Meta-analysis and reviews

1   Meta-analysis and reviews

APHASIA REHABILITATION – A COCHRANE SYSTEMATIC REVIEW UPDATE OF THE EVIDENCE FOR SPEECH AND LANGUAGE THERAPY (SLT) COMPARED WITH NO SLT

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Background: Each year more than 1 million Europeans experience a stroke. A third acquire aphasia, a language impairment affecting the expression and understanding of speech, reading and writing. The original Cochrane Review of SLT for aphasia after stroke (Greener et al., 1999) reviewed 12 trials but a lack of available data meant that the evidence was inconclusive. In this review update we identified and synthesised current evidence from 30 trials that compared SLT with a) no SLT, b) social support and stimulation, and c) different approaches to SLT. Here we report the evidence from (a).
Methods: We searched the Cochrane Stroke Group Trials Register, MEDLINE and CINAHL, hand searched key journals, screened reference lists of relevant articles and contacted researchers to identify other published, unpublished and ongoing randomised controlled trials (RCTs) that compared SLT with no SLT. Two review authors independently extracted the data and assessed the quality of included trials. We sought missing data from trialists.
Results: We included 14 randomised SLT versus no SLT comparisons (n = 1064). Approaches evaluated included "conventional", computer-mediated, group, functional, intensive, operant training and volunteer-facilitated SLT. Outcomes measured included functional communication, receptive and expressive language, severity of impairment, psychosocial impact, number of drop-outs, compliance with allocated intervention and economic outcomes. A meta-analysis of four comparisons found that participants that received SLT had better receptive language scores than those that did not have SLT (MD 8.04, 95% CI [1.55, 14.52]) P = 0.02. We found no other evidence of between-group differences, though we noticed a promising consistency in the direction of the Results which favoured the provision of SLT.
Conclusion: More data are required to inform this comparison. Improved design and reporting of trials in this field will further contribute to the evidence for SLT for aphasia following stroke.

2   Meta-analysis and reviews

GROWING INTEREST IN STROKE REHABILITATION IN CHINA: A SYSTEMATIC REVIEW OF 30 RANDOMIZED CONTROLLED REHABILITATION TRIALS

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Background: Rehabilitation is not standard in stroke care in China. However, growing interest in the efficacy of rehabilitation is evident.
Aims: To systematically review randomized controlled trials (RCTs) comparing rehabilitation versus no rehabilitation after stroke in China.
Methods: We searched 24 databases including Wanfangdata (China) MEDLINE, EMBASE, CENTRAL and Cochrane Stroke Group Register. The primary outcome of interest: Activities of daily living (Barthel Index (BI)), secondary outcome: Disability (Fugl-Meyer Score (FMS)). Random-effect meta-analysis was performed.
Results: 62 papers were identified, 95% published since 2000. 32 papers were excluded because they were not-RCTs or the authors failed to report BI and/or FMS data or data were missing. This left 30 included trials with a total of 4,574 patients, 931 patients with haemorrhagic stroke (20.4%) and 2,525 were males (55.2%). The rehabilitation interventions were mixed but all included additional exercise therapy. Control patients had no or limited rehabilitation. The weighted average effect of rehabilitation on primary outcome was a 20.03 points (95%CI: 16.9-23.2) improvement on BI Scale and 17.34 points (95%CI, 12.60-22.08) improvement on FMS. Patients who received rehabilitation showed marked improvements in BI (Standardized Mean Difference (SMD): 1.16, 95%CI: 0.96-1.35) and FMS (SMD: 1.54, 95%CI: 1.03-2.04) compared to controls. Reporting quality was often low however, with randomization method and time to start of rehabilitation unclear. Reasons for loss to follow up were frequently not stated.
Conclusions: Recent interest in stroke rehabilitation in China has resulted in a large number of trials on the topic. Although reporting quality of many RCTs was low, there is evidence of overwhelmingly positive Results of rehabilitation after stroke.

3   Meta-analysis and reviews

META-ANALYSIS OF INSULIN USE FOR POST-STROKE HYPERGLYCEMIA

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Background: Post-stroke hyperglycemia (PSH) is associated with poor clinical outcomes. Clinical guidelines advocate insulin for PSH, but no clinical benefit has been evident in several clinical trials, and there is a risk of hypoglycaemia.
Methods: Systematic review of papers identified from databases and reference lists was undertaken. Data from randomised controlled trials (RCTs) that reported mortality or functional outcome were extracted. Favourable functional outcome was defined as modified Rankin score (mRS) ≤2 or favourable extended Glasgow Outcome Scores (eGOS).
A DerSimonian-Laird random effects model was used to generate odds ratios and 95% confidence intervals.
Results: We identified 16 studies (2459 patients) including 1 large RCT of 933 patients, 9 pilot RCTs of between 10 and 116 patients and 6 cohort studies, one of which included 851 patients. One study involved a mixed population of neuroscience ITU patients with a subset of 15 stroke patients. One paper used the control group from another paper by the same group. 1421 patients were in RCTs while 1038 were in cohort studies.
Minimum glucose levels for study inclusion varied from 5.6-9.4mmol/L. Mean onset to treatment time ranged from 9.1h to 20.8h. Glucose targets varied from 3.8-11.1mmol/L. Treatment Duration varied from 24h to 5 days.
Eight RCTs reported mortality data and seven reported functional outcome.
Insulin infusions had a neutral effect on mortality (OR 1.1, 95% CI 0.9 to 1.5, p = 0.29, n = 1236) and on good functional outcome (OR 1.03, 95% CI 0.7 to 1.5, p = 0.88, n = 1217). Incidence of hypoglycaemia varied from 8%-80%. Definitions of hypoglycemia varied from <3 to <5mmol/L.
Conclusions: Despite the consistent association of hyperglycaemia in the 48h after stroke with higher risk of death or dependence, insulin has not affected mortality or favourable functional outcome in RCTs to date. There is wide variation in treatment threshold, target, and duration, and in reporting of hypoglycaemia.

4   Meta-analysis and reviews

POST STROKE INFECTION RATES – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Patients with acute stroke are at risk for infections. Reported post-stroke infection rates vary strongly. We performed a systematic review and

meta-analysis to assess the pooled post-stroke infection rate and to estimate the effect of infections on outcome.

Methods: MEDLINE and EMBASE were searched for studies on post-stroke infection. Cohort studies and randomized clinical trials were included when post-stroke infection rate was reported. Rates of infection were pooled after assessment of heterogeneity. In addition, in a multivariate model, associations between patient- and study characteristics and infection rates were quantified. Finally, we reviewed the association between infection and outcome in patients with stroke.

Results: 87 studies were included involving 137 817 patients. 8 studies included patients admitted on the intensive care unit (ICU). There was significant heterogeneity between studies (P<0.01, I2 =97%). The overall pooled infection rate was 30% (24-36%); rates of pneumonia and urinary tract infection were 10% (95% confidence interval [CI] 9-10%) and 10% (95%CI 9-12%). For ICU studies, these rates were substantially higher with 45% (95% CI38-52%), 28% (95%CI 18-38%) and 20% (95%CI 0-40%). Rates of pneumonia were higher in prospective studies and in studies with more patients with a lowered level of consciousness. Studies including patients with more severe strokes reported higher rates of urinary tract infection. Pneumonia was associated with death (pooled odds ratio (OR) of 3.60 (95%CI 2.75-4.70).

Discussion: Infection frequently complicates acute stroke with a pooled rate of 30% of patients. Pooled rates of post-stroke pneumonia and urinary tract infection are both 10%. Pneumonia is associated with death.

5 Meta-analysis and reviews

DIFFERENCE IN VASCULAR RISK FACTOR PROFILE BETWEEN ISCHAEMIC STROKES OF UNDETERMINED AETIOLOGY AND OTHER STROKE SUBTYPES: POPULATION-BASED STUDY AND META-ANALYSIS

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Background: Up to one-third of ischaemic strokes are of undetermined aetiology despite standard diagnostic workup, potentially undermining effective primary and secondary prevention. However, it has been suggested that strokes of undetermined aetiology may often be due to occult atheroma or cardioembolism. If so, we hypothesized that the risk factor profile should resemble that of large-vessel stroke or cardioembolic stroke.

Methods: We compared the risk factor profile of ischaemic stroke subtypes (TOAST classification) in a large population-based study of TIA and stroke (Oxford Vascular Study; OXVASC) and included these data in a meta-analysis of associations in all published population- and hospital-based studies.

Results: Risk factor associations in OXVASC (1669 patients) were broadly similar to those in 9 other population-based studies. Although associations in 24 hospital-based studies were more heterogeneous, the pooled estimates were also similar. We therefore calculated pooled estimates from all studies. There were strong associations (all p<0.0001) of large-vessel stroke with male sex (OR=1.48, 95%CI 1.25-1.75), smoking (1.77, 1.50-2.09) and previous TIA (1.69, 1.39-2.07), while hypertension was consistently associated with small-vessel stroke (1.43, 1.28-1.59). Stroke of undetermined aetiology, however, was negatively associated with conventional risk factors when compared with other subtypes e.g. in comparison with large vessel stroke: male sex (0.57, 0.47-0.69), hypertension (0.70, 0.59-0.83), diabetes (0.77, 0.63-0.93), smoking (0.52, 0.43-0.63) and previous TIA (0.54, 0.43-0.68).

Conclusion: Stroke of undetermined aetiology had a different risk factor profile from large-vessel stroke and had a lower prevalence of most conventional risk factors than all other subtypes. Control of standard risk factors may therefore be less effective in primary and secondary prevention of stroke of undetermined aetiology and more research on novel risk factors is required.

6 Meta-analysis and reviews

FEMALE RISK OF SUBARACHNOID HEAMORRHAGE: A SYSTEMATIC REVIEW WITH EMPHASIS ON HORMONAL, MENSTRUAL AND REPRODUCTIVE FACTORS

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Background: Incidence of subarachnoid haemorrhage (SAH) is higher in women than in men, in particular after age 50. We performed a systematic review and meta-analysis of the literature on female risk factors for SAH with emphasis on hormonal and reproductive factors.

Methods: We searched Medline and EMBASE for articles published between January 1985 and June 2010. For each of the studies fulfilling predefined inclusion criteria, we obtained risk ratios (RRs) or odds ratios (ORs) with corresponding 95% confidence intervals (CIs) for the different risk factors studied. We pooled crude and adjusted ORs (aORs) with a general variance based random effects method.

Results: We included 12 case-control, one longitudinal, and one case-crossover study. The overall aORs were 1.31 (95% CI: 1.05-1.64) for current use of oral contraceptives (OCP) and 0.90 (95% CI: 0.74-1.09) for ever use of OCP, 0.75 (95% CI: 0.56-0.99) for current use of hormone replacement therapy (HRT) and 0.74 (95% CI: 0.54-1.00) for ever use of HRT. Women who had their menarche at a young age (<13y) were at higher risk of SAH (aOR 2.81; 95%CI: 1.61-4.68). No statistically significant effects were found for premenopausal status (aOR 0.74; 95% CI: 0.51-1.07), older age (>50y) at menopause (OR 1.04; 95% CI: 0.72-1.49) and older age (>26y) at first childbirth (aOR 1.45; 95% CI: 0.91-2.33). Data on parity were heterogeneous. The risk of SAH was not increased during pregnancy, labour and the puerperium (RR 0.4; 95% CI: 0.2-0.9).

Conclusion: Female hormone levels characteristic for reproductive age, i.e., the physiological premenopausal state or HRT during the postmenopausal state, are associated with a lower risk of SAH. These observations, however, do not provide a straightforward explanation for the difference in incidence of SAH between the sexes from age 50 onwards.

7 Meta-analysis and reviews

EFFECT OF DOSE AND COMBINATION OF ANTIHYPERTENSIVES ON INTER-INDIVIDUAL BLOOD PRESSURE VARIABILITY: A SYSTEMATIC REVIEW

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Background: Recent studies have shown that visit-to-visit blood pressure variability is a powerful risk factor for stroke, is reduced by calcium channel blockers (CCBs) and diuretics, and increased by beta-blockers. However, it is unknown whether these effects are dose-dependent and persist in combination with other drugs.

Methods: Cochrane and Medline databases were searched for systematic reviews and randomised controlled trials of antihypertensive drugs. Eligible trials randomised all patients to a combination of drug-classes or different doses of the same drug. Baseline and follow-up data for mean (SD) systolic blood pressure (SBP) and diastolic BP were extracted. Differences in inter-individual variance (SD2) in BP were expressed as a ratio (VR). Estimates were pooled by random-effects meta-analysis.

Results: CCBs reduced inter-individual variability in SBP when added to another agent (VR=0.75; 95%CI 0.64-0.87; p=0.0002; 12 trials; 1565 patients), with a smaller reduction with diuretics (VR=0.85; 0.71-1.01; p=0.07; 17 trials; 3217 patients). Adding other agents to CCBs did not significantly affect SBP variability (VR=1.06; 0.83-1.34; p=0.65; 12 trials; 1460 patients) despite a 5.8mmHg reduction in mean SBP. Randomisation to a higher dose of CCBs reduced SBP variability (VR=0.84; 0.74-0.94; p=0.004; 25 trials; 2179 patients) whereas randomisation to a higher dose of beta-blockers increased SBP variability (VR=1.31; 1.01-1.69; p=0.034; 6 trials; 486 patients).

Conclusions: Effects of antihypertensive drugs on SBP variability are dose-dependent and persist when used in combinations. Use of a high-dose of a CCB alone or in combination with other agents is therefore likely to be particularly effective in prevention of stroke.

8 Meta-analysis and reviews

CEREBRAL MICROBLEEDS ARE ASSOCIATED WITH A GREATER RISK OF FUTURE INTRACEREBRAL HAEMORRHAGE THAN ISCHAEMIC STROKE: POPULATION-BASED STUDY AND META-ANALYSIS

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Background: Cerebral microbleeds (MB) may be associated with an increased risk of recurrent ischaemic stroke as well as intracerebral haemorrhage (ICH). Accurate estimates of these risks are needed to inform clinical decisions regarding antithrombotic treatment.

Methods: Risk of recurrent stroke was determined in all patients with ischaemic stroke or TIA who were investigated with gradient-echo MRI to identify MB in the population-based Oxford Vascular Study (OXVASC). These data were pooled with

other prospective cohort data on recurrent stroke risk in patients with vs without MB identified from a systematic review of published studies.

Results: In OXVASC, MB were identified in 33/291 (11%) patients with ischaemic stroke or TIA (51% male, mean age 66 years). After a mean follow up of 2.9 years, 20 patients had a recurrent stroke (2 ICH,18 ischaemic stroke). MB were associated with an increased risk of any stroke on follow up (OR=2.9, 1-8.5, p=0.05) and were present on the baseline scan in 2/2 with ICH and 3/18 with ischaemic stroke (Fisher exact test – p=0.05), The systematic review identified 5 cohort studies (2990 cases) reporting risk of ischaemic stroke and 8 cohort studies (3652 cases) reporting risk of ICH. In the pooled analysis, MB were associated with an increased risk of ischaemic stroke (OR=1.6, 1.2-2.2, p=0.004), but the increase in relative risk of ICH was greater (OR=6.4, 3.7-11.2, p<0.001).

Conclusions: MB are markers of increased risk for all causes of stroke, but the relative risk for ICH appears to be greater than the relative risk for recurrent ischaemic stroke. As clinical outcomes following ICH are in general more severe than those of ischaemic stroke, these Results suggest that long-term antithrombotic agents should be used with caution in patients with ischaemic stroke or TIA and MB, unless there are additional risk factors for recurrent ischaemic stroke.

9   Meta-analysis and reviews

QUALITY OF FOCAL CEREBRAL ISCHAEMIA MODELLING IN TRANSGENIC ANIMALS - A SYSTEMATIC REVIEW

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Background: The modelling of focal cerebral ischaemia in transgenic animals has contributed to our understanding of the ischaemic cascade and stroke pathophysiology. However, we are yet to successfully translate the efficacy of neuroprotective agents observed in animal studies to clinical trial. One reason for this might be if candidate targets were based on findings from transgenic studies which had limited validity. Here we describe a systematic review of study quality in transgenic stroke studies.

Methods: Electronic searching of three online databases was used to identify publications reporting the use of transgenic animals in models of focal cerebral ischaemia. Studies were assessed against the 10-point CAMARADES study quality score (including random allocation to group, blinded assessment of outcome and sample size calculation).

Results: 296 publications met our inclusion criteria reporting 810 experiments using animals with 120 different genetic manipulations. 79% of genetic manipulations were knockouts. 54% of studies used transient models of ischaemic stroke. Study quality was low; 4% of papers report random allocation to group and 12% report blinded assessment of outcome.

Conclusion: The data describing transgenic animals in the modelling of focal cerebral ischaemia is large and heterogeneous. Understanding the pathophysiology of the ischaemic cascade is likely to be beneficial in identifying putative neuroprotective agents and translating their efficacy. However, study quality was low and has been reported in the preclinical data of wild-type animals to be a potential source of bias.

Intracerebral/subarachnoid haemorrhage and venous diseases A

1   Intracerebral/subarachnoid haemorrhage and venous diseases A

SILENT ISCHAEMIC LESIONS IN PATIENTS WITH ACUTE SYMPTOMATIC SPONTANEOUS INTRACEREBRAL HAEMORRHAGE: RELATIONSHIP TO LOBAR MICROBLEEDS AND CEREBRAL AMYLOID ANGIOPATHY

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Background: Cerebral amyloid angiopathy (CAA) is a common cause of spontaneous intracerebral haemorrhage (ICH). Neuropathological studies have shown small areas of infarction in CAA, but this has not been widely studied in vivo. We hypothesized that silent ischaemic lesions could be detected using diffusion-weighted magnetic resonance imaging (MRI) in patients with ICH due to probable CAA (defined using the Boston criteria). We compared the prevalence of silent ischaemic lesions in CAA-related ICH to that in non-CAA related spontaneous ICH, and in age-matched controls.

Methods: Cases were ascertained from consecutive patient cohorts with ICH from 4 stroke centres. MRIs were performed ≤ 3 months of symptomatic ICH. Age-matched controls were consecutive patients referred to the stroke service with a final non-stroke diagnosis. Ischaemic lesions were assessed on diffusion-weighted imaging (DWI) and apparent diffusion coefficient maps. We also rated white matter changes (WMC) and cerebral microbleeds (CMBs). We investigated the associations between DWI lesions, clinical and radiological characteristics.

Results: The prevalence of DWI lesions was 9/39 (23%) in subjects with probable CAA vs 6/75 (8%) in non CAA-related ICH (p=0.024); we found no DWI lesions in controls. Factors associated with DWI lesions were mean total WMC (OR 1.13, 95%CI 1.02-1.26, p=0.019) and presence of lobar CMBs (OR 10.75, 95%CI 1.36-84.96, p=0.024). In multivariate analysis, diagnosis of probable CAA (OR 3.52, 95%CI 1.11-11.18, p=0.033) and mean total WMC score (OR 1.13, 95%CI 1.01-1.27, p=0.026) predicted DWI lesions.

Conclusions: Silent ischaemic lesions are common in spontaneous ICH. The association of DWI lesions with a diagnosis of probable CAA suggest that small vessel dysfunction in CAA is a risk factor for silent ischaemia, as well as ICH. These findings show that acute ICH and subclinical ischaemia show a previously unsuspected dynamic interaction.

2   Intracerebral/subarachnoid haemorrhage and venous diseases A

GENETIC ASSOCIATIONS WIITH BRAIN MICROBLEEDS: SYSTEMATIC REVIEW AND META-ANALYSES

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Background: The frequency of brain microbleeds (BMBs) increases with age, and with a history of hypertension, smoking and stroke (particularly intracerebral haemorrhage), but genetic associations with BMBs are less clear. Since identifying genetic associations may improve our understanding of the aetiology of BMBs, we aimed to assess the existing evidence for these associations with a systematic review and meta-analysis.

Methods: We sought all published studies of the association between any genetic polymorphism and BMBs studied in a total of >100 people. We critically appraised studies, and calculated pooled odds ratios (ORs) using the generic inverse variance fixed effects method. We used I2 and χ^2 statistics to assess heterogeneity, and failsafe N estimates to assess the robustness of our Results.

Results: Only the apolipoprotein E (APOE) e2/3/4 polymorphism had been studied in >100 people (10 studies, 7,351 participants). Compared with people with the e3/e3 genotype, carriers of the e4 allele (e4+) were statistically significantly more likely to have BMBs in any location (e4+ versus e3/e3: pooled OR 1.22, 95% CI 1.05 to 1.41, p=0.01). For strictly lobar BMBs, this association appeared slightly stronger (e4+ versus e3/e3: pooled OR 1.35, 95% CI 1.10 to 1.66, p=0.005). The association of e4+ genotypes with strictly lobar BMBs was reasonably robust to potential publication and reporting biases.

Conclusions: Given the known associations of APOE alleles with lobar intracerebral haemorrhage and cerebral amyloid angiopathy, these findings support the concept that strictly lobar BMBs may be an imaging biomarker of cerebral amyloid angiopathy. In the future, genome wide association studies may identify other important genetic influences on BMBs.

3   Intracerebral/subarachnoid haemorrhage and venous diseases A

GENETIC ASSOCIATIONS OF CEREBRAL AMYLOID ANGIOPATHY – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives: Cerebral amyloid angiopathy (CAA) is characterized by amyloid deposition in cortical and leptomeningeal vessels. It is an important cause of cerebrovascular disorders, in particular lobar cerebral haemorrhage. Many studies have attempted to find associations between polymorphisms in various candidate genes (mostly the apolipoprotein gene [APOE]) and CAA. Identifying genetic associations with CAA may help us better to understand its underlying aetiology,

Oral Session
Intracerebral/subarachnoid haemorrhage and
venous diseases A

Cerebrovasc Dis 2011;31(suppl 2):1–322   3

and so we aimed to evaluate the evidence for these associations with a systematic review and meta-analysis.

Methods: We used a comprehensive search strategy to identify studies of the association between any genetic polymorphism and pathologically diagnosed CAA (on autopsy or biopsy). For studies of the association between the APOE and CAA, we extracted data on the study populations, methodology, and number of subjects with and without CAA or the mean CAA score for different APOE genotypes. We compared the effects of ε4 allele possession (e4+) versus absence (e4-) on the presence or absence of CAA by calculating study-specific and random effects pooled odds ratios (OR). We used the generic inverse variance method with continuous data (CAA standardised mean differences) converted to a dichotomous (OR) format.

Results: We identified 45 relevant studies (6541 subjects) of association between APOE and CAA. Of those, 23 studies (3524 subjects, <50% of the total) provided enough data for meta-analysis. The pooled OR demonstrated a statistically significant association of e4+ genotypes with CAA (OR 3.4, 95% confidence interval [CI] 2.5 to 3.5). There was some variability but no significant heterogeneity between the studies' Results (p 0.15, I2 22%).

Conclusion: Although our Results suggest a clear association between APOE and CAA, it will be important to exclude reporting bias by confirming these findings in the substantial proportion of studies without published data for meta-analysis.

4 Intracerebral/subarachnoid haemorrhage and venous diseases A

LESION LOCATION OF MOYAMOYA RELATED HEMORRHAGE: COMPARISON WITH PRIMARY INTRACEREBRAL HEMORRHAGE

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Background: Moyamoya disease (MMD) occasionally presents with intracranial hemorrhage. However the precise mechanisms of hemorrhage are not fully understood. We sought to investigate whether the lesion location of MMD related hemorrhage differs from that of the primary intracerebral hemorrhage (ICH).

Methods: We assessed 86 MMD patients who presented with intracranial hemorrhage. For each, one primary ICH patient was selected as control. The location of hemorrhage was classified into 7 regions: putaminal; thalamic; lobar; caudate; primary intraventricular; pontine; and cerebellar region. The location of hemorrhage in MMD patients was compared with that of the primary ICH patients.

Results: MMD related hemorrhage patients were younger (40.4±12.9 years) and had lower prevalence of vascular risk factors than the primary ICH patients. The most commonly affected location was the primary intraventricular (44%) followed by lobar (22.6%), putaminal (20.2%), thalamic (4.8%), and caudate (3.6%) region. These frequencies were different from that of the primary ICH patients, which showed putaminal (45.2%), thalamic (21.4%), pontine (13.1%), lobar (9.5%), caudate (4.8%), cerebellar (3.6%), and primary intraventricular (2.4%) region (p<0.001). Presence of intraventricular hemorrhage was observed more frequently in the MMD related hemorrhage than in the primary ICH (83.3% vs 21.4%, p<0.001).

Conclusion: Lesion location of MMD related hemorrhage was different from that of the primary ICH, and MMD patients had higher prevalence of intraventricular hemorrhage. Differences in lesion location and prevalence of intraventricular hemorrhage suggest that MMD related hemorrhage has a different pathogenesis compared with that of the primary ICH.

5 Intracerebral/subarachnoid haemorrhage and venous diseases A

TRIGGER FACTORS AND THEIR ATTRIBUTABLE RISK FOR RUPTURE OF INTRACRANIAL ANEURYSMS: A CASE-CROSSOVER STUDY

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Background: Little is known about activities that trigger rupture of an intracranial aneurysm. Knowledge on what triggers aneurysmal rupture increases insight in the pathophysiology and facilitates development of prevention strategies. We therefore aimed to identify and quantify trigger factors for aneurysmal rupture and to gain insight into the pathophysiology.

Methods: During a 3-year period 250 patients with aneurysmal subarachnoid hemorrhage (SAH) filled in a structured questionnaire regarding exposure to 30 potential trigger factors in the period shortly before SAH (hazard period) and for usual frequency and intensity of exposure. We assessed relative risks (RR) of rupture after exposure to triggers with the case-crossover design comparing exposure in the hazard period with the usual frequency of exposure. Additionally we calculated population attributable risks (PAR).

Results: Eight triggers increased the risk for SAH: coffee consumption (RR:1.7, 95%CI:1.2-2.4), cola consumption (RR:3.4; 95%CI:1.5-7.9), anger (RR:6.3; 95%CI:4.6-25), startling (RR:23.3; 95%CI:4.2-128), straining for defecation (RR:7.3; 95%CI:2.9-19), sexual intercourse (RR:11.2; 95%CI:5.3-24), nose blowing (RR:2.4; 95%CI:1.3-4.5), and vigorous physical exercise (RR:2.4; 95%CI:1.2-4.2). The highest PARs were found for coffee consumption (10.6%) and vigorous physical exercise (7.9%).

Conclusions: We identified and quantified eight trigger factors for aneurysmal rupture. All triggers induce a sudden and short increase in blood pressure, which therefore seems a possible common cause for aneurysmal rupture. Some triggers are modifiable, and further studies should assess whether reduction of exposure to these factors or measures preventing sudden increase in blood pressure decrease the risk of rupture in patients known to have an intracranial aneurysm.

6 Intracerebral/subarachnoid haemorrhage and venous diseases A

CLINICAL PRESENTATION, AETIOLOGY AND LONG-TERM PROGNOSIS IN PATIENTS WITH ATRAUMATIC CONVEXAL SUBARACHNOID HEMORRHAGE

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Objective: To systematically investigate clinical symptomatology, aetiology and long-term prognosis in patients with nontraumatic convexal subarachnoid hemorrhage (cSAH).

Methods: For a 6 year period, we searched our radiologic database for patients with non-traumatic, non aneurismal, subarachnoid hemorrhage (n=132) and amongst those identified 25 patients with cSAH as defined by intrasulcal bleeding restricted to the hemispheric convexities. Subsequent data collection was done by a review of the medical records and standardized interpretation of neuroimaging studies. Follow up data after a mean of 32 months (range 1-61 months) were obtained by telephone or a clinical visit whenever possible.

Results: The 25 patients with cSAH had a mean age of 70 years (range 37 to 88 years) and 13 (52%) were women. 21 patients (84%) were >60 years. The majority of patients (n=11, 44%) presented with partly recurrent transient sensory or motor symptoms. Seizures were the presenting symptom in 5 patients. Headaches were indicated by 11 patients (44%), with only 4 experiencing thunderclap headaches. Symptoms were not typical of a SAH in almost all patients >60 years. MRI revealed a high frequency of previous bleedings and their pattern was often suggestive of cerebral amyloid angiopathy. In 5 patients, cSAH was associated with acute ischemic lesions. Fourteen patients (61%) had an unfavorable outcome (modified Ranking Scale score 3 to 6) at follow-up with 5 deaths. Unfavorable outcome was associated with age >60 years and evidence for multiple bleedings. Recurrent cSAH was not observed.

Conclusions: cSAH often mimics transient ischemic attacks and thus may be an under recognized disorder. In older patients, it shows a high association with imaging features of cerebral amyloid angiopathy and carries a bad prognosis.

7 Intracerebral/subarachnoid haemorrhage and venous diseases A

THE EFFECT OF VASOSPASM ON CEREBRAL PERFUSION: A COLOR DUPLEX STUDY OF THE EXTRA- AND INTRACRANIAL CEREBRAL ARTERIES

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Background: In patients with subarachnoid hemorrhage (SAH), vasospasm is considered the main cause of delayed ischaemic neurological deficits. The purpose of this study was to assess whether middle cerebral artery (MCA) vasospasm reduces the blood flow volume in the corresponding extracranial internal carotid artery (ICA) or global cerebral blood flow volume (CBFV).

Methods: A color duplex ultrasound study of extra- and intracranial cerebral arteries was performed in 28 SAH patients developing vasospasm. Altogether, 337 measurements were completed. MCA vasospasm was defined as a time-averaged maximum flow velocity (TAMX) exceeding 120 cm/s. A "true" Lindegaard index (TAMX MCA/TAMX ICA; angle-corrected values) was determined. Intravascular flow volumes were calculated as the product of time-averaged mean flow velocity (TAV) and the cross-sectional area of the vessel. CBFV was determined as the bilateral sum of ICA and vertebral artery flow volumes. ICA flow volumes and CBFV were compared in each patient: (1) at maximum TAMX recorded in one MCA ("maximum-vasospasm"), (2) when TAMX in the same vessel was closest to mean reference values ("no-vasospasm"). The CBFV course during the first 3 weeks after SAH was evaluated longitudinally.

Results: CBFV was reduced starting from day 3 after SAH. When comparing "maximum-vasospasm" and "no-vasospasm", neither TAMX in ICA (median, 34 vs. 30 cm/s), nor ICA flow volumes (197 vs. 187 ml/min), nor CBFV (558 vs. 527 ml/min) were different, while TAMX in MCA (184 vs. 74 cm/s) and the "true" Lindegaard index (5.8 vs. 2.4) were markedly different.

Conclusion: Vasospasm did not further diminish the ipsilateral ICA inflow and CBFV, which both were reduced already before the onset of vasospasm. Hence, increased TAMX in MCA and Lindegaard indices, reflecting vasospasm, do not point to a reduction in ICA flow volume or CBFV. The sole use of transcranial Doppler monitoring in SAH patients appears to be questionable.

8 Intracerebral/subarachnoid haemorrhage and venous diseases A

SIGNIFICANCE OF ADMISSION TEMPERATURE AND IMPACT ON OUTCOME AFTER INTRACEREBRAL HEMORRHAGE

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Introduction: The purpose of this study is to test the hypothesis that early hyperthermia is associated with poor outcome after intracerebral hemorrhage (ICH), using a robust multi-center Intensive Care Unit (ICU) database.

Methods: Multi-center cohort study using the Project IMPACT critical care database of ICUs at 120 United States hospitals between 2003 and 2008. Patient inclusion criteria were age older than 17 years, acute ICH, and admission to the ICU. Patients were divided into three main groups and based on definitions of hyperthermia and hypothermia in the ICU. Hyperthermia was defined as admission temperature greater than 37.5 °C, hypothermia as a temperature lower than 36.5°C, and normothermia, not classified as hyperthermia or hypothermia. The outcome measure was a composite of severe disability or death at hospital discharge.

Results: Over the 8-year period, the Project IMPACT database contained data on more than 700,000 ICU admissions. We found 4192 patients that met the inclusion criteria. The median age was 67 (Interquartile range [IQR] 54-77), 1970 (47%) were male, and 3030 (75%) were white. The mean admission temperature in the poor outcome group was 37.84±1.1°C vs. 37.42±0.7°C (p<0.00001). Of the total cohort, 1984 (48%) had hyperthermia, 200 (5%) had hypothermia, and 1979 (47%) were normothermic. The hyperthermia group had a higher proportion of poor outcome (1213/1972 [62%]) compared to normothermia (699/1969 [36%]) but the hypothermia group had a significantly higher proportion of poor outcome (132/200 [66%]). In a preliminary multivariate model controlling for potential confounders (age, gender, and pre-morbid functional status) hyperthermia (OR, 1.2; 95% CI, 1.1-1.4) and hypothermia (OR, 1.6; 95% CI, 1.2-2.0) increased the odds of poor outcome.

Conclusions: Among critically-ill ICH patients admitted to the ICU, hyperthermia but also hypothermia are associated with higher odds of poor outcome compared to normothermia. The implications of these findings require further study.

9 Intracerebral/subarachnoid haemorrhage and venous diseases A

THE EFFECT OF ANTITHROMBOTIC THERAPY ON HEMORRHAGE FROM CEREBRAL CAVERNOUS MALFORMATIONS

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Background: Cerebral cavernous malformations (CCMs) are the most frequently diagnosed vascular malformations in the brain and are often asymptomatic. The potential risk of hemorrhage often precludes antithrombotic treatment in patients with cardiovascular disease, but no systematic study has been undertaken to evaluate the effect of blood-thinning therapy on the risk of CCM hemorrhage.

Patients and Methods: Overall, 78 consecutive patients (59% women, mean age 46 years, SD ±18) have been followed at a tertiary referral center for brain vascular malformations. N=41 (53%) had a single lesion, 37 (47%) had multiple CCMs (leading to a total of 351 CCMs under observation or average 4.5 CCMs per patient). The diagnostic event was symptomatic hemorrhage in 12 (15%) patients, epileptic seizure in 9 (12%), focal neurological deficits unrelated to hemorrhage in 14 (18%), while 43 (55%) patients were asymptomatic at diagnosis.

Results: The mean follow-up was 4.7 years (SD ±3.2) leading to 1638 CCM-years of observation. Overall, 9 (12%) patients experienced symptomatic hemorrhage on follow-up (mean rate 2.5%/patient/year or 0.5%/CCM/year). Hemorrhage occurred more frequently in patients with prior CCM hemorrhage (5.7%/patient/year or 1.0%/CCM/year) as compared to those without (1.9%/patient/year or 0.4%/CCM/year). During follow-up, n=14 (18%) patients received ongoing antithrombotic (i.e., anticoagulant or antiplatelet) treatment, including 5 on oral anticoagulants. During 130 CCM-years of observation, no hemorrhagic complications were observed.

Conclusion: Overall, the risk of symptomatic CCM hemorrhage appears to be low, particularly in patients without hemorrhagic presentation. Antithrombotic treatment does not seem to increase the frequency of CCM-related hemorrhage.

Acute stroke: new treatment concepts A

1 Acute stroke: new treatment concepts A

GRANULOCYTE-COLONY STIMULATING FACTOR FOR MOBILISING BONE MARROW STEM CELLS IN SUB-ACUTE STROKE: THE STEM CELL TRIAL OF RECOVERY ENHANCEMENT AFTER STROKE-2 (STEMS-2) RANDOMISED CONTROLLED TRIAL (ISRCTN 63336619)

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Background: Granulocyte-colony stimulating factor (G-CSF) is neuroprotective in experimental stroke, and mobilises CD34+ peripheral blood stem cells into the circulation. We assessed the safety of G-CSF in recent stroke in a phase IIb single-centre randomised controlled trial.

Methods: G-CSF (Filgastrim 10 μg/kg [=1×10^6 U/kg]) or vehicle placebo (ratio 2:1) was given subcutaneously for 5 days to 60 patients 3-30 days post ischaemic or haemorrhagic stroke. The primary outcome was the frequency of serious adverse events (SAE). Peripheral blood CD34+ count (flow cytometry), blood counts and functional outcome were measured. MRI assessed change in lesion size and the presence of iron-labelled CD34+ cells re-injected on day 6. Post-mortem analyses evaluated immunostaining of G-CSF and its receptor and CD34+ cells within infarcted brain.

Findings: 60 patients were recruited at mean 8 days (SD 5) post ictus, with mean age 71 (12) years, and 53% male. The groups were well matched for baseline minimisation/prognostic factors. There were no significant differences between groups in the number of participants with a SAE: G-CSF 15/40 (37.5%) versus placebo 7/20 (35%), death or dependency (modified Rankin Scale 3, interquartile range 2-4) at 90 days, or the number of injections received. G-CSF increased CD34+ and total white cell counts 9 and 5-fold respectively. There was a trend towards reduction in MRI final ischaemic lesion volume and change from baseline in G-CSF treated patients (p=0.08 and 0.054 respectively). In one participant, there was a suggestion that labelled CD34+ cells had migrated to the ischaemic lesion. G-CSF and its receptor are expressed in peri-infarct brain tissue.

Interpretation: This randomised triple-blind placebo-controlled trial suggests that G-CSF is safe when administered sub-acutely. G-CSF may reduce lesion size and mobilise CD34+ cells to migrate to the ischaemic stroke.

2 Acute stroke: new treatment concepts A

IMMUNOTHERAPY FOR STROKE: A NEW HOPE?

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Background: Tissue-type plasminogen activator (tPA) is the only available emergency treatment for acute ischemic stroke. tPA (endogenous and exogenous) has two faces in acute ischemic stroke: beneficial fibrinolysis in the vascular bed, but damaging effects on the neurovascular unit and the brain parenchyma. All together, the limitations lead to only 10% of stroke patients being treated with tPA, among which only 40% actually display neurological improvement. To improve this profile, we aimed at developing a novel treatment strategy for stroke, relying on antibodies targeting the pro-neurotoxic effects of tPA.

Methods and Findings: We have previously shown that tPA can worsen ischemic brain damages in rodents, thanks to its ability to interact with the amino terminal domain of the NR1 (ATD-NR1) subunit of glutamatergic NMDA receptors. Accordingly, we first used recombinant protein engineering and immunoglobulin production technologies in order to obtain antibodies that specifically recognize the ATD-NR1 in mice and humans. In vitro, these antibodies prevented the potentiating effect of tPA on NMDA glutamatergic receptors, without altering basal neurotransmission. Then, based on a dedicated model of murine thrombo-embolic stroke coupled to MRI, NIRF, confocal microscopy, behavior assessments, we demonstrate the efficiency of immunotherapy in a complete pre-clinical screen: after a single administration alone or with late tPA-induced thrombolysis, antibodies dramatically reduce ischemic brain injuries, improve long-term neurological outcome and, in parallel, attenuate critical ischemic events including blood-brain barrier leakage and activation of matrix metalloproteinases -3 and -9, and the Platelet-Derived Growth Factor-CC pathway.

Conclusions: Our immunotherapy strategy is thus able to limit ischemic histological and neurological damages in mice, and extends the therapeutic window of tPA-driven thrombolysis. Thus, the prospect of this immunotherapy is an extension of the range of treatable patients, whether used as a monotherapy or, in combinations, to extend the therapeutic window for thrombolysis.

3 Acute stroke: new treatment concepts A

EFFECT ON STUDY SAMPLE SIZE OF AN EXTENDED TIME WINDOW FOR INITIATION OF NEURORESTORATIVE THERAPY AFTER STROKE: AN EXPLORATORY ANALYSIS ON THE VIRTUAL INTERNATIONAL STROKE TRIALS ARCHIVE (VISTA)

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Introduction: The large sample size required for acute stroke trials may result from natural population heterogeneity and variation in NIHSS severity score collected hyperacutely when patients are unstable. For neurorestorative treatments that may be initiated later after stroke onset, e.g. at 24h, a more homogeneous population with more predictable outcome may be available. We postulated that deferred selection would permit more powerful and thus smaller trials.

Methods: We examined the relation between baseline (<6h) vs. 24 hour NIHSS recordings and 90 day modified Rankin Score (mRS) outcome in patients from VISTA, assessing r2 values from basic correlations with dichotomised mRS followed by ordinal analysis of the mRS.

We undertook simulations to model the sample size required to detect a "shift" in mRS outcome equivalent to a 5% absolute difference in proportion achieving mRS 0-2 versus 3-6, setting power at 80% and assuming adjustment for entry age and NIHSS, and an NIHSS entry criterion of 4-20.

Results: Among patients with entry NIHSS 4-20, baseline (<6h) NIHSS explained only 19% (r=0.44) of the variation in outcome measured by the full scale of mRS whereas 24h NIHSS explained 34% (correlation=0.58).

After adjustment for age and treatment with thrombolysis, each NIHSS point is responsible for odds of poorer mRS at 90 days of 1.23 (1.22,1.25) if NIHSS is measured hyperacutely, but 1.31 (1.29,1.33) when recorded at 24h.

Across 10,000 simulated trials, those that selected patients immediately with entry NIHSS 4-20 and adjusted 90 day mRS outcome for NIHSS, on average required 640 patients per group whereas if selection and treatment were delayed until 24h after stroke onset, fewer than 400 patients per group were required to detect the same simulated treatment effect with equal power.

Conclusion: Trial selection and analysis based on a delayed measurement of NIHSS selects a population in whom untreated outcome is more predictable and may allow trial samples to be reduced by 35-40%.

4 Acute stroke: new treatment concepts A

INFARCT SIZE DETERMINATION IN ACUTE ISCHEMIC STROKE: A COMPARATIVE STUDY OF ASPECTS SCORES FROM NONCONTRAST CT (NCCT) AND CT ANGIOGRAPHY (CTA) SOURCE IMAGES

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Background: Estimation of infarct size is gaining increasing prominence in the imaging-based patient triage for more aggressive reperfusion therapies in acute ischemic stroke (AIS). Preliminary Results suggest that CTA source images (CTA-SI) may provide a more accurate assessment of irreversibly injured tissue in the acute stroke setting than NCCT. We sought to evaluate these two techniques in the determination of infarct size in a stroke cohort treated by a mechanical thrombectomy device, the Penumbra Stroke System.

Methods: This was a multicenter retrospective study of AIS patients with anterior circulation proximal artery occlusions (PAO) who underwent neuroimaging and were subsequently treated with the Penumbra Stroke System. Patients with both NCCT and CTA-SI data were included in this analysis. Images were independently analyzed by a central core imaging laboratory using the Alberta Stroke Program Early CT Scale (ASPECTS) blinded to clinical information except stroke side. Statistical analysis was performed to compare these two modalities with significance set at p<0.05.

Results: A total of 45 patients were enrolled, of whom 48.8% (21/43) were female. The mean age was 63.0±17.8 years, and the median NIHSS score was 16 (IQR 12-19). The median pre-treatment ASPECTS scores for NCCT vs. CTA-SI were 8 vs. 6. In pair wise comparison, CTA-SI ASPECTS scores were significantly lower than NCCT (p<0.0001). The median difference between NCCT and CTA-SI ASPECTS was 1 (IQR 0-3). The proportion of patients with ASPECTS ≤7 was 33.3% vs. 71.1% for NCCT vs. CTA-SI (p=0.0007), respectively.

Conclusion: Analysis of CTA source images Results in a significantly larger region of ischemic injury compared to NCCT, with a higher proportion of patients categorized with extensive ischemic injury (ASPECTS ≤7). These findings might have important implications for imaging-based patient triage, and further investigation into the relative diagnostic accuracy between the two modalities is warranted.

5 Acute stroke: new treatment concepts A

SERUM LEVELS OF IL-10 FACILITATE SELECTION OF ISCHEMIC STROKE PATIENTS WITH CLINICAL-DIFFUSION AND PERFUSION-DIFUSSION MISMATCH FOR SYSTEMIC FIBRINOLYSIS

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Background: Clinical-Diffusion mismatch (CDM; NIHSS score ≥8 & DWI lesion volume ≤25 mL) and Perfusion-Difussion mismatch (PDM; difference >20% between initial DWI and MMT lesion volumes) have been suggested as a surrogate of ischemic brain at risk of infarction. Likewise, previous studies by our group have demonstrated that salvageable brain may be predicted with a number of molecular signatures of ischemic but not infarcted brain. Then, our aim was to study if serum levels of several biomarkers could facilitate the selection of ischemic stroke patients with CDM or PDM for systemic fibrinolysis.

Methods: We prospectively studied 595 patients (70.9±10.8 years, 54.3% male) with hemispheric ischemic stroke within 12h from the onset of symptoms. One hundred and eighty-four patients were treated with t-PA following SIST-MOST criteria. NIHSS score and MRI DWI and MMT volumes (manual segmentation method) were measured at admission (median, 186.0 min). Serum levels of glutamate (Glu), IL-10, TNF-α, IL-6, NSE, and active MMP-9 were determined by ELISA or HPLC in blood samples obtained at admission. The best predictive cut-off values were calculated by ROC analysis.

Results: Patients treated with t-PA who presented PDM had higher IL-10 levels at admission (p<0.0001). By contrast, patients with CDM showed higher levels of IL-10 (p<0.0001) as well as Glu, and TNF-α (all p<0.05), and lower levels of NSE and active MMP-9 (all p<0.0001). On the other hand, IL-10 ≥ 30 pg/mL predicts good functional outcome at 3 months with a specificity of 88% and a sensibility of 86% (area under curve, 0.952; p<0.0001). A multivariate logistic model identified only IL-10 ≥ 30 pg/mL as significantly independent molecular predictor of good

functional outcome after adjustment for age and basal stroke severity in both patients with PDM (OR, 18.9) as CDM (OR, 7.5).

Conclusion: Serum levels of IL-10 facilitate selection of ischemic stroke patients with CDM and PDM for systemic fibrinolysis.

6 Acute stroke: new treatment concepts A

NEUROFLO TREATMENT AND MORTALITY – RESULTS FROM THE SENTIS RANDOMIZED, MULTI-CENTER TRIAL

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Background: The SENTIS multi-national randomized trial evaluating the NeuroFlo catheter as a treatment for acute ischemic stroke has recently been completed. The trial included 515 subjects with presumed cortical ischemic stroke, ineligible for IV tPA or thrombectomy and presenting for treatment up to 14 hours after last known normal. This cohort was randomized to standard medical management according to AHA guidelines or to NeuroFlo treatment plus the same medical management. The treatment involves temporary, partial aortic occlusion of the supra- and infra-renal aorta with an endovascular dual-balloon catheter.

Methods: Mortality, by cause, was tracked as a secondary endpoint of the trial and compared between treatment and control groups. All deaths were independently adjudicated by a Data Safety and Monitoring Board, who also assigned stroke-relatedness.

Results: There was a trend toward lower mortality in the treatment group vs. controls (16.3% vs. 11.2%; p=0.104). Post-hoc analysis of stroke-related mortality revealed a potential difference with a treatment mortality of 7.4% and a control rate of 14.4% (p=0.015). We will present the cause of death in the two groups and discuss that the lower mortality in the treated patients was associated with better outcome.

Conclusion: The SENTIS trial indicated that there is a reduction in stroke related mortality when treated with cerebral perfusion augmentation up to 14 hours. Hypothesized mechanisms may involve an impact on stroke progression in specific patient groups. Additional study will be required to further evaluate this finding.

7 Acute stroke: new treatment concepts A

INTRAVENOUS ADMINISTRATION OF RT-PA IN STROKE PATIENTS LEADS TO INCREASED PLASMA CELLULAR-FIBRONECTIN LEVEL

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Background: Disruption of the vascular endothelium and blood-brain barrier (BBB) after cerebral ischemia may play important role in pathogenesis of hemorrhagic transformation (HT). The aim of this study was to assess the dynamic of markers that reflects endothelium injury in acute ischemic stroke (IS) patients treated with rt-PA.

Methods: We prospectively included 34 IV rt-PA treated patients according NINDS protocol within the first 3 hs (mean age: 62.6, 73.5% males, mean NIHSS score at admission: 14.5) and 20 IS patients in control group without HT admitted between 3 and 6 hs after IS onset comparable with rt-PA group. A blood samples were obtained at admission, in 24 hs, 3 and 7 days after stroke onset in both groups and additionally in 1 h after rt-PA infusion to measure plasma levels of Matrix Metalloproteinase-9 [MMP-9 (ng/ml)], cellular Fibronectine [c-Fn (microg/ml)] and Homocystein [Hm (micromol/L)]. HT rates were calculated from CT or MRI scans done 3-4 and 22-36 hs after IV rt-PA and symptomatic HT (sHT) was defined according to ECASS III criteria.

Results: HT was observed in 15 (44.1%) patients after rt-PA (all in 22-36 hs scans), sHT in 2 (5.9%). At admission no differences between groups on concentration of all markers were observed. In 1 h after rt-PA the level of c-Fn was higher in patients with all types of HT (203,8±115.4 microg/ml, p<0.05) in comparison with patients without HT (88±30.2) and controls (95.5±53.1). At 24 hs in patients with HT the concentrations of c-Fn (174.9±77.2 microg/ml), MMP-9 (371.3±416 ng/ml) and Hm (30.9±13.1 micromol/L) were increased vs patients without HT (86.6±57.2 microg/ml, p=0.09; 110.4±104.9 ng/ml, p=0.044 and 20.7±8.1 micromol/L, p=0.023, respectively) and control group (all p<0.05).

Conclusion: High plasma c-Fn level just after IV rt-PA might be indicative of endothelial damage and increased permeability of BBB leading to HT, probably due to proteolytic properties of rt-PA.

8 Acute stroke: new treatment concepts A

PRECEDING INTRAVENOUS THROMBOLYSIS FACILITATES ENDOVASCULAR MECHANICAL RECANALIZATION IN LARGE INTRACRANIAL ARTERY OCCLUSION

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Background: Acute occlusions of the large intracranial arteries are relatively resistant to intravenous thrombolysis. Therefore, multimodal approaches combining intravenous thrombolysis with endovascular mechanical recanalization are increasingly applied. In this setting intravenous thrombolysis may facilitate subsequent mechanical thrombectomy. To test this hypothesis we analyzed the influence of intravenous thrombolysis on net intervention time in subsequent endovascular mechanical recanalization.

Methods: In this retrospective single center analysis we compared net intervention time with and without preceding intravenous thrombolysis in patients treated by endovascular mechanical recanalization between 01/2003 and 06/2010. Net intervention time was defined as the interval between onset of endovascular thrombus manipulation and successful vessel recanalization.

Results: We identified 65 eligible patients, 35 of them were treated by intravenous thrombolysis prior to mechanical therapy. Recanalization was achieved in 26 patients with (74%) and 23 patients without preceding intravenous thrombolysis (77%). In the case of successful recanalization, net intervention time was significantly shorter in patients with preceding intravenous thrombolysis (24.8 +- 22.8 vs. 44.2 +- 40.5 minutes; p<0.05). This difference remained significant after restricting analysis to the patients treated by the Penumbra Stroke System© (n=32). After three months, patients with preceding intravenous thrombolysis were more likely to be functionally independent (mRS ≤ 2) than those without (p<0.05).

Conclusions: Our findings suggest that preceding intravenous thrombolysis may shorten intervention time in patients treated by endovascular mechanical recanalization. However, due to the retrospective design of our study, these findings have to be interpreted with caution and need confirmation in a larger patient population.

9 Acute stroke: new treatment concepts A

PDGF-CC ISOFORM IS ASSOCIATED WITH HEMORRHAGIC TRANSFORMATION AND EDEMA IN ISCHEMIC STROKE PATIENTS TREATED WITH TPA

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Background: Platelet derived growth factor (PDGF) are a family of molecules that play a significant role in angiogenesis. Importantly, PDGF-CC isoform is activated by tissue plasminogen activator (tPA) regulating Blood Brain Barrier permeability after ischemia. Our aim was to study the association of serum levels of PDGF isoforms with hemorrhagic transformation (HT) and edema after thrombolysis in ischemic stroke.

Methods: We studied 129 patients with ischemic stroke treated with iv t-PA within the first 4.5 h from stroke onset. Serum levels of PDGF-AA, PDGF-AB, PDGF-BB and PDGF-CC were analyzed by ELISA in serum samples obtained on admission (before t-PA bolus) and at 24 and 72h. CT was performed on admission and at 24-36 hours. On the 2nd CT, HT was classified according to ECASS II definitions and severe brain edema was diagnosed if extensive swelling causing any shifting of the structures of the midline was detected.

Results: PDGF-AA, PDGF-AB and PDGF-BB showed greater levels on admission, followed by a decrease at 24 and 72h. By contrast, PDGF-CC levels were greater at 24h (131.3±67.6 ng/mL) than on admission (69.1±40.5 ng/mL) or at 72 h (108.8±51.6 ng/mL) (all p<0.0001).Patients who developed HT showed only higher levels of PDGF-CC isoform on admission (95.6±13.9 vs. 66.9±41.2 ng/mL) and at 24h (222.9±33.2 vs.123.6±64.0 ng/mL) (all p<0.0001). In the multivariate analysis, PDGF-CC levels on admission (OR, 1.02) and at 24h (OR, 1.05) were independently associated with HT. On the other hand, patients with severe edema showed only higher levels of PDGF-CC on admission (89.6±18.2 vs.66.6±41.8 ng/mL) and at 24 h (198.7±43.3 vs.123.1±65.5 ng/mL).

Conclusions: PDGF-CC levels increase after tPA treatment and are associated with HAT and edema. These Results suggest that PDGF-CC could be a therapeutic target for thrombolytic treatment in acute ischemic stroke.

Vascular biology

1   Vascular biology

INCREASED PLATELET COUNT AND LYMPHOCYTE-PLATELET COMPLEX FORMATION IN PATIENTS WITH RECENTLY SYMPTOMATIC VERSUS ASYMPTOMATIC CAROTID STENOSIS-RESULTS FROM THE PLATELETS AND CAROTID STENOSIS (PACS) STUDY

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Introduction: The precise mechanisms responsible for the disparity in stroke risk between asymptomatic and symptomatic carotid stenosis patients are unclear. We hypothesised that recently symptomatic patients would have excessive platelet activation compared with their asymptomatic counterparts.

Methods: We performed an observational analytical study to compare haematological parameters and platelet activation status in asymptomatic versus early ($\leq$4 weeks after TIA or stroke onset) and late phase ($\geq$3 months) symptomatic moderate or severe ($\geq$50%) carotid stenosis patients. The sensitive and specific technique of whole blood flow cytometry was used to quantify platelet surface CD62P and CD63 expression, and the % circulating leucocyte-platelet complexes. Unpaired non-parametric comparisons were performed with the Wilcoxon rank sum test.

Results: Data from 31 asymptomatic carotid stenosis patients were compared with those from 46 symptomatic patients in the early phase, and 35 of these patients in the late phase after symptom onset, 23 of whom underwent intervention. Median platelet count was higher in early symptomatic than asymptomatic carotid stenosis patients (211 vs. 200×10^9/L; p=0.03), but the differences between the late symptomatic and asymptomatic groups were not significant (219 vs 200×10^9/L, p=0.1). The median % lymphocyte-platelet complexes was higher in early symptomatic than asymptomatic patients (2.8 vs. 2.4%, p=0.001; Figure 1). There were no significant differences in the expression of other activation markers between the groups.
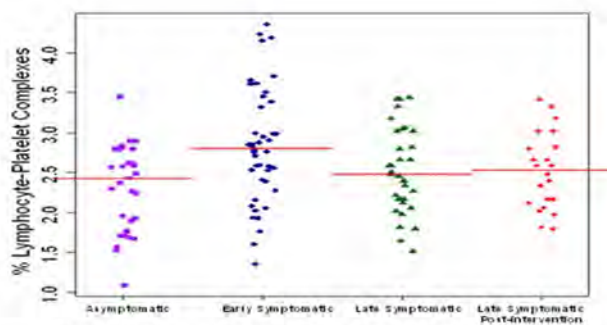

Figure 1: Scatterplot of percentage circulating lymphocyte-platelet complexes in the asymptomatic, early symptomatic, late symptomatic, and late symptomatic post-intervention subgroups. Each point on the graphs represents an individual patient's result; horizontal lines represent median values. P values refer to comparisons between the asymptomatic and symptomatic patients at different stages after symptom onset. * represents a statistically significant result.

Discussion: These findings improve our understanding of the haemostatic/ thrombotic profile in carotid stenosis. Increased platelet count and leucocyte-platelet complex formation could predispose to recurrent ischaemia or infarction in patients with recently symptomatic carotid stenosis. Longitudinal studies are warranted to assess the prognostic value of these biomarkers in asymptomatic and symptomatic carotid stenosis.

PENTRAXIN-3 IS A MARKER FOR ADVANCED, NOT EARLY ATHEROSCLEROSIS. RESULTS FROM THE BRUNECK, ARMY AND ARFY STUDIES

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Background: Pentraxins like C-reactive protein are key components of the innate immune system. Recently, pentraxin-3 has been proposed to be a specific marker of vascular inflammation.

Methods and Results: Pentraxin-3 levels were measured in three cross-sectional studies of 132 young men (ARMY Study), 205 young women (ARFY Study) and 562 individuals 55 to 94 years old (Bruneck Study). In contrast to C-reactive protein, pentraxin-3 showed little relationships with classic vascular risk factors and inflammatory conditions. Pentraxin-3 levels were independently associated with prevalent cardiovascular diseases (odds ratio [95%CI] 3.07 [1.64-5.74]) and severe but not early carotid and femoral atherosclerosis in the Bruneck Study. No association with increased intima-media thickness was demonstrated in young men and women.

Conclusion: Level of pentraxin-3 is independently associated with advanced atherosclerosis and manifest cardiovascular disease. Unlike C-reactive protein, pentraxin-3 appears not to be a component of the classic acute phase response (systemic inflammation) but specific for vascular inflammation.

3   Vascular biology

OVER-EXPRESSION OF CYCLIN-DEPENDENT KINASE 5 STIMULATES CELL MIGRATION IN HUMAN BRAIN MICROVASCULAR ENDOTHELIAL CELLS

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Background: Abnormal activation of neuronal and blood vessel cell death/ angiogenic pathways are common features in acute stroke. Spatial and temporal regulation of cytoskeletal dynamics critically modulates this process. We showed that the pharmacological inhibition of cyclin-dependent kinase 5 (Cdk5) with kinase inhibitor r-roscovitine and the deregulation of its activators p35/p25 with calpain inhibitor can affect angiogenesis in human brain microvascular endothelial cells (hCMEC/D3).

Methods: Using in vivo cell imaging system (Chip-Man Technologies Ltd) we monitored the effects of stable GFP-Cdk5 over-expression (Cdk5ov) on hCMEC/ D3 angiogenesis. Capillary branch chain formation and migration were studied in Matrigel and wounding assays, respectively. A hypoxia-chamber was used to mimic the effects of stroke on cell migration. Protein levels were estimated by Western blot. Cdk5/p35 involvement in cytoskeletal organization was investigated by confocal microscopy.

Results: Over-expression of cdk5 reduced cell adhesion, associated with increased p35 and talin protein levels. Cell migration was increased in Cdk5ov transfectants and this was augmented in hypoxic conditions (p<0.05). Cdk5ov transfectants showed a greater formation of neocapillary branch structures but their appearance was more chaotic. Similar to the controls, Cdk5 was distributed with actin fibres alongside the branch structures. Confocal analysis in untransfected cells, demonstrated co-localization of p35 and activated pTyr(15) Cdk5 with actin fibres in all phases of cell motility. P35 and talin co-localized with activated Cdk5 and integrin beta-1 at the leading edge of moving cells, indicating their interplay in cytoskelatal dynamics. Microarray analysis showed reduced expression of pro-angiogenic protein MEF2C and Jagged-1 in mutated (D144N) Cdk5 transfectants.

Conclusions: A pathway operating through Cdk5 may critically modulate cell dynamics during hypoxia/brain injury associated conditions.

4 Vascular biology

SINGLE-PARTICLE AGGREGATION ANALYSIS OF RECOMBINANT NOTCH3: IMPLICATIONS FOR CADASIL

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Background: CADASIL is the most frequent monogenic cause of stroke. The underlying small vessel disease is determined by mutations in NOTCH3. Mutations are highly uniform in that all mutations change the number of cysteine residues. Accumulation of the NOTCH3 (N3) extracellular domain in small blood vessels of patients and CADASIL-mutant transgenic mice led to the hypothesis, that protein aggregation is a central mechanism in the disease. Previous in vitro experiments using cell lysates of N3-overexpressing cells suggested enhanced formation of higher order multimers for mutant N3 compared to wild-type (WT).

Methods: We established a robust assay to assess multimerization of N3. The assay is based on recombinant protein purified from cell culture supernatant. After fluorescent dye labeling the multimerization process can be monitored on a single particle level in a confocal setup. Fluorescence autocorrelation spectroscopy, scanning for intensely fluorescent targets and fluorescence resonance energy transfer were used to quantify and characterize multimer formation. Western Blot analysis was used to validate the findings.

Results: We show that aggregation is unique to CADASIL mutant N3. WT N3 did not show any multimer formation under physiological conditions. Multimerization is facilitated by crosslinking of sulfhydryl groups. Although WT N3 does not exhibit multimerization itself, it can participate in multimer formation together with mutant N3. We further show that other proteins engage in multimer formation of mutant N3.

Conclusions: Using correctly folded protein from cell supernatant we demonstrate a qualitative difference in aggregation behavior between WT and mutant N3. Our findings imply that aberrant sulfhydryl groups from unpaired cysteine residues play a major role in the aggregation process. Sequestration of WT N3 and other proteins into multimers from mutant N3 may provide a basis for a potential new disease mechanism.

5 Vascular biology

APOLIPOPROTEIN-E CONTROLS ATP-BINDING CASSETTE TRANSPORTERS IN THE ISCHEMIC BRAIN

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We have previously shown that ABC transporters exhibit profound expression changes on ischemic cerebral microvessels, impeding drug accumulation in stroke brain. As such, the luminal transporter ABCB1, which extrudes drugs from the brain into blood, is upregulated, whereas the abluminal transporter ABCC1, which carries drugs in the opposite direction from the blood to brain, is downregulated upon stroke. The signal pathways controlling ABC transporters expression after stroke were unknown.

By means of genetic knockout and protein delivery studies, which we combined with protein expression analysis and pharmacological experiments, we found out that the expression patterns of ABCB1 and ABCC1 in ApoE-/- mice fundamentally differed from wildtype mice.

As such, ABCB1 was downregulated in ischemic brain capillaries, whereas ABCC1 was upregulated. Moreover, ApoE is de novo expressed on ischemic brain capillaries together with its receptor, ApoER2. We demonstrate that ApoER2 interacts with Jun N-terminal kinase (JNK)-1/2 interacting protein (JIP)-1/2. JIP1/2 in turn targets MKK-7 and MKP-7, to either phosphorylate or dephosphorylate JNK1/2, depending on the presence or absence of ApoE, thus influencing ABC transporter expression.

Selective inhibitors of luminal ABC transporters increased drug accumulation in rodents, studies in humans were disappointing. As such, it was realized that larger sets of transporters may have to be modulated pharmacologically or by transcriptional regulation to facilitate drug brain entry. The surface receptor ApoER2 is a promising target for drug delivery purposes, as its deactivation resets those transporters regulated by the stroke. Future studies have to demonstrate whether ApoER2 deactivation improves neurological therapies efficacy.

6 Vascular biology

RETICULATED PLATELETS IN THE EARLY AND LATE PHASES AFTER TIA AND ISCHAEMIC STROKE - RESULTS FROM THE TRINITY ANTIPLATELET RESPONSIVENESS (TRAP) STUDY

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Background: Reticulated platelets are young platelets, recently released into the circulation, that contain a residual amount of megakaryocyte-derived mRNA. There are limited data on this potentially functionally-important platelet fraction in ischaemic cerebrovascular disease (CVD). We hypothesised that reticulated platelets would be elevated in CVD patients.

Methods: We performed a case-control study to compare the % circulating reticulated platelets (%RP) in patients with TIA or ischaemic stroke (N=86) with healthy controls (N=24). %RP was quantified with the sensitive and specific technique of whole blood flow cytometry in patients ≤4 weeks of TIA or stroke onset (baseline), and again 14 days (14d) and ≥90 days (90d) later. The underlying mechanism responsible for the TIA or stroke was categorised according to the TOAST classification.

Results: %RP was not increased in the overall CVD patient population at baseline or 14d vs. controls (P≥0.1), but was significantly higher in CVD patients at 90d than in controls (P=0.008, Fig. 1). Subgroup analysis revealed that the %RP was elevated in patients with "lacunar" TIA or stroke at baseline (P=0.03), and in patients with TIA or stroke secondary to small vessel occlusion, cardioembolism or of undetermined aetiology at 90d compared with controls (p≤0.0496).
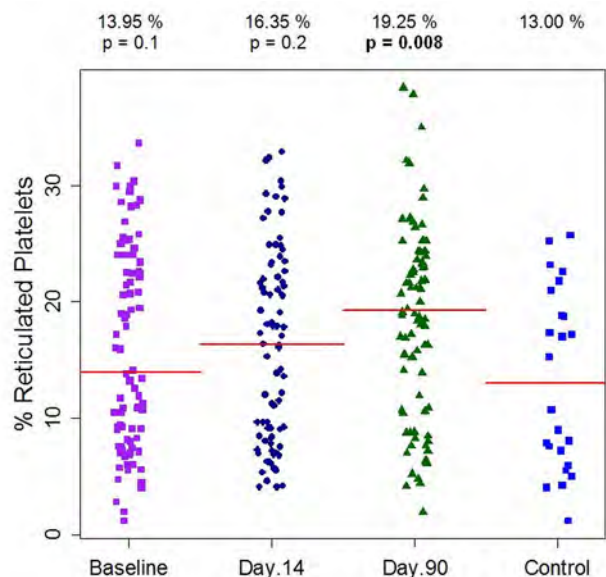

Figure 1 Scatterplot of circulating reticulated platelet levels in CVD patients at baseline, 14 days, and > 90 days versus control subjects.
Each point represents a single patient. Red lines and numbers above indicate median values. P values refer to comparison of median %RP between CVD patients at different time points with controls.

Conclusions: To our knowledge, this is the largest study of reticulated platelets in a well-characterised cohort of ischaemic CVD patients, and is the first study to investigate circulating reticulated platelets in the same patients in the early, subacute and late phases after symptom onset. The findings suggest that increased platelet production/turnover does not precede TIA or ischaemic stroke onset, but is a consequence of the ischaemic event, except perhaps in the subgroup with small vessel occlusion. The impact of reticulated platelets on platelet hyper-reactivity and non-responsiveness to antiplatelet therapy during follow-up deserves study.

ASSOCIATION OF DIMETHYLARGININES AND THE INFLAMMATORY RESPONSE AFTER ACUTE ISCHEMIC STROKE

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Background: Asymmetric dimethylarginine (ADMA) the most potent endogenous inhibitor of the nitric oxide synthase and its analogon symmetric dimethylarginine (SDMA) have been implicated in endothelial dysfunction and stroke outcome. Early inflammation represents an important factor contributing to unfavourable prognosis after acute ischemic stroke. In the present study we aimed to investigate the association between dimethylarginines and inflammation after acute ischemic stroke.

Methods: Blood samples of 58 patients with acute ischemic stroke were taken at the time points 6, 12 and 24 hours, as well as 3 and 7 days after symptom onset. ADMA and SDMA were determined using high-performance liquid chromatography–tandem mass spectrometry. Monocyte chemotactic protein-1 (MCP-1), matrix metalloproteinase-9 (MMP-9), tissue inhibitor of matrix metalloproteinase-1 (TIMP-1), interleukin-6 (IL-6) and C-reactive protein (CRP) were measured as mediators of inflammation in addition to S100B as marker for brain damage. For analysis of an independent association of dimethylarginine levels with inflammation markers a multiple stepwise linear regression analysis was performed adjusted for age, gender, stroke severity at admission and all tested markers at a respective time point.

Results: Plasma ADMA and SDMA levels are significantly correlated to markers of inflammation during the first hours but also days after stroke onset. ADMA is positively correlated to TIMP-1 at 6h, 24h and 3d after stroke onset. ADMA was also found to be inversely correlated to MMP-9 at 12h and positively correlated to IL-6 at 7d. SDMA is positively correlated to MCP-1 at 6h, 24h, 3d and 7d and to IL-6 at 3d and 7d after stroke onset.

Conclusion: Our data show that ADMA and SDMA are independently but differentially associated with the inflammatory response after acute ischemic stroke. To demonstrate the mechanisms behind further investigations are needed.

VALIDATION OF `REVERSED ROBIN HOOD SYNDROME' BY ACETAZOLAMIDE-CHALLENGED HMPA-SPECT IN PATIENTS WITH SEVERE STENO-OCCLUSIVE DISEASE OF INTRACRANIAL CAROTID OR MIDDLE CEREBRAL ARTERY

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Background: Intracranial stenosis is associated with stroke recurrence. In severe stenosis, perfusion is maintained by collateral pathways and cerebral autoregulation (CA). CA may be impaired due to inadequate cerebral vasodilatory reserve (CVR) & intracranial steal phenomenon ("reversed-Robin Hood (RRH) syndrome"). Identification of patients with inadequate CVR and RRH may help in selecting high-risk patients.

Methods: We prospectively included patients with symptomatic and severe stenosis of intracranial carotid (ICA) & middle cerebral artery (MCA), defined according to validated transcranial Doppler (TCD) criteria. CVR was evaluated with TCD & breath-holding index (BHI) <0.69 determined inadequate CVR. RRH was detected as transient velocity reduction in affected artery when flow increased in the reference artery. Patients with RRH were further evaluated with acetazolamide-challenged HMPAO-SPECT.

Results: 112 patients (79 males, mean age 57yrs; range 23-79yrs) with severe intracranial stenosis fulfilled our TCD criteria of inadequate CVR. 35 (31%) patients demonstrated RRH with a median steal magnitude of 17% (inter-quartile range, IQR 10). HMPAO-SPECT demonstrated perfusion deficit (median 8%; IQR 13%) in 33 out of these 35 cases (sensitivity 78%, specificity 96% with positive predictive value 96%). A strong relationship between RRH on TCD and SPECT was noted on ROC curve analysis (area under curve 0.93; 95% confidence interval 0.88-0.98; p<0.00001). Linear relationship was noted between TCD steal magnitude and SPECT (Pearson correlation coefficient, r=0.643;p<0.0001). Patients with RRH were at a higher risk of developing recurrent cerebral ischemia (p=0.04; RR 1.7, 95%CI 1.2-3.6).

Conclusions: RRH syndrome in patients with severe intracranial stenosis is associated with high risk of cerebral ischemic events. Acetazolamide-challenged HMPAO-SPECT is reliable in the diagnosis of reversed Robin Hood syndrome in patients with severe steno-occlusive disease of intracranial carotid and middle cerebral artery. Identification of RRH might help in identifying a target group of patients for possible revascularization.

PREDICTORS OF POOR LEPTOMENINGEAL COLLATERAL STATUS IN ACUTE ISCHEMIC STROKES: ANALYSIS OF DATA FROM THE KEIMYUNG STROKE REGISTRY

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Introduction: We plan to comprehensively evaluate factors responsible for reduced leptomeningeal collateral status in patients presenting with acute ischemic strokes.

Methods: The study population included patients with acute ischemic strokes included in the Keimyung Stroke Registry, Korea (2005-2009). Detailed clinical and biochemical data was collected prospectively. Imaging analysis including leptomeningeal collateral status on CTA was done at the University of Calgary. Clinical outcome was assessed at 90 days using the modified Rankin Scale.

Results: Of 250 patients with anterior circulations occlusions, 168 patients (mean age 66.8 years, 51.8% male, median NIHSS 14) with M1 MCA+/- intracranial ICA occlusions were included in the study. Median time from stroke onset to CT was 117 minutes (IQR 78-190). Significant leukoaraiosis as measured by the van Swieten scale was noted in 33/168 (22.3%) patients. The distribution of leptomeningeal collateral status was as follows (poor:33.3%, moderate:48.2% and good:18.5%). On univariate analysis, increased waist diameter, blood glucose at baseline, HbA1c, INR, serum uric acid and CRP along with low HDL levels were associated with poor collateral status (p < 0.05). In a multivariable logistic regression model including age, sex, presence of proximal carotid disease and significant leukoaraiosis along with the statistically significant variables in the univariate analysis, the only predictors of poor collateral status were raised blood glucose at baseline (OR 1.007 95% CI 1.001-1.013, p=0.02) and low serum HDL level (OR 0.96 95% CI 0.94-0.98, p=0.01). Good leptomeningeal collateral status, absence of significant leukoaraiosis and recanalization (TIMI 2-3) were independent predictors of good clinical outcome (mRS 0-2) (p<0.05).

Conclusion: Poor leptomeningeal collateral status is associated with raised blood sugar and low serum HDL level at baseline, suggesting the possibility of endothelial dysfunction in leptomeningeal collaterals. Interventions aimed at modulating endothelial dysfunction may alter collateral flow and be an area of future acute stroke intervention.

Brain imaging A

MULTISPECTRAL ANALYSIS OF CEREBRAL ISCHEMIA IN WHOLE BRAIN CT PERFUSION: SALVAGE OF PENUMBRA WITHOUT VISUALIZATION OF MISMATCH IS POSSIBLE

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Background: In acute stroke imaging, the concept of mismatch between reduced cerebral blood flow (CBF) and normal cerebral blood volume (CBV) has been used to visualize salvageable penumbra. Reduced CBV has been shown to represent infarct core specifically, however there are rare cases of reversible CBV perfusion deficits after thrombolysis. The purpose of this study was to assess the frequency of reversible apparent infarct core shown by reduced CBV in CT perfusion (CTP) using voxel based multispectral analysis.

Methods: Retrospectively, datasets of 1200 acute stroke protocols during a time span of 18 month were evaluated. All patients received whole brain CTP (Siemens Definition AS+) and follow up imaging within 48 hours. In 110 proximal MCA occlusive strokes, CBV and CBF perfusion maps were co-registered in normalized MNI-152 space for automated multispectral analysis (Analyze10.0). Within the

CBV-CBF spectrum, voxels of mismatch were defined by normal CBV and lowered CBF, and voxels of infarct core were defined by lowered CBV and lowered CBF using established thresholds for penumbra and infarct core. We defined significant reversibility of CBV as the total percentage of voxels of apparent infarct-core that did not represent infarct on follow up.

Results: An average of 48% mismatch voxels and 4% infarct-core voxels were identified within ischemic hemispheres. Only 2.1% of apparent infarct-core voxels did not infarct on follow up. A total of only 2 cases showed visually reversible CBV lesions. Both patients suffered from M1 occlusion and succesful recanalization was achieved within a short time after onset of symptoms. Follow up imaging revealed absence of infarction in the region of aparent infarct core.
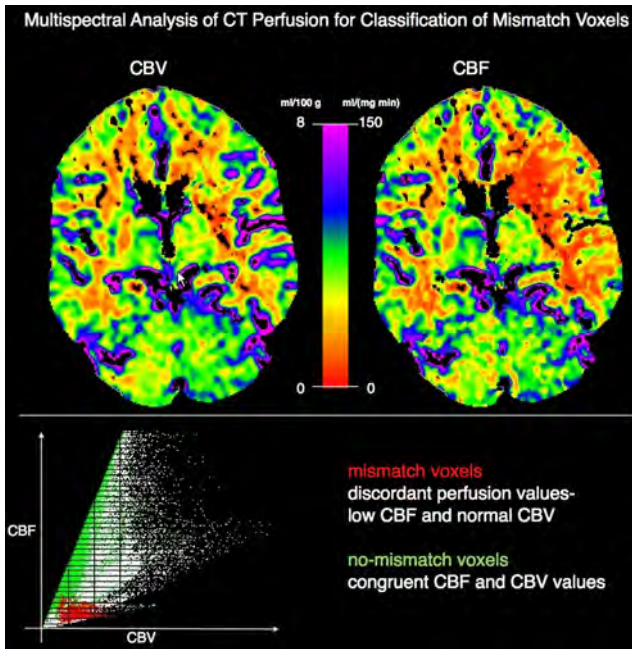
Conclusion: Multispectral analysis of ischemic stroke identified salvageable apparent infarct core. In rare cases penumbra without mismatch is possible possibly due to early recanalization. CBV thresholds that define infarct core may depend on the timing of reperfusion.

2 Brain imaging A

HYPERINTENSE VESSELS ON FLAIR-MRI: A MARKER OF SLOW PROGRESSION OF THE ISCHEMIC AREA DURING THE ACUTE STROKE PHASE

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Background: Hyperintense vessels (HV) on FLAIR-MRI have been associated with higher grade of arterial collaterals and smaller infarct volume in acute stroke patients. Our aim was to study the association of the HV sign with the recruitment of penumbra into infarction in acute stroke patients.

Methods: From a prospective stroke database, we selected acute stroke patients with a large artery occlusion of the anterior circulation admitted at our comprehensive stroke center for endovascular therapy, in whom a multimodal MRI was performed before treatment. Baseline CT and MRI were reviewed to evaluate the ASPECTS score and the presence of HV on FLAIR sequence. Hypodensity volume was measured on a follow-up CT at 24 hours. Good outcome was considered as a mRS 0-2 at three months.

Results: A total of 56 patients were selected (37 had received intravenous alteplase). Median time between baseline CT and MRI was 110 minutes [IQR, 75-187]. ASPECTS score on baseline CT was 10 in 39% of patients, 9 in 49% and 8 in 12%. ASPECTS score was 2 [1-3] points lower in the DWI-MRI and this decrease did not correlate to the time elapsed between the two exams. HV sign was present in

29/56 patients (M1 70%, M2 30%, TICA 44%). There were no differences in stroke severity, stroke subtype and ASPECTS score on baseline CT between patients with and without HV. HV was associated with a smaller decrease of ASPECTS score (1 [1-2] vs 3 [2-4], p<0.001) and with a smaller hypodensity volume (40±61mL vs 92±90mL, p=0.01). There was a trend toward a better outcome in patients with HV (50% vs. 28%, p=0.1). HV sign was independently associated with a higher probability of penumbra stability after adjustment for delay between exams, systolic blood pressure and serum glucose (OR 10.4 [IC95% 2.3 to 47]).

Conclusion: Hyperintense vessels sign on FLAIR is associated with a slow progression of the ischemic area in acute stroke patients with cerebral artery occlusion of the anterior circulation.

3 Brain imaging A

PATHOLOGICAL MICROVASCULAR MORPHOLOGY IN ISCHEMIC PENUMBRA REVEALED BY VESSEL SIZE IMAGING

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Background: Vessel size imaging is a novel magnetic resonance imaging (MRI) technique to quantitatively assess the morphological properties of microvasculature by providing two quantities: microvessel density related quantity Q and mean vessel size index (VSI). These parameters enable the assessment of pathological changes of ischemic tissue and may provide useful information to describe the penumbra.

Methods: Over a period of two months, non-selected acute ischemic stroke patients (n=89) were admitted to our institution were examined in a 3T MRI scanner in the application of vessel size imaging protocol, which was embedded into clinical imaging routine without time extension. Seventy-five patients had a perfusion-diffusion mismatch were included into further analysis. Two ROIs were defined for comparison: the ROI of ischemic penumbra corresponding to the hyperintensities of mean transit time (MTT) minus diffusion-weighted imaging (DWI) and the mirrored region of mismatch ROI to the contralateral hemisphere containing healthy brain tissue.

Result: Comparing the voxel-wise distribution between two ROIs, and for all patients, the value of Q in the ischemic region is significantly smaller than that in the mirrored healthy tissue (p<0.05) and the value of VSI is higher for (p <0.05). In case-wise studies, 39 patients (52%) show significantly decreased Q and increased VSI in the ischemic tissue, while Q and VSI display no significant changes in 20 patients (27%). The MTT volume was larger in the 39 patients with predominate changes in microvasculature than in those without obvious variation.

Discussion: Our findings in acute stroke patients match the Results from a rat stroke study. These observations of reduced microvessel density and increased mean vessel diameter could be explained by a more pronounced effect of edema on compression of small capillaries as compared to large-sized vessels, leading to a shift in the calculated average vessel size.

4 Brain imaging A

PREDICTING INFARCT CORE USING CT PERFUSION - CEREBRAL BLOOD FLOW THRESHOLDS PERFORM BEST

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Background: CT perfusion (CTP) is potentially widely applicable in acute ischemic stroke but validation of infarct core definitions and the effect of post-processing is limited. We analyzed common CT perfusion parameters as predictors of infarct core using contemporaneous diffusion MRI.

Methods: Acute ischemic stroke patients <6 hours after onset had CTP (2×2 4mm slabs, 16 slice Philips) and diffusion MRI (1.5T Siemens) within 1hr. Images were motion corrected, co-registered and smoothed (Gaussian) to varying degrees. CTP maps of time to peak (relTTP), absolute and relative cerebral blood volume (CBV), cerebral blood flow (CBF), mean transit time (MTT) and time to peak of the deconvolved tissue residual function (Tmax) were generated. The diffusion lesion was manually outlined to its maximal visual extent. Receiver operating characteristic (ROC) analysis area-under-the-curve (AUC) was

calculated within the manually outlined maximal extent of TTP perfusion lesion. Optimal thresholds were determined (Youden's index) both globally and for individual cases.

Results: There were 98 CTP slabs (54 patients) analyzed, 46% treated with thrombolysis. Median onset to CT 190 min, median CT to MR 30 min. In ROC analysis, increased smoothing improved AUC values for prediction of DWI lesion (globally and individually). Relative (<31% mean contralateral) CBF performed best followed by absolute CBF (<15mL/100g/min) and then CBV (Table). Applied to maps, CBF thresholds were clearly visually superior to CBV. Specificity was limited by undetectable CBF/CBV in normal white matter in cases with reduced contrast bolus intensity.

Parameter*	AUC	Threshold (from Youden's index)		
		Value	Sensitivity	Specificity
Relative CBF	0.79	31%	0.72	0.72
Absolute CBF	0.75	15 mL/100g/min	0.70	0.69
Relative CBV	0.75	54%	0.70	0.68
Absolute CBV	0.74	1.8%	0.66	0.72
Tmax	0.66	8.9 sec	0.55	0.74
Relative TTP	0.67	8.8 sec	0.56	0.74
MTT	0.63	13.0 sec	0.55	0.64

*Using 6-pixel width Gaussian smoothing kernel.

Conclusion: In contrast to previous reports, CBF predicted the acute DWI lesion better than CBV. However, no simple threshold avoids detection of significant false positive regions in normal white matter. This relates to low signal to noise ratio in CTP maps and indicates the need for optimized acquisition and standardized, sophisticated post-processing.

5 Brain imaging A

PATTERNS OF ISCHEMIC LESION PERFUSION IN THE FIRST MONTH AFTER STROKE. THE "NO REFLOW" PHENOMENON

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Background: Use of perfusion imaging (PI) has largely focussed on acute stroke, whereas changes in lesion perfusion patterns occurring subacutely or later might provide alternative opportunities for intervention. We assessed perfusion patters from <6hrs to 30 days after stroke in a prospective multicentre cohort study.

Methods: We recruited adult patients with ischemic stroke in 3 stroke centres. Patients underwent CT or MR structural, PI and angiographic imaging <6 hours of onset, at 72 hrs and 30 days. We recorded NIHSS at <6hrs, 3, 7 and 30 days; mRS at 1 and 3 months. We used imaging equipment and protocols harmonised to a common framework. Image data were processed qualitatively (structural lesion, vessel patency, PI defect) and quantitatively (by in house and commercial software) using 7 PI parameters (CBF, CVF, MTT, ATF, Tmax, TTP, raw image).

Results: We recruited 83 eligible patients, median age 70.5yrs (max 89), of median baseline NIHSS 7 range 1-30, median time to imaging 2.75 hr range 1.25:6:00. 46% received rt-PA. Most baseline imaging was with CT (78%); most follow-up imaging was MR: 60/76 (79%) at 72hr, 44/48 (92%) at 30d. At baseline, 63 (77%) patients had a visible ischemic lesion; 47 (64%) had a Tmax PI defect of whom 31 (38%) had mismatch. 40 patients (50%) had impaired arterial patency at baseline. The PI lesion shrank in 32 patients, was unchanged in 13 and worsened in 3 at 72hrs or 30d. Mismatch persisted in 5 at 72 hrs and 1 at 30d. 50% of occluded arteries recanalised by 72hr and a further 13% by 30d. 13/40 patients showed arterial recanalisation but persistent perfusion defect (ie "no reflow") at 72hrs (9 at 30d).

Conclusion: Tissue perfusion defects persist despite recanalisation in about 33% of stroke patients who present with arterial occlusion. This may equate to the "no reflow" phenomenon seen in experimental models. This offers scope to identify interventions to enhance tissue reperfusion and outcome.

6 Brain imaging A

MRI-BASED USE OF INTRAVENOUS TISSUE PLASMINOGEN ACTIVATOR IN WAKE-UP STROKE

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Background and purpose: Patients waking up with symptoms of stroke are often excluded from treatment with tissue Plasminogen Activator (tPA). In our Stroke Unit equipped with a 3T-MRI we studied the safety and efficacy of MRI-based use of intravenous tPA in wake-up stroke.

Methods: We analyzed data of 152 patients (including 18 wake-up strokes) who received tPA after MRI between January 2008 and October 2010.

Results: Patients with wake-up strokes were older, had longer median door-to-needle time and a trend towards higher median NIHSS on admission compared to those thrombolysed within 4.5h (79.8 years, SD ±8.9 vs 73.6 years, SD ±12.2, p< 0.05; 86.5 min, IQR 50-110.5 vs. 60 min, IQR 49-75, p=0.01; 14, IQR 8-16 vs 8, IQR 5-16, p=0.08, respectively). Time between the moment patients were last seen well and thrombolysis was significantly longer in patients who woke up with symptoms of stroke (12.4 h, IQR 11.5-15.2 h vs. 2.1 h, IQR 1.8-2.8 min, p < 0.01). Good functional outcome (mRS <3) 3 months after thrombolysis was achieved in 6 patients who woke up with stroke symptoms and 66 patients who received tPA within 4.5h (33.3% vs. 49.3%, p=0.21). One symptomatic intracerebral hemorrhage occurred in patients with wake-up strokes as compared to 4 in patients with known time of symptom onset (5.6% vs. 3%, p=0.56). Mortality after 3 months did not differ significantly in both groups (20, 14.9% vs 1, 5.6%, p=0.27). In multivariate analyses including age, gender, baseline NIHSS and atrial fibrillation wake-up strokes were not independently associated with unfavourable outcome after 3 months (OR 1,19; 0,34-4,17).

Conclusion: Despite unfavorable baseline characteristics of patients who woke up with stroke symptoms functional outcome after three months was not worse compared to patients who received tPA within 4.5h. Overall this study encourages those who prepare prospective MRI-based trials of thrombolytic agents in patients with unknown time of symptom onset.

7 Brain imaging A

WHICH ARTERIAL INPUT FUNCTION IN ACUTE STROKE PWI? – A COMPARISON WITH O15-WATER-PET

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Background: The arterial input function (AIF) is a precondition for MR perfusion imaging. However so far there is no validation of the optimal localisation of the AIF in acute stroke. We assessed the different AIF's from the M1, M2 and M3 branches of the Middle Cerebral Artery (MCA) to detect the penumbral flow threshold defined by 15O-water positron emission tomography (CBF-PET) (<20 ml/100g/min).

Methods: In acute and subacute stroke patients, the CBF-PWI maps generated with AIF's from the different MCA branches (M1, M2, M3) contralateral to the ischemic hemisphere were compared on a voxel based approach with CBF-PET. In a receiver operating characteristic comparison (ROC-analysis), the influence of the AIF on PW derived maps was assessed using quantitative CBF-PET maps as the gold standard with respect to penumbral flow <20ml/100g/min. The performance of the AIF to define the penumbral flow was calculated for each MCA branch.

Results: In an analysis of 8 stroke patients (median time MRI to PET: 66 minutes; patients imaged within 22 hours after stroke) the best MCA branch for the definition of the AIF with the highest area under the curve (AUC) to identify penumbral flow (<20ml/100g/min on CBF-PET) was the M3 segment. Median AUC was 0.94 (IQR 0.87-0.96), 0.91 (IQR 0.84-0.95), 0.86 (IQR 0.79-0.90) in M3, M2 and M1 respectively.

Discussion: Quality in terms of AUC was enhanced in more distal MCA branches. In Conclusion, our data support that AIF's for the generation of PW-CBF maps in acute stroke should be defined via selection of distal branches of the MCA.

8 Brain imaging A

FREQUENCY OF UNEXPECTED MAJOR FINDINGS IN ACUTE STROKE PATIENTS ON CT ANGIOGRAPHY

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Background: Standard neuroradiological evaluation of acute stroke patients for the possibility of thrombolysis with 64-MDCT angiography from arcus to vertex covers anatomically the lung apices, the superior mediastinum with central vessels and the neck. We determined the frequency of major findings in acute stroke patients that are unrelated to their primary complaint but have therapeutic consequence.
Methods: 532 acute stroke patients underwent standard neuroradiological evaluation at Copenhagen University Hospital Bispebjerg 2009-2010. This study is a retrospective review of prospectively collected standardized data over two years to assess the frequency of unexpected but potentially clinically serious findings and was approved by the Danish data protection agency, file no. 2010-41-5205.
Results: 26 of 532 acute stroke patients 2009-2010 at Copenhagen University Hospital Bispebjerg showed unexpected major findings: 16 patients had lung tumors, 2 pulmonary emboli, 3 lymph node metastases, 4 central aneurysms (3 on the proximal aorta and one on the brachiocephalic trunc) and one was suspect of gas gangrene.
Conclusion: Unexpected major findings with therapeutic consequence are found in 5% of acute stroke patients.

9 Brain imaging A

PERSISTENCE OF HYPERDENSE MIDDLE CEREBRAL ARTERY SIGN ON FOLLOW-UP CT SCAN IS ASSOCIATED WITH POOR OUTCOME IN ISCHEMIC STROKE PATIENTS TREATED WITH INTRAVENOUS THROMBOLYSIS

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Background: Significant numbers of acute ischemic stroke (AIS) patients recover with optimal care & timely intravenous thrombolysis with tissue plasminogen activator (IV-TPA). However, rates & extent of recovery remain highly variable. Early identification of reliable predictors of functional outcomes is important for planning interventions & rehabilitation strategies. Hyperdense middle cerebral artery sign (HMCAS) on pre-treatment CT scan represents presence of thrombus, often associated with severe disability & poor clinical outcome. However, it is reliable only in AIS patients managed conservatively. In thrombolysed cases, it may disappear (clot dissolution) or persist (persisting clot) on the follow up CT scan. We aimed at evaluating whether disappearance or the persistence of HMCAS on follow-up scan predicts final outcome.
Methods: Consecutive AIS patients treated with IV-TPA from Jan2007 to March2010 were included. Posterior circulation strokes were excluded. HMCAS was assessed by 2 independent stroke neurologists, blinded to the patient data or outcomes. The data were analyzed for the early predictors of function outcome.
Results: Of the total of 1918 AIS patients admitted to our center, 189 (9.9%) eligible cases were thrombolysed; mean age 64±13 years; 102 (59%) males; mean onset-to-treatment time 157±38 minutes & median NIHSS 16 points. Hypertension was the commonest vascular risk factor in 144 (76%) & 63 (33%) patients suffered from atrial fibrillation (AF). HMCAS was observed on the pre-TPA scan in 95 (50%) patients and persisted in 47 (50%) of them. Overall, 96 (51%) patients achieved good functional outcome (mRS 0-1 at 3 months). On the univariable anlaysis, age, AF, pre-TPA NIHSS score and HMCAS on the follow-up CT scan were associated with poor functional outcome. However, only pre-TPA NIHSS score (OR1.09; 95%CI 1.04-1.16, p=0.001) & HMCAS on follow-up CT scan (OR 22.93; 95%CI 8.81-54.52, p <0.0001) remained significant on multivariate analysis.
Conclusion: Persistence of HMCAS on the follow up CT scan in AIS patients treated with IV-TPA can be used as an early predictor of poor functional outcome.

Vascular surgery and neurosurgery/interventional neuroradiology

1 Vascular surgery and neurosurgery/interventional neuroradiology

RISK OF IPSILATERAL ISCHEMIC STROKE RECURRENCE BEFORE CAROTID ENDARTERECTOMY

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Background: Carotid endarterectomy (CEA) reduces the risk of ipsilateral ischemic stroke in patients with symptomatic 50-99% carotid stenosis. The risk reduction is high if CEA is performed within 2 weeks of the last cerebrovascular symptom. We aimed to investigate the risk of ipsilateral ischemic stroke recurrence before CEA.
Methods: This is a primary analysis of the Additional Neurological SYmptoms before Surgery of the Carotid Arteries – a Prospective study (ANSYSCAP). We prospectively ascertained 230 consecutive patients with symptomatic 50-99% carotid stenosis who underwent evaluation before CEA. We followed the patients for 90 days or until CEA. The primary endpoint was ipsilateral ischemic stroke that occurred after the presenting event.
Results: The risk of ipsilateral ischemic stroke recurrence before CEA was 4.8% (n=11) within two days, 7.9% (n=18) within seven days, 11.2% (n=25) within 14 days, and 18.7% (n=33) within 90 days of the presenting event. The risk of ipsilateral ischemic stroke recurrence was higher if the presenting event was a stroke (adjusted HR 12.3, p=0.016) or TIA (adjusted HR 10.4, p=0.025) compared with an amaurosis fugax. Age, sex, or degree of carotid stenosis on the symptomatic side did not affect the risk of ipsilateral ischemic stroke recurrence.
Conclusions: The risk of recurrent ipsilateral ischemic stroke was high within the first days of the presenting event. Many recurrences would likely have been avoided if CEA had been performed within 24 hours of the presenting event.

2 Vascular surgery and neurosurgery/interventional neuroradiology

RISK OF WOUND HEMATOMA AT CAROTID ENDARTERECTOMY UNDER DUAL ANTIPLATELET THERAPY

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Background: Early intensive antiplatelet therapy is recommended in patients with acute ischemic stroke or transient ischemic attack (TIA). Moreover, in those suffering their ischemic event from severe internal carotid stenosis guidelines also recommend endarterectomy within 14 days of the onset of a minor stroke or TIA. Thus, patients with recently symptomatic severe carotid stenosis may undergo endarterectomy when on dual antiplatelet therapy and may be at an increased bleeding risk.
Methods: During a 16 year period, 688 consecutive patients (mean age 66.5 years, SD 9.2; 75.7% male) underwent first carotid endarterectomy at a single center under dual antiplatelet therapy, i.e. ASA and clopidogrel (16.4%) or single antiplatelet therapy, i.e. ASA or clopidogrel (83.6%). All patients underwent standardized operative procedure with patch endarterectomy. The amount of intraoperative heparin and protamine were assessed. Bleeding complications were evaluated as local hematoma without and with the need of operative revision and as amount of local wound drainage.
Results: Local hematoma occurred in 108 (15.7%) patients. In 19 (2.8%) patients re-surgery for local wound hematoma was necessary. Hematoma more often occurred in patients under dual than single antiplatelet therapy (24.1% vs. 15.0%; OR 1.094, 95% CI 1.797 - 2.952, p=0.028). Hematoma needing operative revision occurred in 4 patients with dual and 15 with single antiplatelet therapy and did not differ in both groups (21.1% vs. 16.1%; OR 1.370, 95% CI 0.446 - 4.207, p=0.812). The amount of intraoperative given heparin and whether this was antagonized with protamine did not influence the presence of postoperative wound hematoma.
Summary: Our study suggests that patients with recently symptomatic severe carotid stenosis can undergo early endarterectomy without increased severe local bleeding complications also when under dual antiplatelet therapy with ASA and clopidogrel.

3 Vascular surgery and neurosurgery/interventional neuroradiology

EARLY CAROTIDENDARTERECTOMY - INCREASED PER-OPERATIVE RISK?

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Background: The strategy towards performing carotid endarterectomy within two weeks in patients with a TIA or minor stroke has been implemented gradually into clinical practice in Sweden.
However, uncertainty as to the optimal timing of CEA (carotid endarterectomy) is still unclear. Is there a higher risk to intervene within two weeks after the onset of symptoms? The aim of this study was to assess if early intervention for symptomatic carotid stenosis results in increased procedural risk.
Method: All interventions for symptomatic carotid stenosis from May 2008 to December 2010 were prospectively recorded in the Swedish Vascular Registry (Swedvasc). Time to intervention was set by the date of onset of symptoms that caused the patient to seek medical attention and the date for surgery. Stroke rate and mortality at 30 days post-operatively was analyzed for the cohorts of patients with the following time to intervention: 0-14 days (early) and>14 days (delayed).
Results: During the period of observation, 1989 patients underwent CEA for symptomatic carotid disease and were followed up at 30 days after surgery. 1186 (59.6%) underwent early intervention and 803 (40,4%) had a delayed treatment. The frequency of major stroke or death within 30 days was for the early group 2,1% and for the delayed group 3,6% (ns).
Conclusion: There is no significant higher procedural risk after early intervention. Even though early intervention prevents more strokes, there is no evidence that surgery performed within two weeks after onset of symptoms cause more complications.

4 Vascular surgery and neurosurgery/interventional neuroradiology

SHORT-TERM PREDICTORS OF STROKE AFTER CAROTID STENTING AND CAROTID ENDARTERECTOMY: DATA FROM THE INTERNATIONAL CAROTID STENTING STUDY (ICSS)

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Background: ICSS (ISRCTN25337470) is a randomized controlled trial comparing carotid stenting (CAS) to endarterectomy (CEA) for recently-symptomatic carotid stenosis. Interim analysis showed an excess of stroke in the CAS group at 30 days, driven mainly by non-disabling events. We hypothesised that baseline vascular risk factors would increase the risk of procedural stroke.
Methods: Baseline factors influencing the risk of any stroke within 30 days after CAS and CEA were investigated sequentially in a per-protocol analysis of patients in whom the allocated procedure was initiated. Binomial regression was used to calculate the risk ratios in each subgroup in univariable and multivariable models. Patients with missing information were excluded from individual analyses.
Results: CAS was initiated in 828/853 patients allocated stenting, of whom 58 (7.0%) suffered a stroke. CEA was initiated in 821/857 allocated endarterectomy, of whom 27 (3.3%) suffered a stroke. In univariable analysis, the 30-day stroke risk in CAS patients was significantly higher (p<0.05) with each additional year of age, with increasing Rankin Score at baseline, the presence of atrial fibrillation (15.4% vs 6.3%), in those who never smoked vs current smokers (9.3% vs 2.5%), in left-sided stenoses vs right (9.0% vs 4.8%), and with stroke as the index event vs amaurosis fugax (8.6% vs 1.4%). Results were attenuated in multivariable analysis. The 30-day risk of stroke after CAS increased significantly with increasing number of risk factors (0%, 4.9%, and 15.7% in those with 0-1, 2-3 and 4-5 risks respectively, p<0.001). The risk of CEA showed no clear association with the number of risk factors (1%, 3.7%, and 3.4% respectively). In those with 4-5 risk factors, the risk of CAS was nearly 5 times higher than CEA (risk ratio 4.61, 95%CI 2.08 to 10.22, p<0.001).
Conclusions: CAS should be avoided in patients with multiple risk factors, but might be a safe alternative to CEA in those with few vascular risk factors.

5 Vascular surgery and neurosurgery/interventional neuroradiology

CHARACTERISTICS OF PERI-PROCEDURAL BRAIN ISCHAEMIA DIFFER BETWEEN PATIENTS RANDOMISED TO STENTING VERSUS ENDARTERECTOMY FOR SYMPTOMATIC CAROTID ARTERY STENOSIS – RESULTS FROM THE ICSS-MRI SUBSTUDY

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Background: In the MRI substudy of the International Carotid Stenting Study (ICSS, ISRCTN25337470), 50% of patients treated with stenting (CAS) and 17% of patients treated with endarterectomy (CEA) had new ischaemic brain lesions on diffusion-weighted imaging (DWI) after treatment. In the present analysis, we compared characteristics of ischaemic lesions between CAS and CEA.
Methods: The total number of new ischaemic lesions on post-treatment DWI (lesion count), and total and individual lesion volumes were compared between patients randomised to CAS (n=124) or CEA (n=107) in the ICSS-MRI substudy, using generalised linear models.
Results: CAS patients had significantly higher lesion counts than CEA patients (1 lesion, CAS: 15% vs. CEA: 8%; 2-5 lesions, 19% vs. 5%;>5 lesions, 16% vs. 4%; RR of having a higher lesion count with CAS vs. CEA: 8.77, 95% CI 4.40-17.51, p<0.001). Individual lesions were significantly smaller in the CAS group than in the CEA group (p<0.001). Total lesion volume did not differ between groups (p=0.18). The increase in lesion count with CAS over CEA was higher among patients with stroke as the qualifying event (interaction p=0.004) and diabetes (interaction p=0.03). The estimated statistical power to find a significant difference between CAS and CEA for the count model (number of DWI lesions) and the model based on dichotomised, binary outcome (presence of DWI lesions) was 76% and 65% for a sample size of 50 patients, 91% and 87% for 75 patients, and 96% and 95% for 100 patients, respectively.
Conclusion: Patients treated with CAS had higher numbers of ischaemic brain lesions on post-treatment DWI than patients undergoing CEA, but individual lesions were smaller. These findings may reflect differences in underlying mechanisms of ischaemia. Comparison of lesion counts increased statistical power compared with binary outcome analysis, and may be the preferred method to analyse DWI outcome data in future studies of carotid revascularisation.

6 Vascular surgery and neurosurgery/interventional neuroradiology

LENGTH OF STENOSIS PREDICTS TREATMENT RELATED ISCHEMIC LESIONS AFTER CAROTID ARTERY STENTING

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Background: Carotid artery stenting (CAS) is associated with the risk of periprocedural embolic events. We aimed at determining predictors of procedure-related ischemic events.
Methods: We analyzed new ischemic lesions in diffusion-weighted MR imaging (DWI) after CAS in 123 patients with symptomatic high-grade carotid stenosis. Ten covariates were assessed as potential risk factors for new DWI lesions: age, gender, hypertension, diabetes, dyslipidemia, smoking status, severity of stenosis, side of intervention, length of the target carotid lesion, and irregularity of the surface of the target plaque.
Results: From the ten covariates assessed, only the length of the target lesion was independently associated with new DWI lesions. Among patients with carotid lesions<10 mm in length, the proportion of subjects with new DWI lesions was 13.2% (95% CI, 6.5-22.9), whereas among patients with lesions of 20 mm or longer, this proportion was 53.8% (95% CI, 25.1-80.8) (relative risk 4.1, 95% CI, 1.6-8.4, p=0.002). There was a trend towards higher rates of new lesions in older subjects, but this result was not significant.
Conclusion: The length of carotid lesions is independently associated with the risk of CAS-related ischemic events.

7 Vascular surgery and neurosurgery/interventional neuroradiology

THE COGNITIVE IMPACT OF MICROEMBOLI IN CAROTID ENDARTERECTOMY: "SOLID" EVIDENCE FOR "VICIOUS" BUBBLES

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Background: Few studies have investigated the influence of perioperational microembolism on neuropsychological parameters. Although data are lacking, gaseous microemboli are allegedly innocent compared to solid particles. We investigated the differential effect on cognition of microemboli depending on the nature of the underlying material.

Methods: 87 patients with a>70% stenosis were studied with an extensive battery of neuropsychological tests preoperatively (baseline), at 3-7 days and at 3 months postoperatively. Patients were monitored over both middle cerebral arteries preoperatively (30†min), intraoperatively and immediately postoperatively (60†min) using a multi Dop T2 ultrasound device (DWL, Germany). Microemboli were identified according to standard criteria and analyzed by an offline automated system to predict their gaseous (G) or solid (S) nature.

Results: The number of all emboli (S+G), and the number of solid emboli that were detected during the whole operation, was 1) negatively correlated to the verbal learning index (Kendall's tau 0.69, p=0.009; 0.67, p=0.01) 2) positively correlated to the degree of loss of initial improvement of the number of correctly identified signs in the d2 test (tau=0.58, p=0.03; 0.63, p=0.01), and 3) to the number of errors in the nonverbal learning task (tau=0.55, p=0.04; 0.58, p=0.02). Patients in whom we detected≥22 emboli regardless of their nature during the whole operation, or≥11 solid emboli had adverse neuropsychological outcome [1] OR: 0.73 (0.55-0.89); 0.68 (0.47-0.91); 2) OR: 1.69 (1.33-2.02); 1.45 (1.12-1.71); 3) 1.91 (1.57-2.35); 1.77 (1.49-2.22)].

Conclusion: We demonstrated the association between the number of microemboli that were recorded during the operation regardless of their nature and the development of specific neuropsychological deficits. Gaseous emboli may have a cognitive impact and we suggest that a minimum load/threshold of microemboli is required for the development of neuropsychological deficits.

8 Vascular surgery and neurosurgery/interventional neuroradiology

A NEW GENERATION OF FLOW-DISRUPTION DEVICE FOR ENDOVASCULAR TREATMENT OF INTRACRANIAL ANEURYSMS - CLINICAL AND ANGIOGRAPHIC RESULTS OF A MULTICENTER FEASIBILITY STUDY

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Background: Based on previous in vitro and in vivo experimental studies a new generation of flow disruption (FD) device (Surpass FD, Tel Aviv, Israel) was developed and evaluated in a multicenter feasibility study for the treatment of intracranial aneurysms.

Methods: A total of 56 aneurysms in 49 patients were treated. Thirty-seven aneurysms were smaller than 10mm in diameter, and 19 were larger than 10mm. The aneurysms originated in 74% of the cases from the internal carotid artery (ICA). Single devices, tailored to local boundary conditions, were placed endovascularly in parent arteries and covering the aneurysm. Implanted devices measured 2.9-5.3mm in diameter with a length of 10-80mm.

Results: Immediate control angiography (DSA) demonstrated various degree of flow reduction within aneurysm up to a complete flow stagnation. Up to six-month follow-up DSA available in 10 patients showed a complete/near-complete occlusion in 9 aneurysms and size reduction in 1 aneurysm. In 2 patients tortuosity of ICA prevented a successful device deployment with the first generation of delivery system. All perforating arteries covered by the implant remained patent during the follow-up period of up to 15 months. Procedure related thromboembolic complications were seen in 3 patients and resolved in 2. Another patient experienced a wire perforation during device deployment that led to an intracerebral hematoma necessitating a surgical intervention. At 90-day follow-up the patient presented with an improving upper extremity hemiparesis and dysphasia. Another patient with a preexisting aneurysm-associated partial CN III palsy developed a complete ptosis. None of the aneurysms ruptured during follow-up. One patient with a basilar trunk aneurysm died during follow-up period due to a pseudomonas pneumonia resistant to antibiotics.

Conclusion: Preliminary data demonstrate the safety and effectiveness of a new generation of FD device in treating aneurysms without the need for coiling.

9 Vascular surgery and neurosurgery/interventional neuroradiology

TIMI SCORE IN SUCCESSFUL RECANALIZATION AFTER ENDOVASCULAR REPERFUSION THERAPIES FOR ACUTE STROKE: SHOULD WE REDEFINE RECANALIZATION END-POINTS IN ENDOVASCULAR ACUTE STROKE TRIALS?

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Background: Endovascular reperfusion trials for acute stroke show up to 60-80% recanalization (RE) rates but good functional outcome in only 30-40%. Definition of RE is usually considered as final Thrombolysis In Myocardial Infarction (TIMI) 2-3 score. We hypothesized that clinical course, infarct volume and outcome vary widely across TIMI grades in successful RE as defined in trials.

Methods: Consecutive patients treated with IA reperfusion therapy were analyzed. Vascular occlusion and RE were classified according to TIMI. Infarct volume was measured on 24h CT. Early clinical evolution was determined by NIHSS (baseline, 24h and discharge). Clinical improvement was defined as decrease≥4p from baseline NIHSS. Long-term outcome was evaluated by modified Rankin Scale at 3months (good functional outcome: mRS†≤†2).

Results: 120 patients were included; 56 (46.6%) female, mean age 70.5 ± 11. 8y and median baseline NIHSS 19 (IQR 15-23). Arterial occlusions were: 62 (51.6%) MCA, 43 (35.8%) TICA, 13 (10.8%) BA and 2 (1.7%) PCA. 81 (67.5%) patients achieved RE defined as TIMI 2-3. Patients who RE had better clinical evolution (24h: 55.6 vs 16%; discharge 64.4 vs 12%), smaller infarct (mean 111.6 ± 153 vs 239.8 ± 168.2 cc), lower mortality (25.3 vs 56.7%) and better functional outcome (41.5 vs 3.8%) than patients who didn't (p<0.01).

However, significant differences between TIMI grades were detected in the RE group (Table). Patients who achieved TIMI 3 had 5-times smaller infarct and 2-times better early clinical course than those with TIMI 2a. In patients who RE, achievement of TIMI 3 independently predicted good functional outcome after adjusting for baseline NIHSS and time to RE (OR 5.8; 95% CI 1.4-23.9; p=0.014).

N (%)	TIMI 2a 21 (17.5)	TIMI 2b 27 (22.5)	TIMI 3 33 (27.5)	p A: TIMI 2a vs 2b B: TIMI 2b vs 3 C: TIMI 2a vs 3
Improvement after 24h	5 (23.8)	13 (48.1)	24 (72.7)	A: 0.163 B: 0.017* C: 0.001*
Improvement at discharge	9 (42.9)	17 (62.9)	26 (78.8)	A: 0.221 B: 0.151 C: 0.017*
Infarct volume	252.3±54.7	77.6±25.3	49.7±17.3	A: 0.221 B: 0.358 C: 0.003*
Mortality	7 (33.3)	9 (33.3)	3 (9.1)	A: 0.995 B: 0.038* C: 0.038*
mRS≤2	4 (19)	8 (29.6)	21 (63.6)	A: 0.381 B: 0.031* C: 0.006*

Conclusion: RE after endovascular treatment is associated with clinical improvement but relevant differences are detected between TIMI grades. More strict RE end-points in IA trials are required to adjust the translation of RE into good clinical outcome after endovascular procedures.

Large clinical trials (RCTs) A

1 Large clinical trials (RCTs) A

A RANDOMISED BLINDED TRIAL OF TERUTROBAN VERSUS ASPIRIN IN PATIENTS WITH CEREBRAL ISCHAEMIC EVENTS: RESULTS OF THE PERFORM STUDY

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Worcester, MA, USA; [5]Roberston Center for Biostatistics, Glasgow, United Kingdom; [6]Royal Brompton Hospital, London, United Kingdom; [7]University of Heidelberg, Mannheim, Germany; [8]Inselspital, University of Bern, Bern, Switzerland; [9]John Radcliffe Hospital, Oxford, United Kingdom

Background: Patients with ischaemic stroke or transient ischaemic attack (TIA) are at high risk of recurrent stroke or other cardiovascular events. We aimed to evaluate the superiority of the specific TP (thromboxane A2/prostaglandin endoperoxide) receptor antagonist, terutroban, over aspirin in the prevention of cerebrovascular and cardiovascular events in such patients.

Objectives and Methods: Patients were randomised in the PERFORM study if they had an ischaemic stroke or a TIA in the previous 3 months or 8 days, respectively. They received either terutroban (30 mg o.d.) or aspirin (100 mg o.d.). The primary efficacy endpoint was a composite of ischaemic stroke (fatal or non-fatal), myocardial infarction (fatal or non-fatal) or other vascular death (excluding haemorrhagic death of any origin). A sequential statistical analysis of non-inferiority (margin 1.05) followed by superiority was performed.

Results: Following an interim analysis based on the main efficacy endpoint, the Data Monitoring Committee recommended to prematurely stop the study for futility. A total of 19 120 patients were analysed with a mean follow-up of 28.3 months. Primary endpoint occurred in 1091 patients (5.1%PY) receiving terutroban and 1062 patients (5.0%PY) receiving aspirin (HR 1.02, 95% CI 0.94–1.12). There was no evidence for a difference between terutroban and aspirin for any of the secondary or tertiary endpoints. There was a moderate increase in minor bleedings with terutroban (1147 [12%] versus 1045 [11%]), while no relevant differences were observed in other safety aspects.

Conclusions: Terutroban has a clinical efficacy similar to aspirin without safety advantages in stroke patients.

2 Large clinical trials (RCTs) A

EFFECTS OF CANDESARTAN ON VASCULAR EVENTS AND FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE STROKE AND HIGH BLOOD PRESSURE: THE SCANDINAVIAN CANDESARTAN ACUTE STROKE TRIAL

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Background: Systolic blood pressure>140 mm Hg is common in acute stroke. Current clinical guidelines do not recommend routine blood pressure lowering, but the evidence is conflicting. Beneficial effects of blood pressure lowering with the angiotensin receptor blocker candesartan have been suggested by animal studies and one clinical trial.

Methods: SCAST is a multicentre, randomised- and placebo-controlled trial of candesartan in patients with acute stroke (ischaemic or haemorrhagic) and systolic blood pressure≥140 mm Hg. Treatment with candesartan or placebo was started within 30 hours of symptom onset and given for 7 days, doses increasing from 4 to 16 mg daily over the first three days. There were two co-primary effect variables: i) Composite end-point of vascular death, stroke or myocardial infarction during the first 6 months and ii) Functional status at 6 months. Recurrent stroke was pre-specified as a secondary effect variable.

	Candesartan (n=1017)	Placebo (n=1012)
Female gender, n (%)	405 (40)	448 (44)
Age, years (SD)	70.8 (11.2)	71.0 (11.0)
Qualifying event		
Acute ischaemic stroke, n (%)	862 (85)	871 (86)
Intracerebral haemorrhage, n (%)	144 (14)	130 (13)
Other, n (%)	9 (1)	11 (1)
Systolic blood pressure, mm Hg (SD)	171.2 (19.0)	171.6 (19.2)
Diastolic blood pressure, mm Hg (SD)	90.3 (13.9)	90.6 (14.2)
Duration of symptoms, hrs (SD)	17.6 (8.1)	17.9 (8.1)
Scandinavian Stroke Scale score (SD)	40.6 (12.3)	40.5 (12.6)
Pre-morbid modified Rankin Scale score, median (IQR)	0 (0-0)	0 (0-0)
OCSP classification		
Total anterior	79 (8)	79 (8)
Partial anterior	502 (49)	486 (48)
Posterior	153 (15)	132 (13)
Lacunar	279 (27)	309 (31)
Other	4	6
Medical history		
Hypertension, n (%)	676 (69)	670 (70)
Diabetes mellitus, n (%)	163 (16)	157 (16)
Current or previous atrial fibrillation, n (%)	190 (19)	186 (19)
Previous stroke or TIA, n (%)	252 (25)	204 (21)
Current use of an ACE inhibitor, n (%)	270 (27)	264 (27)
Thrombolytic treatment before randomisation, n (%)	69 (8)	82 (9)

Results: 2,029 patients were included at 146 centres in 9 North-European countries. Data are 99% complete for the primary effect variables. Baseline characteristics are presented in the table.

Summary: SCAST is to date the largest trial of blood pressure lowering treatment in acute stroke. The main results and the analysis of recurrent stroke will be presented.

3 Large clinical trials (RCTs) A

RELATION BETWEEN CHANGE IN SYSTOLIC BLOOD PRESSURE AND RISK OF STROKE PROGRESSION, STROKE RECURRENCE AND POOR FUNCTIONAL OUTCOME IN THE SCANDINAVIAN CANDESARTAN ACUTE STROKE TRIAL

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Background: Up to 80% of acute stroke patients have elevated systolic blood pressure when admitted to hospital. SCAST has tested whether careful blood

pressure lowering treatment with candesartan is beneficial in this setting, and the main results have been submitted for presentation at the conference. The aim of this sub-study is to investigate the relationship between level of blood pressure lowering and the risk of stroke progression, early recurrence and poor long-term functional outcome.

Methods: SCAST is a multicentre, randomised- and placebo-controlled trial of candesartan in patients with acute stroke and elevated blood pressure. Patients with stroke (ischaemic or haemorrhagic) and systolic blood pressure≥140 mm Hg were included within 30 hours of symptom onset and randomised to candesartan or placebo for 7 days, doses increasing from 4 to 16 mg daily the first three days. Blood pressure was measured once daily following 5 minutes of rest using a validated monitor. We defined groups of patients with different levels of reduction in systolic blood pressure, and assessed the effects on stroke progression, symptomatic hypotension, early stroke recurrence and functional status at 6 months

Results: 2 029 patients were recruited from 146 centres in 9 North-European countries. Baseline characteristics are presented in the table.

	Candesartan (n=1017)	Placebo (n=1012)
Female sex, n (%)	405 (40)	448 (44)
Age, years (SD)	70.8 (11.2)	71.0 (11.0)
Qualifying event		
Acute ischaemic stroke, n (%)	862 (85)	871 (86)
Intracerebral haemorrhage, n (%)	144 (14)	130 (13)
Other, n (%)	9 (1)	11 (1)
Systolic blood pressure, mm Hg (SD)	171.2 (19.0)	171.6 (19.2)
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Duration of symptoms, hrs (SD)	17.6 (8.1)	17.9 (8.1)
Scandinavian Stroke Scale score (SD)	40.6 (12.3)	40.5 (12.6)
Pre-morbid modified Rankin Scale score, median (IQR)	0 (0-0)	0 (0-0)
OCSP classification		
Total anterior	79 (8)	79 (8)
Partial anterior	502 (49)	486 (48)
Posterior	153 (15)	132 (13)
Lacunar	279 (27)	309 (31)
Other	4	6
Medical history		
Hypertension, n (%)	676 (69)	670 (70)
Diabetes mellitus, n (%)	163 (16)	157 (16)
Current or previous atrial fibrillation, n (%)	190 (19)	186 (19)
Previous stroke or TIA, n (%)	252 (25)	204 (21)
Current use of an ACE inhibitor, n (%)	270 (27)	264 (27)
Thrombolytic treatment before randomisation, n (%)	69 (8)	82 (9)

Conclusion: SCAST is to date the largest trial of blood pressure lowering treatment in acute stroke. Results of this subgroup analysis will be presented at the conference. Please see abstract AID 1271 for the main results of the trial.

4 Large clinical trials (RCTs) A

RIVAROXABAN VERSUS WARFARIN IN PATIENTS WITH AF AND PRIOR CEREBROVASCULAR DISEASE: RESULTS FROM THE ROCKET-AF TRIAL

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Background: In the ROCKET-AF trial (ClinicalTrials.gov, NCT00403767), rivaroxaban 20 mg once daily without monitoring produced similar stroke and systemic embolism rates compared with warfarin by intention-to-treat, and lower rates on treatment in patients who had atrial fibrillation and were at increased risk of stroke.

In predefined substudy e aimed to assess the effects of rivaroxaban compared with warfarin in the subgroup of patients with AF and a history of stroke or TIA.

Methods: In the ROCKET AF trial, 14,264 moderate to high-risk patients with nonvalvular AF were randomly allocated to rivaroxaban, 20 mg daily or dose-adjusted warfarin (target INR range 2.0–3.0) in a double-blind fashion. Median follow-up was 707 days. The primary efficacy endpoint was stroke or systemic embolism. The primary safety outcome was major and non-major clinically relevant haemorrhages. In predefined analyses of the 7,662 (55%) patients with previous stroke or TIA enrolled in ROCKET-AF, we investigated the effect of rivaroxaban compared with warfarin in the secondary prevention of major outcome.

Results: We will reportthebaseline demographics and risk for stroke in the two cohorts with or without previous cerebrovascular events and the results for the primary and secondary efficacy and safety endpoints,according to treatment group among patients with a previous cerebrovascular. We will also show the results of subgroup analyses of the primary outcome in patients with a history either stroke or TIA. WThe results of the treatment effect accordingto the "time warfarin was controlled in the therapeutic range"and study drug discontinuation will also be presented.

Summary: The analyses will provide reliable estimates of the effectiveness and safety of Rivaroxaban compared with warfarin in the secondary prevention of major vascular events among a large international cohort of 7,662 fibrillating patients with AF previous stroke or TIA.

5 Large clinical trials (RCTs) A

FLUOXETINE FOR MOTOR RECOVERY AFTER ACUTE ISCHAEMIC STROKE (FLAME): A RANDOMISED PLACEBO-CONTROLLED TRIAL

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Background: Hemiplegia and hemiparesis are the most common deficits caused by stroke. A few small clinical trials suggest that fluoxetine enhances motor recovery but its clinical efficacy is unknown. We therefore aimed to investigate whether fluoxetine would enhance motor recovery if given soon after an ischaemic stroke to patients who have motor deficits.

Methods: In this double-blind, placebo-controlled trial, patients from nine stroke centres in France who had ischaemic stroke and hemiplegia or hemiparesis, had Fugl-Meyer motor scale (FMMS) scores of 55 or less, and were aged between 18 years and 85 years were eligible for inclusion. Patients were randomly assigned, in a 1:1 ratio to fluoxetine (20 mg once per day, orally) or placebo for 3 months starting 5–10 days after the onset of stroke. All patients had physiotherapy. The primary outcome measure was the change on the FMMS between day 0 and day 90 after the start of the study drug. Secondary outcomes assessed NIHSS, Rankin scale and MADRS variations between D0 and D90. Participants, carers, and physicians assessing the outcome were masked to group assignment. Analysis was of all patients for whom data were available (full analysis set). This trial is registered with ClinicalTrials.gov, number NCT00657163

Findings: 118 patients were randomly assigned to fluoxetine (n=59) or placebo (n=59), and 113 were included in the analysis (57 in the fluoxetine group and 56 in the placebo group). Two patients died before day 90 and three withdrew from the study. FMMS improvement at day 90 was significantly greater in the fluoxetine

group (adjusted mean 34.0 points [95% CI 29.7–38.4]) than in the placebo group (24.3 points [19.9–28.7]; p=0.003). NIHSS showed no differences while motor part of NIHSS showed a greater improvement in the Fluoxetine (-5.2 ± 2.4) than in the placebo group (-4 ± 2.5) p=0.016. The number of independent patients (Rankin: 0-2) was significantly higher in the Fluoxetin group at D90.

Interpretation: In patients with ischaemic stroke and moderate to severe motor deficit, the early prescription of fluoxetine with physiotherapy enhanced motor recovery after 3 months.

Experimental studies A

1   Experimental studies A

EXPRESSION AND ALBUMIN PROMOTER BINDING ACTIVITY OF HEPATOCYTE NUCLEAR FACTOR- 1ALPHA (HNF-1ALPHA) IN FOCAL TRANSIENT ISCHEMIC RAT BRAIN

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Background: Exogenous human albumin has been shown neuroprotective in experimental ischemic stroke and it is currently investigated in clinical trials. We have previously found for the first time the de novo synthesis and upregulation of albumin at both mRNA and protein level (at 0 and 22 hours of reperfusion after 2 hours of ischemia) in the ischemic rat brain. To study the transcriptional regulation of endogenously expressed albumin, we analysed the role of transcription factors in albumin expression in ischemic rat brain.

Methods: We have analysed the putative transcription factor binding sites for the albumin promoter using TFSEARCH computational tool and validated in rat middle cerebral artery occlusion (MCAO) model of ischemia. mRNA and protein expression of selected transcription factors were analysed by qRT-PCR and western blotting respectively. Immunoprecipitation and chromatin immunoprecipitation was done to see protein-protein interaction and protein-albumin promoter interaction respectively.
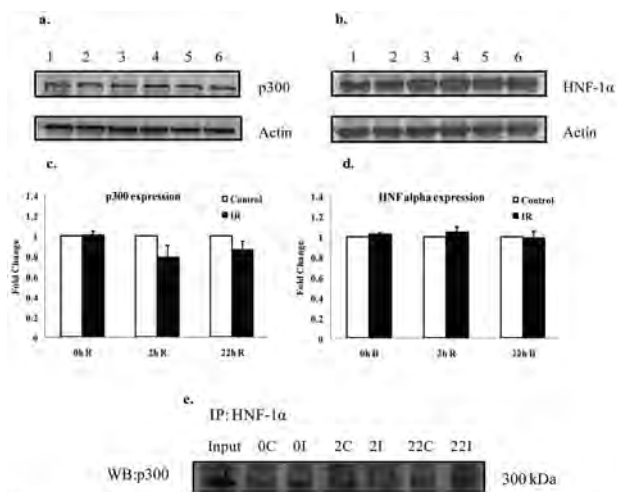
Figure 1 a) & b) Representative image of western blot. Lane 1: 0h R - control animals; Lane 2: 0h R- ischemic animals; Lane 3: 2h R - control animals; Lane 4: 2h R- ischemic animals; Lane 5: 22h R - control animals; Lane 6: 22h R- ischemic animals. c) & d) Western blotting band density quantification. Open bar indicates data for control animals and filled bar indicates data for ischemic animals. e) Representative images of western blot of p300 done after immunoprecipitation using HNF1α antibody. 0h R: 0 hours of reperfusion after 2 hours of MCAO; 2h R: 2 hours of reperfusion after 2 hours of MCAO; 22h R: 22 hours of reperfusion after 2 hours of MCAO. All the data represented as mean ± SEM n=3 per group.
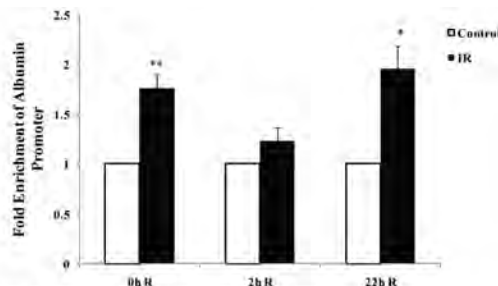
Figure 2 Quantitative real time PCR data for fold enrichment of albumin promoter by chromatin immunoprecipitation using HNF-1alpha antibody. 0h R: 0 hours of reperfusion after 2 hours of MCAO; 2h R: 2 hours of reperfusion after 2 hours of MCAO; 22h R: 22 hours of reperfusion after 2 hours of MCAO. All the data represented as mean ± SEM n=3 per group. * p <0.05, ** p<0.01 vs respective control, student t-test.

Results: Computational analysis predicted approximately 20 transcription factor binding sites including HNF-1alpha. We found for the first time mRNA and protein expression of HNF-1alpha in the control and ischemic rat brain. There was no significant difference in mRNA and protein expression of HNF-1alpha between control and ischemic (0, 2 and 22 hours of reperfusion) but there was increased interaction of HNF-1alpha with p300 (known interacting partner for HNF-1alpha, a histone acetyl-transferase) in 0 hour reperfusion and 22 hours reperfusion group. Also albumin promoter binding activity of HNF-1alpha in 0 and 22 hours reperfusion group increased compared to respective control group animals.

Conclusion: HNF-1α is mainly expressed in the rat liver and involved in hepatic expression of albumin. Our result shows for the first time de novo synthesis of HNF-1alpha in control and ischemic rat brain. Interaction of HNF-1alpha with p300 and also with albumin promoter was found elevated in ischemic conditions, and these interactions are probably responsible for overexpression of albumin in ischemic conditions.

2   Experimental studies A

AUTOLOGOUS BONE-MARROW MONONUCLEAR CELLS (BM-MNC) IN MIDDLE CEREBRAL ARTERY ACUTE ISCHEMIC STROKE. A SINGLE-BLIND CONTROLLED PHASE I/II TRIAL

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Background: BM-MNC intra-arterial transplantation has proven beneficial effects in experimental models of ischemic stroke, probably related to secretion of a broad spectrum of growth factors and cytokines. However, safety and efficacy of BM-MNC in human ischemic stroke is not known. We aimed to assess the safety, feasibility and efficacy of autologous BM-MNC transplantation in acute stroke patients. The study was approved by the national ethics committee (TCI 0107). Registered at ClinicalTrials.gov as: NCT00761982.

Methods: A single-blind (outcomes assessor) controlled phase I/II trial was conducted in acute ischemic stroke patients. In BM-MNC-treated patients, autologous BM-MNC was obtained by iliac crest aspirated and injected intra-arterially between 5 and 9 days after stroke. Follow-up visits were done at 1, 30, 90 and 180 days after procedure. Primary outcome was safety and feasibility of the procedure. Secondary outcome was improvement in neurological function assessed by modified Rankin Scale, Barthel index and NIHSS.

Results: Ten cases (BM-MNC-treated) and ten controls (BM-MNC-non-treated), all with MCA ischemic strokes, were included. Mean age was 67.4 (vs. 66.9 in controls, p=ns). Intra-arterial injection of BM-MNC was done at 6.4 days after stroke and NIHSS before procedure was 15.0 (vs 15.6 in controls, p=ns). 159×10e6 (±121×10e6) MNC were injected. There was no transplantation complications during procedure or in follow-up. At 180 days, there were no significant differences in neurological function compared to control group: NIHSS was 8.1±6.5 (vs 8.3±4.2 in control group), m-Rankin scale was 3.5 (vs 3.4) and Barthel index was 56.5 (vs 56.6).

Conclusion: BM-MNC intra-arterial transplantation in acute ischemic stroke is feasible and safe. Further research is necessary for elucidating the efficacy of autologous transplantation of BM-MNC in ischemic stroke patients.

TROPHIC AND REPAIR EFFECTS OF THE CDP-CHOLINE ADMINISTRATION IN THE CEREBRAL INFARCT. EXPERIMENTAL STUDY IN RATS

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Introduction: Pharmacological agents such as trophic factors might promote one or more repair mechanisms can improve the functional status following a stroke. Animal experimental data have demonstrated that CDP-choline administration is effective in repair processes and recovery.

Aims: To analyze the possible trophic and repair mechamism of CDP-choline in a model of focal cerebral ischemia in rats.

Material and Methods: 40 Sprague Dawley male rats distributed in 4 groups: 1) Normal; 2) Sham (surgery without infarct); 3) Control (surgery plus infarct); 4) CDP-choline (surgery plus infarct plus ip CDP-choline (500 mg/kg). We analyzed: Functional evaluation score and lesion volumen by Magnetic Resonance Imaging (MRI) at 24h and 14 days and by H-E at 14 days. At 14 days: Celll death by TUNEL and Endogenous Cellular Proliferation (BrdU) by inmunohistochemistry. In peri-infarct zone LRP, synaptophysin, GFAP and VEGF by Western Blot and inmunofluorescence. Rats were sacrificed at 14 days.

Results: CDP-choline significantly improved functional recovery, decreased the lesion volume by MRI, cell death (necrosis and apoptosis) and LRP at 14 days. In addition, CDP-choline significantly increased cellular proliferation (BrdU), VEGF and Synaptophysin and decreased GFAP (gliagenesis) compared to Control Group.

Conclusions: CDP-choline improved functional recovery with reduction in infarct volume, cell death and LRP expression (protective effect), and increased neurogenesis, synaptogenesis and VEGF and reduction of gliagenesis (trophic and repair effect) in the peri-infarct area after ischemic stroke.

THE ADMINISTRATION OF ANTAGONISTS FOR ENDOTHELIN-1 (ET-1) RECEPTORS MEDIATES NEUROPROTECTION IN AN EXPERIMENTAL MODEL OF CEREBRAL ISCHEMIA

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Background: Endothelin-1 receptor antagonists are being investigated to prevent neuronal loss after cerebral ischemia. The aim of this study was to assess the effects of Clazosentan, an antagonist of ET-1 receptor A; BQ-788, an antagonist of ET-1 receptor B; and a combination of both, on the development of edema, infarct volume and sensorial-motor deficits, in rats subjected to ischemia by occlusion of the middle cerebral artery (MCAO).

Methods: Wistar rats (280-320 g) (n=24) submitted to ischemia by intraluminal transient (90 min) occlusion of the middle cerebral artery. After ischemia, rats were randomized into 4 groups (n=6) treated with; 1) control group (saline), 2) Clazosentan group (Clazosentan 10mg/kg iv), 3) BQ-788 group (BQ-788 3mg/kg iv), and 4) combined treatment (Clazosentan 10mg/kg plus BQ-788 3mg/kg iv). Cerebral edema and infarct volumes were measured by MRI at baseline, 24 and 72 h and 7 days after ischemia. In addition, functional recovery was assessed using the cylinder test, and serum levels of ET-1 were obtained from peripheral blood.

Results: rats treated with clazosentan showed a reduction of edema at 72h and at 7 days (both p<0.0001), a better sensorial-motor recovery at 24h (p=0.003), 72h (p=0.006) and 7 days (p=0.002), and a decrease in the serum levels of ET-1 at 72h (p=0.02) and at 7 days (p=0.009) in comparison with the control group. The combined treatment induced a reduction of edema at 24 hours (p=0.004), 72hours (p<0.0001) and at 7 days (p=0.001) and a reduction on infarct volume at 24h (p=0.008), 72h (p=0.007) and at 7 days (p=0.004). Effects on BQ-788 group were not significantly different from controls.

Conclusions: These Results demonstrate that ET-1 receptors could be a good therapeutic target for cerebral ischemia.

RAPID REVERSAL OF ANTICOAGULATION PREVENTS EXCESSIVE SECONDARY HEMORRHAGE AFTER THROMBOLYSIS IN A THROMBOEMBOLIC MODEL IN RATS

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Background and purpose: Thrombolysis is the only approved therapy for ischemic stroke but secondary hemorrhage is a severe complication. Because oral anticoagulants are believed to increase the risk of hemorrrhage, thrombolysis is usually contraindicated in patients on vitamin K antagonists. We studied whether thrombolysis in a thromboembolic MCAO model in rats pre-treated with warfarin increases secondary hemorrhage, and whether substitution of coagulation factors prior to thrombolysis prevents hemorrhagic complications.

Methods: Wistar rats were anticoagulated using warfarin in drinking water (0.4 mg/kg/24 h). Strength of anticoagulation was monitored using benchside international normalized ratio (INR) coagulometry. Two hours after injection of 12 blood clots into the internal carotid artery, rt-PA (9mg/kg) was administered. Two of five groups of animals received prothrombin complex concentrate (PCC, 50 U/kg) 15 min before thrombolysis. Serial MR-imaging was performed 20 min, 2.5 h and 24 h after MCAO. Secondary hemorrhage was quantified on T2* MR images as previously established.

Results: Severity of hypoperfusion on initial PWI-MR did not differ among groups. Thrombolysis resulted in successful reperfusion in all groups. Anticoagulated animals had significantly more secondary hemorrhage and a higher mortality rate compared to non-anticoagulated animals. PCC rapidly reversed the increased INR. While PCC failed to prevent hemorrhage in strongly anticoagulated, it reduced the incidence of severe hemorrhage in moderately anticoagulated rats (INR=2-3) to the level of nonanticoagulated controls.

Conclusions: Preceding anticoagulation increases the risk and extent of secondary hemorrhage after thrombolysis. Reversal of anticoagulation using PCC may allow thrombolytic therapy without increasing the risk of secondary hemorrhage.

SODIUM IMAGING IN A MOUSE MODEL OF STROKE

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Background: Sodium imaging in stroke models is of growing interest because of its availability for the use as an intrinsic marker for brain integrity. The small anatomical size of the rodent still remains a limiting factor for stroke MRI imaging in experimental models. The aim of this study was to develop a novel MRI technique high resolution in a mouse model of stroke.

Methods: Thromboembolic stroke was induced by local injection of purified thrombin directly into the right MCA of C5 black/6J mice. MRI was performed on a 9,4 Tesla Biospec 94/20 USR (Bruker, Germany) small animal system in combination with a two-winding 105 MHz inductively coupled surface resonator element. The center slice of each scan was used for further data analysis to calculate SO and T2* parameter maps.

In addition, MRI histology was performed to evaluate/correlate the data.

Results: The combination of the high field of 9.4 Tesla, the surface coil and the weighted 23Na-CSI sequence enable a spatial resolution of $0.6 \times 0.6 \times 1.2$ mm^3 in a measurement time of one hour. Cerebral ischemia resulted in a significant increase of sodium concentration in the ischemic territory, ranging from 260 to 360%, compared to contralateral healthy tissue (Figure 1). There is also a sodium T2*-increase in the infarcted hemisphere of 110% to 175%. Regions of hyperintense sodium correspond to the T2 weighted images and the infarcted area investigated by histology.
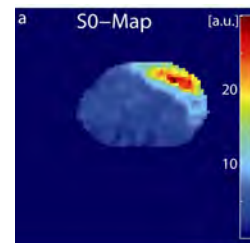
Conclusions: This work demonstrates that 23Na-CSI is feasible for sodium imaging with high resolution for the small anatomical size of the murine brain. Furthermore, the acquired data, allows the calculation of S0 and T2* parameter maps and therefore a quantitative evaluation of the sodium signal change in stroke.

Intracerebral/subarachnoid haemorrhage and venous diseases B

10 Intracerebral/subarachnoid haemorrhage and venous diseases B

SYSTOLIC BP LOAD PREDICTS HEMATOMA GROWTH AND MORTALITY IN PATIENTS WITH ACUTE INTRACEREBRAL HEMORRHAGE

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Background: High blood pressure (BP) is considered an important therapeutic target in acute intracerebral hemorrhage (ICH). However, association between BP and hematoma growth (HG) has not been clearly demonstrated. We aimed to determinate the impact of BP changes and course on HG in patients with acute ICH. **Methods:** We prospectively studied 107 patients with acute supratentorial ICH. Patients underwent baseline (<6h) and 24h CT scans, and a CTA (<6h) for the blinded detection of SS. HG was defined as ICH enlargement >33%–6mL at 24h. On admission, all patients underwent noninvasive BP monitoring at 15 min interval over first 24h with a validated oscillometric device. BP variability was calculated as the SD of mean systolic (S), diastolic (D), mean (M) BP, and pulse pressure (PP) values. Max BP, min BP, max BP increase (max - baseline), and max BP drop (baseline - min) values were calculated. SBP and MBP loads were defined as the proportion of readings >180 and >130 mmHg, respectively. 90-day mortality was recorded. **Results:** Although baseline BP variables were unrelated to HG, 24h-BP variables including BP variability, max BP increase and BP loads were significantly associated with HG (Table). In a logistic regression model, SBP 180-load >10.9% (OR 4.6, 95% CI 1.6–13.4, p=0.006), CTA-SS (OR 3.86, 95% CI 1.1–14.2, p=0.042), and GCS <11 (OR 6.6, 95% CI 1.1–42.1, p=0.047) predicted independently HG. The combination of CTA-SS and SBP 180-load >10.9% increased in 6-fold the risk of HG (20.5±21.9 vs. 3.4±8.5 mL, p=0.02). At 90 days, independent predictors of mortality were SBP 180-load >10.9% (OR 5.9, 95% CI 1.3–26.4, p=0.022), age >74 years (OR 14.4, 95% CI 2.6–80, p=0.002), and baseline ICH volume >17.7 mL (OR 22.3, 95% CI 4–123.8, p<0.001).

Table 1. 24h-BP variables significantly related to hematoma growth (HG) after acute ICH

	HG (n=36)	No HG (n=62)	P-value
BP variability (mmHg)			
SBP	17.5±9.2	13.8±5.3	0.048
DBP	11.4±5.8	8.9±3.3	0.029
MBP	13.3±8.3	9.8±3.7	0.035
PP	13.5±6.2	10.9±3.3	0.039
Max BP increase (mmHg)			
SBP	23.1±20.9	13.8±15.3	0.040
DBP	20.3±13.3	14.6±12.2	0.049
MBP	17.2±13.6	11.3±11.3	0.039
PP	24.2±24.7	13.7±12.6	0.037
BP load			
SBP 180-load	37.8%	12.5%	<0.001
MBP 130-load	19.2%	7.2%	0.013

Conclusions: In patients with acute ICH, only one-tenth of SBP readings above 180 mmHg are needed to increase in 5-fold the risk of HG. SBP 180-load >10.9% emerged as independent predictor of HG and 90-day mortality after acute ICH.

11 Intracerebral/subarachnoid haemorrhage and venous diseases B

SPEED OF ULTRA-EARLY HEMATOMA GROWTH IN INTRACEREBRAL HEMORRHAGE: A POWERFUL PREDICTOR OF FURTHER HEMATOMA GROWTH AND POOR OUTCOME

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Background: The impact of initial intracerebral hemorrhage (ICH) volume on hematoma growth (HG) and outcome may vary widely depending on the time from symptom onset to baseline CT scan (onset-imaging time, OIT). Thus, we aimed to investigate the impact of the speed of HG prior to baseline CT (speed of ultra-early HG, SuHG) on further HG and outcome in patients with acute ICH. **Methods:** We prospectively studied 133 consecutive patients with primary supratentorial ICH evaluated within 6 hours from symptoms onset. Patients underwent baseline (<6h) and 24h CT scans for ICH volume measurement, and a CTA (<6h) for the blinded detection of spot sign. We defined SuHG as the relation between initial ICH volume/OIT, HG as ICH enlargement >33% or >6mL at 24h, early neurological deterioration (END) as increase ≥4 points in the NIHSS score or death at 24 hours, and poor functional outcome as mRS score >2 at 90 days (90d). **Results:** Median initial ICH volume was 13.6 (7.2–34.9) mL, median OIT was 144 (103–225) minutes, and median SuHG was 6.7 (2.8–14.1) mL/h. SuHG was significantly faster in patients with the spot sign than those without (14.5 [6.8–27] vs. 4.2 [1.8–8.5] mL/h, p<0.001). SuHG was well correlated with baseline (r=0.631, p<0.001) and 24h (r=0.745, p<0.001) NIHSS scores. The SuHG markedly improved the accuracy of initial ICH volume in the prediction of END and 90d mortality (Table). SuHG >10.2 mL/h independently predicted HG (OR 3.6, 95% CI 1.4-9.1, p=0.008), END (OR 70.2, 95% CI 14.6-337, p<0.001), 90d mortality (OR 17, 95% CI 5.3-54, p<0.001), and poor functional outcome (OR 6.2, 95% CI 1.3-29, p=0.021) after adjusting for baseline NIHSS score, initial ICH volume and CTA spot sign.

Table 1. Predictive values of SuHG and initial ICH volume for END and 90d mortality

	END		90d mortality	
	SuHG >10.2 mL/h	ICH volume >25 mL	SuHG >10.2 mL/h	ICH volume >25 mL
Sensitivity	93.1%	82.8%	77.5%	70%
Specificity	85.3%	82.4%	87.9%	84.6%
PPV	64.3%	57.1%	73.8%	66.7%
NPV	97.8%	94.4%	89.9%	86.5%

Conclusions: The speed of ultra-early hematoma growth represents a novel approach for improving the prediction of further HG and outcome in patients with acute ICH. SuHG >10.2 mL/h emerged as the most powerful predictor of HG, END, 90d mortality and poor functional outcome after acute ICH.

12 Intracerebral/subarachnoid haemorrhage and venous diseases B

RELEVANCE OF PLASMA B-AMYLOID ON THE RISK OF HEMATOMA GROWTH IN PATIENTS WITH ACUTE INTRACEREBRAL HEMORRHAGE

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Background: The cerebrovascular deposition of the β-amyloid peptide (Aβ) impairs the function and structural integrity of brain blood vessels. The influence of the levels of plasma Aβ on the risk of hematoma growth (HG) is unknown. We tested the hypothesis that the levels of Aβ may influence the risk of HG in patients with intracerebral hemorrhage (ICH). **Methods:** We prospectively included patients with spontaneous ICH within the first 6 hours after ICH onset in a multicentre study (6 hospitals). We excluded etiology due to anticoagulants, tumor or arterial-venous malformation. HG was defined as an increase >33% in the volume of hematoma on the CT obtained 24-72 hours after the onset of symptoms, in comparison with the admission CT. Volumes were calculated using the formula (AxBxC)/2. We measured plasma Aβ40 and Aβ42 using standard ELISA techniques. We recorded age, sex, time to admission CT, localization, etiology (arterial hypertension, AA according to the Boston criteria, unknown), vascular risk factors, Glasgow coma scale score, blood glucose, temperature and

blood pressure at admission, intraventricular hemorrhage (IVH), and volume of the admission hematoma. Bivariate and multivariate regression analyses were performed.

Results: We studied 80 patients (mean age 71.8±12 y, 54% were men). HG was observed in 21 patients (26.2%). In bivariate analysis, HG was associated with absence of IVH (p=0.017) and decreasing time to admission CT (p=0.050), and there was a trend for lobar localization (p=0.087) and decreased levels of plasma Aβ42 (p=0.073). The multivariate analysis showed that IVH (OR 0.23, 95%CI 0.01-0.95, p=0.045), lobar location (OR 4.04, 95%CI 0.95-17.2, p=0.057) and time to admission CT (OR 0.991, 95%CI 0.983-0.999, p=0.02) were independently associated with HG.

Conclusion: Levels of plasma Aβ are not an independent predictor for HG. However, lobar location increases the risk of HG, while longer time-to-admission and IVH decrease the risk.

13 Intracerebral/subarachnoid haemorrhage and venous diseases B

ASSOCIATION BETWEEN HYPERTHERMIA, FUNCTIONAL OUTCOME, AND HEMATOMA GROWTH AFTER ICH: ON BEHALF OF VISTA-ICH INVESTIGATORS

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Introduction: The purpose of this study is to test the hypothesis that hyperthermia is associated with poor functional outcome and hematoma growth after ICH.

Methods: Patients from placebo arms of acute ICH trials registered in the Virtual International Stroke Trials Archive (VISTA) were analyzed. Data for temperatures at baseline and 24h, were compared to the functional outcome at 90 days and hematoma growth at 72 hrs after admission. Poor outcome was defined as a modified Rankin Scale (mRS) ≥ 4 at 90 days and hematoma growth was defined as change in hematoma volume ≥ 30% from baseline. Candidate variables were selected at the univariate level and logistic regression models were then fitted to identify predictors of poor outcome and hematoma growth.

Results: In total, 303 patients were included in the analysis. The average age of the cohort was 66±12 years, 200 (66%) were males, the median admission NIHSS was 13 (Interquartile range [IQR 25-75], 9-18), median GCS was 15 (IQR, 14-15), mean baseline temperature was 36.4±0.5 °C and at 24h was 36.7±0.6°C. The median hematoma volume at baseline CT scan was 15cc (IQR, 8-33) and 17cc (IQR, 8-39) at 72 hrs. IVH was present in 104 (34%) of patients and hematoma growth ≥ 30% occurred in 37% of patients. After adjustment, hyperthermia at 24h was associated with hematoma growth (odds ratio [OR], 2.2; 95% confidence interval [CI], 1.1-4.4) but not with poor functional outcome at 90 days. Poor functional outcome at 90 days was independently associated with age (OR, 1.1; 95% CI, 1.01-1.1), history of diabetes mellitus (OR, 2.6; 95% CI, 1.3-5.1), admission NIHSS (OR, 2.6; 95% CI, 1.4-4.8), IVH (OR, 1.8; 95% CI, 1.04-3.1), and hematoma growth (OR, 1.8; 95% CI, 1.01-3.3).

Conclusions: This data suggests that in ICH patients, age, history of diabetes mellitus, admission NIHSS, IVH, and hematoma growth at 72 hrs, are independently associated with poor outcome at 90 days; and that hematoma growth is independently associated with hyperthermia at 24hrs after admission. This data does not support empiric use of temperature modulation in ICH patients, but a randomized, controlled trial is needed to clarify this point.

14 Intracerebral/subarachnoid haemorrhage and venous diseases B

MODERATELY AGGRESSIVE BLOOD PRESSURE LOWERING USING INTRAVENOUS NICARDIPINE FOR ACUTE INTRACEREBRAL HEMORRHAGE: AN INTERIM REPORT OF A MULTICENTER, PROSPECTIVE, OBSERVATIONAL STUDY

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Background: Moderately aggressive blood pressure (BP) lowering with target systolic BP (SBP) ≤160 mmHg using IV nicardipine is the major strategy for

patients with acute intracerebral hemorrhage (ICH) in Japan (Koga M, et al: Hypertens Res 2009). We aimed to assess whether this strategy is safe and feasible.

Methods: This is an interim report of a prospective, observational study from 10 centers. The inclusion criteria include: supratentorial ICH, initiation of IV nicardipine ≤3 hrs, admission SBP ≥180 mmHg, GCS ≥5, and hematoma volume ≤60 ml. Some of these criteria followed those of the ATACH study. A final sample size is scheduled to be 200 patients. Patients were initially treated with 5mg/hr of IV nicardipine and the dose was increased up to a maximum of 15 mg/hr to maintain SBP between 120 and 160 mmHg with tight BP monitoring for initial 24 hrs. The primary endpoints were neurological deterioration (ND) corresponding to an increase ≥4 points from initial NIHSS within 72 hrs (estimated 90% CI based on previous reports: 27.4-38.0%) and serious adverse effects (SAE) within 24 hrs which need to stop IV nicardipine (3.1-8.9%). The secondary endpoints included hematoma enlargement (HE) >33% on follow-up CT at 24 hrs (18.6-29.0%) and unfavorable outcome (mRS 4-6) at 3 months (55.0-66.8%), and death within 3 months (5.1-11.9%).

Results: 143 patients (86 men, 66+-12 years old) were enrolled until November 2011. The median initial SBP was 192 mmHg. The median initial hematoma volume was 10.5 ml and the median NIHSS score was 13. ND was found in 7 patients (5%). SAE was observed in one patient (1%). HE was identified in 22 patients (15%). Of 113 patients, 47 patients (42%) had unfavorable outcome and 5 patients (4%) died.

Conclusions: SBP lowering (range 120-160 mmHg) using IV nicardipine with tight BP monitoring appears to be safe and feasible for acute ICH. We are planning to participate in ATACH 2 trial for seeking better BP target based on this observational study.

15 Intracerebral/subarachnoid haemorrhage and venous diseases B

GCSF PROMOTES LONG-TERM FUNCTIONAL RECOVERY AFTER EXPERIMENTAL INTRACEREBRAL HEMORRHAGE

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Background: The hematopoietic factor GCSF is a neuronal ligand, that activates neurogenesis and counteracts apoptosis in experimental stroke. Therefore it is currently used in clinical trials as a promising therapy for patients with acute cerebral ischemia. To date, its long-term effects after intracerebral hemorrhage (ICH) have not been investigated sufficiently.

Methods: The effects of GCSF after experimental intracerebral hemorrhage were studied in male wistar rats. After striatal injection of 70 μl autologous blood, the animals were subjected to either (1) daily intraperitoneal application of GCSF (60 μg/kg) or (2) intraperitoneal injection of vehicle for 5 days. A third group received a one-time intracerebral injection of 60 μg/kg GCSF. Neurologic deficits, lesion volume and the extent of neurogenesis were assessed up to day 42 after ICH.

Results: 45 animals underwent the procedure. The mortality rate during the study was 4,4%. The ICH was located in the right striatum and caused mild to moderate neurologic deficits with subsequent improvement over time in all animals. Compared to control, animals with a single intracerebral injection of GCSF showed a significantly accelerated functional recovering on day 7 and day 14 after ICH (p<0,05). Beneficial effects were less pronounced after intraperetoneal treatment. Differences in functional status equalized until day 42. Histologic data are outstanding at the time of submission and will be available shortly.

Conclusion: GCSF promotes functional recovery after experimental intracerebral hemorrhage in rats. Antiedematous, antiapoptotic or neurogenetic effects are discussed as possible mechanisms.

16 Intracerebral/subarachnoid haemorrhage and venous diseases B

PREVALENCE AND DETERMINANTS OF FATIGUE 1 YEAR AFTER SPONTANEOUS INTRACEREBRAL HAEMORRHAGE

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Background: Fatigue is a common and important cause of long term morbidity after stroke. However, it remains unexplored and the few published data only focused on ischaemic strokes. We aimed to determine prevalence and associated factors of fatigue in a cohort of survivors one year after a spontaneous intracerebral haemorrhage (ICH).

Methods: The PITCH cohort is a prospective, hospital-based cohort of consecutive adults admitted for an ICH. It has been shown to have similar characteristics as a population-based cohort. Survivors are followed-up every year with standardized

Oral Session
Intracerebral/subarachnoid haemorrhage and
venous diseases B

Cerebrovasc Dis 2011;31(suppl 2):1–322

21

questionnaires including: Chalder fatigue Scale (cut-off of 3 to define fatigue), depression (MADRS cut-off of 14 to define depression) and anxiety (HAD cut-off of 8 to define anxiety). Predictive and associated factors of fatigue were identified using multivariate analyses (logistic regression model).

Results: Among a cohort of 562 patients, 244 survived at 1 year. Fatigue was evaluated in 153 (63%) patients (median age 63; 60% of men). In multivariate analysis, excluded patients were older (OR 1.03 per 1 year increase; 95%CI, 1.01-1.05) and more dependent (modified Rankin score of 3 or more) (OR 2.07; 95%CI, 1.17-3.68). Seventy-nine (51%) patients were fatigued. Among characteristics at admission, a severe neurological deficit (OR 1.06 per 1 point increase at NIHSS; 95%CI, 1.01-1.11) and severe leucoaraiosis on CT-scan (OR 1.42 per 1 step increase; 95%CI, 1.04-1.96) were associated with fatigue 1 year after ICH. At 1 year, fatigue was associated with a severe neurological deficit (OR 1.15 per 1 point increase at NIHSS; 95%CI, 1.03-1.29) and with depression (OR 34.9; 95%CI, 4.51-269.69).

Conclusion: Fatigue is very frequent 1 year after ICH, therefore patients should systematically be screened for it. Despite large confidence intervals, the strong association with depressive symptoms requires further studies focusing on the impact of depression and its treatment on fatigue symptoms.

17 Intracerebral/subarachnoid haemorrhage and venous diseases B

LONG TERM CLINICAL AND NEUROIMAGING OUTCOME OF ARTERIOVENOUS MALFORMATIONS TREATED WITH STEREOTACTIC RADIOSURGERY

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Background: patients with cerebral arteriovenous malformations (AVM) that undergo stereotactic radiosurgery (SRS) can develop late neuroimaging changes ranging from edema to necrosis. Their prevalence and clinical correlation are poorly understood.

Methods: we describe a consecutive series of AVM treated with SRS between 1993 and 2009, and followed with contrast enhanced brain MRIs semesterly for the first 2-3 years and annually afterwards. Patients lost in the follow up were contacted and invited to participate in the study. Brain edema, blood-brain barrier breakdown and necrosis were defined as radiological endpoints, and classified according to their intensity by an independent radiologist. Clinically, appearance or worsening of seizures or focal symptoms, development of headaches or signs of endocranial hypertension, brain haemorrhage and AVM-related death were recorded.

Results: 110 patients, 52% male, mean age 38 years. Eleven were excluded due to incomplete records or loss of follow up. The rest was followed for a mean of 74 months, after receiving a median dose of 18 Gy prescribed to the 80% isodose. Thirty nine percent of patients had minimal o mild edema, and 15% developed moderate to severe lesions (AMV size and radiation dose being risk factors). Most of the latter (71%) were symptomatic, being 5,5 times more likely to suffer seizures and 11 times more likely to develop focal symptoms or endocranial hypertension. These complications appeared a median of 23 months after the SRS. Brain haemorrhage was equally common in all patients, with annual bleeding rate of 2,7% during the first year, 0,9% until the 4th year and 0,4% afterwards. Overall AVM-related mortality was 1,8%.

Conclusions: moderate to severe radiation-induced changes appear in 15% of patients, who usually become symptomatic years after treatment. More efforts are needed both to detect the problem during daily clinical practice and to determine the optimal management, that remains unclear.

18 Intracerebral/subarachnoid haemorrhage and venous diseases B

DECOMPRESSIVE HEMICRANIECTOMY IN SEVERE CEREBRAL VENOUS THROMBOSIS: A PROSPECTIVE STUDY OF 10 CASES

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Background: Small retrospective case series suggest that decompressive hemicraniectomy may be life saving in patients with cerebral venous thrombosis (CVT) and impending brain herniation. Prospective studies of consecutive cases are lacking.

Methods: Single centre, prospective study. In 2006 we adapted our protocol for CVT treatment to perform acute decompressive hemicraniectomy in patients with impending herniation, in whom the prognosis with conservative treatment was considered infaust. All consecutive CVT patients between 2006 and 2010 who underwent hemicraniectomy were included. Outcome was assessed at 12 months with the modified Rankin Scale (mRS).

Results: Ten patients (8 women) with a median age of 41 years (range 26-55) were included. Before surgery 5 patients had GCS<9, 8 had normal pupils, 2 had a unilateral fixed and dilated pupil. All had space-occupying intracranial hemorrhagic infarcts. The median preoperative midline shift was 9 mm (range 0-15). Unilateral hemicraniectomy was performed in 9 patients and bilateral hemicraniectomy in one. Postoperative median midline shift was 4 mm (range 0-11). Three patients died. Death was caused by progressive oedema and expansion of the hemorrhagic infarcts, with elevated intracranial pressure. In one of these patients CVT was not recognized preoperatively, and the craniectomy was too small. The patient with bilateral hemicraniectomy also died. Five patients recovered without disability at 12 months (mRS 0-1). Two patients had some residual handicap (one minor handicap, mRS 2; one moderate, mRS 3).

Conclusion: These prospective data show that decompressive hemicraniectomy in the most severe cases of cerebral venous thrombosis was life-saving in 7/10 patients, with an excellent outcome in 5. In 3 patients death was caused by enlarging hemorrhagic infarcts.

Acute stroke: new treatment concepts B

10 Acute stroke: new treatment concepts B

RESCUE, COMBINED AND STANDALONE THROMBECTOMY FOR STROKE MANAGEMENT IN LARGE VESSEL OCCLUSION USING THE SOLITAIRE™ FR DEVICE. A PROSPECTIVE SINGLE CENTER STUDY. (RECOST STUDY)

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Background: Ischemic stroke (IS) secondary to large vessel occlusions are associated with poor outcome despite intravenous rt-PA therapy. The objective of this present study was to report the experience of a stroke unit in patients with M1 or carotid occlusion treated with combined procedure (rtPA IV and the Solitaire™ FR mechanical thrombectomy device) and to evaluate the safety, the technical and clinical Results.

Methods: Consecutive IS patients with a relevant deficit on admission, a major large vessel occlusion were included in one of three therapeutic arms: (1) Rescue therapy in MCA occlusion < 4.5 hours (intravenous rt-PA, and thrombectomy, if 50 minutes after the NIHSS was still over 8; (2) Combined therapy (intravenous rt-PA and associated thrombectomy) in terminal or tandem ICA occlusions < 4.5 hours or BA occlusions < 24 hours; (3) Standalone Thrombectomy in patients between 4.5 and 6 hours or contraindications for IV rtPA. Outcome was evaluated by a stroke neurologist, at 24 hours, discharge and 3 months. Good neurological outcome was defined as a NIHSS of 0 or 1 and/or a NIHSS improvement of more than 9 points at discharge. At 3 month, it was defined by a rankin scale ≤2.

Results: 50 patients (mean age of 68, sex ratio of 1) were included, 12 in the Rescue, 28 in the Combined, and 10 in the Thrombectomy therapy. Recanalisation TICI3 was achieved in 84% of cases. Overall symptomatic complication rate was 10% with 4 cases of embolic events during thrombectomy, and one case of symptomatic hemorrhagic complication. At discharge, mean NIHSS was 6 (compared to an initial mean NIHSS of 15), 60% of patients had a good neurological outcome. The 3-month clinical outcome will be presented during ESC.

Conclusion: In our study, the use of the Solitaire device has allowed a high rate recanalization and good initial clinical outcome. Other studies and randomized studies are necessary to validate this attractive treatment.

11 Acute stroke: new treatment concepts B

STENT-ASSISTED MECHANICAL RECANALIZATION IN ACUTE ISCHEMIC STROKE

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Purpose: The purpose of this study was to demonstrate a new approach to the use of a self-expanding stent in the treatment of acute ischemic stroke.

Methods: 38 consecutive patients with acute intracerebral artery occlusions were treated with a self-expandable intracranial stent, which was withdrawn in its unfolded state. For this technique, we used the Solitaire AB/FR, which is the only intracranial stent that is fully recoverable. 10 patients had an occlusion of the basilar artery, 23 had a middle cerebral artery occlusion, and 5 had terminal carotid artery occlusions; 6 of these had to be treated first for an acute occlusion originating in the internal carotid artery. Recanalization Results were assessed by follow-up angiography immediately after the procedure. Neurologic status was evaluated before and after treatment (90-day follow-up) according to the National Institutes of Health Stroke Scale and modified Rankin scale.

Results: Successful revascularization was achieved in 34 of 38 (89%) patients (thrombolysis in cerebral infarction [TICI] 2a/b and 3. There was immediate flow restoration in 36 of 38 (94%) cases after deployment of the device. The stent was removed in its unfolded state in all patients. The mean time from stroke symptom onset to recanalization was 277 minutes, with a standard deviation of 118 minutes. Mean National Institutes of Health Stroke Scale score on admission was 19.4, with a standard deviation of 5.7. 23 of the patients (60.5%) improved by >10 points on the National Institutes of Health Stroke Scale at discharge, and 44% showed a modified Rankin scale score of 0-2 at 90 days. Mortality was 18%. In 1 case, an asymptomatic intracranial hemorrhage was detected on control computed tomography, and 3 patients had a symptomatic intracranial hemorrhage.

Conclusion: Withdrawal of an unfolded, fully recoverable, intracranial stent yielded very promising angiographic and clinical Results. It combines the advantages of prompt flow restoration and mechanical thrombectomy.

12 Acute stroke: new treatment concepts B

1-YEAR RESULTS FOR MECHANICAL THROMBECTOMY WITH THE SOLITAIRE STENT IN ACUTE STROKE

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Background: To report the effectiveness of mechanical thrombectomy with the Solitaire stent in severe acute ischemic stroke in conjunction with intravenous systemic thrombolysis.

Methods: Prospective single center study of patients with acute ischemic stroke based on proven large artery occlusion via CT-angiography in anterior or posterior circulation. Patients were triaged for eligibility for mechanical thrombectomy, independently of intravenous thrombolysis with tissue plasminogen activator (rTPA). Clot retrieval was performed with the Solitaire stent (AB and FR, ev3 Inc, Plymouth, MN) with up to 4 maneuvers. NIHSS and mRS scores were assessed on admission, discharge, after 90 days and after one year. For evaluation of outcome patients were stratified in early, intermediate and late treatment subgroups.

Results: Till January 2011 54 patients were eligible for mechanical thrombectomy with the Solitaire stent since October 2009. 92% had a NIHSS score of ≥ 10 and 96% mRS 4 or 5 on admission. 40 of 54 patients received intravenous rTPA prior to mechanical thrombectomy (bridging technique), 14 were treated with thrombectomy alone. 27 of 54 had tandem stenosis and were a priori stented. Recanalization rate was 88%; in 50% of cases the first attempt led to recanalization. There were no procedural complications. Overall 37% (20 of 54) patients had a good clinical outcome (mRS ≤ 2) in the 90 days follow up interval. In the early treatment subgroup (n=21) with recanalization in ≤ 4,5 h from symptom onset good outcome was reached in 50%. Of 13 patients with carotid-T-occlusions 6 had a good outcome after 90 days. Patients who received a combined treatment with intravenous rTPA (bridging) had a higher NIHSS score reduction (p=0.06) than non-bridging patients. By May 2011 the 1-Year Results of 25 patients will be available for analysis and Discussion.

Conclusions: rTPA and mechanical thrombectomy is safe. The Solitaire can be deployed safely and quickly. Current Results are encouraging, especially in combination with i.v. rTPA; the Solitaire may play a key role in further improvement of outcome in severe acute stroke based on large vessel occlusions.

13 Acute stroke: new treatment concepts B

THE MINDFRAME DEVICE FOR FLOW RESTORATION AND CLOT REMOVAL IN ACUTE ISCHEMIC STROKE PATIENTS. RESULTS FROM THE PRIISM STROKE TRIAL

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Background and purpose: Early flow restoration in large vessels occluded by emboli have potential as a treatment for patients experiencing acute ischemic stroke. This clinical study was to assess the safety and performance of the MindFrame System in flow restoration.

Methods: The MindFrame System EU-PRIISM-01 Stroke Trial was a prospective, single arm, multi-center trial that was independently monitored and core laboratory adjudicated enrolling subjects with an acute neurologic deficit consistent with acute large vessel stroke. The primary endpoints were to establish TIMI II or III grade flow within 30 minutes of guide catheter placement, achieve 50% or greater TIMI II or III grade flow at the end of the procedure and to achieve 28% or greater mRs 0-2 at 90 days in patients treated. Secondary endpoints were serious adverse events, mortality, incidence of symptomatic inctracranial hemorrhage and neurological condition.

Results: 48 patients at 8 international centers were enrolled. 40 were treated. Mean age was 64, mean pre-stroke mRs score was 0.3 and mean NIHSS was 17. 75% of patients treated had initial flow restored with the MindFrame System to TIMI II or III grade within 30 minutes of guide catheter placement. 82% of patients treated achieved TIMI II or III grade flow. Prior IV thrombolysis had been administered in 63%. In 60% of patients treated, adjuvant intra-arterial mechanical thrombectomy was required. 47% received low dose IA rTPA. Preliminary Results indicate that 47% of patients treated will have mRs 0-2 at 90 day follow up. There were no device related adverse events.

Conclusion: Early clinical experience suggests that the MindFrame System is a safe and effective treatment for the restoration of blood flow and the removal of intracranial occlusion.

14 Acute stroke: new treatment concepts B

MECHANICAL EMBOLECTOMY FOR THE TREATMENT OF ACUTE ISCHEMIC STROKE: INITIAL RESULTS FROM THE TREVO STUDY (THROMBECTOMY REVASCULARIZATION OF LARGE VESSEL OCCLUSIONS IN ACUTE ISCHEMIC STROKE)

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Background: Clinical outcome in acute ischemic stroke (AIS) has been shown to be strongly correlated with clinically relevant revascularization in multiple, independent studies. Restoration of blood flow to at-risk brain tissue is an obvious therapeutic target, yet pharmacologic lysis of thrombus is often not successful or feasible in large vessel stroke. Mechanical thrombectomy has been pursued as an alternative method for restoring blood flow in large vessel ischemic stroke. Some challenges with previous devices have been predictable procedural Results, procedure time, and ease of use. Newer devices are reported to offer benefits in these areas. The Trevo™ system utilizing Stentriever™ technology is a novel device for removal of thrombus in patients suffering an acute ischemic stroke. This device has been engineered to maximize thrombus integration to potentially provide an easier and more predictable method of mechanical thrombectomy. We report the preliminary Results of The TREVO (Thrombectomy REvascularization of large Vessel Occlusions in acute ischemic stroke) Study.

Methods: Seven centers in four European countries participated in this multi-center, prospective, single-arm trial evaluating mechanical thrombectomy with the Trevo™ system. Patients with persistent large vessel occlusion aged 18-79 with an NIHSS of 8-30 were included. Patients with occlusions in either the anterior or posterior circulation were enrolled. Patients were required to be treated within 8 hours from symptom onset. The trial utilized an independent imaging core lab and clinical events committee (CEC).

Results: Enrollment is on-going, with 24 enrolled to date. Median age is 67 and median NIHSS is 17. The occlusions were located in the ICA (28%), MCA M1 (61%), MCA M2 (5.5%), and Vertebrobasilar (5.5%). Revascularization was assessed with the TICI scale, and 82% achieved TICI 2b or 3 post-Trevo use.
Late-breaking Results, including updated demographics, procedural and 90d outcomes will be reported at the time of presentation.

Conclusions: High rates of revascularization were achieved and the Trevo device shows promising clinical Results and procedural success.

15 Acute stroke: new treatment concepts B

CEREBRAL PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY WITH STENTING IN PATIENTS WITH ACUTE MCA OCCLUSION - CASE- CONTROL STUDY

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Background: Early recanalization of brain artery occlusion predicts 3-month independency in acute ischemic stroke (AIS) patients. Cerebral percutaneous

transluminal angioplasty with stenting (cPTAS) is an experimental method tested in AIS treatment.

Methods: Prospective, bicentric, case-control study was used. 106 patients (62 males, age 25-86, mean 65.8±12.2 years) with AIS due to middle cerebral artery (MCA) main stem occlusion were enrolled. 75 patients fulfilling criteria received intravenous thrombolysis (IVT) within 4.5 hours since AIS onset. No further recanalization therapy was used in 26 (35%) IVT treated patients with achieved MCA recanalization (Group 1). Patients with IVT failure after 60 minutes were randomized into 2 subgroups - 23 patients were treated with cPTAS (Group 2), no further recanalization therapy was used in 26 patients (Group 3). CPTAS within 8.0 hours since AIS onset was applied also in all 31 nonIVT patients (Group 4). Neurological deficit on admission (using NIHSS), MCA recanalization at the end of IVT/cPTAS, occurrence of symptomatic intracerebral hemorrhage (SICH), and 3-month clinical outcome (using mRS) were evaluated.

Results: In the particular groups, median NIHSS on admission was 13.5, 16.0, 15.5, 15.0 (p>0.05); SICH occurred in 4%, 4%, 4%, 3% patients, resp. (p>0.05); favorable 3-month clinical outcome (mRS 0-3) was achieved in 65%, 31%, 52%, 52% patients, resp. (statistically significant difference between Groups 2 and 3, p=0.048). Favorable 3-month clinical outcome difference was not statistically significant between IVT only (Groups 1+3) and cPTAS only (Group 4) treated patients (48% vs. 51%, p>0.05). Complete MCA recanalization after cPTAS was achieved in 29 (54%) patients.

Conclusion: In the presented study, cPTAS seems to be a safe and effective treatment option in AIS patients with MCA occlusion contraindicated to IVT or with IVT failure. Supported by IGA MH CR grants NT/11386-5/2010, NT/11046-6/2010.

16 Acute stroke: new treatment concepts B

GASOMETRIC ANALYSIS OF BLOOD SAMPLES DIRECTLY OBTAINED BEYOND ARTERIAL MCA OCCLUSION DURING ENDOVASCULAR PROCEDURES PREDICTS RESPONSE TO REVASCULARIZATION

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Background: Endovasclar procedures for acute stroke may last several hours until recanalization is achieved. During this time, measures offering information about the degree of damage to the affected brain tissue may help physicians taking decisions about whether to pursue or not efforts to achieve recanalization. We studied gasometric parameters of blood samples drawn through the microcatheter.

Methods: During endovascular procedures, after clot was first crossed with the 2.3 French microcatheter a 1-2 ml. Blood sample was obtained from the arterial segment distal to the occlusion (Post). Simultaneously another sample was obtained from femoral artery (Pre). A gasometric study was immediately performed. We defined clinical improvement as NIHSS decrease ≥4 points at discharge. Infarct volumes were measured on 24 hour CT.

Results: Blood sampling was performed in 12 patients with MCA occlusion. No complications related to procedure were observed. Gasometric analysis showed differences between Pre and Post blood samples in mean oxygen partial pressure (Post-paO2 73.2 Vs Pre-paO2 79.3; p=0.007) and mean oxygen saturation (Post-Sat O2 93.08% Vs Pre-Sat O2 94.4%: p=0.006). Despite that neither Post-paO2 (r=0.07;p=0.8) nor Post-SatO2 (r=0.1; p=0.8) were correlated with time from symptom onset to gasometry, final infarct volume was inversely correlated with Post-paO2 (r=-0.722, p=0.018) and Post-SatO2 (r=-0.664, p=0.036). We identified a cut point value of Post-paO2>70 mmHg that better predicted differences in final infarct volume (386 Vs 69 cc; p=0.032) and discharge NIHSS (27 Vs 12; p=0.011). Only Post-paO2>70 (p=0.014) and dyastolic blood pressure (p=0.03) were associated with clinical improvement. In a logistic regression adjusted for time to recanalization Post-paO2>70 emerged as the only independent predictor of clinical improvement (OR:27 95%CI:1,043-689,790; p=0.047).

Conclusion: Direct local blood sampling from the ischemic brain is feasible during endovascular procedures. A gradient in oxygenation parameters was demonstrated between Pre and Post occlusion blood samples. This information may be used to predict clinical outcome and help in decision making in the angio-suite.

17 Acute stroke: new treatment concepts B

PROXIMAL MIDDLE CEREBRAL ARTERY MAINSTEM OCCLUSION: MIGHT THE COMBINATION OF INTRAVENOUS THROMBOLYSIS AND ULTRASOUND (SONOTHROMBOLYSIS) SERVE AS AN ALTERNATIVE TO INTRA-ARTERIAL THROMBOLYSIS?

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Background: In middle cerebral artery mainstem (MCA-M1)-occlusion, treatment with intravenous tissue plasminogen activator (IV-TPA) leads to a low rate of early recanalization. Data from an observational study comparing Results of patients with hyperdense MCA sign (HMCAS) undergoing either IV-TPA or intra-arterial thrombolysis (IA-TPA) showed an improved outcome on the mRS after 90 days for the IA-TPA group (Mattle et al. Stroke 2004). By retrospective analysis of our registry of proximal MCA-M1, we sought to evaluate the effect of sonothrombolysis (1 hour 2 MHz insonation) plus IV-TPA (So+IV-TPA) in comparison to IV-TPA alone and in comparison to the Results of Mattle et al. using IA-TPA.

Methods: Patients were included in the registry when proximal MCA-M1-occlusion without residual flow on the Thrombolysis in Brain Ischemia Doppler score was shown by transcranial duplex sonography at baseline and if they were admitted within 6 hours from symptom onset. Data of the patients receiving IV-TPA or So+IV-TPA were retrospectively analyzed.

Results: A total of 72 patients receiving IV-PTA were analyzed, 28 of those received So+IV-TPA. There was no difference of demographic parameter (age 64.5±12 years vs. 64.0±10, male 61% vs. 71%, n.s.) or severity of stroke at baseline (NIHSS median/range 18/16 vs. 18/22). One hour after IV-TPA bolus, recanalization was more frequent in the So+IV-TPA group (partial 11% vs. 39%; complete 14% vs. 25%, p=0.003). After 3 months, favorable outcome (mRS 0-1) was more frequent in the So+IV-TPA group 6% vs. 28% (p=0,01); mRS 0-2 14% vs. 32%; and 19% vs. 12% had died (n.s.). Symptomatic intracerebral hemorrhage (sICH) occurred in 1 vs. 3 patients, (n.s.).

MCA-M1 Occlusion treated with IV-TPA alone (No US=no Ultrasound,) versus Sonothrombolysis+IV-TPA (US=Ultrasound): Outcome after 90 Days
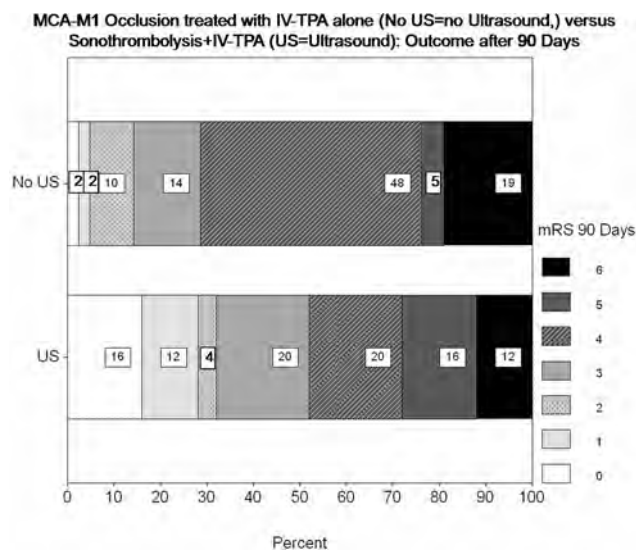
Conclusion: When comparing the data of proximal MCA-M1 occlusion and IV-TPA with the data of patients with HMCAS and IV-TPA (Mattle et al.), outcome of our group was worse. However, early recanalization and Results after 3 months of the So+IV-TPA group were nearly comparable to the Results from the IA-TPA group. In proximal MCA-M1 occlusion, So+IV-TPA should be considered as an alternative to IA-TPA.

18 Acute stroke: new treatment concepts B

TRANSCRANIAL LASER THERAPY (TLT) DOES NOT INDUCE LONG-TERM NEOPLASTIC OR HEMORRHAGIC RESPONSE IN BRAINS OF STROKED RATS

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Background and purpose: The aim of the present study was to explore whether near infrared photobiomodulation with Transcranial Laser Therapy (TLT) promotes hemorrhage or neoplasia in stroked rats.

Methods: Stroke was induced in rats by middle cerebral artery (MCA) occlusion using a filament insertion technique. TLT (near infrared (NIR) laser energy, 808nm) was applied at different skull locations 24 hours after stroke at a cortical surface dose of 7.5mW/cm^{2} for either 2 or 4 minutes, (0.9J/cm^{2} or 1.8J/cm^{2} respectively), and compared to a sham-control group with no laser treatment. Two sets of experiments were performed. Experiment 1 assessed for neoplasia in 142 animals at 3 time

points: 28, 56 and 84 days. Experiment 2 assessed for hemorrhagic transformation in 37 rats at 72 hours poststroke. All evaluations were made by histopathology.
Results: In Experiment 1, no proliferative cells were found in any of the brains (laser treated or control) at the 28 day time interval, and no neoplastic changes were noted in any of the examined brain sections that were observed for the 56 or the 84 day time intervals. In Experiment 2, there was no statistically significant difference in the incidence of hemorrhage in the laser-treated and sham-control groups. Signs of hemorrhage were found in 18.3% of control rats and 18.9% of laser treated rats.
Conclusion: TLT at doses of 7.5mW/cm^2 at the cortical surface for either 2 or 4 minutes does not promote hemorrhagic transformation or induce a neoplastic response in stroked rat brains up to three months post-treatment.

Experimental studies B

7 Experimental studies B

EFFECTIVE HEMOSTATIC THERAPY IN EXPERIMENTAL INTRACEREBRAL HEMORRHAGE ASSOCIATED WITH THE DIRECT THROMBIN INHIBITOR DABIGATRAN

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Background and Purpose: The direct oral thrombin inhibitor dabigatran-etexilate (DE) is expected to replace vitamin K antagonists for stroke prevention in atrial fibrillation in millions of patients. However, the lack of an effective antagonist in case of intracerebral hemorrhage (ICH) is a major concern for stroke neurologists. The Aims of the present study were to establish a murine model of ICH associated with dabigatran, and to test how effectively different hemostatic factors prevent hematoma growth.
Methods: In C57BL/6 mice receiving dabigatran-etexilate (4.5 or 9mg/kg i.p.) in vivo and in vitro coagulation assays and dabigatran plasma levels were measured repetitively. Thirty min after ICH induction by striatal collagenase injection, anticoagulated mice with either DE dose received an intravenous injection of either saline, prothrombin complex concentrate (PCC, 100U/kg), murine fresh frozen plasma (FFP, 200µl), or recombinant factor VIIa (FVIIa, 8mg/kg, Novo7®). ICH volume was determined on brain cryosections 24h later.
Results: Intraperitoneal DE led to a substantial prolongation of tail-vein-bleeding-time and ecarin-clotting-time for 4-8h corresponding to dabigatran plasma levels. Intracerebral hematoma expansion occurred mainly during the first hours on serial T2* MRI. Anticoagulation with either dose of DE increased the hematoma volume significantly compared to non-anticoagulated mice. PCC prevented excess hematoma growth caused by DE dose-dependently and more consistently than FFP and FVIIa after injection of either DE dose (n=60/experiment), and also reduced mortality significantly.
Conclusions: Our translational study provides strong evidence that PCC prevents excess intracerebral hematoma formation most effectively in a newly established murine ICH model associated with dabigatran. The effectiveness and safety of this strategy has to be further evaluated in clinical studies.

8 Experimental studies B

CLEARANCE OF ALBUMIN FOLLOWING ULTRASOUND-INDUCED BLOOD-BRAIN BARRIER OPENING IS MEDIATED BY ACTIVATED MICROGLIA

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Background: Ultrasound-mediated opening of the blood-brain barrier in the presence of gas-filled microbubbles is a potential strategy for drug delivery across the blood-brain barrier (BBB) to promote regeneration after ischemic stroke. Therapeutic options include transfer of growth factors like BDNF or genes. However, related bioeffects and potential side-effects that could limit a translation into clinical application are poorly understood so far. We therefore examined the clearance of extravasated albumin following ultrasound-mediated BBB opening.
Methods: 16 male Wistar rats underwent insonation of one hemisphere (1 MHz, intracranial pressure 1,27 MPa, pulse length 10 ms, repetition frequency 1Hz, duration 1 min) together with IV administration of ultrasound contrast agent (Optison

0.1 ml/kg) and Evans Blue dye. Animals were sacrificed at different time points, and immunofluorescence for detection of cellular marker proteins was performed.
Results: Autofluorescence of albumin-bound Evans Blue dye indicated cellular albumin uptake as soon as 1 hour after insonation (2±1 cells/optical field). Cellular albumin uptake increased constantly over 24 hours (22±2 cells/optical field, p<0.05). The majority of albumin-positive cells were located in the periphery of brain capillaries. Most albumin phagocyting cells stained positive for CD163 and Iba-1. The combination of both markers identifies these cells as activated microglia. Some perivascular cells with intracellular albumin expressed the endothelial marker protein EN4. All albumin uptaking cells stained negative for the glial marker proteins GFAP and S100beta as well as for the neuronal TubulinIII.
Conclusion: Ultrasound-induced BBB opening leads to albumin extravasation which is phagocytized predominantly by microglial cells. As albumin uptake into neurons has been shown to be neurotoxic, rapid albumin clearance by microglia might prevent neuronal cell death.

9 Experimental studies B

KININOGEN DEFICIENCY PROTECTS MICE FROM ISCHEMIC STROKE BY REDUCING BLOOD BRAIN BARRIER DAMAGE, INFLAMMATION AND THROMBUS FORMATION

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Background: Inflammation and brain edema, caused by the breakdown of the blood-brain barrier (BBB), are key pathophysiological steps after ischemic stroke leading to secondary brain damage. Kininogen (KNG) is an important member of the kallikrein-kinin system (KKS). Activation of the KKS triggers the release of kinins from their precursor KNG. Kinins are proinflammatory peptide hormone involved in inflammatory processes, attraction of immune cells and increased vascular permeability.
Methods: Focal cerebral ischemia was induced by middle cerebral artery occlusion for 60 minutes (tMCAO) in KNG-/- and wild-type mice followed by 24 or 72 h of reperfusion. Neurological deficits were assessed and infarct volumes were calculated from 2,3,5-triphenyltetrazolium chloride (TTC)-stained brain slices. Evan's Blue tracer was applied to quantify the extent of BBB damage. The local inflammatory response was evaluated by real-time reverse transcription-polymerase chain reaction and immunhistochemistry. The extent of thrombus formation within the infarcted brain areas was analyzed by immunoblot.
Results: KNG-/- mice developed significantly smaller brain infarctions and less neurological deficits compared to wild-type controls (119.6±26.1 mm^3 vs 42.4±29.1 mm^3; P<0.0001). Reduced BBB breakdown (Evan's Blue extravasation: 5.7±2.3 µg vs 2.3±1.7 µg; P=0.0076) and mitigation of tissue inflammation could be identified as underlying mechanisms. Moreover, KNG deficiency largely protected from intracerebral thrombus formation after tMCAO.
Conclusion: Our present as well as previous findings (Austinat et al., 2009) demonstrate that the KKS is critically involved in the pathophysiology of acute ischemic stroke at different levels. Targeted inhibition of distinct constituents of the KKS such as KNG might be a promising strategy to treat ischemic brain damage in the future.
Reference: 1. Austinat et al., 2009: Blockade of bradykinin receptor B1 but not bradykinin receptor B2 provides protection from cerebral infarction and brain edema. Stroke 40:285–293.

10 Experimental studies B

ISCHEMIC LESION DEVELOPMENT AND LONG TERM BEHAVIOURAL DEFICITS OF A RAT PHOTOTHROMBOTIC BRAIN STEM STROKE MODEL

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Background: So far no appropriate animal model of brain stem ischemia exists that allows comprehensive preclinical testing of candidate drugs. To address this issue we developed a rat photothrombotic brain stem stroke model and tested whether this model can be used to investigate neuroprotective and neuroregenerative therapies.
Methods: Adult male Wistar rats were anaesthetized with an intraperitoneal injection of ketamine hydrochloride and xylazine hydrochloride. In spontaneously breathing rats a midline neck incision was performed and the skull base was approached by blunt separation. After injection of Bengal rose (infarct group, n=7)

or saline (sham group, n=7), a circular area of the skull (diameter 2mm) between the canalis caroticus and the midline was illuminated with a laser for 7 minutes. The infarct size was assessed by magnetic resonance imaging (MRI) after 2, 24 and 48 hours. For the evaluation of neurobehavioural deficits the Rotarod test and the beam balance test were performed weekly for four weeks.

Results: Animals of the infarct group showed homogenous infarcts of the brain stem on coronal MRI images (Figure A). Between 2 and 24 hours significantly expanding ischemic lesions were observed on sagittal MRI images (P<0,05) (Figure B). The neurological outcome was significantly impaired in the infarct group as measured by the Rotarod test and the beam balance test.
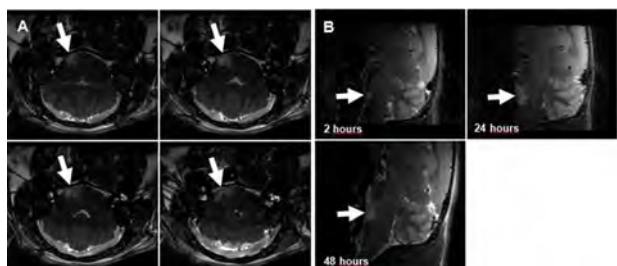
Conclusions: In our study we found an infarct growth of photothrombotic brain stem lesions over 24 hours indicating that this stroke model is suitable to investigate candidate neuroprotective stroke drugs that have infarct volume as therapeutic target. Moreover, our brain stem stroke model allows long-term survival in combination with stable neurological deficits. Therefore it can also be used for the analysis of neuroregenerative stroke therapies.

11 Experimental studies B

SECONDARY DAMAGE IN IPSILATERAL THALAMUS FOLLOWING CEREBRAL CORTICAL INFARCTION IN HYPERTENSIVE RATS CAN BE MODIFIED BY BECLIN 1 KNOCKDOWN

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Background: Focal cerebral cortical infarction can cause secondary neuronal degeneration in ipsilateral thalamus remote from ischemic lesion which delays functional recovery. However, the molecular mechanisms underlying the secondary damage remain undetermined. Here, we investigated if autophagy occurred and possible role of Beclin 1 on autophagy as well as secondary neurodegeneration in ipsilateral thalamus after cerebral infarction.

Methods: Cerebral cortical infarction was introduced by distal middle cerebral artery occlusion (MCAO) in hypertensive rats. Autophagy Inhibitor, 3-methyladenine (3-MA), or dimethyl sulfoxide (control) was intraventricularly administrated to block autophagy. Expression of Beclin 1 was knocked down using siRNA delivered into the thalamus prior to unilateral MCAO. Autophagic activation or expression of Beclin 1 was evaluated by immunochemistry, Western blot or electron microscopy. The neuronal loss and glial activation were examined by Nissl staining or immunochemistry.

Results: We found that LC3-II/LC3-I ratios and Beclin 1 expression were markedly increased in neurons and astroglia cells within ipsilateral thalamus at 3, 7 and 14 days after distal MCAO compared to controls (P<0.05 or 0.01). Formation of autophagic vacuoles was observed in damaged neurons and astroglia cells within ipsilateral thalamus. Autophagic activation in the ipsilateral thalamus was markedly inhibited by treatment of 3-MA compared to controls (P<0.01). Beclin 1 knockdown significantly reduced conversions of LC3-I to LC3-II, which was accompanied by obvious decrease in neuron loss and glial activation in ipsilateral thalamus at 7 days after distal MCAO compared to controls (P<0.05 or 0.01).

Conclusions: Our Results demonstrate that autophagic cell death occurs within the ipsilateral thalamus and secondary damage in ipsilateral thalamus following cerebral cortical infarction in hypertensive rats can be modified by Beclin 1 knockdown.

12 Experimental studies B

FUNCTIONAL CEREBRAL BLOOD VOLUME RESPONSE TO NORMOBARIC OXYGEN THERAPY AFTER STROKE VARIES SPATIALLY AND TEMPORALLY

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Background: High flow normobaric oxygen (NBO) therapy transiently improves clinical deficits and reduces DWI lesions in acute stroke patients. The therapeutic mechanism of NBO is not well understood. We investigated NBO-induced functional cerebral blood volume (fCBV) changes using MRI after stroke in rats.

Methods: Stroke was induced in adult male rats (n=8) by filament occlusion of the right middle cerebral artery. Rats were scanned on a 9.4T imager post-stroke. DWI and arterial spin labeling (ASL) perfusion, and gradient echo (GRE) MRI were obtained at baseline prior to injection of the MION contrast agent. Post-MION, rats were exposed to periods of 2 min room-air (RA), 10 min NBO and 10 min RA while imaged. This was repeated approximately every 30 min, interleaved with DWI scans. fCBV responses at 1h and after 3 h post-stroke were analyzed using generalized linear model.

Results: All rats showed DWI lesions within larger ASL lesions. Fig A shows the concatenated fCBV response across all rats to NBO at 1 h (77±7 min) for 8 rats. Fig B shows the response of the animals at time points > 3 h (225±18 min) for 6 rats across 11 epochs (2 rats died before 3h). Only responses with P-value < 0.01 are shown. The graphs represent CBV changes measured at the crosshairs along with fitted model (gray regions show NBO-exposure time-points). No significant responses are evident in the core. In peri-infarct regions, there are transient elevations in fCBV in response to NBO at 1 h. By 4 h, the same region shows decreases.

A. Functional CBV response to NBO at 1 h post-stroke

B. Functional CBV response to NBO at 4 h post-stroke
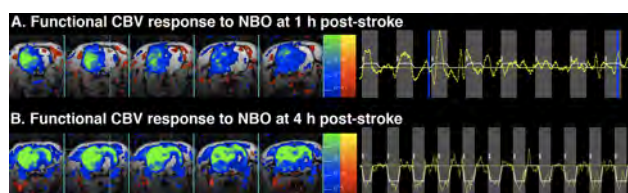
Discussion: CBV changes to NBO are both spatially and temporally heterogeneous. The mechanisms of peri-infarct tissue salvage as a result of NBO therapy may be due to vasoconstriction in normal regions with slight elevation in the penumbra. Hemodynamic changes may be a key neuroprotective mechanism of NBO, but relatively short lived. NBO may therefore be of most benefit to patients who exhibit substantial DWI and perfusion mismatch.

13 Experimental studies B

NECDIN MODULATES RESIDENT MICROGLIAL CELLS IN EXPERIMENTAL STROKE

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Necdin has been shown to promote neuronal survival, differentiation and restricts proliferation in hematopoietic stem cells. We tested the hypotheses that necdin is expressed in inflammatory cells and modulates inflammation in stroke. Mice were subjected to 60 min of middle cerebral artery occlusion (MCAO) and sorted for CD11b with magnetic-activated cell sorting (MACS) and further analyzed with immunoblots and immunohistochemistry. Necdin was specifically upregulated at 72h reperfusion time point in CD11b+ MACS sorted leukocytes from the ipsilateral hemispheres. Additionally, a high number of necdin+/Iba1+ were observed in the brain sections. To test the role of necdin in growth arrest in inflammatory cells, we generated lentiviral particles (LVPs) to downregulate necdin at protein levels via RNA interference (RNAi). In concurrent with MCAO,LVPs were intra-arterially injected at the ipsilateral side. Cell counts showed significantly higher number of BrdU+, Iba1+, BrdU+/Iba1+ double positive and BrdU+/Iba1+/LVPs-EGFP+ triple positive cells at the ipsilateral cortex (RNAi with necdin versus control non-targeting microRNA).

Analysis of EGFP expressing bone marrow chimeric mice showed that necdin+ cells were not derived from the peripheral macrophages invading the brain after MCAO (72h reperfusion). The hyperactivated resident microglia assumed the "ameboid" morphology were necdin+, meanwhile the resting state "ramified" phenotypic microglia were devoid of necdin. To corroborate, CD11b+ cells were sorted for

CD45 high and low in expression using fluorescence absorbed cell sorting (FACS). Necdin mRNA levels in the ipsilateral hemisphere were 8 fold higher in CD11b+/CD45low and 20 fold higher in CD11b+/CD45high cells in comparison to the contralateral hemisphere of CD11b+/CD45low cell fraction. In summary, necdin is expressed in the hyperactivated subpopulation of resident microglia and not in bone marrow derived macrophages and, restricts their proliferation and thereby might modulate stroke outcome.

14 Experimental studies B

VARIABILITY OF RTPA RESPONSE IN A MOUSE MODEL OF THROMBOEMBOLIC STROKE

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Objectives: Although several treatment strategies have shown a beneficial effect in animal models of ischemia, translation to major clinical trials has been poor. Apart from a multitude of factors related to poor study design, the animal model itself may contribute to this lack of translation through its inability to adequately represent the pathophysiology of naturally occurring cerebral ischemia. This study characterized a novel reproducible mouse model of thromboembolic stroke that may provide new insights into the mechanisms of ischemic stroke.

Methods: Thromboembolic stroke was induced by local injection of thrombin directly into right MCA of C57 black/6J mice. CBF velocity was measured continuously by laser Doppler flowmetry allowing determination of spontaneous clot dissolution. The efficiency of rtP to induce thrombolysis was examined at different time points after clot formation. The effect of different concentration of thrombin (1,5 and 3 UI) and rtPA (5 and 10 mg/kg) was examined. The efficiency of rtPA to induce thrombolysis and its subsequent effect on infarct volume were measured by laser Doppler, histology and MRI.

Results: Thrombin injection resulted in clot formation and cortical brain injury (n= 13). The clot is stable up to 2 hr after formation, subsequently 20% of the animals (n=8) recanalize spontaneously. There is a significant variability in the response to rtPA at different time-points after clot formation. At 20 min after the clot formation, rtPA treatment Results in 100% recanalization. However, rtPA-induced thrombolysis only dissolves the clot in 30% of the animals (n=6) when administrated 40 min after clot formation (Fig 1).
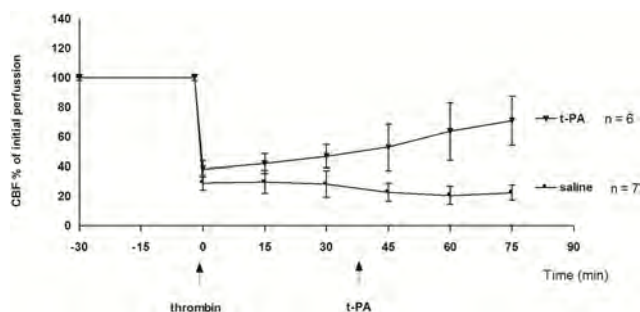
Conclusion: Similar to human ischemic stroke of embolic origin, the model shows variability in the response to rtPA at different time periods after stroke onset. The model may be useful for investigating the pathophysiology of clot lysis and for studying new acute treatment regimes.

15 Experimental studies B

PROGNOSTIC IN VIVO BIOMARKERS FOR LESION DEVELOPMENT AFTER CEREBRAL ISCHEMIA

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A better prediction of the outcome after ischemia and estimation of onset time at early time points would greatly facilitate clinical decisions. Therefore, the aim of the present study was to use magnetic resonance spectroscopy to identify neurochemical markers for outcome prediction at early time points after ischemia.

ICR-CD1 mice were subjected to 10-minute, 30-minute or permanent middle cerebral artery occlusion (MCAO). The regional cerebral blood flow (CBF) was monitored in all animals by laser-Doppler flowmetry. All MR studies were carried out in a horizontal 14.1T magnet. Fast spin echo images with T2-weighted parameters were

acquired to localize the volume of interest and evaluate the lesion size. Immediately after adjustment of field inhomogeneities, localized 1H MRS was applied to obtain the neurochemical profile from the striatum (6-8 μl) or the cortex (2.2-2.5 μl). Six animals (sham group) underwent nearly identical procedures without MCAO.

By comparing the evolution of several metabolites in ischemia of varying severity, we observed that glutamine increases early after transient ischemia independently of severity, but decreases in permanent ischemia. On the opposite, GABA increased in permanent ischemia and decreased in transient. We also observed a decrease in the sum of N-acetyl aspartate + glutamate + taurine in all irreversibly damaged tissues, independently of reperfusion and severity. Finally, we have observed that some metabolites decrease exponentially after ischemia. This exponential decrease could be used to determine the time of ischemia onset in permanent ischemia.

In Conclusion, magnetic resonance spectroscopy can be used as a prognostic and diagnostic tool to monitor reperfusion, identify reversibly and irreversibly damaged tissue and evaluate the time of ischemia onset. If these Results can be translated to stroke patients, this technique would greatly improve the diagnosis and help with clinical decisions.

Brain imaging B

10 Brain imaging B

NO EVIDENCE OF ACUTE OR PREDISPOSING STRUCTURAL ABNORMALITIES IN PATIENTS WITH TRANSIENT GLOBAL AMNESIA (TGA): A TRACT BASED SPATIAL STATISTICS (TBSS) STUDY

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Background: Until today, delayed MRI has detected small punctuate lesions in the lateral hippocampus on diffusion-weighted imaging (DWI) in patients with TGA. We sought to elucidate a possible underlying more extensive disturbance of the hippocampal network in a prospective explorative approach using diffusion tensor imaging (DTI) and TBSS.

Methods: DTI data were acquired on a 3T MRI scanner (Siemens Trio) in 10 subjects with TGA and proven typical DWI lesions in the hippocampus, and processed in the TBSS framework comparing TGA patients with healthy control subjects matched for age, sex and extent of chronic white matter lesions. Furthermore, all patients underwent a standardized diagnostic protocol including a detailed neurological and neuropsychological examination.

Results: There were 9 women and 1 man in the study population; the mean age was 66 years. All patients reported an emotional trigger before onset of the TGA episode. Persisting mild cognitive deficits could be demonstrated in the subacute phase after the end of the episode in all patients. On DWI, all patients had single (six patients) or multiple (four patients) focal hyperintensities in the lateral hippocampus (Figure 1A). Regarding the extent of chronic white matter lesions, six patients had no white matter lesions (Fazekas grade 0) and four patients had mild white matter lesion load (Fazekas grade 1). Tract-based spatial statistics revealed no significant differences in fractional anisotropy and mean diffusivity values (p<0.05) between TGA patients and healthy controls (Figure 1B).
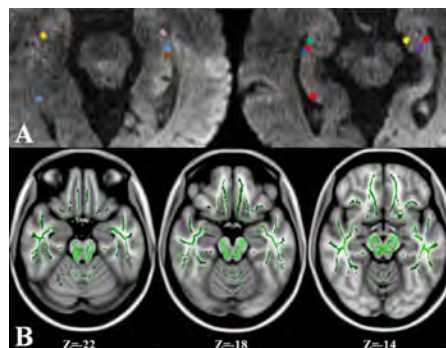

Figure 1. A. Schematic drawing of focal DWI lesions located in the hippocampus in 10 patients with transient global amnesia (each color represents a specific patient). B. Axial images demonstrating skeletal voxels without significantly (p<0.05) reduced FA values in patients with TGA compared to healthy controls. The background image is the MNI152 standard space T1 template; the slice localizations are in the MNI152 coordinate system.

Discussion: In patients with TGA neither preexisting lesion burden/structural tissue damage nor disturbed hippocampal network integrity could be demonstrated by tract-based spatial statistics. This finding suggests a transient functional perturbation rather than an impaired structural integrity of hippocampal and/or mesiotemporal memory circuits to be responsible for TGA.

11 Brain imaging B

MIGRAINE ATTACKS MIMICKING STROKE: MR PERFUSION IS HELPFUL!

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Background: In a subset of cases acute migraine attacks may present clinically as stroke. Due to therapeutical implications it is essential to differentiate these patients from true stroke patients. Therefore, the aim of this study was to evaluate patterns of MR perfusion abnormalities in these patients.
Methods: In a retrospective analysis of more than 1500 consecutive patients 20 patients (7 male, 13 female) were identified suffering from acute migraine attacks and not from stroke. All patients were referred to emergency MR with the suspicion of acute stroke and examined with a standard protocol including perfusion weighted imaging (PWI). Two radiologists reviewed color coded time to peak (TTP), relative mean transit time (rMTT), relative cerebral blood volume (rCBV), and relative cerebral blood flow (rCBF) maps in consensus for presence, vascular territory and grade of perfusion abnormality. Clinical follow up as well as MR follow up studies were available.
Results: Hypoperfusion was found in 14/20 acute migraine patients (70%) with delayed rMTT and TTP and decreased rCBV and rCBF, not restricted to a dedicated vascular territory. Bilateral hypoperfusion was seen in 3/14 cases, in 11/14 cases hypoperfusion with a posterior predominance was found. TTP and rMTT were the best maps to depict perfusion changes, but also rCBF maps were positive in 13/14 patients with hypoperfusion. In every case, clinical and imaging follow up were negative for brain infarction.
Conclusion: Perfusion abnormalities, untypical for stroke, may be seen in patients with acute onset hemiplegic migraine. In those cases, the MR perfusion pattern is helpful to differentiate hemiplegic migraine from acute stroke.

12 Brain imaging B

LONGITUDINAL MRI STUDY OF THE ENHANCED THERAPEUTIC EFFECTS OF LIPOSOME-ENCAPSULATED CITICOLINE IN STROKE

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Background: Citicoline is considered a therapeutic agent for the treatment of stroke. The unclear Results obtained from clinical trials may be based on its delivery form (oral versus I.V.), which affects its bioavailability in the brain. Encapsulation of citicoline in liposomes may increase its bioavailability in the brain and therefore its therapeutic effects. So far, available data on this regard is restricted to models of global ischemia, or to the use of invasive techniques (with data only at 24 hours after stroke). Here, we describe an in vivo longitudinal study of citicoline-treated animals after focal ischemia, showing the time profile of the evolution of the disease for a period of 7 days, allowing us to have a clearer vision of the therapeutic effects of citicoline, in regard to its administration form.
Methods: 19 rats were submitted to a permanent occlusion of the middle cerebral artery and treated with: 1) saline, 2) Intraperitoneal citicoline (I.P. 500 mg/kg), 3) Intravenous citicoline (I.V. 48 mg/kg), and 4) Intravenous liposome-encapsulated citicoline (containing 48 mg/kg of citicoline). Lesion volumes were measured using a 9.4 T MRI system at days 0 (DWI) and 1, 3 and 7 (T2-MRI) following surgery.
Results: Liposome-encapsulated citicoline induces a change on infarct volumes (respect initial values) of +14%, +6% and -32% at days 1, 3 and 7 post ischemia, in contrast with animals treated with saline (+64%, +65%, +39%), I.P. citicoline (+62%, +69%, +10%) or I.V. iticoline (+52%, +41%, -9%). A slight reduction of edema formation was observed for animals treated with citicoline in all delivery forms.
Conclusions: Liposome-encapsulated citicoline causes a noticeable reduction of lesion volumes at days 1, 3 and 7 following stroke. I.P. and I.V. administration of free citicoline also induces positive although smaller effects on treated animals, starting at later time-points that liposome-encapsulated citicoline.

13 Brain imaging B

CLINICAL OUTCOME AND IMAGING FOLLOW-UP IN ACUTE STROKE PATIENTS WITH NORMAL PERFUSION CT AND NORMAL CT ANGIOGRAPHY

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Introduction: Acute stroke multimodal CT imaging (MMCT: Non enhanced CT, CT angiography and CT perfusion (CTP)) may show normal Results despite persistent clinical stroke. We prospectively evaluated the sensitivity/specificity of MMCT infarct detection and the clinical outcome in patients with normal MMCT findings.
Methods: From April 2007 to April 2008, all patients with acute hemispheric stroke within 6 hours of symptom onset who underwent complete MMCT and MRI follow-up imaging were included. MMCT analysis included occlusion type, early infarct hypodensities (EIH), mean transit time (MTT), and cerebral blood volume (CBV) maps according to Alberta Stroke Program Early CT Score (ASPECTS). Clinical assessment included symptom onset to CT scan ($\leq$ 3h/> 3h), the National Institute of Health Stroke Scale score (on admission/discharge), and the modified Ranking Scale (mRS) 90 days after stroke onset.
Results: 107 patients were included (mean age 68,4 years; $\leq$ 3h n=84, > 3h n=23; intravenous thrombolysis (IVT) n=51 ($\leq$ 3h n=40, > 3h n=11). In patients with normal MMCT on admission (n=54), follow-up MRT detected brain infarctions in 23 patients (lacunar strokes n=16; infratentorial strokes n=4; territorial infarction n=3). Sensitivity/specificity/positive predictive value/negative predictive value of any infarct detection was 69.5%/99.8%/99.9%/57,2% and of any territorial infarct detection was 93,9%/99,9%/99,9%/93,6%, respectively. In univariate regression analysis (time to CT scan $\leq$ 3h/>3h; IVT: yes/no; ASPECTS EIH/CBV/MTT, 10/<10), only the evidence of normal CTP (ASPECTS MTT=10) had a statistically significant impact (p=0,02) on a good outcome (mRS 0-1).
Conclusion: MMCT sensitivity in acute lacunar or infratentorial stroke was poor. But we found a high specificity and a fairly good sensitivity in territorial infarct detection. In acute stroke patients with normal MMCT findings on admission, a good clinical prognosis can be expected.

14 Brain imaging B

ASSESSMENT OF HYPOXIA IN ACUTE ISCHEMIC STROKE PATIENTS WITH 18F-MISONIDAZOLE PET AND COMPARISON WITH MRI: A PROSPECTIVE PILOT STUDY

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Objectives: 1- to identify and to locate hypoxic tissues in acute stroke patients with a specific hypoxic cells PET tracer (18F-fluoromizonidazole) (FMISO), 2- to compare FMISO PET with 3T MRI.
Background: FMISO PET has been used to identify hypoxic tissues (potentially salvageable) in animals and patients. No published study has compared FMISO PET and 3T MRI in acute stroke patients.
Design/Methods: From October 2009 to June 2010, consecutive patients aged > 18 years admitted for a first symptomatic hemispheric stroke with NIHSS 5-20/42, in whom FMISO PET and MRI were available < 36 hours after stroke onset, were included after signed informed consent. The PET was acquired 2 hours after intravenous administration of 3.7 MBq/kg of 18F-MISO. All acquisitions were performed on Siemens Truepoint 6 PET-CT system. MRI were performed 2 hours after PET on 3T Philips MRI. FMISO PET were coregistered on DWI MRI. Mean uptake in the normal hemisphere was used as a reference (SUVref). All areas with a FMISO PET uptake > SUVref + 3DS were considered as hypoxic.
Results: Ten patients were included (6M-4F, mean age 66.5 years, 2 subcortical and 8 large cortical infarcts). FMISO PET were performed in a mean delay of 24 hours after stroke onset (6.5-30.00) and MRI 2 hours later (77-300 min). An increased uptake of FMISO was detected in 9/10 patients (large areas encompassing all stroke volume in 3, peripheric areas in 6). Areas of increased uptake were mainly included in DWI+ lesions (8/9). In 3/9, these hypoxic areas were associated in the infarct with regions of absent uptake, probably necrosed brain. No uptake was observed in the infarct in 1 patient.

Conclusions: Combining acquisition of FMISO PET and MRI within the first 30 hours after stroke onset appeared feasible. Hypoxic tissues were detected by FMISO in 90% of patients mainly in DWI+ lesions. DWI lesions appeared heterogeneous, including areas of hypoxic tissues (with uptake of F-MISO) and necrotic areas.

15 Brain imaging B

SEARCH FOR A MAP AND THRESHOLD IN PERFUSION MRI TO ACCURATELY PREDICT TISSUE FATE: A PROTOCOL FOR ASSESSING LESION GROWTH IN PATIENTS WITH A PERSISTENT VESSEL OCCLUSION

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Background: Based on multiple studies addressing the topic of magnetic resonance perfusion imaging it seems highly unlikely that any one combination of a map and threshold will ever yield a reliable prediction of radiological or clinical outcome for all patients with acute ischemic stroke (AIS). The goal of our study was to, in a minimally biased way, assess the usefulness and predictability of perfusion maps in AIS patients while additionally attempting to find a perfusion imaging protocol which could, at least in a subgroup of patients, offer the treating physician a useful estimate of tissue fate.

Methods: Our study included 145 AIS patients, from which 41 presented with a persistent vessel occlusion. Using three different software packages (Perfscape/Neuroscape, PMA and Stroketool) maps of mean transit time, cerebral blood flow (CBF) and Tmax were created. Three different thresholds were applied to each parameter map and subsequent volumes of hypoperfused tissue were calculated.

Results: The maps and thresholds showing the highest correlation coefficient to final infarct volume were: Tmax 4s in Perfscape/Neuroscape, CBF 20 ml/100g/min in PMA and CBF 15% (of the highest value on the scale for a given patient) in Stroketool. Using a CBF map with a restrictive threshold had, depending on the software used and in patients with a persistent vessel occlusion, shown volumes of tissue at definite risk of infarction in up to a 100% of patients. The additional use of a CBF map with a high threshold had enabled identification of patients without penumbra.

Conclusions: No one combination of software, map and threshold was able to give a reliable estimate of tissue fate for all patients. However, in patients with a vessel occlusion, a combination of a CBF map with a low threshold and a high threshold can provide a calculation of the minimum volume of brain tissue inevitably to be lost if the occlusion persists.

16 Brain imaging B

CTASI MUCH MORE RELIABLE THAN NCCT FOR DETECTION OF CEREBRAL ISCHEMIA IN PATIENTS SCANNED LESS THAN 90 MINUTES FROM STROKE ONSET

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Background: Hypoattenuation on CT-angiography source image (CTA-SI) are easily visualized and approximates to final infarct volume better than hypodensity on non contrast CT (NCCT). However, little is known regarding how the reliability and predictive ability of these modalities changes over time from stroke onset. We compared relationships between CTA- SI and NCCT at different time points after stroke.

Methods: Acute ischemic stroke patients with proximal anterior circulation occlusions (ICA, MCA M1, proximal M2) from Calgary CTA database were studied. Cohort was categorized in four groups based on time from stroke onset to NCCT/CTA: 0-90 min; 91-180 min; 181-360 min; > 360 min. Two neuroradiologists and two stroke neurologists evaluated 128 scans each (64 NCCT and 64 CTASI) in a random fashion. The scan were equally distributed in all time frame groups (n=32 in each time group). ASPECTS was scored to determine extent of early ischemic changes. NCCT Brain and CTASI were interpreted at separate sessions weeks apart for all readers. Reliability was assessed using interclass correlation coefficient.

Results: Among 64 subjects included in the study, median NCCT ASPECTS was 7.3 (IQR6-9) and the median CTASI ASPECTS was 5.5 (IQR4-6).

Unadjusted interclass correlation coefficient showed least agreement among readers to detect early ischemic changes on NCCT Brain in ultraearly phase (<90 minutes) from stroke onset in comparison to later time periods (Table 1). Identifying CTA SI abnormality had an uniform agreement irrespective of time period (Table 1).

Conclusion: Using ASPECTS methodology, NCCT brain is not reliable to identify the extent of ischemia in the ultraearly (<90 minute from stroke onset) phase of stroke. CTASI abnormalities were reliable irrespective of the time from stroke onset. Acute ischemic stroke trials can consider using CTASI to estimate the extent of ischemia in the very early phase after stroke when using imaging criteria for eligibility.

Table 1. Interclass correlation coefficient comparing NCCT brain and CTASI in different time categories from stroke onset

Time	NCCT		CTASI	
	ICC	95% CI [upper, lower]	ICC	95% CI [upper, lower]
0-90	0.48	0.719, 0.282	0.96	0.984, 0.931
91-180	0.80	0.906, 0.668	0.94	0.976, 0.898
181-360	0.81	0.910, 0.690	0.87	0.941, 0.784
>360	0.89	0.954, 0.810	0.89	0.954, 0.809
Overall	*0.78*	*0.844, 0.694*	*0.93*	*0.951, 0.905*

17 Brain imaging B

THE FACTORS RELATING TO DWI LESIONS IN PATIENTS WITH TRANSIENT ISCHEMIC ATTACK

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Background and Aims: The purpose of this study was to clarify the factors relating to acute ischemic lesions on diffusion-weighted MRI (DWI) in patients with transient ischemic attack (TIA).

Methods: A multicenter retrospective study was conducted to elucidate the characteristics of inpatients with TIA. The subjects of this study were TIA patients admitted to 13 stroke centers in Japan within 7 days after onset between 2008 and 2009. TIA was defined as focal neurological symptoms ascribable to a vascular etiology lasting less than 24 hours. We assessed the associations of baseline characteristics with positive DWI lesions.

Results: 464 patients (292 men, mean age of 69 years) were registered. MRI examinations were performed in 458 patients (99%), and DWI lesions were positive in 96 patients (21%). 56 patients had a single DWI lesion and 40 patients had multiple DWI lesions. Positive DWI lesions were associated with longer time from onset to imaging (p=0.014), but not with duration of symptom. Multivariate analysis revealed that men (OR 1.86, 95%CI 1.12-3.18; p=0.016), facial palsy (OR 2.72, 95%CI 1.46-5.03; p=0.002), and large-artery atherosclerotic (LAA) lesions responsible to ischemia (OR 2.03, 95%CI 1.19-3.40; p=0.009) were significantly related to positive DWI lesions. As compared to patients with a single DWI lesion, those with multiple DWI lesions were more likely to have longer time from onset to imaging (p=0.015), hypertension (p=0.008), smoking habit (p=0.031), LAA lesions (p=0.012), and previous TIA episodes within 90 days before hospitalization (p<0.001). In contrast, atrial fibrillation was found more often in patients with a single DWI lesion than in those with multiple lesions (p = 0.002).

Conclusion: This study demonstrated that DWI lesions in patients with TIA were correlated with men, facial palsy, and LAA lesions. As DWI lesion was classified into single or multiple, there might be some differences of baseline characteristics between the two groups.

A PILOT PATHWAY FOR THE DIRECT TRANSFER OF ALL STROKE PATIENTS FROM AMBULANCE TO THE CT SCANNER 24HRS A DAY – RESULTS AND CONSEQUENCES

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Background: On the basis of local and national targets a decision was made to attempt to improve the time to CT head scan for stroke patients at our hospital (a 960 bed teaching hospital in the UK). Target was admission to scan time of 1hr for all stroke patients 24 hrs a day.

Method: Prior to the pilot patients were brought to ED and seen by a senior stroke nurse and general physicians; the doctor would request a CT head scan. After Discussion with radiology, ED, ambulance service and stroke nurses a decision was made to pilot a protocol of "direct from ambulance to CT scan" for potential stroke patients. Nurses would request the CT head scans which should avoid ED assessment and consequent delay. If adopted this would provide a unique service in the UK which traditionally has struggled to provide adequate 24hr hyperacute stroke imaging. Risks identified included potentially inappropriate scanning of non-stroke patients.

Results: 182 patients went through the pilot pathway from 1/11/10 to 20/12/10. Pre-alert by the ambulance crews to the stroke teams increased from 25% before the pilot to 75% during. Prior to the pilot 15% stroke patients had their CT head scan in <1hr, during the pilot 136 (75%) had their scan within 1hr. In Nov out of 111 patients scanned 79 (71%) were strokes, 16 TIA (20%) and 16 (20%) non-strokes. These figures improved in December out of 71 scanned 59 (83%) were strokes, 7 TIA (10%) and 5 non-stroke (7%). Non-stroke diagnosis included migraine, epilepsy, sepsis and in many of these cases CT was indicated anyway. Overall after review only 4 patients in Nov and 1 patient in Dec should not have had a head scan at all.

Discussion: This pilot was considered successful. The Results improved significantly between Nov and Dec after education and further Discussion to sharpen criteria for inclusion. The rate of inappropriate scanning (5 patients/2months - 3%) is felt to be acceptable for the benefit of improved early scanning for stroke patient management.

Heart and brain

1   Heart and brain

WARFARIN LOADING DOSE GUIDED BY PHARMACOGENETICS IS EFFECTIVE AND SAFE IN CARDIOEMBOLIC STROKE PATIENTS

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Background: The clinical practice of starting the warfarin treatment with fixed loading dose driven by an effort to shorten hospitalization time is discouraged by the current guidelines but is nonetheless very prevalent. Specific group at risk of more frequent bleeding complications are patients after recent ischemic stroke.
Aim: To compare safety and efficiency of warfarin loading dose compared to maintenance dose guided with pharmacogenetics in the initiation of warfarin treatment. Primary end point was time in the treatment range (TTR, fraction of INR in range in the first 10 days). Secondary end points were: Time to the first INR in range, time to the first INR above range, the proportion of patients with serious adverse events (INR>4, bleeding, thromboembolic events, death).
Methods: Consenting cardioembolic stroke patients being initiated on warfarin were randomized to loading dose group (LDG) or maintenance dose group (MDG). Treatment was initiated either with loading dose for the first 3 days (double the estimated dose) or directly from day 1 with estimated dose. Included patients were genotyped for CYP 2C9 and VKORC1 polymorphisms and dose was estimated with published algorithm. Patients were followed up for 90 days. International normalized ratio (INR) was measured routinely on days 0-10,15,20,30 and 90. The target INR range was set as 1,8 to 3,2.
Results: 25 patients were included (13 in LDG, 12 in MDG). TTR during the first 10 days was significantly higher for the LDG (0,46 vs. 0,33 in MDG, p=0,003). Time to the first INR in range was shorter for LDG 5,4 vs. 7,6 days, ns. INR above range was reached only in 2 patients in LDG (after mean 4,5 days) and in 5 patients in MDG (21,4 days, p<0,001). The number of patients with serious adverse events was not significantly different (2 LDG, 3 MDG).
Conclusion: Warfarin loading dose guided by pharmacogenetics improved the efficiency of warfarin dose initiation without increasing the risk of adverse events.

2   Heart and brain

CONTINUOUS STROKE UNIT ECG MONITORING DETECTS INTERMITTENT ATRIAL FIBRILLATION MORE SENSITIVELY THAN 24 H HOLTER ECG AFTER ACUTE STROKE AND TIA

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Background and Purpose: The effectiveness of stroke prevention with anticoagulants has been firmly established in stroke/TIA patients suffering from atrial fibrillation (AF). Although detection of intermittent AF (iAF) in this high-risk population is important, the optimal diagnostic work-up is currently unclear. The aim of the present study was to compare the effectiveness of continuous ECG monitoring (CEM) with 24h Holter ECG for detection of iAF.
Methods: A prospective, consecutive single-center study enrolling all patients with ischemic stroke or TIA admitted to our stroke unit (SU) was performed between March 2010 and January 2011. All patients received a 12-channel ECG upon admission, and 24h Holter ECG was started within48h. CEM consisted of 2 modes. In the conventional mode, diagnosis of AF was based on the frequency-triggered arrhythmia alarm of the monitor system confirmed by 12 channel ECG. In the automatic mode, monitoring data were transferred via internet to a central server where a dedicated AF detection software based on heart rate dynamic analysis (SRAclinic®) generated AF diagnosis.
Results: Of the 824 patients admitted to the stroke unit, 564 patients fulfilled all predefined criteria for entering the data analysis. Mean age was 69±13 years, 60.1% were male. 81.1% of patients had a stroke, 18.9% a TIA. Prevalence of all AF based on documentation on the SU was 21.9%. AF was sustained in 12.6% and intermittent in 9.3% of the study population. Intermittent AF was detected by admission ECG in 34.6%. Additional CEM detected intermittent AF significantly more frequently (96.2%) than additional 24 h Holter ECG (61.5%) (p<0,01, McNemar).
Conclusions: Prevalence of iAF detected in stroke unit patients is high. CEM including an automatic dedicated AF analysis software and ECG data storage for physician review is more sensitive and sufficiently specific to replace 24 h Holter ECG for detection of iAF on stroke units.
Disclosure: Investigator-initiated study, support by ApoplexTechnologies.

3   Heart and brain

PROGNOSIS OF CEREBRAL INFARCTION ACCORDING TO CORONARY ARTERY DISEASE STATUS

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Background: there is no large study on the risk of cardiovascular events in patients with recent cerebral infarction according to presence/absence of silent coronary artery disease (CAD).
Objective: to stratify the risk of vascular event recurrence in BI patients according to CAD subgroups (no disease, silent coronary stenosis <50%, silent coronary stenosis ≥50%, and known symptomatic CAD).
Method: From June 2005 and December 2008, 378 consecutive acute BI patients regardless of stroke subtype underwent coronary angiography (n=315, median delay from stroke onset, 8 days) except if they had known CAD (n=63). Follow-up was 4 years. Follow-up visits were scheduled between three and six months after enrolment and every year thereafter. All patients had carotid and femoral artery, thoracic, and abdominal aorta ultrasound examinations at baseline. All patients signed informed consent and the study was approved by local ethics committee.
Main outcome measure: Two-year rate of a composite of vascular death, cardiac events (myocardial infarction, resuscitation after cardiac arrest, hospitalisation for unstable angina or cardiac insufficiency), stroke or peripheral arterial disease.
Results: In December 2010, the median follow-up was 37 months (interquartile range, 27 to 49); 32 patients died (20 before the two-year contact) and 6 patients had no follow-up information. At two-year, a total of 40 patients had at least 1 vascular event giving an overall estimated risk of 11.2% (95%CI, 8.3-14.9). According to the CAD subgroups at baseline, vascular event risk was 3.6% in 119 patients with no CAD, 8.4% in 112 patients with silent coronary stenosis <50%, 16.7% in 80 patients with silent coronary stenosis ≥50%, and 23.4% in 61 patients with known CAD (log-rank, p<0.0001). Using patients with no CAD as reference, the age-gender-adjusted HR (95%CI) of vascular events was 2.10 (0.63-6.96) for silent coronary stenosis <50%, 4.41 (1.36-14.27) for silent coronary stenosis ≥50% and 6.63 (2.06-21.35) for known CAD.
Conclusion: In patients with cerebral infarction, silent CAD is a strong predictor of any future cardiovascular events within two years after stroke onset.

4   Heart and brain

HIGH SENSITIVE TROPONIN (HSTNI) IN ACUTE STROKE PATIENTS

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Background: Acute ischemic stroke may occasionally be complicated by concomitant acute coronary symptoms (ACS). However, the diagnosis of myocardial infarctions in stroke patients may be missed due to the predominant neurological symptoms. A biomarker with high positive predictive value for ACS in stroke patients would therefore be desirable. For this purpose, we examined the application of high sensitive troponins (hsTNI) in an acute stroke cohort.

Methods: In a prospective study, we examined 697 consecutive patients with acute ischemic stroke from March to December 2010. HsTNI (Siemens Centaur TNI Ultra) was measured on admission day and after 3-6h if initial hsTNI was >0.045 µg/l. All patients received a 12 lead-ECG and continuous ECG monitoring according to the stroke guidelines. Laboratory and ECG findings as well as cardiac symptoms were evaluated by a cardiologist. Coronary angiography was initiated if ECG abnormalities or clinical symptoms suspective of STEMI were present.

Results: Out of 697 stroke patients, 141 (20.2%) patients showed elevated hsTNI levels at admission. By using the former standard Beckman cTrop T System, elevated troponin levels were found in 23/697 (3.3%, p<0.001, Fisher's exact test). Of the hsTNI positive patients, 30/141 (21.3%) had normalized hsTNI values after 3-6 hours. 62/141 (44.0%) showed a hsTNI increase of >30%, while 49/141 (34.8%) displayed stably elevated hsTNI levels in the follow-up measurement. 9/141 (6.4%) underwent coronary angiography followed by stenting or coronary artery bypass graft in 7/141 (5.0%). 4/141 (2.8%) were classified as having STEMI.

Conclusion: Our data demonstrate that hsTNI is elevated in about 20% of acute ischemic stroke patients. As a therapeutically relevant ACS was diagnosed in only 5%, the positive predictive value of elevated hsTNI levels in patients with acute ischemic stroke is very low. We therefore assume that elevated hsTNI levels in this cohort may rather be a systemic stress marker.

5 Heart and brain

REDUCTION OF CEREBRAL INFARCT SIZE BY DRONEDARONE

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Background and purpose: In the ATHENA trial, dronedarone reduced the incidence of stroke in patients with atrial fibrillation. Since smaller cerebral infarcts are sometimes asymptomatic, the reduced incidence of stroke might reflect reduction of infarct size (IS) by dronedarone. However, no data on this effect of dronedarone are available.

Methods: In 60 rats, the middle cerebral artery was occluded (MCAO) for 1h followed by reperfusion. IS was assessed at day 7. Animals were examined using a neurological 5 points score. Twelve animals served as controls (group A), 12 animals received 30mg/kg (group B) and 100mg/kg (group C) dronedarone daily starting 3 days before MCAO; 12 animals received 30mg/kg (group D) starting 2h after MCAO. In all groups treatment was maintained until day 7. In 12 additional animals (6 controls, 6 pretreated animals) fractional anisotropy (FA) was assessed using magnetic resonance imaging (MRI).

Results: IS in group A was 151±45mm³ versus 94±42mm³ in group B, 79±29mm³ in group C, and 127±51mm³ in group D, respectively (B,C,D P<0.05 vs. A). Neuroscores and weight loss (expressed as percent of initial weight) were less in treatment groups: 1.8±0.6 and 91% in group B, 1.4±0.5 and 93% in group C, and 2.1±0.6 and 89% in group D compared to 2.4±0.5 and 83% in controls (B,C,D P<0.05 vs. A). FA in the ischemic penumbra was significantly higher in treated than in control animals (0.44±0.2 vs. 0.35±0.17; P<0.05).

Conclusions: Dronedarone administered before and after MCAO reduces IS and improves FA and neurological outcome in transient cerebral ischemia.

6 Heart and brain

INCREASED P-WAVE DURATION ASSOCIATED WITH CRYPTOGENIC STROKE AND WITH PFO

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Introduction: P-wave abnormalities on the 12-lead electrocardiogram (ECG), including increased p-wave duration, dispersion and interatrial block (IAB), are associated with paroxysmal atrial fibrillation. Atrial arrhythmia may be a cause of stroke in some younger people with unexplained stroke. It has been suggested that the association between PFO and cryptogenic stroke may be due to associated atrial arrhythmias.

We investigated whether p-wave abnormalities were more common in cryptogenic stroke than control subjects, and if there is an association with the presence of PFO.

Methods: Patients aged ≤55 years with cryptogenic stroke and controls were recruited. A resting ECG was performed and analysed in a blinded manner using electronic callipers. Interatrial block (IAB) was defined as a duration ≥110ms.

The primary outcome was the difference in p-wave parameters between stroke patients and controls. The secondary outcomes were the difference in p-wave parameters between stroke patients with and without PFO.

Results: ECGs were obtained on 52 stroke cases (36 with a PFO; 27 large) and 23 controls.

P-wave duration was higher in cases than controls (105.0 vs 98.4 ms; p=0.024). IAB was more frequent in cases than in controls (35% vs 13%; p=0.055). P-wave duration was not significantly longer for stroke patients with a PFO, or a large PFO. IAB occurred in 13% of controls, 25% with no PFO, 33% with a small PFO and 41% with a large PFO (Chi squared test for trend 4.613; p=0.032).

In a significant linear regression model (R²=0.174, p=0.001), case-control status remained a significant predictor of p-wave duration (Beta 0.326; p=0.004).

Conclusion: P-wave duration is longer in patients with cryptogenic stroke than controls. IAB is more frequent in those with stroke, and increases in frequency with occurrence and size of PFO. The association between PFO and stroke may be in part due to atrial arrhythmia. Extended rhythm monitoring is required in younger patients with unexplained stroke.

7 Heart and brain

THE RISK OF PARADOXICAL EMBOLISM (ROPE) STUDY: INITIAL DESCRIPTION OF THE COMPLETE DATABASE

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Background: Paradoxical embolism (PE) may be a major cause of cryptogenic stroke (CS). How to determine that a discovered patent foramen ovale (PFO) is pathogenic and to predict recurrence risk for individuals is unknown. Prior studies have been limited by extremely low statistical power. The RoPE Study Aims to identify and combine extant CS databases to support robust risk modeling. Here we describe the development of the RoPE cohort.

Methods: To create the RoPE database, we identified existing databases of CS patients with known PFO status; obtained variable definitions; determined independent variables of interest; specified outcomes; defined inclusion/exclusion criteria; determined missingness across databases; and obtained additional primary data to complete each database.

Results: Twelve databases from 7 countries were obtained of patients with CS, known PFO status, and follow-up data. Eight included CS patients (with and without PFO), and 4 included only those with PFO. Of the former, PFO prevalence ranged from 21% to 64%. There was considerable variation in the definitions of several key variables (e.g. shunt grade). Many variables of potential scientific interest were not collected in most databases (e.g. comorbid DVT, Valsalva at onset, migraine). New data were acquired to complete some databases, including: outcome ascertainment (3 databases); transesophageal echocardiograms obtained and re-read (n=250); neuroimages obtained and re-read (n=1092). Characteristics of the 3634 patients in the RoPE cohort are shown in the table.

Conclusion: The RoPE Study database represents the largest database of cryptogenic stroke patients investigated for PFO and followed for recurrent events. Harmonizing the data was labor intense owing to heterogeneity across databases. Future efforts at pooled analyses may be helped by more standardization in data definitions and data collection procedures.

	Total	CODICIA	PFO-ASA	APRIS	Bern	Bern (Unpub)	PICSS	Lausanne	Toronto	Sapienza	Tufts	German	NOMASS
Total N	3634	485	581	90	159	249	250	91	121	343	81	1124	60
% with PFO	52%	62%	46%	21%	100%	100%	39%	64%	100%	39%	100%	34%	38%
Mean age (y)	54.6	56.2	42.5	69.9	51.1	51.9	57.8	46.5	46.2	61.6	57.8	58.1	63.8
Male	59%	60%	57%	50%	58%	65%	57%	57%	53%	58%	62%	62%	45%
CAD	10%	5%	–	26%	8%	18%	18%	0%	–	8%	9%	10%	15%
DM	13%	12%	4%	37%	9%	6%	19%	5%	6%	17%	16%	18%	21%
HTN	42%	35%	15%	82%	32%	33%	47%	27%	17%	57%	44%	57%	65%
Chol	29%	–	18%	34%	30%	40%	–	48%	23%	24%	44%	32%	21%
Smoker	33%	32%	48%	20%	33%	22%	29%	33%	15%	34%	16%	32%	24%

8 Heart and brain

POSTURE AFFECTS RIGHT TO LEFT SHUNT DETECTION BY CONTRAST TRANSCRANIAL DOPPLER

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Background: Right-to-left shunting (RLS) has been detected among patients with cryptogenic ischemic stroke, migraine headache with aura, during neurosurgery on a patient in a sitting position, and among divers. The best patient position to detect RLS is controversial. This study was performed to further investigate which patient position best detects RLS using contrast-enhanced transcranial Doppler examination (cTCD).
Methods: Consecutive patients with ischemic stroke or transient ischemic attack referred to our Institute's Non-invasive Cerebrovascular Laboratory for suspected paradoxical embolism were prospectively evaluated. The standard protocol for RLS detection recommended by the International Consensus Criteria was used. Each subject was examined at rest and after Valsalva maneuver (VM) in four positions - supine, right lateral decubitus, right lateral leaning, and upright sitting – in random order. RLS was graded 0 (no microbubbles [mB] detected), I (1-10 mB), II (>10 mB but no curtain), or III (curtain, shower of mB). Blood pressure, heart rate and neurological symptoms were monitored. Data were analysed using SPSS v17.0.
Results: A total of 240 patients participated in the study. RLS was detected in at least one position in 89 of the 240 patients (37.1%, 95% CI 33.1% – 43.3%). The detection of at least one mB during normal breathing was lowest in the supine position, and highest in the right lateral decubitus position. With VM, the detection of at least one mB was highest in the upright sitting position (20.4% vs 8.3%, p<0.0002). If mB were not detected in the upright sitting position, they may still be detected in other body positions. Changes in the position of the body and the injection of agitated saline were well-tolerated.
Conclusions: RLS is best detected in the upright sitting position with VM. If negative, other positions may be employed. Confirmation of our findings by other centers would be helpful.

9 Heart and brain

DETECTION OF UNDIAGNOSED SILENT AF IN PATIENTS WITH ACUTE STROKE

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Background: Stroke in patients with AF is often severe and Results in long-term disability or death. Approximately one out of five strokes is due to AF. The proportion of cardioembolic strokes may be higher than currently known because "silent AF" is underdiagnosed. Paroxysmal AF carries the same stroke risk as permanent or persistent AF. Patients with silent AF suffering a stroke and remaining undiagnosed will not receive appropriate treatment and are exposed to a higher risk of second stroke. Therefore, a more intense screening for asymptomatic AF may allow identification of more patients at risk and may lead to an initiation of an appropriate treatment to prevent future AF-related events.
Methods: We performed a prospective cohort study involving 9 German stroke-units including 1200 consecutive patients with an ischemic stroke who had no history of AF and were in sinusrhythm on admission. All patients underwent 72-hour Holter ECG within 12 hours of hospital admission. Any arrhythmia that fulfilled the ECG criteria for AF and lasted for 30 s or longer was considered as AF. The study Aims to determine the proportion of silent AF patients in this cohort, also analysing the added value of routine 72-hours Holter compared to 24-h Holter. All ECGs are additionally analysed using a computer-aided algorithm which evaluates the deformation of the PQRST-complex.
Patients will be reevaluated clinically and by 72-h ECG one year after the first visit.
Results: Until today 1160 patients are included. The inclusion period ends on January 31. The data will than be analyzed and will be ready for presentation at the ESC meeting.

Acute stroke: emergency management, stroke units and complications A

1 Acute stroke: emergency management, stroke units and complications A

THE ACUTE BRAIN CARE UNIT (ABC-UNIT) – THE INITIATION OF A MULTIDISCIPLINARY TREATMENT PROTOCOL AND SPECIAL UNIT FOR IV THROMBOLYSIS IN STROKE REDUCES THE MEDIAN DOOR-TO-NEEDLE TIME TO 26 MINUTES

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Background: The efficacy of iv thrombolysis for ischemic stroke rapidly decreases in the first few hours after stroke onset. The number needed to treat for a good outcome increases from 4 if treated within 1 hour to 14 if patients are treated 4½ after stroke onset. This means that during the first few hours following stroke onset, every second counts. The purpose of the study was to set up an Acute Brain Care Unit (ABC-Unit) and protocol to reduce the length of time between the arrival of the patient at the Emergency Room and initiation of treatment - the door-to-needle time (DNT) - in most patients below 30 minutes.
Methods: The first phase of the study consisted of a detailed evaluation in a prospective cohort of the DNT in patients treated between 2001-2005. Based on these Results an Acute Brain Care Unit protocol involving the ambulance service and the ER, radiology and neurology departments was written in the second phase of the study to improve the door-to-needle time. This protocol was also based on similar experiences in cardiology and in trauma care. Finally, the effects of this new protocol on the DNT were measured in the years 2006-2008.
Results: Table 1 shows both the Results of the first phase and after initiation of the ABC-Unit. The DNT was reduced from a median of 86 minutes to 26 minutes. Because more patients could be treated within the 3 hour (later 4½ hour

time-window) the number of patients treated at the ABC-Unit almost doubled in the first year. Over 70% of the patients were treated within 2 hour after stroke onset (Figure 1). Regarding safety, in the first 2 years of the ABC-Unit only three patients had a hemorrhage. At the conference Results covering 2006-2010 will be presented.

Table 1. Detailed time analysis (on average in minutes) before (2001-2005, n=103) and after (2006-2008, n=97) the initiation of the Acute Brain Care Unit

	Before ABC-Unit	After start ABC-Unit
Symptom onset till arrival of the ambulance at the patient	29	36
Arrival ambulance till arrival in hospital	38	32
Arrival emergency ward till CT-scan	32	6
CT-scan till start of treatment	54	19
Door-to-needle time	*86*	*26*
Symptom-to-Needle (STN-time)	*153*	*93*
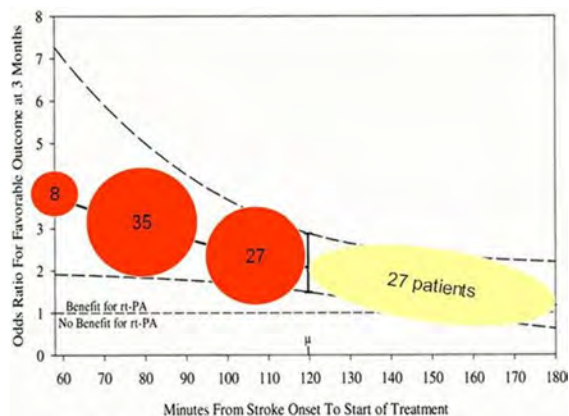
Figure 1. The number of patients and their symptom-to-needle time in the first two years of the Acute Brain Care Unit (ABC-Unit).

Conclusion: The initiation of an ABC-Unit for iv thrombolysis in stroke reduced the DNT in our centre from 86 to 26 minutes. This ABC-Unit can serve as an example for similar Units in other hospitals. At www.abc-unit.com the exact operation of the ABC-Unit is shown in a movie.

2 Acute stroke: emergency management, stroke units and complications A

DEVELOPMENT OF A DECISION ANALYTIC MODEL (DAM) TO SUPPORT DECISION-MAKING AND RISK COMMUNICATION FOR THROMBOLYTIC TREATMENT IN ACUTE STROKE CARE

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Background: Thrombolysis with iv rt-PA has improved the prognosis for acute ischaemic stroke. Decision support during the hyperacute stroke period is needed to expedite appropriate clinical assessment of eligibility for rt-PA, and communication of risks and benefits to patients/families.
Methods: A DAM was constructed to establish the likely balance of benefits and risks of thrombolytic treatment in individual patients. Probability of independence (mRS 0-2) three months post-stroke was based on a predictive equation reported in the literature (Stroke-Thrombolytic Predictive Instrument [STPI], derived from large scale trials) calibrated using data from stroke patients in the SITS-UK database. Probabilities for death at three months were derived from regression analyses of SITS-UK data; whereas, probability of symptomatic intracerebral haemorrhage (SICH) used an equation derived from SITS data.
Results: The DAM expresses probabilities for short-term (SICH, death, independence and dependence at 6-months) and long-term outcomes (QALYs), with and without rt-PA, as a function of 11 patient characteristics (age, gender, diabetes, previous stroke, NIHSS score, systolic BP, onset time to treatment, weight,

aspirin use, blood glucose and signs of current infarction on imaging). Adding blood glucose and signs of current infarction to the S-TPI predictive equation increased prediction accuracy (area under the curve increased from 0.728 to 0.741). The DAM identifies sub-groups of patients with a different balance of risks and benefits from thrombolytic treatment, including no benefit and likely harm.
Conclusion: Outcomes generated by the DAM show improved discrimination between stroke patients who may and may not maintain their independence. The DAM has been embedded within a computerised tool for supporting clinical decision-making on rt-PA and risk communication (and where appropriate engagement of patients/family members in decision-making) within the hyperacute stroke period.

3 Acute stroke: emergency management, stroke units and complications A

THROMBOLYSIS RATE AND IMPACT OF A STROKE CODE: A FRENCH HOSPITAL EXPERIENCE AND SYSTEMATIC REVIEW

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Background: Intravenous (IV) rt-pa is effective in hyperacute (HA) ischemic stroke (IS) but is administered only in few patients. Our aim was to prospectively estimate the thrombolysis rate in a stroke unit (SU) of a French hospital using a stroke code (SC) protocol with a prehospital notification system and to compare our Results with a systematic review in order to study the influence of a SC on the thrombolysis rate.
Methods: We report, from December 2005 to July 2009, the IV rt-pa rate among potentially eligible strokes in our prospective registry. The systematic review was conducted in searching PubMed and EMBASE for prospective studies from the last ten years reporting thrombolysis rates and their use of a SC. We categorized SC between those with a pre-hospital notification and those with only an in-hospital SC system.
Results: Among the 1450 stroke patients hospitalized in our stroke unit, 349 were admitted via the SC protocol as suspicions of HA strokes; 127 patients were thrombolysed, corresponding to 12.9% of IS admitted in the SU, 36% of the suspected HA strokes and 59.6% of the HAIS. We found 23 prospective studies reporting thrombolysis rates, which ranged from 10.3% to 58% of HAIS. Ten studies gave data regarding the use of a SC in HAIS and were relevant for statistical analysis. Thrombolysis rate among HAIS in the hospitals with an in-hospital restricted SC was better than those without SC (OR: 2.75, 95% CI: 1.92-3.97). Thrombolysis rate was higher in the hospitals with a prenotification (54.7%) compared with both those with no specific organization (18.2%) (OR=5.43, 95% CI: 3.84-7.73) and those with an in-hospital restricted SC (37.9%) (OR=1.97, 95% CI: 1.53-2.54).
Conclusion: Thrombolysis rate for IS is improved with a SC, especially when a pre-hospital notification system is used. This organization allows for a better cooperation between the Emergency Medical Services and the SU and could reduce pre-hospital and in-hospital delays.

4 Acute stroke: emergency management, stroke units and complications A

DEVELOPMENT AND VALIDATION OF A STROKE IDENTIFICATION INTERVIEW ALGORITHM AT DISPATCHER LEVEL

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Background: Recent innovations such as CT-installation in ambulances promise pre-hospital diagnostic stroke workup and may lead to earlier specific treatment. However, efficient use of such expensive mobile facilities requires an effective pre-selection of emergency activations by identifying patients with stroke at dispatcher level. Stroke specific interview algorithms have not yet been prospectively validated.
Methods: Information given by callers in emergency calls were analysed by two independent raters using a systematic analysis protocol for stroke or TIA (N=117), other neurological (N=39) and non-neurological (N=51) diseases. A new stroke identification interview algorithm was then established and dispatchers of the Berlin fire brigade were trained in the use of this algorithm. Sensitivity and positive predictive value were determined prospectively in patients admitted to the three Charité hospitals between Oct 16 and Dec 16, 2010.

Results: Dysphasic/dysarthric symptoms (33%), unilateral symptoms (22%) and expressed suspicion of stroke (47%) were typical information in stroke cases but infrequent in non stroke diseases (all < 10%). Convulsive symptoms (41%) were frequent in other neurological diseases but not in strokes (3%). Pain (26%) and breathlessness (31%) were often expressed in non neurological diseases (6% and 7% in strokes).

5774 patients were admitted to Charité hospitals during the validation period. Of these, 222 patients had a final diagnosis of stroke. The sensitivity of the new algorithm for detecting stroke in this sample was 53.3% and the positive predictive value for stroke and TIA was 58.5%. Of all 275 patients with stroke dispatcher code admitted to Charité hospitals, 216 (78.5%) were subsequently diagnosed with a neurological disease.

Conclusion: More than half of all strokes admitted via ambulance were correctly identified in the emergency call interview. Most of false positive stroke codes were cases with other neurological diagnoses.

5 Acute stroke: emergency management, stroke units and complications A

THROMBOLYSIS IN CERVICAL ARTERY DISSECTION - DATA FROM THE CERVICAL-ARTERY-DISSECTION-AND-ISCHEMIC-STROKE-PATIENTS (CADISP) DATABASE

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Background: Whether thrombolysis for stroke attributable to cervical artery dissection (CADStroke) is beneficial remains unclear.

Methods: We used the CADISP-database to compare outcomes of CADStroke-patients treated with and without thrombolysis. Main outcome measures were favorable 3-month-outcome (modified Rankin scale 0-2) and "major hemorrhage" (any intracranial hemorrhage (ICH), major extracranial hemorrhage). Unadjusted and adjusted odds ratios (OR[95%-confidence-intervals] were calculated.

Results: Among 612 CADStroke-patients, 68 (11.1%) received thrombolysis. Thrombolysis was applied intravenously in 81%. Thrombolysed patients had more severe strokes (median NIHSS-score 16 versus 3; p<0.001), and more often occlusions of the dissected artery (67.6% versus 39.5%; p<0.001) Fewer thrombolysed (54.4%) than nonthrombolysed CADStroke-patients (85.3%) recovered favorably.(ORunadjusted 0.21[0.12-0.35],p<0.001). After adjustment for stroke severity and presence of vessel occlusion, the odds to recover favorably were virtually identical for both treatment groups.(ORadjusted 0.95[95%CI 0.45-2.00],p=0.89). In a further analysis using a propensity matching score to reduce the effects of bias, favorable outcome was not different between 64 thrombolysed and 64 nonthrombolysed CADStroke-patients (OR 1.0[0.49-2.0]).Major hemorrhages occurred in 4 (5.9%) thrombolysed patients. All were asymptomatic ICHs. In the nonthrombolysis group, 3 (0.6%) patients had major hemorrhages (asymptomatic ICH[n=2], major extracranial hemorrhage[n=1]).

Conclusion: As thrombolysis was neither independently associated with unfavorable outcome nor with an excess of symptomatic bleedings, thrombolysis should not be withhold in CADStroke-patients. The lack of any trend towards a benefit of thrombolysis indicates the legitimacy to search for more efficient treatment options. As most patients were treated intravenously, endovascular procedures deserve testing in a comparative trial.

6 Acute stroke: emergency management, stroke units and complications A

EARLY AND ULTRAEARLY THROMBOLYSIS IN ACUTE STROKE: SEX DIFFERENCES IN STROKE OUTCOME

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Background: A recent study has shown that ultraearly thrombolysis treatment (≤70 min) is associated with better outcome in patients with moderate to severe strokes. Our objective is to study this effect according to sex.

Methods: multicenter prospective study of acute ischemic stroke patients treated with intravenous (IV) tPA at five stroke units sharing a common extra hospital stroke code and stroke care protocols (Madrid Stroke Network) (2003-2009). Variables analysed: onset to treatment time (OTT), demographic data, vascular risk factors, baseline blood pressure and glycaemia, stroke etiology according with the International Classification of stroke, basal NIHSS and 3-months modified Rankin scale (mRS) score (worse outcome was defined as mRS >2). Using multivariate logistic regression, the association between OTT and 3-months favourable outcome (mRS 0-2) according sex was studied.

Results: a total of 1140 patients were included, 53% men. Mean age (SD) was higher in women than in men (69.2 [14.2] vs. 66 [13.4], P <0.0001). Median NIHSS was 13 and median OTT 140, without sex differences. Ultraearly thrombolysis (≤ 70 min) was associated with a better outcome only in severe strokes (NISHH > 16), both in women and men: OR 3.21 (1.11 to 9.23) and 9 (1.02 to 78.69) respectively. Early treatment (<90 min) was associated with better outcome in severe strokes, but it reached the statistic significance only in women: OR 2.76 (1.26 to 5.86) and 2.64 (0.95 to 7.29) respectively.

Conclusion: Ultraearly thrombolysis (≤ 70 min) is associated with better outcome in severe strokes in both sexes. However, women could get great benefits than men from early treatment (< 90 min).

7 Acute stroke: emergency management, stroke units and complications A

EARLY SEIZURES AS AN INDEPENDENT PREDICTOR OF HIGHER MORTALITY IN INTRAVENOUS THROMBOLYSIS

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Background: early seizures (ES) have been related with bad outcome in acute ischemic stroke but there are few studies regarding to patients receiving intravenous (iv) thrombolysis.

Methods: Multicenter observational study, including consecutive acute stroke patients treated with iv tPA in 5 university hospitals during a 6 year period (2004-2009). Seizures occurring in the first 24 hours after treatment, baseline characteristics, risk factors, stroke severity (NIHSS) and etiology were recorded. Stroke outcome (NIHSS at 24 hours, 7th day and modified Rankin Scale [mRS] at 3 months) as well as hemorrhagic complications and oedema were compared between patients with and without ES. Type of seizures and antiepileptic drugs were also registered in the group of patients with ES.

Results: 824 acute stroke patients were studied, 16 with ES (1.94%). There were not differences in baseline characteristics, time to treatment or in risk factors between both groups, although those patients with ES scored higher in the NIHSS at stroke onset (17 [12-21] vs 13 [9-18] p= 0.016). Those with ES were associated with a higher mortality: OR 4.9 (95% CI 1.45-17), adjusted with confounding variables like baseline NIHSS, age and sex. There was a non-significant trend towards poorer outcome mRS ≤2: adjusted OR (aOR) 0.26 (95% CI 0.05-1.3), symptomatic cerebral hemorrhage: aOR 1.12 (95% CI 0.1-9.3) and oedema: aOR 1.22 (95% CI 0.3-3.8) in the ES group. Among patients with ES, 87.5% had an ischemic stroke in the anterior circulation and 75% had recurrent seizures during the first 24 hours. Valproate was the drug most frequently administered (50%).

Conclusion: Seizures during the first 24 hours is an independent predictor of higher mortality among patients with ischemic stroke treated with iv thrombolysis. ES may also increase the risk of complications and decrease the probability of good outcome.

Oral Session
Acute stroke: emergency management, stroke
units and complications A

Cerebrovasc Dis 2011;31(suppl 2):1–322

35

8 Acute stroke: emergency management, stroke units and complications A

EXTENDING TIME WINDOW FOR ENDOVASCULAR PROCEDURES ACCORDING TO COLLATERAL PIAL CIRCULATION

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Presence of collateral pial circulation (CPC) predicts favorable outcome in patients undergoing intra-arterial (IA) procedures. We aimed to determine if CPC may be used during the procedure to decide about pursuing recanalization efforts: Pial Collateral Score (PCS 0 to 6) was used to assess collateral flow on initial angiogram in stroke patients undergoing IA procedures. We considered good CPC when PCS was<3. We defined total time of ischemia (TTI) as onset to recanalization time and clinical improvement as>4 point decline in the discharge NIHSS. Infarct volume was measured on CT at 24 hours.

Results: We studied CPC in 61 patients (31 MCA, 30 ICA/NIHSS 18). 21 patients (34%) had good CPC. Although there were no differences at baseline between patients with good and poor CPC including NIHSS (good CPC 18 Vs 19; p=0.06), patients with good CPC had better clinical outcome (median discharge NIHSS 7 Vs 21; p=0.02) and smaller infarct volume (56 Vs 238cc; p<0.001). For patients with poor CPC a ROC curve defined<300 TTI minutes (Sens. 67%, Spec. 75%) as best predictor of improvement (TTI<300:66.7% Vs TTI>300:25%;p=0.05). In patients with good CPC degree of clinical improvement was not related to TTI. While the rate of clinical improvement was similar for patients recanalizing within 300†minutes (poor CPC 66.7% Vs good CPC 85%; p=0.38) the likelihood to experience improvement was 3 fold higher after 300†minutes only in patients with good CPC (25% Vs 86%: p=0.01).Infarct volume was also reduced by 4 fold when TTI>300†minutes (poor CPC 93cc Vs good CPC 22cc; p<0.01).

After adjusting for age and baseline NIHSS, TTI<300 emerged as an independent predictor of clinical improvement in patients with poor CPC (OR:6.6 95%CI 1.01-44.3; p=0.05) but not in patients with good CPC. In a logistic regression model presence of good CPC independently predicted improvement after adjusting for TTI, admission NIHSS and age (OR: 12.5; 95%CI: 1.6-74.8; p=0.02).

Conclusion: The presence of good CPC predicts better clinical response to IA treatment beyond 5 hours from symptom onset. Identification of good CPC may help physicians when considering to continue recanalization efforts in late time window.

9 Acute stroke: emergency management, stroke units and complications A

ADMISSION PERFUSION-CT CBV-LESION VOLUME DOES NOT PREDICT NEUROLOGIC OUTCOME OR FINAL INFARCTION VOLUME AFTER INTRAARTERIAL THROMBOLYSIS FOR ACUTE ANTERIOR CIRCULATION ISCHEMIC STROKE

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Background: In acute stroke, areas of CBV decrease in Perfusion-CT (PCT) are thought to show final infarction. Recent data indicates that CBV lesions can be reversible in patients undergoing intravenous thrombolysis. We aimed to evaluate the predictive value of PCT CBV-lesion volume (CBV-LV) for neurologic outcome and final infarction volume after intraarterial thrombolysis (iaT).

Methods: In a prospective study, 26 consecutive patients (17 w, 9 m, mean 67.5yrs ±12.1) with M1, proximal M2 or distal ICA occlusion underwent iaT within 6 hours after symptom onset (mean 4±1.2h), after noncontrast CT, PCT and CT angiography. Three raters blinded for clinicoradiologic data independently created color-coded CTP maps for CBV and processed these for volumetry of CBV lesion in comparison to the contralateral side. CBV-LVs were analyzed for their relationship with final infarct volume on CT five days post intervention, improvement of NIHSS score between admission and discharge and modified Rankin Scale (mRS) at 90d after stroke.

Results: The reperfusion rate (=TIMI 2&3) was 72%. Two patients (8%) each had asymptomatic and symptomatic parenchymal hemorrhage. Median improvement of NIHSS between admission and discharge was 7.5 (range: -12 – 19) and 58% had favourable functional outcome (mRS≤2) 90 d after stroke onset. Mean CBV-LV was 43.2 - 67.6 ccm (SD 20,7 – 26,1), whereas final infarct volume was 64.6±74.2 cccm. CBV-lesion volume showed no correlation with functional outcome at 90 days or final infarct volume, but was inversely associated with improvement on the NIHSS score (r≤0.514, p≤0.016).

Conclusion: Admission PCT CBV-LV is not a predictor for neurologic outcome and final infarction volume after iaT in our cohort. The inverse correlation between CBV-LV and improvement of NIHSS score adds to increasing data suggesting a potential reversibility of CBV lesions in the context of successful recanalization therapy.

Stroke prognosis A

1 Stroke prognosis A

PREDICTORS OF 3-DAY, 7-DAY AND 30-DAY CASE-FATALITY IN 26 818 PATIENTS WITH FIRST-EVER-ISCHEMIC STROKE

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Background: Predictors of 3-day, 7-day and 30-day case-fatality in first-ever-ischemic stroke were identified and compared to predictors of 3-months and 1-year case fatality.

Methods: A registry designed to register all hospitalized stroke patients in Denmark since 2001, holds 26 818 patients with first-ever ischemic stroke. Patients underwent evaluation including stroke severity (Scandinavian Stroke Scale, SSS), CT-scan and cardiovascular risk factors: hypertension, atrial fibrillation (AF), diabetes mellitus (DM), intermittent arterial claudication, previous myocardial infarction, smoking, and alcohol consumption; 96% were treated in Stroke Units. Survival was followed up to 1 year through the Danish Central Person Registry. Predictors of 3-day to 1-year case-fatality were identified using multiple regression analysis.

Results: In the study 48.5% were women; 51.5% were men. Mean age 71.2 (SD 13.4) years; mean SSS score 43.9 (SD 15.2). Three-day /7-day case-fatality: Stroke severity (SSS) and age were the only significant predictors of 3-day and 7-day case-fatality (non-linear effect of age/SSS); sex and cardiovascular risk factors had no predictive power. Thirty-day case-fatality: Significant predictors were age and stroke severity (non-linear effect of age/SSS), AF (no, OR 0.6) and smoking (yes, OR 1.3). Three-months/1-year case-fatality: Significant predictors were age and stroke severity (non-linear effect of age/SSS), sex (male OR 1.2/1.3), AF (no, OR 0.7/0.6) and smoking (yes, OR 1.3/1.3), ischemic heart disease (no, OR 0.7/0.7), DM (no, OR 0.8/0.8). Alcohol consumption, intermittent arterial claudication and hypertension did not influence 3-months/1-year case-fatality.

Conclusion: Only age and stroke severity were significant predictors of stroke mortality within the first 3 and 7 days after stroke. While cardiovascular risk factors influenced 3-months and 1-year case-fatality they were of no significant influence on early case-fatality rates.

2 Stroke prognosis A

FUNCTIONAL STATUS AT THREE MONTHS AS PREDICTOR OF LONG TERM SURVIVAL AND FUNCTIONALITY IN PATIENTS WITH ISCHAEMIC STROKE

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Background: Costs of long term survival after stroke represent about 50% of total healthcare expenditure with stroke. It is important to know the impact of treatment in the acute phase in a subsequent long term functional status. The objective of this study is to estimate the effect of functional status at three months on long term survival and functional status.

Methods: In a prospective community study from October 1998 to September 2000, 380 patients were registered with an ischaemic stroke among 95 816 persons registered at three health centres from Northern Portugal. Initial evaluation included socio-demographic profile, previous vascular risk factors and the OCSP classification. Patients were followed-up at 3 months, one and seven years and functional status was assessed with the modified Rankin scale.

Results: Patients had on average 72 years of age (sd=12) and 44.7% were men. The OCSP subtype was 22.9% TACI, 18.4% PACI, 40.5% LACI and 18.2% POCI. About 60% had HBP, 26.3% were diabetic and 36.3% had cardiac disease. At 3 months 46.3% were independent (Rankin<3), 36.1% dependent and 17.6% deceased. More than 50% of patients independent at 3 months were alive at 7 years, the median survival decreased to 6, 5.4 and 1.6 years in patients with Rankin equal to 3, 4 or five, respectively. Using a logistic regression model, the odds ratio of being independent at 7 years (Rankin<3 vs. others) decreased with age (0.89, 95% CI: 0.86-0.93), is 6.6 (95% CI: 2.8-15.5) in persons independent at 3 months,

3.5 (95% CI: 1.6-7.4) in women and 4.7 (95% CI: 1.7-12.8) when there was no recurrence after the first episode. Among the 133 survivors at 7 years, 96 (72.2%) kept the functional status at three months, 75 as independent and 21 as dependent.
Conclusion: The functional status three months after ischaemic stroke is associated with long term survival and functionality. Treatments that improve functionality in the short term may have major repercussions on long term functionality.

3 Stroke prognosis A

MORE SEVERE STROKES IN WOMEN THAN IN MEN IN SURVIVORS AT 3 MONTHS AFTER FIRST-EVER-ISCHEMIC STROKE. A NATIONWIDE DANISH STUDY OF 26 818 PATIENTS

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Background: Three months after stroke women are more dependent than men. Hence, outcome is believed to be worse in women. However, more women survive stroke than men, i.e. female stroke survivors are living with more severe strokes than men. We tested the hypothesis that worse functional outcome reported in women is due to female superiority in survival forcing women to live with more severe strokes than men.
Methods: A Danish registry of all hospitalized stroke patients in Denmark since 2001 holds 26 818 patients with first-ever-ischemic stroke. Patient evaluation included stroke severity (Scandinavian Stroke Scale, SSS), CT-scan and cardiovascular risk factors. Survival was followed for 3 months. Admission stroke severity was classified according to SSS: very severe 0-14; severe 15-29; moderate 30-44; mild 45-58.
Results: Mean age was 71.2 years; 48.5% women; mean SSS score 43.9. Survival, at 3-months after stroke of patients with admission SSS 0-14: Men/women 60-69 years 70/71%, 70-79 years 65/68%, 80+ years 50/55%. Survival at 3-months, admission SSS 15-29: Men/women 60-69 years 88/88%, 70-79 years 87/84%, 80+ years 72/79%. Survival at 3-months, admission SSS 30-44: Men/women 60-69 years 97/98%, 70-79 years 93/94%, 80+ years 89/91%. Survival, at 3-months, admission SSS 44-58: Men/women 60-69 years 99/99%, 70-79 years 99/99%, 80+ years 97/97%.
Conclusion: Women survived stroke better that men. Hence, female survivors at 3 months are living with more severe strokes than men of the same age. This was in particular true for patients with initially very severe and severe strokes and the oldest. The difference in stroke severity between men and women who survived at 3 months increased as age and stroke severity increased. Due to female superiority in survival women are forced to live with more severe strokes than men explaining why functional outcome is worse in women.

4 Stroke prognosis A

PREDICTION OF THE RISK OF INTRACEREBRAL HEMORRHAGE IN PATIENTS WITH ISCHEMIC STROKE TREATED WITH IV T-PA WITH 3H - APPLICATION OF THE "HAT SCORE" IN A STROKE UNIT

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Background: Intracerebral hemorrhage (ICH) is the most feared complication of thrombolytic treatment in ischemic stroke (IS). The HAT score (risk of hemorrhage after thrombolysis) has been developed to predict the risk of ICH and the prognosis at 3 months after thrombolysis in IS patients. This score is based on four risk factors: history of diabetes mellitus (DM) and pretreatment serum glucose, NIH Stroke Scale (NIHSS) score and extent of hypodensity on CT scan. We applied the HAT score in a cohort of patients admitted to our stroke unit, and we compared the Results with those previously published.
Methods: We evaluated IS patients treated with IV t-PA (tissue-plasminogen activator) within 3 hours, between 2003 and 2008, prospectively registered in a stroke database. HAT score was retrospectively applied. Predictive ability of HAT score for ICH and 3 months outcome (modified rankin scale -mRS) was calculated by receiver-operator curves (confidence interval of 95%).
Results: We analyzed 245 patients and excluded 17 (9 false stroke, 1 intra-arterial t-PA, 6 underwent t-PA after 3 hours, 1 had incomplete data). Mean age was 66.9 years (±10.73), 40.8% were female. 22% of patients had DM, 8% serum glucose at baseline>200mg/dl, 44% NHISS>15 and 9% visible hypodensity on the CT scan. The c-statistic showed a good discriminative value for symptomatic ICH (0.86 [0.79 to 0.94]), weak for total ICH (0,64 [0,56-0,72]) and exceptional for fatal ICH (0,95 [0,0-1,0]). Those c-statistic values were similar to the data calculated in 2 cohorts previously published. C-statistic values were acceptable for 3 months outcome (0.71 [0,64-0,77] for mRS≤1; 0,73 [0,66-0,79] for mRS≤2; 0,78 [0,69-0,88] for mRS≥5).

Conclusion: In our cohort, HAT score predicted the risk of total, symptomatic and fatal ICH and outcome 3 months afterwards. The Results are in accordance with those previously published, contributing to the validation of the scale and its application in clinical practice.

5 Stroke prognosis A

PREDICTORS OF HEALTH-RELATED QUALITY OF LIFE AND COGNITIVE FUNCTION AFTER INTRACEREBRAL HAEMORRHAGE: RESULTS FROM THE INTERACT PILOT PHASE

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Background: As limited data exists on health-related quality of life (HRQoL) and cognitive function after intracerebral haemorrhage (ICH), we aimed to determine the predictors of these outcomes at 90-days among patients enrolled in the pilot phase of the Intensive Blood Pressure (BP) Reduction in Acute Cerebral Haemorrhage Trial (INTERACT).
Methods: INTERACT1 (N=404) was a randomised controlled trial of early intensive BP lowering in patients with CT-confirmed ICH (<6 hrs of onset) and elevated systolic BP (systolic 150-220 mmHg) undertaken during 2005-07. HRQoL and cognitive function were determined using the EuroQoL questionnaire and Mini-Mental State Examination, respectively, by in-person interviews with 90-day survivors. Multivariate logistic regression analysis (with significant univariate variables forced with age, sex, ethnicity, time from onset to presentation, and randomised treatment) was performed to identify predictors of "low" HRQoL (according to overall utility score < median [0.77]; domain scores 2 or 3 versus 1; visual analogue scale (VAS) score <80) and "low" MMSE (≤23).
Findings: Predictors of low overall HRQoL (n=328) were high NIHSS (≥9 vs <9, odds ratio [OR] 4.23, 95% confidence interval [CI] 2.50-7.15) and age (per 10 yr, OR 1.32, 95%CI 1.08-1.61). Haematoma volume (per 1 ml) predicted low levels of mobility (OR 1.03, 95%CI 1.01-1.06), self-care (OR 1.03 95%CI 1.01-1.06) and usual activity (OR 1.02 95%CI 1.00-1.05) but not pain and discomfort or anxiety scores. The predictors for low MMSE (n=214) were age (OR 2.50, 95%CI 1.76-3.54), time from onset to presentation (per 1 hr) (OR 1.56, 95%CI 1.14-2.13) and high NIHSS (OR 4.87, 95%CI 2.25-10.58).
Interpretation: HRQoL and cognitive function appear related to age and initial clinical severity of ICH. Size of initial hematoma volume influenced subsequent physical outcomes, but not the non-physical parameters of pain/discomfort, anxiety and cognition.

6 Stroke prognosis A

HIGH SERUM GLUCOSE AND FUNCTIONAL OUTCOME IN PATIENTS WITH ACUTE ISCHEMIC STROKE AND MECHANICAL THROMBECTOMY

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Background and purpose: Hyperglycemia has been associated with poor outcome and resistance to recanalization in patients treated with intravenous (i.v.) tPA. Hyperglycemia may increase PAI-1 and decrease tPA activity. We aimed to study the impact of hyperglycemia in patients with acute stroke treated with mechanical thrombectomy compared to those who received i.v. tPA.
Methods: From May 2005 to April 2010, we prospectively registered 237 consecutive patients treated with reperfusion therapies and documented arterial occlusion. Of them, 176 were treated only with i.v. tPA (TPA group) and 61 with mechanical thrombectomy (MT group). In 27 patients MT was performed after i.v. tPA. Complete recanalization was considered, using transcranial Duplex, if it was achieved TIBI IV or V in TPA group, and graded using the TICI criteria, if it was achieved 2b or 3 in the MT group. Poor outcome at 3 months was considered as a Rankin>2. We evaluate the interaction of baseline serum glucose by treatment group on functional outcome at 3 months by logistic regression analysis.
Results: Median baseline NIHSS was 13.5[9,18] in TPA and 18,5[15,22] in the MT, and mean serum glucose was 129 ± 43 mg/dl and 132 ± 39 respectively. Complete recanalization (within 2 hours from tPA or after MT) occurred in 58 patients (33%) of the TPA and in 44 (72%) of the MT group, and poor outcome was recorded in 86 (48%) and in 42 (68%) patients, respectively. High NIHSS (OR:1.16 CI 1.1 to 1.2;p<0.001), older age (OR:1.04 CI 1.01 to 1.07;p=0.02), higher basal glycemia

(OR:1.9 CI 1.01 to 3.8;p=0.049) and absence of complete recanalization (OR:4.1 CI 2.06 to 8.5; p<0.001) were independently associated with poor outcome. There was negative serum glucose by treatment interaction: The adjusted OR for poor functional outcome was 1.8 in the TPA and 1.6 in the MT group.

Conclusions: These findings can not support the idea of a distinct harmful effect of high serum glucose levels in patients treated with i.v. TPA or with MT.

7 Stroke prognosis A

LONG-TERM MORTALITY AND STROKE RECURRENCE IN PATIENTS WITH ISCHEMIC STROKE AND ATRIAL FIBRILLATION ARE ASSOCIATED WITH THE TYPE OF ATRIAL FIBRILLATION

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Background: There are only scarce data whether long-term outcome and mortality is different among different types of atrial fibrillation (AF). Aim of this study was to determine whether the type of atrial fibrillation is an independent predictor of long-term outcome in patients with ischemic stroke.

Methods: We used data from all consecutive patients registered in the Athens Stroke Outcome Project registered between 2003 and 2009. Outcome was assessed by all-cause mortality, stroke recurrence or a composite endpoint of the main cardiovascular complications. Kaplan –Meier curves of the probability to remain free of stroke recurrence, of all-cause death and of the composite event during 10-years follow up were generated. Uni- and multivariate Cox Proportional Hazard models were used to determine whether the type of AF is an independent predictor of 10-year all-cause mortality and 10-year composite CVD event.

Results: 846 patients with AF were identified from a pool of 2445 patients. 366 patients (43.2%) had permanent AF, 214 (25.3%) newly diagnosed AF, 166 (19.6%) paroxysmal AF and 101 (11.9%) persistent AF. 152 (18%) of patients had a recurrent stroke during the 10 years follow up. The 10-years rate of being free of stroke recurrence was significantly less in patients with permanent AF (log-rank p=0.01). During the first 10 years after the index event, 485 patients (57.3%) died and 206 (24.1%) composite events occurred. The 10-years probability of survival as well as of being free from the composite event was statistically significantly higher in patients with paroxysmal AF (log-rank p<0.001). The type of AF was an independent predictor of 10-years all-cause mortality.

Conclusion: Long-term mortality and stroke recurrence in patients with ischemic stroke and atrial fibrillation are associated with the type of atrial fibrillation.

8 Stroke prognosis A

DEVELOPMENT AND EXTERNAL VALIDATION OF A BASIC CLINICAL SCORE (A²DS²) FOR PREDICTING PNEUMONIA AFTER ACUTE ISCHEMIC STROKE: THE BERLIN STROKE REGISTER AND THE STROKE REGISTER NORTHWEST-GERMANY

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Background: Post-stroke pneumonia is a potentially modifiable complication after stroke showing consistent association with poor outcome. We developed and externally validated a prognostic score for predicting risk of post-stroke pneumonia based on clinical data.

Methods: The prognostic score was developed based on routinely collected clinical parameters from the Berlin Stroke Register (BSR), a network of 14 acute care stroke units in Berlin, Germany. Association of demographics, comorbidities and clinical characteristics with post-stroke pneumonia during hospitalisation was investigated using multivariable logistic regression analyses. Variables to be identified as independent predictors of post-stroke pneumonia were translated into a point scoring system. The properties of the developed basic score were externally validated using an independent data set from the Stroke Register Northwest-Germany, consisting of 140 acute care hospitals.

Results: Between 2007 and 2009 15.335 patients with ischemic stroke were registered within the BSR; mean age was 71 years, 51% were female. 7% of the patients suffered from post-stroke pneumonia. A 10-point score was derived for prediction of post-stroke pneumonia (Age [≥75 years=1], Atrial fibrillation [presence=1], Dysphagia [presence=2], Sex [male=1], Stroke severity [NIHSS 0-4=0, 5-15=3, ≥16=5], A²DS²). The score demonstrated excellent discrimination properties in the derivation and the validation cohort (c-statistics: derivation 0.84; validation 0.84). Defining patients with a A²DS² score of ≥5 to be at high risk for post-stroke pneumonia yields to sensitivity of 82.6% and specificity of 71.5% in the derivation and of 83.3% and 70.2% in the validation cohort.

Conclusions: The A²DS² score is a valid tool for predicting post-stroke pneumonia based on routinely available data that might be useful in clinical routine to justify increased monitoring and tailored prophylactic measures in patients at high risk for post-stroke pneumonia.

9 Stroke prognosis A

DEVELOPING PREDICTIVE MODELS OF EXCELLENT AND DEVASTATING OUTCOME AFTER STROKE

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Background: Functional status following stroke has been used as a primary outcome in stroke research, most commonly using the modified Rankin score (mRS). Models to predict such outcomes may be useful; in balancing groups in randomised trials, for comparison of outcomes between stroke centers and may assist clinically in outcome prediction. The aim of this study was to firstly identify variables predictive of both excellent (mRS 0-1) and devastating outcomes (mRS 5-6), and to develop models of these outcomes.

Methods: Patients admitted with a diagnosis of ischemic or hemorrhagic stroke in 2001-02 to the Halifax Infirmary, Nova Scotia, Canada, were enrolled in the Stroke Outcomes Study. Sixteen clinical variables from the first neurological assessment and six radiological variables from the acute CT scan were used to model outcome at six months (mRS) using multivariate analysis.

Results: Of 538 stroke patients enrolled, 30% had an excellent outcome and 30% had a devastating outcome six months after stroke. Three models of excellent outcome were developed (AUC 0.866-882) including different combinations of the variables age, pre-stroke functional status, stroke severity, being able to lift both arms and walk independently, normal verbal GCS and leukoaraiosis. Predictive models of devastating outcome produced three models (AUC 0.859-0.874) including the aforementioned variables and in addition living alone, total anterior circulation stroke, but not ability to walk. Leukoaraiosis was the only independent radiological predictor in models of both outcomes. There was no statistical difference between model performance for either outcome (p>0.05, ANOVA). The simplest models were externally validated for both excellent and devastating outcomes in the Oxfordshire community stroke project dataset (AUC 0.856 and 0.885 respectively).

Conclusion: This study demonstrates two new externally validated predictive models of excellent and devastating outcome. The importance of leukoaraiosis in outcome prediction may relate to risk of cognitive impairment and infarct growth post stroke. Living alone pre-stroke is an independent predictor of a devastating outcome post-stroke.

Etiology of stroke and risk factors A

1 Etiology of stroke and risk factors A

PREVOTELLA INTERMEDIA INFECTION ASSOCIATE WITH ATHEROTHROMBOTIC STROKE – PERIODONTAL BACTERIA ANTIBODY TITRATION IN ISCHEMIC STROKE (PERIODONTITIS) STUDY

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Periodontal bacterial infection is observed in around 80% of Japanese adults. It was reported that some periodontal bacteria were observed in atherosclerotic region. In the present study, we have evaluated serum antibody titer of periodontal bacteria, and its association with ischemic stroke.

Methods: Acute ischemic stroke patients (n=132; 74 male and 58 female, 71.3±10.7 years) who had been treated in Kagawa University Hospital and non-stroke patients (n=111; 46 male and 65 female, 57.6±14.9 years) who were admitted to Osaka Neurosurgical Hospital outpatient clinic were enrolled in the present study. Stroke subtype was determined with NINDS classification. Serum was obtained from each patient with consent to this study. Serum antibody titer of Actinobacillus actinomycetemcomilans (Aa), Porphyromonas gingivalis (Pg), and Prevotella intermedia (Pi) were evaluated.

Results: Antibody titer of Pi, but not Aa and Pg, was significantly higher in acute ischemic stroke patients compared with non-stroke patients (Pi: 383.8±293.9U/ml vs. 317.1±183.1U/ml, p<0.005; Aa: 78.0±15.7U/ml vs. 126.9±17.1U/ml; Pg: 135.6±13.2U/ml vs. 110.8±14.4U/ml, respectively). Among ischemic stroke subtype, the patients with atherothrombotic stroke had the highest antibody titer of Pi (465.2±324.0U/ml, n=52; p<0.001). To access the reason of high antibody titer of Pi in the patients with atherothrombotic stroke patients, we have next evaluated an association of carotid artery atherosclerosis and antibody titer of Pi. In the patients with carotid artery atherosclerosis, antibody titers were higher than those of the patients who had no carotid artery atherosclerosis (453.0±292.0U/ml vs. 309.7±218.1U/ml, p<0.001).

Conclusion: From our Results, Pi infection, but not Aa and Pg, may be associated with carotid artery atherosclerosis. And, through this association, Pi infection may lead the occurrence of atherothrombotic stroke.

2 Etiology of stroke and risk factors A

SERUM LIVER ENZYME LEVELS AND THE RISK OF STROKE IN THE GENERAL POPULATION: THE ROTTERDAM STUDY

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Background: Liver diseases are putative risk factors for both cerebral infarction and intracerebral hemorrhage, through impairment of metabolic processes and coagulation. However, this association has not been investigated thoroughly at a population-based level. The aim of this study was to investigate the association between liver enzyme levels and the long-term risk of stroke in a large prospective cohort of community-dwelling elderly people.

Methods: The study was part of the Rotterdam Study and included 4876 participants aged 55 years or older who were stroke-free at baseline (1990-1993). Non-fasting serum levels of the following enzymes were determined at baseline: aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), gamma-glutamyltranspeptidase (GGT), alkaline phosphatase (AP), and lactate dehydrogenase (LD). Follow-up for incident stroke was complete up to January 1, 2009. Cox-regression models were used to determine associations between liver enzyme levels and stroke risk, adjusted for age and sex and for potential confounders.

Results: During 58,089 person years of follow-up (median 13.9 years), 716 participants developed a stroke, of which 368 were classified as cerebral infarction, 64 as intracerebral hemorrhage, and 284 as unspecified. AP levels were associated with risk of intracerebral hemorrhage [hazard ratio (HR) per SD increase: 1.20; 95% CI: 1.04-1.39], but not with cerebral infarction. Increasing LD levels were also associated with risk of intracerebral hemorrhage [HR per SD: 1.42; 95% CI: 1.14-1.78], but not with cerebral infarction. ASAT, ALAT and GGT levels were not significantly associated with risk of stroke or any of its subtypes.

Conclusion: Serum AP and LD levels, but not ASAT, ALAT and GGT levels, are associated with the long term risk of intracerebral hemorrhage in the general elderly population. None of the liver enzyme levels were associated with the long-term risk of cerebral infarction.

3 Etiology of stroke and risk factors A

LACK OF ASSOCIATION BETWEEN GENETIC VARIATIONS IN THE KALRN LOCUS AND ISCHEMIC STROKE

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Background: Kalirin is a multifunctional brain specific Rho guanine nucleotide exchange factor, and association between genetic variants in the kalirin gene (KALRN) locus and ischemic stroke (IS) and coronary artery disease has been

reported. The aim of the present study was to investigate if genetic variants in the KALRN locus are associated with IS and/or IS stroke subtypes.

Method: Five SNPs were analyzed in the Sahlgrenska Academy Study on Ischemic Stroke (SAHLSIS). SAHLSIS comprises 844 patients, who suffered from IS before reaching the age of 70 years, and 668 healthy controls. The patients were classified according to TOAST criteria into the IS etiologic categories large-vessel disease (n=111), small-vessel disease (n=165), cardioembolic stroke (n=151), other determined cause of stroke (n=92), cryptogenic stroke (n=206), and undetermined stroke (n=119). Two other Swedish case-control materials, Lund Stroke Register with 1864 patients and 960 controls and Malmö Diet and Cancer Study with 898 patients and 900 controls, were used to replicate Results on overall IS.

Results: Associations between ischemic stroke and genetic variants in the KALRN locus (rs9289231 and rs13075202) were found in SAHLSIS, but they could not be replicated in any of the other two samples. Additionally, independent associations with the IS subtype of cardioembolic stroke were detected for both rs9289231 and rs1307520 in SAHLSIS.

Conclusion: In these Swedish samples genetic variants in the KALRN locus are not associated with overall IS.

4 Etiology of stroke and risk factors A

SEARCHING FOR A SHARED GENETIC BACKGROUND IN INTRACRANIAL AND ABDOMINAL AORTIC ANEURYSMS USING A META-ANALYSIS AND POLYGENIC ANALYSIS

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Background: A genetic predisposition for intracranial aneurysms (IA) and abdominal aortic aneurysms (AAA) has been proven, with evidence for at least one shared genetic risk locus (9p21.3). We suggest additional shared genetic risk factors for IA and AAA. We performed a meta-analysis and polygenic analysis using genotyping Results from Dutch IA and AAA patients genotyped in previous genome wide association studies (GWAS).

Methods: We tested associations of over 2 million genotyped and imputed SNPs in a Dutch IA (709 cases, 2692 controls) and AAA (807 cases, 1909 controls) cohort. We used a meta-analysis to combine the IA and AAA association Results. For polygenic analysis, we selected sets of SNPs from the IA GWAS with p-values below different thresholds, ranging from 5e-8 to 0.5. For these SNP sets, we calculated risk scores by counting the number of risk alleles in each AAA sample. We tested the difference in risk scores between AAA cases and controls. We repeated this for IA samples, with scores based on SNPs from the AAA GWAS.

Results: The meta-analysis reveals genome-wide significant (p<5e-8) associations for SNPs at locus 9p21.3. Risk scores based on large numbers of SNPs associated with IA are significantly different between AAA cases and controls, and vice versa. This difference increases when more SNPs are included in the model, by changing the p-value threshold. The largest risk score difference between IA cases and controls (p=1.5e-10) is based on 50665 SNPs (p<0.2 in AAA) and explains 1.85% of IA disease variance. A difference between AAA cases and controls (1.6e-10) based on 73818 SNPs (p<0.4 in IA) explains 2.14% of disease variance in AAA.

Conclusion: This study confirms locus 9p21.3 as a shared genetic risk factor in IA and AAA. Furthermore, thousands of common variants with small individual effect sizes in IA collectively contribute to the risk of AAA, and vice versa. This suggests an additional overlap in the genetic Background of IA and AAA.

5 Etiology of stroke and risk factors A

FGG GENE VARIATIONS ARE ASSOCIATED WITH LEVELS OF FIBRINOGEN GAMMA' IN STROKE PATIENTS BUT NOT WITH STROKE RISK

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Introduction: Fibrinogen gamma', an isoform of fibrinogen, is associated with the risk of thromboembolic disorders, such as stroke. It is produced after alternative mRNA processing of the FGG transcript. Genetic variations in the FGG gene have been shown to decrease levels of fibrinogen gamma' and increase risk of

thromboembolic disorders. For ischemic and hemorrhagic stroke these associations have been studied sparsely, and studies on FGG gene variations on stroke risk have conflicting Results. Therefore we aimed to determine the associations of FGG haplotypes with fibrinogen gamma' levels and risk of stroke.

Methods: We included 157 controls, 38 patients with intracerebral hemorrhage and 157 with ischemic stroke. Three common haplotypes were formed by 2 tagging SNPs, rs2066861 and rs1049636. We measured fibrinogen gamma' levels and total fibrinogen levels. Multiple linear regression and multiple logistic regression, adjusted for age and sex, were used to study the associations.

Results: The allele frequencies of haplotype (H)1, H2 and H3 were 44%, 27% and 29%, respectively. In the total group H2 was associated with lower fibrinogen gamma' levels and gamma'/total fibrinogen ratio, compared with H1 (186.8 vs 255.2 mg/l, p=1.5e-8 and 0.071 vs 0.089, p=6.7e-10, respectively). Similar associations were seen in (ischemic and hemorrhagic) stroke patients and controls. H3 gave significantly higher levels of the gamma' ratio (0.098; p=0.001 vs H1) in controls and patients with ischemic stroke, but not in patients with intracerebral hemorrhage. We found no associations between haplotypes and risk of ischemic or hemorrhagic stroke.

Conclusions: Genetic variations in the FGG gene are associated with both increased and decreased levels of fibrinogen gamma'. We found no association between FGG haplotypes and risk of ischemic or hemorrhagic stroke.

6 Etiology of stroke and risk factors A

LOW VITAMIN D LEVELS ARE ASSOCIATED WITH INCREASED RISK OF STROKE IN OLDER ADULTS

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Background: Accumulating evidence suggests that vitamin D deficiency may increase the risk of cardiovascular disease. However, it is uncertain whether low vitamin D levels are associated with an increased risk of stroke.

Methods: As part of the German Epidemiological Trial on Ankle-Brachial Index (getABI), serum levels of 25-hydroxyvitamin D (25(OH)D) were measured in 6803 ambulatory primary-care patients aged ≥65 years (mean age 73 years; 58% women). Participants had their baseline examination in October 2001 and were followed for up to 7 years. The association between baseline vitamin D status and the risk of stroke during follow-up was examined by Cox proportional hazards analysis.

Results: During a mean follow-up of 5.7 years, 249 participants had a stroke (84% ischaemic), a stroke rate of 6.5 per 1000 person-years. Across quartiles of 25(OH)D levels, the risk of any stroke and the risk of ischaemic stroke increased with decreasing 25(OH)D (p for trend <0.001 and 0.02, respectively); compared to participants in the highest 25(OH)D quartile (> 53.7 nmol/L), participants in the lowest 25(OH)D quartile (< 24.5 nmol/L) had twice the risk of any stroke (HR 2.0, 95% CI 1.4-2.9) and a 70% higher risk of ischaemic stroke (1.7, 1.1-2.6) in Cox regression analysis adjusted for potential confounders (age, sex, education, smoking status, body mass index, renal function, prior stroke). Additional adjustment for conventional risk factors and cardiovascular disease as potential causal intermediates slightly attenuated these associations (any stroke: 1.8, 1.2-2.6; ischaemic stroke: 1.5, 1.0-2.3). Excluding 310 participants with prior stroke from analysis did not substantially change the Results.

Conclusion: Low vitamin D levels were associated with an increased long-term risk of stroke in this prospective cohort study. This association was independent of potential confounders and only partly mediated by conventional risk factors and cardiovascular disease.

7 Etiology of stroke and risk factors A

POPULATION BASED STUDY OF THE PREVALENCE OF FABRY DISEASE IN UNSELECTED PATIENTS WITH TIA OR STROKE

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Background: Fabry disease is an X-linked recessive lysosomal storage disorder which can be, among other symptoms, associated with cerebrovascular disease.

In recent years the prevalence of Fabry disease, especially in young patients with stroke/TIA, has been reported to be up to 1.2% in cryptogenic stroke patients aged ≤55 years. However, there have been no population-based studies in unselected patients with TIA or stroke across the full range of ages.

Methods: We determined the prevalence of Fabry disease mutations in consecutive patients from a population-based study of acute TIA or ischaemic stroke (Oxford Vascular Study). DNA samples were diluted to optimal concentration and then all exons of the GLA gene, including all intron/exon boundaries, were amplified by PCR in seven separate reactions. All PCR products were submitted to DHPLC analysis, and all samples where the DHPLC indicated a possible mutation were reamplified, using a second set of PCR primers, and sequenced using standard automated sequencing protocols. Sequencing analysis was carried out using Mutation Surveyor software (Softgenetics).

Results: Samples of 1113 patients (52% females; mean age 73 years; 10% age ≤55; 613 stroke; 500 TIA) were tested. No patient had a known gene mutation responsible for Fabry disease. However, in 252 (23%) samples, a known polymorphism or sequence variation in the GLA gene was identified. This rate of polymorphisms was similar to that found in a control cohort of 1700 patients with myocardial infarction tested in our laboratory and is likely to be the normal population Background rate.

Conclusion: Fabry disease is rare in an unselected group of UK patients with TIA or stroke. Larger studies in unselected younger patients with cryptogenic stroke are required to determine whether routine screening is justified in this group.

8 Etiology of stroke and risk factors A

STROKE AND LONG-TERM EXPOSURE TO AIR POLLUTION: A COHORT STUDY

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Background: Short-term exposure to air pollution can trigger stroke. Whether long-term exposure to air pollution can lead to the development of stroke is not yet established. We examined the association between exposure to traffic-related air pollution over 35 years and stroke incidence in a prospective cohort study.

Methods: We followed 57 053 participants of the Danish Diet, Cancer and Health cohort in the Hospital Discharge Register for first-ever hospital admission for stroke (incident stroke) between baseline (1993-1997) and 2006 and denoted fatal strokes in those who died within 30 days of stroke admission. We estimated the annual mean levels of nitrogen dioxide (NO2) at residential addresses of the cohort participants since 1971. We assessed the association between exposure to air pollution and incident and fatal stroke by Cox regression analyses for the full cohort, separately for stroke sub-types (ischemic, hemorrhagic stroke, and non-specified), and for participants with and without co-morbid conditions including heart disease, asthma, or chronic obstructive pulmonary disease.

Results: Over a mean follow-up of 9.8 years of 52 215 eligible subjects, there were 1 984 (3.8%) first hospital admissions for stroke, of whom 142 (7.2%) died within 30 days. An increase of 5.7 μg/m³ of NO2 levels was associated with a 5% increase in the risk of stroke hospitalization, (hazard ratio 1.05; 95% confidence interval 0.99-1.11), and a 22% increase in the risk of a death from stroke (1.22; 1.00-1.50). Ischemic but not hemorrhagic stroke was associated with air pollution.

Conclusions: Long-term exposure to traffic related air pollution may contribute to the development of and death from ischemic but not hemorrhagic stroke. Air pollution is risk factor for ischemic stroke.

9 Etiology of stroke and risk factors A

HAZARDOUS WORKING CONDITIONS AND INCREASED RISK OF HEMORRHAGIC STROKE

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Background: Physical and psychological stresses confronted during labor may harm worker's health, thereby increasing the risk of stroke. However, such an association has not been documented in hemorrhagic stroke (HS). We aim to investigate whether demanding working conditions are associated with increased risk of HS.

Methods: The Acute Brain Bleeding Analysis (ABBA) study was a multicenter case–control study in which subjects were recruited from 33 hospitals in Korea with nationwide coverage. Each HS case was 1:2 matched to hospital and community controls (age- and sex- matched), and 940 HS cases with 1880 controls were recruited. Highly structured questionnaires were used to collect information on working conditions including occupation, regular working hour, duration of strenuous activities in regular work, and shift work, directly from HS cases and their controls. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated by conditional logistic regression analyses, adjusted for family history of stroke, hypertension, current smoking and regular alcohol drinking.

Results: Compared to white-collar workers, blue-collar workers had significantly higher odds of HS (aOR 1.46, CI 1.19–1.79) but not those in housewives or unemployed (aOR 0.92, CI 0.68–1.23). With increment of regular working time, the risk of HS was also elevated (aOR 0.87, CI 0.66–1.15 for 5–8 hour/day; aOR 1.35, CI 1.03–1.77 for 9–12 hour/day; aOR 1.98, 95% CI 1.36–2.87 for ≥13 hour/day; compared to ≤4 hour/day). The duration of strenuous activities in regular working time was also associated with HS (aOR 1.27, CI 0.93–1.72 for 1–7 hour/week; aOR 1.89, CI 1.51–2.37 for ≥8 hour/week; compared to none). However, shift work was not associated with increased odds of HS (aOR 1.02, CI 0.56–1.82).

Conclusions: This study shows that physically demanding working conditions, such as blue-collar job, extended working time and longer duration of strenuous activities, may be a risk factor for HS.

Rehabilitation and reorganisation after stroke A

1 Rehabilitation and reorganisation after stroke A

PROFILE OF VISUAL FIELD LOSS FOLLOWING STROKE

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Background: Purpose of this study was to document the profile of visual field loss occurring in stroke survivors including associated symptoms and visual impairment, types of field loss, type of stroke, management, quality of life and outcome.

Methods: Prospective, multi-centre, observation study with standardised referral and assessment forms across 21 UK sites. Visual field assessment included confrontation and quantitative perimetry Methods. Multi-centre ethical approval and informed patient consent was obtained.

Results: 1345 patients were referred with suspected visual difficulty. 915 patients were recruited with mean age of 69.18 years (SD 14.19). 479 (52.3%) had visual field loss: 404 patients had been referred with symptoms of field loss. 3.5% had ocular pathology to explain their field loss. Visual field loss was significantly more left-sided (52.8%) than right sided (37.5%) or bilateral (p=0.0001 t-test). 1.4% of field loss was longstanding from a prior stroke. The most common type of loss was homonymous hemianopia (75%) followed by quadrantanopia (15.4%). Stroke type was infarct in 86.2% and most common area of lesion was occipital and parietal lobes (60.3%). Mean vision-related quality of life was 65.69 (SD: 18.07). Treatment included compensatory strategies, refraction, prisms, low vision aids and partial sight registration. 13.4% of patients were discharged, 74.9% were reviewed and 11.7% were referred for specialist assessment. Of those reviewed, 50.7% had static field loss, 38% improved and 7.3% had normal visual fields.

Conclusions: Visual field loss occurred in approximately 50% of stroke survivors with suspected visual difficulty. This was mostly homonymous hemianopia of complete or partial extent and often left sided. Quality of life score for vision was less than normal subject scores. Field loss was mostly due to occipital or parietal lobe infarcts. All patients received treatment and advice. The extent of field loss remained unchanged over time in 50%, improved in 38% and returned to normal in 7%.

2 Rehabilitation and reorganisation after stroke A

IMPROVEMENTS OF PARAFOVEAL VISUAL FIELD ARE ASSOCIATED WITH INCREASED READING SPEED AFTER VISION RESTORATION TRAINING

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Background: Subjects with homonymous visual field defects (HFD) frequently suffer from reduced reading speed. It was studied whether increased visual functioning after vision restoration training (VRT) would coincide with improved reading abilities.

Methods: Reading speed of 11 subjects 1.5 years after posterior-parietal stroke was measured with Radner Charts before and after 6-months VRT (1h daily repeated light stimulation in partially damaged visual field). VRT outcome measures were the number of detected light stimuli in eye-tracker controlled high resolution perimetry (HRP) and the spared visual field within the affected hemifield up to the relative and absolute defect visual field border (square degrees). Enlargements of spared visual field within the affected hemifield were correlated with changes of reading speed after VRT.

Results: After VRT, the number of detected light stimuli increased by 5.02±4.31% (M±SD) (p=0.03). Visual field enlargements were observed for relative (18.09±32.35 before, 137.40±53.32 after VRT; p=0.006) and absolute defect visual field borders (36.95±33.77SD before, 152.02±49.70 after VRT; p=0.005). In parallel reading speed increased from 108.95±33.95 words/min. before VRT to 122.26±30.35 after VRT (p=0.017) which significantly correlated with enlargements of spared visual field up to the relative defect visual field border (r=0.73, p=0.016). Interestingly, this did not correlate with the area of sparing up to the absolute defect visual field border nor with the global increase of detected light stimuli. Eye movements (post/pre-difference) did not correlate with VRT outcome measures.

Conclusion: VRT improved visual fields in parafoveal areas which are most relevant for reading. This can not be explained by changes in eye-movement behaviour. Because of a significant association between improvements of parafoveal vision and reading speed, we propose that HFD patients with reading deficits may benefit from visual stimulation by training.

3 Rehabilitation and reorganisation after stroke A

CIRCUIT CLASS THERAPY FOR IMPROVING MOBILITY AFTER STROKE. AN UPDATED COCHRANE REVIEW

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Background: Circuit class therapy (CCT) offers a supervised group training forum that enables increased task-specific practice time without increasing staffing. The aim of this review was to examine the effectiveness of CCT on mobility in adults with stroke.

Method: Update of a Cochrane systematic review including randomised or quasi-randomised controlled trials involving adult stroke participants receiving CCT.

Results: An additional four trials (492 participants) were included, taking the total number of included trials to six (total 784 participants). CCT remained superior to the comparison intervention (standard care therapy or no therapy) on a number of variables: the positive effect for 6 minute walk test reduced (MD, fixed 65.88m, 95%CI 33.26 to 98.49) and the effect for walking speed increased (MD, fixed 0.15m/s, 95% CI 0.04 to 0.25). No change was found with balance: CCT was superior to comparison on some tests (Step Test: MD, fixed 3.09 steps, 95%CI 0.31 to 5.86, p=0.03; Activities-specific Balance and Confidence: MD, fixed 7.76, 95% CI 0.66 to 14.87, p=0.03) but not others (BBS: MD 0.32 points, 95% CI -0.82 to 1.45). The effect of CCT reducing length of hospital stay was lost (MD, fixed -0.39 days, 95%CI -2.87 to 2.08) although the statistical heterogeneity of this analysis is unacceptable (I2=71%). Risk of bias was assessed as low across the studies.

Conclusion: CCT is effective in improving mobility for people after moderate stroke. In contrast to the Results of the original review, CCT may not reduce hospital length of stay. Further research investigating the differential effects of stroke severity, latency and age, as well as the economic impact of this model of service delivery is required. A current large Australian multicentre trial (CIRCIT) is examining the effectiveness and cost-effectiveness of CCT for people receiving rehabilitation early after stroke.

4 Rehabilitation and reorganisation after stroke A

EARLY SAFETY AND EFFICACY OF THEOPHYLLINE TO PROMOTE POST-STROKE MOTOR RECOVERY

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Background: There is evidence that GABA mechanisms play an important role in stroke recovery, shown by animal models when GABA is inhibited, and by transient re-emergence of stroke deficits in recovered patients after administration of GABA agonists. We studied whether low-dose theophylline, a GABA-A antagonist, would be safe for patients during acute stroke rehabilitation and whether there would be early evidence of efficacy for improved motor recovery.

Methods: In a double-blinded study, we enrolled 12 first-time ischemic stroke patients who had weakness 2 weeks after stroke and assigned them randomly to receive theophylline 300 mg each day before their usual rehabilitation for a period of two weeks, or to receive a placebo dose before therapy. Patients had baseline assessment with the Fugl-Meyer Motor Scale (FM), repeated again the day after the medication period.

Results: There were 4 males/8 females with a mean age of 74.5 years old (range 38-93). On average, they were 16.8 days since stroke onset (range 8 – 30). The mean pre-drug FM score (0 – 100) of patients assigned to theophylline was 58 (SD =17.98) and placebo 54.8 (SD=23). After the drug period, the mean FM Score for the theophylline group was 68.3 (SD=15.3), a significant increase compared to baseline (p =.02). The placebo group had a mean score of 56.7 (SD=24.2) which was not a significant change. There were no seizures, headaches, dizziness, nausea, vomiting, insomnia or any other unanticipated adverse effects among any patients assigned to active drug.

Conclusions: No patient experienced any adverse events and only the group receiving theophylline prior to daily therapy demonstrated significant improvement. These early findings suggest that antagonism of GABA mechanisms after stroke can be safe at low doses and may be beneficial in facilitating motor function after stroke. These data support the feasibility of a randomized controlled study to determine efficacy and safety in larger numbers of patients.

5 Rehabilitation and reorganisation after stroke A

THE TIMING IT RIGHT STROKE FAMILY SUPPORT PROGRAM: PHASE 2 PILOT RANDOMIZED CONTROLLED TRIAL

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Background: Family caregivers play a central role in the recovery, rehabilitation, and community re-integration of individuals who have experienced a stroke. We developed the Timing it Right Stroke Family Support Program (TIRSFSP) to provide stroke families with timely education and support as they are caring for and supporting stroke survivors' across the care continuum. The objective if this research was to conduct a pilot randomized controlled trial of the TIRSFSP.

Methods: We conducted a multi-site mixed methodology randomized controlled pilot trial of the TIRSFSP. Caregiver participants were recruited from acute care hospitals in Toronto and Pembroke Ontario and Calgary Alberta. Caregivers were randomized using sealed envelopes into one of three intervention arms: 1) standard care, 2) Self-directed TIRSFSP, or 3) TIRSFSP delivered by a stroke support person in person and by telephone for the first 6 months post stroke. Participants completed standardized measurement instruments prior to randomization and then again 1, 3 and 6 months post-stroke. Participants were also invited to participate in qualitative interviews that explored their needs for support as well as their experiences receiving their specific arm of intervention. Stroke support persons recorded time spent with each participant.

Results: 31 family caregivers consented to participate in the study and 19 participated in the qualitative phase of this study. As expected with this small sample size, no significant changes were observed in any of the outcome variables. Stroke support persons held an average of 5 sessions and spent an average of 2 hours and 35 minutes with each participant. Qualitative findings describe caregivers' experiences with support received and the need for further support.

Conclusions: Findings from this pilot research suggest that the TIRSFSP may benefit family caregivers. We are now conducting a multi-site mixed methodology randomized controlled trial of the intervention.

6 Rehabilitation and reorganisation after stroke A

THE INTERACTION OF LOCAL AND GLOBAL PROCESSING IN THE VISUAL PERCEPTION OF STROKE PATIENTS

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Introduction: In several studies with hierarchical stimuli it has been shown that the left and the right hemispheres are specialized for the processing of local and global information, respectively. Using visual search tasks that require different levels of processing (global vs. local figures) we investigate the lateralization of deficits in visual perception of stroke patients. In particular we want to assess whether patients with left hemisphere stroke (LH) have more difficulties in processing the local properties of a visual search task while patients with right hemisphere lesions (RH) show an impaired global processing. In our analysis we have in particular considered the context of perceptual processing: i.e. whether the prior exposure to a global or local task has an effect in the performance of the patients in the opposing task, depending of the lesion side.

Methods: 24 controls and 24 stroke patients (15 RH and 9 LH, N male = 8) were asked to indicate the presence or absence of a global or local target in a visual search task. The visual search task consisted of finding a local target (a single visual element) or a global target (a Kanizsa triangle) among 52 distracters. The experimental session consisted of three blocks (local or global) randomly ordered in 4 different combinations comprising 24 trials each.

Results: Consistent with the literature we found that patients with RH lesions needed in general more time in finding the global target, compared to the local task. The RT was especially slower for target positions closer to the contralateral side of the lesion. The accuracy in the global task was also significantly lower for these patients, but only when the global task was presented in the third block.

Discussion: The Results revealed the presence of an order effect in the performance in global or local visual search task together with a position effect of the target on the screen. Overall, the Results provide evidence for relative hemispheric specialization for global and local processing in accordance with previous studies. These findings have important implications for the design of visuo-perceptual rehabilitation technology.

7 Rehabilitation and reorganisation after stroke A

ANALYSIS ON THE STATUS OF STROKE REHABILITATION AND MAJOR INFLUENTIAL FACTORS FOR URBAN COMMUNITY PATIENTS IN CHINA

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Background: Normative rehabilitation system can reduce the rate of disability due to stroke and abate the burden on families and the whole society effectively in developed countries. The objective of our study was to investigate the awareness and status of stroke rehabilitation for urban community survivors, so as to provide a theoretical basis for establishing and improving standardized and effective stroke rehabilitation system in China.

Methods: Cross-section study From May. 2010 to Jun. 2010, 400 stroke patients, who were all community residents in Chengdu, China, were investigated in the form of face-to-face questionnaire. Descriptive analysis was used to described the socio-demographic characteristics of patients, rehabilitation system, the awareness of rehabilitation, the therapy of community-based rehabilitation and The correlation of rehabilitation with its possible associated factors was analyzed by multivariate regression analysis. Simultaneously, the whole status of community rehabilitation about 994 patients reported in China was reviewed.

Results: The survivor is mainly elder in urban community of China, age distribution of age group 71-80 years old show large proportion, about 45%.The main problem is they have low educational level and consciousness to rehabilitation after discharge and could not access to information effectively. More than 75% of patients did not receive community rehabilitation services, but 90% of them desire for further treatment. Multiple regression analysis showed that only age, having information and treatment in hospital and service about Improving hemiplegia provided by their own community were independent determinants of rehabilitation after discharge in these patients, respectively.

Conclusions: The stroke patients is mainly elder in the community of China. The main problem is that the survivors have low awareness of rehabilitation and community-based rehabilitation is insufficient. We should draw the experience from developed countries and regions to set up and optimize a standardized and effective community- and home-based rehabilitation service system in China as soon as possible.

8 Rehabilitation and reorganisation after stroke A

IMPACT OF STROKE IN EVERYDAY LIFE THE FIRST YEAR AFTER STROKE

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Background: In a Swedish survey of people with stroke 50% reported that they still had unmet rehabilitation needs 12 months after stroke onset. To be able to develop client-centered rehabilitation interventions, knowledge is needed regarding the perceived impact of stroke in everyday life; specifically in participation in activities and if and how the impact of stroke changes. The aim of the study was to explore the perceived impact of stroke on everyday life the first year after stroke and changes over time.

Methods: From a longitudinal study including people with stroke admitted to stroke units at Karolinska University hospital in Stockholm, data from baseline, 3 and 12 months was used. Impact of stroke was measured by the Stroke Impact Scale in 8 domains as well as Perceived recovery at 3 and 12 months. Multivariate analyses will be used to identify changes over time and we will take contextual, stroke-specific and functioning aspects into account.

Results: The sample consisted of 204 persons, with a mean age of 70 years and 57% were men. Analyses are ongoing. Preliminary Results show that the impact of stroke had changed significantly in the domain Emotions (p<.05) and in Perceived recovery (p<.001) over the year. Men reported significantly higher scores than women on these variables at 12 months. There were no significant changes over time in the domains Strength, Memory, ADL/IADL, Mobility, Hand function and Participation in the whole sample. Regardless of having mild, moderate or severe stroke, significant changes were seen in Perceived recovery. Significant changes in Emotions were only found in those with mild stroke; in Memory among those with moderate stroke; and in Strength among those with severe stroke.

Conclusion: The perceived impact of stroke on everyday life seems to be rather stable over time in the majority of the domains in the Stroke Impact Scale, which needs further exploration.

9 Rehabilitation and reorganisation after stroke A

STROKE CANADA OPTIMIZATION OF REHABILITATION BY EVIDENCE: IMPLEMENTATION TRIAL (SCORE: IT)

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Background: Knowledge Transfer refers to the strategies involved in closing knowledge gaps to promote the rapid uptake of research findings and evidence-based clinical practice to benefit patients. The study goal was to compare stroke patient outcomes after rehabilitation by therapists and nurses who used either a "Process Oriented (PO)" or an "Outcome Oriented (OO)" knowledge transfer, intervention implementation strategy.

Methods: 20 research sites in participating rehabilitation centers across Canada were randomized and personnel were trained to provide the assigned strategy to facilitate the uptake of the SCORE stroke rehabilitation, evidence-based recommendations in practice. Both groups received educational materials, a continuing education session and instruction in using the outcome measures. The PO sites also had 2 part time "champions", who attended a change management workshop and implemented the evidence based protocol with assistance from a local advisory committee, performed monthly audits of guideline adherence and took part in educational teleconferences with study investigators. Consenting, medically stable persons with stroke, admitted to a participating in-patient rehabilitation program for treatment of residual disability received an individualized treatment program that respected the Knowledge Transfer treatment orientation assigned to the site.

Results: Demographic, clinical and functional characteristics of the OO (N=744) and PO (N=773) groups were similar at enrollment. Focus Groups and Practice Audits suggested that practice in the PO sites changed more than the OO sites, but outcome scores on the Functional Independence Measure, the Box and Block Test, the Chedoke Arm and Hand Index and the Chedoke-McMaster Stroke Assessment were similar as was discharge status. The Six Minute Walk distance was somewhat longer (219 versus 170 meters) in the PO sites.

Conclusion: A PO knowledge transfer strategy resulted in better adherence to evidence based practice but brought about very modest benefits for stroke patient recovery. Possible reasons will be discussed.

Behavioral disorders and post-stroke dementia

1 Behavioral disorders and post-stroke dementia

IS TIA INDEPENDENTLY ASSOCIATED WITH COGNITIVE IMPAIRMENT? A COMPARISON WITH STROKE AND MI

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Background: Although the stroke lesion contributes to post-stroke cognitive impairment, stroke and vascular dementia may also coincide partly as a result of a shared association with increased cerebral susceptibility to ischaemia. If so, more cognitive impairment should be seen in patients with TIA than in other groups with similar vascular risk factors, such as myocardial infarction (MI) without TIA or stroke. We did a population-based study of cognitive impairment in MI, TIA and stroke.

Methods: In the Oxford Vascular Study, cognitive outcome was assessed in consecutive strokes, TIAs without prior stroke, and MIs. MMSE and TICSM were done at 12 months and MMSE and Montreal Cognitive Assessment (MoCA) at 60 months. TIAs with stroke on follow-up were excluded.

Results: Stroke (n=398) and TIA (n=252) patients were older than MI (n=396) patients (mean/SD age 74.2/12.3 and 73.9/12.8 vs 69.6/12.4 years, p<0.0001) and more likely to be female (50% and 57% vs 34%, p<0.0001). For all tests, as expected cognitive scores were lower after stroke (p<0.002) than after TIA or MI at both 12 and 60 months and rates of moderate/severe cognitive impairment (MMSE<24) were highest after stroke at both 12 and 60 months (19% and 21%; both p<0.005 vs TIA or MI). However, despite the difference in age, cognitive scores and rates of moderate/severe cognitive impairment at 12 and 60 months were similar after TIA (11% and 8%) versus MI (9% and 11%). Rates of mild cognitive impairment (MoCA<26 and MMSE >24) were also similar at 60 months: 63% after TIA versus 61% after MI (77% after stroke). Results were comparable when only patients >75 years old were considered.

Conclusion: Rates of mild and moderate/severe cognitive impairment were similar after TIA and MI suggesting that any increased cerebral susceptibility to ischaemia in patients with TIA does not increase the risk of cognitive impairment.

2 Behavioral disorders and post-stroke dementia

IMPAIRMENT OF CEREBRAL HEMODYNAMICS AND COGNITIVE PERFORMANCE IN ATHEROTHROMBOTIC DISEASE PATIENTS

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Background: Patients with pre-existing atherothrombotic disease are prone to cognitive impairment. We tested whether cerebrovascular reactivity (CVR), a marker of cerebral microvascular hemodynamic dysfunction, is associated with poorer cognitive scores.

Methods: A subgroup of non-demented patients with chronic coronary heart disease was assessed after a follow-up of 15±3 years for cognitive function (Mindstreams Computerized Cognitive Battery; computing index scores summarizing performance in each cognitive domain and a global cognitive score) and for CVR using the breath-holding index (BHI) with Transcranial Doppler. We assessed cognitive scores in patients with and without impaired CVR (bottom quartile of BHI; BHI<0.47).

Results: Among 428 patients (mean age 71.7±6.2 yrs, 97% men) median BHI was 0.73 (25% 0.47, 75% 1.04). Impaired CVR was not associated, in our cohort, with any of the traditional vascular risk factors. Multiple linear regressions adjusting for age, sex and education revealed that impaired CVR was associated with 4±1 lower executive function scores (p=0.004) and 3±1 lower global scores (p=0.01), but not with memory performance (p=0.3). Further adjustment to baseline CRP, bilateral carotid plaque, stroke and depressive symptoms did not attenuate these associations (p=0.003 for executive function score and p=0.01 for the global score].

Conclusion: Among non-demented patients with pre-existing atherothrombotic disease, impaired CVR, a marker of cerebral microvascular dysfunction, is associated with poorer global cognitive function and in-particular executive dysfunction.

Disclosure: The Mindstreams Computerized Cognitive Battery was provided by NeuroTrax.

3 Behavioral disorders and post-stroke dementia

RISK OF INCIDENT DEMENTIA AMONG PATIENTS WITH ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Several studies have suggested an association between atrial fibrillation (AF) and dementia. This systematic review and meta-analysis Aims to quantify the risk of incident dementia among patients with AF compared to those without.

Methods: We searched MEDLINE, EMBASE, PSYCHINFO in September 2010 for published prospective studies evaluating the association between baseline AF and incident dementia. Random effects meta-analysis was performed on included studies and heterogeneity was assessed using I2 statistic.

Results: Fifteen studies with 46637 patients were included (mean age 71.7 years). One study that could not be pooled reported no difference in mini-mental state examination score between patients with and without AF. Meta-analysis of fourteen studies showed increased risk of dementia in patients with AF compared to those without (OR 2.0 95%CI 1.4-2.7, p<0.0001) but this analysis was limited by substantial heterogeneity (I2=75%). The subgroup of seven studies of stroke patients showed a significant association (OR 2.4 95%CI 1.7-3.5, p<0.001, I2=10%) while the seven studies of the broader population showed borderline significant (OR 1.6 95%CI 1.0-2.7 p=0.04, I2=87%). For the conversion of mild cognitive impairment to dementia, one study showed a significant association in patient with AF compared to those without (OR 4.6 95%CI 1.7-12.5).

Conclusions: Evidence suggests that patients with AF are at greater risk of incident dementia than those without. Stroke patients with AF are found to have the higher risk of dementia compared to the broader population. These at risk groups of patients may benefit from cognitive monitoring.

4 Behavioral disorders and post-stroke dementia

COGNITIVE IMPAIRMENT PREDICTS POOR QUALITY OF LIFE IN CAROTID OCCLUSION: BASELINE ANALYSIS FROM THE RANDOMIZED EVALUATION OF CAROTID OCCLUSION AND NEUROCOGNITION (RECON) TRIAL

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Background: Cognitive impairment is variably reported to have an effect on quality of life in stroke. Demonstration of this association is especially important in a setting in which a surgical intervention is being proposed as a means to reverse cognitive decline. We assessed the association between cognition and quality of life among participants in the NIH-sponsored Randomized Evaluation of Carotid Occlusion and Neurocognition (RECON) Trial, an ancillary study of the Carotid Occlusion Surgery Study (COSS).

Design/Methods: Patients were enrolled in RECON within 120 days of TIA or minor stroke secondary to carotid artery occlusion. We used multivariable regression to predict Stroke-Specific Quality of Life (SSQOL) from a composite Z-score on an age-adjusted neurocognitive battery that included both global and hemisphere-specific tests. Depression and stroke severity were controlled for by including the Center for Epidemiological Studies Depression Scale (CES-D) and NIHSS. Age, gender, and education were also included as covariates.

Results: Among the 67 enrolled patients (mean age=58, 22F) who completed baseline cognitive testing, CES-D and SSQOL, average composite Z-score was 1.36 SD below age-adjusted population means (range 0.5 SD above to 3.8 below). The range of scores on the CES-D was 0-48 (mean=18). The NIHSS range was 0-15 (mean=3 for those with stroke). Cognitive score predicted SSQOL (P=.049), independent of depression and stroke severity, which were also both significant (P<.001, P=.0002, respectively). Age, gender, and education were not significant.

Conclusions: Cognitive impairment independently predicted poor quality of life in patients with symptomatic carotid occlusion, suggesting that the degree of cognitive impairment in this population is clinically and functionally relevant. Whether the cognitive decline can be reversed to a clinically meaningful degree awaits the 2-year outcome Results of the RECON study.

5 Behavioral disorders and post-stroke dementia

PREVALENCE AND FUNCTIONAL IMPACT OF MEDIAL TEMPORAL LOBE ATROPHY ON COGNITION IN A HOSPITAL-BASED STROKE SERVICE COHORT

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Background: Vascular cognitive impairment (VCI) and Alzheimer's disease (AD) may interact and co-exist. The extent to which AD pathology contributes to cognitive impairment in stroke patients, and its relationship to markers of cerebrovascular disease, is largely unexplored. Medial temporal lobe atrophy (MTA) is a radiological marker for AD pathology. We hypothesized that MTA would be associated with cognitive impairment in a hospital-based stroke cohort.

Methods: All eligible patients underwent detailed neuropsychological testing and standardized magnetic resonance imaging (MRI), including gradient-recalled echo T2* and coronal FLAIR. We assessed MTA on FLAIR images using a new validated visual rating scale based on the Scheltens scale (scored from 0 to 4; severe MTA was defined as ≥2). Cerebral microbleeds (CMBs) and age-related white matter changes (ARWMC) were rated using validated scales. The effect of MTA on cognitive impairment in each cognitive domain was tested using regression analyses, adjusting for other imaging and clinical factors.

Results: Three hundred and ninety-six patients were included. One hundred and seventy-one patients (43%) showed some degree of MTA; in 38 MTA was severe. Patients with severe MTA were older (76 vs 64, p<0.001), more hypertensive (97% vs 66%, p<0.001), had more severe ARWMC (median 9 vs 5.5, p<0.001) and more lobar CMBs than patients with mild or no MTA. In adjusted multivariate analyses, MTA was a predictor of verbal memory impairment (OR 1.81, 95%CI 1.22-2.71, p=0.004).

Conclusions: MTA is common in stroke patients, is independently associated with verbal memory impairment, and is associated with MRI markers of small vessel disease. Although the presence of MTA suggests that AD pathology contributes to cognitive dysfunction in this cohort, confirmation of the underlying pathology requires histological correlation. Nevertheless, our findings may have implications for prevention and treatment of VCI.

6 Behavioral disorders and post-stroke dementia

A COMPARISON OF THE BASELINE MONTREAL COGNITIVE ASSESSMENT (MOCA) AND THE BASELINE MINI-MENTAL STATE EXAMINATION (MMSE) IN PREDICTING MODERATE TO SEVERE POST-STROKE COGNITIVE IMPAIRMENT AT 3-6 MONTHS FOLLOW-UP

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Background: It is important to establish sensitive prognostic tools for cognitive impairment at the sub-acute stroke phase, as stroke patients with moderate to severe cognitive impairment were found to be at increased risk of incident dementia (Narasimhalu, 2009). We aimed to examine the predictive ability of the baseline MoCA and the baseline MMSE for moderate to severe cognitive impairment at 3-6 months after stroke.

Methods: Patients with ischemic stroke and transient ischemic attack were assessed with both MoCA and MMSE within 14 days after acute stroke. They then received

a formal neuropsychological evaluation 3-6 months later. Cognitive outcomes were classified as either "none to mild cognitive impairment" or "moderate to severe cognitive impairment"

Results: Of the 190 patients recruited and due for follow-up, 163 (86%) completed the month 3-6 assessment. 119 had none to mild cognitive impairment and 44 had moderate to severe cognitive impairment. Univariate analyses showed that age, education, baseline MoCA and MMSE scores were significantly different between the two cognitive severity groups. However, logistic regression showed that only baseline MoCA scores were significant (p< 0.002) in predicting for moderate to severe cognitive impairment whilst baseline MMSE scores, age and education categories, baseline neurological measures (NIHSS and mRS scores) and stroke subtype did not. Receiver Operating Curve (ROC) analysis established an optimal baseline MoCA cutoff score of ≤21 (Sensitivity 91%, Specificity 58%, PPV 44%, NPV 95%, correctly classified 67%) in differentiating between cognitive severity groups.

Conclusion: In Conclusion, the baseline MoCA was superior to the baseline MMSE in predicting moderate to severe cognitive impairment at 3-6 months post stroke.

7 Behavioral disorders and post-stroke dementia

COMPARISON OF THE MODIFIED TELEPHONE INTERVIEW OF COGNITVE STATUS (TICSM) WITH THE MMSE AND MOCA FOR THE EVALUATION OF COGNITIVE IMPAIRMENT AFTER TIA AND STROKE

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Background: Cognitive assessment should be routine after stroke in view of high rates of stroke-related cognitive impairment, but face-to-face testing is not always possible in large studies. We therefore assessed the performance of the 13-item (39 point) modified Telephone Interview of Cognitve Status (TICSm) against other short cognitive tests in patients with cerebrovascular disease.

Methods: In the population-based Oxford Vascular Study (2002-2007) of consecutive TIAs and strokes, cognitive outcome was assessed with the MMSE, TICSm and Montreal Cognitive Assessment-MoCA (2007 only) at least 6 months after the index event. Accepted cut-offs of ≥27 on MMSE, ≥25 on TICSM, ≥26 on MoCA were used to indicate normal cognitive function.

Results: in 674 patients (mean/SD age 73.0/12.2 years, 49% female, 60% stroke), MMSE scores were skewed towards higher values (median/IQR=28/26-29), whereas TICSM scores were more normally distributed (23/19-26). 160/376 (43%) patients with normal MMSE had low TICSm but only 22/238 (9%) patients with normal TICSm had low MMSE (p<0.0001). Low TICSm in those with normal MMSE was associated (all p<0.005) with older age, less education, stroke vs TIA, higher Rankin and lower Barthel score. Among 165 patients with a MoCA, of the 65 with normal TICSm, MoCA was low in 27 (42%) with reduced subtest scores for visuoexecutive function (p<0.0001), abstraction (p<0.0001), recall (p=0.01), attention (p=0.03), verbal fluency (p=0.01) and language (p=0.03) compared to those with normal MoCA.

Conclusion: The TICSm has greater sensitivity for mild cognitive impairment than the MMSE in TIA and stroke. However, the lack of frontal/executive tasks makes the TICSm less appropriate than the MoCA in patients with vascular cognitive impairment when face-to-face testing is feasible.

8 Behavioral disorders and post-stroke dementia

CEREBROSPINAL FLUID BIOMARKERS AND EARLY COGNITIVE PROFILE IN ACUTE STROKE

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Background: Stroke-related dementia and Alzheimer's (AD) disease share several risk factors and they are considered to be two ends of a continuum rather than two distinct entities. A characteristic cerebrospinal fluid (CSF) pattern with low level of beta-amyloid (BA) has been found in AD. Few studies have focused, though, on the impact of acute stroke on the CSF biomarkers and their relation to cognition.

Methods: N=28 patients (mean age 75.6 years), with acute stroke were included within 5-10 days after symptom debut; N=28 controls were recruited among age-matched, apparently healthy individuals.
Stroke localization and lesions characteristics were determined by CT-scans. Cerebrospinal fluid was collected by lumbar puncture and the levels of

neurofilament light subunit (NFL), BA 1-42, p-Tau, and total-Tau were measured. Neuropsychological evaluation was done by using a battery of tests covering six cognitive domains; the presence of depressive symptoms was checked by GDS/MADRS.

Results: A surprisingly high number of stroke patients had low BA 1-42 (52.4%) compared with controls (3.6%), p<0.001. As expected, the concentrations of spinal total-Tau (p=0.006) and NFL (p<0.001) were higher in the stroke patients. Mann-Whitney test showed that high NFL was strongly associated with both cognitive impairment (p<0.001) and depression (p=0.034) while low BA 1-42 correlated only with cognitive impairment (p<0.001).
Only 14.3% of the stroke patients had normal cognitive profile compared to 92.9% (p<0.001) of the controls. Depression was found in 25% of the stroke patients and correlated strongly with impaired cognition (p<0.001).

Conclusions: Our novel and most important finding is that roughly half of the stroke patients had low levels of BA 1-42. Further studies are required in order to verify the Results in larger groups and to penetrate the pathogenic mechanisms behind this. Early post-stroke depression is quite common and is strongly related to cognitive impairment.

9 Behavioral disorders and post-stroke dementia

LONGITUDINAL ATTRITION OF COGNITIVE DATA IN A POPULATION-BASED STUDY OF TIA AND STROKE: EXTENT OF POTENTIAL BIAS IN ESTIMATING BURDEN OF COGNITIVE IMPAIRMENT

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Background: Dementia after stroke is associated with increased morbidity and mortality. Thus patient attrition may lead to biased estimates of post-stroke cognitive impairment, high attrition resulting in underestimation of rates depending on the risk-factor profile of patients not assessed. In the absence of previous population-based data, we determined attrition rates of cognitive data over 5-year follow-up of TIA and stroke.

Methods: Participants in the Oxford Vascular Study (2002-2007), a prospective population-based cohort of all TIA and stroke, were tested at baseline (MMSE), 1, 6 and 12 months (MMSE or Telephone Interview for Cognitive Status-TICSM) and 5 years (MMSE and Montreal Cognitive assessment-MoCA). Reasons for lack of valid test were recorded.

Results: In 1290 TIA and stroke patients (879 stroke, mean/SD age 74.7/12.5 yrs, 604 male), 286 (22%) were dead at 12 months and 658 (51%) at 5 years. After exclusion of those unable to fully complete testing (e.g. blind, deaf, severe motor impairment etc) valid cognitive testing was only obtained in 62%, 62%, 70%, 68%, 55% of survivors at 0, 1, 6, 12, and 60 months respectively. Of reasons for lack of valid test, dysphasia (18%) and being too unwell (13%) were more common at baseline whereas moving out of area was more common at 5 years (26%). Rates of severe (untestable) dementia (<4%) and declining to be interviewed (<18%) were relatively constant. Lack of valid test (i.e. dead or unable/unwilling to complete) was associated (all p<0.001) with older age, major stroke, cardioembolic vs lacunar stroke, multiple strokes and leukoaraiosis at baseline.

Conclusion: Death during follow-up and lack of valid cognitive test are associated with known predictors of post-stroke cognitive impairment. Determination of the true burden of stroke-related cognitive deficit should therefore include risk-factor adjusted estimation of probability of impairment in non-tested patients.

10 Behavioral disorders and post-stroke dementia

BRAINSTEM RAPHE HYPOECHOGENICITY CORRELATES WITH DEPRESSION IN SYMPTOMATIC PATIENTS WITH SMALL VESSEL DISEASE: A PILOT STUDY

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Background: Patients with small vessel disaease (SVD) often present with depressed mood. Brainstem raphe hypoechogenicity (BRh) on transcranial sonography (TCS) of the brain parenchyma is increasingly used as a biomarker in bipolar depression and depression in Parkinson's disease. We aimed to investigate TCS correlates of depression in symptomatic SVD patients.

Methods: We conducted a cross-sectional study from April 1st 2009 till April 1st 2010. Neurological, functional and cognitive status, Hamilton Depression Rating Scale (HDRS) score, TCS and magnetic resonance findings (Age-Related

White Matter Changes scale scores), were compared between 30 healthy age- and sex-matched controls and 59 patients with SVD.

Results: Compared to control subjects, patients with SVD were more frequently depressed (p<0.001). None of the controls had cognitive decline, while evidence for vascular cognitive impairment (VCI) was detected in 49% of SVD patients (<0.0001). TCS examination showed that SVD cases more frequently had BRh (61% vs 10%, p<0.0001), SN hyperechogenicity (32% vs 3%, p=0.002) and enlarged third ventricle diameter (mean diameter 7.2 mm vs 5.2 mm, p=0.0001), compared to healthy controls. Parameters associated with depression on HDRS in univariate analysis were VCI (OR 3.5, 95%CI 1.1-11.9, p=0.041) and BRh (OR 7.5, 95%CI 1.5-26.9, p=0.013). In multivariate analysis, independent predictor of depression was only BRh with OR 6.4 (95%CI 1.3-22.2, p=0.025). Excellent correlation was found between BRh and severity of cerebral lesions (p=0.0001).

Conclusions: Substantial number of depressed patients with symptomatic SVD has BRh as a marker of depression. BRh might reflect severity of subcortical ischemic brain lesions in SVD patients, leading to disruption of ascending monoaminergic pathways conecting basal limbic system and frontal lobes. There is a potential in TCS examination to be used in detection and prediction of depression in these patients.

11 Behavioral disorders and post-stroke dementia

DEPRESSION AFTER STROKE PREDICTS HEALTH OUTCOMES IN THE LONG TERM

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Background: Little is known about how depression after stroke affects other health outcomes in the long term. This study investigates the association between depression in the first year after stroke and mortality, stroke recurrence, cognitive impairment, disability and health related quality of life up to 15 years after stroke.

Methods: Data on first ever strokes collected from the population-based South London Stroke Register. 4022 patients were registered between January 1995 and December 2009. Patients were followed up 3 months after stroke and then every year for up to 15 years. Follow up included assessments for depression (Hospital Anxiety and Depression, depression subscale score>7 = depression), disability (Barthel Index), cognition (Abbreviated memory test or Mini-mental estate examination) and health related quality of life (SF-12). Multivariable regression models were used to investigate the association between depression within a year of stroke and mortality, stroke recurrence, disability, cognitive impairment and health related quality of life up to 15 years after stroke. Models were adjusted for age, sex, ethnicity, stroke severity (Glasgow coma score, urine incontinence and hemiparesis) and disability observed during the stroke acute phase.

Results: Depression in year 1 after stroke was associated with higher mortality HR: 1.32 (1.10-1.59) and higher risk of stroke recurrence HR: 1.62 (1.04-2.55). It also predicted higher disability rates up to 8 years post stroke, with RR ranging from 2.25 (1.10-4.58) to 3.29 (2.00-5.42), cognitive impairment in year 2 OR:2.01 (1.20-3.38), lower scores in the mental domain of the SF-12 up to year 7, and lower scores in the physical health domain up to year 8. There were no associations with these outcomes at later time points.

Conclusion: Depression has an impact over the stroke patients in the long term not only because of the distress it causes but because it is associated with very negative health outcomes.

12 Behavioral disorders and post-stroke dementia

THE NATURAL HISTORY OF DEPRESSION UP TO 15 YEARS AFTER STROKE

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Background: Little is known about the long term natural history of depression after stroke. This study investigates the incidence, prevalence, duration and recurrence of depression up to 15 years after stroke.

Methods: Data on first ever strokes were collected from the population-based South London Stroke Register. 4022 patients were registered between January 1995 and December 2009. Patients were assessed with the Hospital Anxiety and Depression scale (HAD) 3 months after stroke and then annually for up to 15 years. Depression was defined as scores>7 in the HAD depression subscale.

Results: During the 15 years of follow up 55% of the patients were depressed at some point, with incident cases ranging from 7% to 21% a year, and prevalence ranging from 29% to 39%. From all the patients who had depression at any time point 59% were depressed within 3 months of stroke, 69% within a year and 82% within the first 3 years. Half of the patients depressed at 3 months had recovered at 1 year and the other half recovered gradually in the following few years with only 4% remaining depressed until year 5. The proportion of newly detected cases of depression dropped gradually from 100% 3 months after stroke to 5% 9 years after stroke, with no new cases diagnosed after that point. In contrast, the proportion of recurrent cases rose consistently from 35% at 2 years to 100% 15 years after stroke.

Conclusion: Depression is a frequent problem that persistently affects one in three patients up to 15 years after stroke. However, its early start, relatively short duration and high proportion of recurrences make its natural history very dynamic. These findings support the view that depression requires periodic clinical attention in the long term after stroke.

Acute stroke: emergency management, stroke units and complications B

10 Acute stroke: emergency management, stroke units and complications B

RISK FACTORS FOR POST STROKE PNEUMONIA IN PATIENTS TREATED IN STROKE UNITS – AUSTRIAN STROKE UNIT REGISTRY

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Background: A significant proportion of stroke pts. develop pneumonia, ranging from 5% to 13% in pts. with dysphagia or 28% in artificially ventilated pts. Aspiration due to dysphagia is the single most important factor for the development of PSP, others are age, stroke severity, chronic pulmonary disease, hemorrhagic transformation of infarct, large basal-ganglia infarct, intensive care treatment, dysarthria or use of proton-pump-inhibitors.

Objective: The aim of this study was to detect predisposing factors for PPS in a large cohort of stroke pts. treated at stroke units (SU).

Methods: The study is based on data from the Austrian Stroke Unit Registry which prospectively collects data from pts. admitted to 34 SUs. Case records of 46009 patients treated between 2004 and Dec. 2010 were analysed. Data were compared in univariate analysis and then included into a multivariate logistic regression model.

Results: Overall 2605 patients (5.7%) had pneumonia while being admitted to the SU. Pts. with pneumonia were older and had higher NIHSS on admission. Other concurrent complications, diabetes, atrial fibrillation and application of nasogastric tubes (NGT) were significantly more prevalent in this group. 51% of pts. with PSP had a NGT, whereas only of 9% pts. without PSP. 27% of pts. with a NGT developed PSP, only 3.4% without a NGT. In the multivariate analysis age, NIHSS, progressive or recurrent stroke, cardiac arrhythmias, cardiac insufficiency, other concurrent infections and application of nasogastric tubes were independently and significantly associated with pneumonia, among which application of NGT showed the highest odds ratio for pneumonia (p<0.00001 OR 3.7 95%CI 3.1 - 4.2).

Conclusion: Many pts. acquire post-stroke pneumonia in spite of enteral feeding via NGTs. This allows to conjecture that feeding through NGT does not reliably prevent aspiration or protect from pneumonia. Other protective measures have to be studied esp. to prevent silent aspiration in stroke.

11 Acute stroke: emergency management, stroke units and complications B

DIAGNOSIS AND TREATMENT OF STROKE-ASSOCIATED PNEUMONIA (SAP). A NATIONWIDE SURVEY IN GERMAN STROKE UNITS

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Background: Stroke-associated pneumonia (SAP) constitutes one of the main complications in acute stroke affecting neurological prognosis. Current guidelines for acute stroke care lack standardized recommendations for the medical approach of SAP. We developed a standardized questionnaire to explore diagnostic and treatment routine in German stroke units (SUs).

Methods: The survey included characteristics of SUs (e.g. presence of standardized operational procedures [SOPs]), questions related to empirical and prophylactic antibiotic treatment of SAP and 5 case vignettes describing relevant scenarios considering CDC criteria of "clinically defined pneumonia". All certified German SUs (N=163) were contacted in April 2010. Association of clinical, imaging or laboratory findings with diagnosis of SAP was investigated by descriptive statistical analyses.

Results: Response rate was 51%. SAP was mainly diagnosed based on clinical criteria. The biomarker C-reactive protein (CRP), which is not a CDC criterion, was often requested as additional diagnostic option (67-76%). Chest X-ray showed only limited influence on diagnosis of SAP. Third-generation cephalosporines, (acyl-) aminopenicillines and ß-lactamase inhibitors were the most frequent used antibiotics in mono- and combination therapy (42%) with a predefined mean treatment duration of 8 days (SD 2) in 45% of SUs. A minority of SUs (5%) used prophylactic antibiotic treatment. The majority (61%) of SUs had SOPs on SAP, but no impact on diagnosis and treatment was found.

Conclusion: Clinical CDC criteria are the main diagnostic and treatment-guiding determinants in SAP. In contrast to its central role in CDC criteria, chest X-ray revealed to be of minor importance. The survey demonstrates that current CDC criteria do not reflect clinical practice and indicate an urgent need for new diagnostic criteria of SAP. The frequent request for CRP as a diagnostic criterion reflects the demand for biomarkers as diagnostic tool in SAP.

12 Acute stroke: emergency management, stroke units and complications B

MODERATE BLOOD PRESSURE REDUCTION DOES NOT REDUCE CEREBRAL BLOOD FLOW IN ACUTE ISCHEMIC STROKE

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Background: Early treatment of hypertension in acute stroke is controversial due to concerns that this may reduce cerebral blood flow (CBF) in the ischemic penumbra. It has been hypothesized that nitric oxide donors may increase CBF in stroke patients. We aimed to assess the CBF response to acute BP reduction with labetalol and nitroglycerin.

Methods: Patients presenting with ischemic stroke <72 h after onset were enrolled. Those with mean arterial pressure (MAP)>100 mmHg received nitroglycerin (sublingual/topical) or intravenous labetalol, aiming for MAP reduction of 10%. All patients underwent MRI with Perfusion (PWI) and Diffusion-weighted (DWI) imaging before and after BP treatment. PWI deficit and DWI lesion volumes were measured planimetrically.

Results: Of 28 patients enrolled, 22 had MAP>100 (median 115.5 mmHg, IQR=19.91) and 6 had MAP of ≤100 (median=93.33 mmHg, IQR=9.75). The median time between first and second perfusion was 24 min (IQR= 63.5). In treated patients, mean penumbral CBF was not affected by antihypertensive therapy (pre-treatment 31.7±11.5 vs post treatment 33.1±11.4 ml/100g/min, p=0.685). Similarly, ischemic core CBF (28.7±11.9 vs 30.2±11 ml/100g/min, p=0.659) and hemispheric CBF (39.0±6.2 vs 39.6±5 ml/100gr/min, p=0.698) were not affected by treatment. Patients who received nitroglycerin did not show improvement in penumbral CBF (median CBF change= -0.5, IQR= 12.2 ml/100g/min) relative to those who did not receive nitroglycerin (median CBF change= -3.0, IQR= 10.7 ml/100g/min, p= 0.30). There was no difference in DWI lesion volume growth, between patients receiving antihypertensives (median= 0.3 ml, IQR= 4.3) and those who were not treated (median =3.8 ml, IQR= 12.5, p=0.71).

Conclusion: Antihypertensive therapy does not result in further reductions in penumbral, core or hemispheric CBF in acute stroke. Nitroglycerin treatment was not associated with CBF improvement. These Results support the safety of moderate BP reduction in the early post stroke period.

13 Acute stroke: emergency management, stroke units and complications B

DOES THE ASOCIATION OF DM AND PREVIOUS CEREBRAL INFARCTION REALLY INCREASE THE RISK OF HAEMORRHAGIC TRANSFORMATION OR POOR OUTCOMES AFTER INTRAVENOUS THROMBOLYSIS IN ISCHEMIC STROKE?

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Background: Intravenous thrombolysis (IVT) is the recommended therapy for acute ischemic stroke (IS). However, licensing approval in Europe does not advocate IVT in diabetic patients with a previous cerebral infarction (PCI). Our aim was to assess whether a history of PCI in diabetic patients is associated with poorer outcomes or higher risk of symptomatic intra-cerebral hemorrhage (SICH) after IVT.

Methods: Prospective multicenter observational analysis of consecutive IVT-treated, acute IS patients at 5 stroke units sharing a common stroke code and care protocols (Madrid Stroke Network), from January 2003 to December 2009. The frequency of SICH and 3-month outcome were compared among the following groups: (1) diabetic patients with PCI (DM+/PCI+); (2) diabetic patients without PCI (DM+/PCI-); (3) non diabetic patients with PCI (DM-/PCI+); (4) patients without prior diagnosis of diabetes neither PCI (DM-/PCI-).

Results: 1140 IVT-treated patients were included. 24 patients (2.1%) had known DM and a history of PCI; 194 (17%) were diabetic without PCI and 87 (7.6%) had a PCI and no history of DM. No differences were found in stroke severity on admission among groups. None of the DM+/ICP+ patients developed SICH whilst 1.3-2.2% of the patients in the other groups. Of the total 1120 patients (98.2%) who completed the 3-month follow-up period, 123 died (12.4%), with no differences among groups. Data regarding mRS at 3 months were available in 1107 patients. 11 (45.8%) patients in the DM+/ICP+ group, 84 (45.7%) in the DM+/ICP-, 31 (36.9%) in the DM-/ICP+ and 332 (41.0%) in the DM-/ICP- were dead or dependent, with no differences among groups. Logistic regresion analysis showed that high glucose levels were associated with increased risk for SICH, mortality and death or dependence with no effect of DM or PCI.

Conclusions: Ischemic stroke patiens with DM and PCI who are IVT-treated had similar outcomes and no increase in risk of SICH than patients without that history.

14 Acute stroke: emergency management, stroke units and complications B

EARLY RECURRENT ARTERIAL EMBOLISM - AN UNDERESTIMATED RISK AFTER THROMBOLYSIS?

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Background: Intracranial hemorrhage is the primary concern when using recombinant tissue-type plasminogen activator (rt-PA) for acute stroke therapy. Bearing in mind the pharmacodynamic of rt-PA within cardio-embolic stroke a recurrent early arterial embolism might also be a significant complication of today's standard therapy. Little is known about this complication, its frequency and risk factors.

Methods: Retrospective Analysis of data for 429 consecutive patients with cardiogenic stroke treated between January 2003 and December 2006 with regard to the occurrence and time pattern of clinically symptomatic secondary embolism.

Results: Fifty-three of the 429 patients with cardiogenic stroke were treated with rt-PA within first 3 hours after symptom onset. Early recurrent embolism occurred in 7.5% of the patients after thrombolysis and in 1.1% of the non thrombolysis group (p=0.01). Within both groups early cerebral recurrent stroke occurred in three patients, and one patient had a systemic embolism in each group.

The time pattern of recurrent embolism differed significantly (p<0.001). In patients with thrombolysis therapy recurrent embolism occurred predominantly within 90 minutes after initiation of rt-PA application. Spontaneous recurrence of embolism occurred generally more than a week after the first event.

As the major risk factor dilated cardiomyopathy could be identified (p<0.001). Atrial fibrillation alone does not mean an increased risk.

Oral Session
Acute stroke: emergency management, stroke
units and complications B

Cerebrovasc Dis 2011;31(suppl 2):1–322

47

Conclusions: Characteristically symptoms of early recurrent embolism take place within the first hours after rt-PA-therapy initiation. The frequency of this complication in patients with cardioembolic ischemic stroke undergoing intravenous thrombolysis is similar to that for symptomatic intracerebral hemorrhage. Physicians should be aware of a recurrent embolism to avoid clinical deterioration.

15 Acute stroke: emergency management, stroke units and complications B

IV THROMBOLYSIS AND STATINS

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Background: Prior use of statins may affect functional outcome and intracranial hemorrhage (ICH) rates in stroke patients receiving IV thrombolysis (IVT).
Methods: In a pooled analysis of 11 IVT-databases we compared outcomes between statin users and nonusers. Main outcome measures were excellent 3-month-outcome (modified Rankin scale 0-1) and intracranial hemorrhage (ICH) in three categories. We distinguished all ICHs (ICHall), symptomatic ICH based on the criteria of the ECASS-II-trial (SICHECASS-II) and those of the NINDS-trial (SICHNINDS). Unadjusted and adjusted odds ratios (OR) with 95%-confidence-intervals were calculated.
Results: Among 4012 IVT-treated patients 918 (22.9%) were statin users. They were older, more often male, and more frequently had hypertension, hypercholesterolemia, diabetes, coronary heart disease, and concomitant antithrombotic use compared with nonusers. Fewer statin users (35.5%) than nonusers (39.7%) reached an excellent 3-month-outcome (ORunadjusted 0.84[0.72-0.98],p=0.02). After adjustment for age, gender, blood pressure, time-to-thrombolysis, and stroke severity, the association was no longer significant (0.89[0.74-1.06],p=0.20). ICH occurred by trend more often in statin users (ICHall 20.1% versus 17.4%; SICHNINDS 9.2% versus 7.5%; SICHECASS-II 6.9% versus 5.1%). This difference was statistically significant only for SICHECASS-II (OR=1.38[1.02-1.87]). After adjustment for age, gender, blood pressure, use of antithrombotics, and stroke severity, the ORadjusted for each category of ICH (ICHall 1.15[0.93-1.41]; SICHECASS-II 1.32[0.94-1.85]; SICHNINDS 1.16[0.87-1.56]) showed no difference between statin users and nonusers.
Conclusion: In stroke patients receiving IVT, prior statin use was neither an independent predictor of functional outcome nor ICH. It may be considered as an indicator of baseline characteristics that are associated with a less favorable course.

16 Acute stroke: emergency management, stroke units and complications B

SHORT-TERM BLOOD PRESSURE VARIABILITY AND EARLY OUTCOME FOLLOWING ACUTE STROKE

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Background: Visit-to-visit blood pressure variability (BPV) has been proposed as a risk factor for stroke, perhaps of greater significance than casual BP. In acute stroke, we have shown that high MAP and DBP variability using non-invasive beat-to-beat BP monitoring (Finapres) was associated with worse prognosis. High systolic BPV (SBPV) was associated with increase in death or early neurological deterioration at day 10 in the TAIST study. However, the prognostic value of BPV in acute stroke remains uncertain.
Methods: We analysed baseline BP data from two studies of blood pressure in acute stroke (CHHIPS and COSSACS), to clarify the relationship between baseline BPV (using two sets of three readings each, five minutes apart, supine position, using a semi-automated validated UA767 monitor) and 2-week death or dependency (modified Rankin Scale >3). BPV was defined as the standard deviation, and binary logistic regression analysis was carried out to assess association with outcome, corrected for baseline prognostic factors, including demography, comorbidity and pre-stroke and post-stroke antihypertensives.
Results: Data from 935 participants were analysed (COSSACS 763, CHHIPS 172). Baseline BP (mean (SD)) was 155 (24)/83 (14) mmHg. Baseline SBPV was 7.2 (4.1) mmHg and DBPV was 5.5 (3.9) mmHg. Age and baseline NIH were the only significant predictors of the primary outcome. The odds of death/dependency at 2 weeks increased by 4.7% per unit increase in age, and by 28.3% per unit increase in baseline NIH.

Table 1. Baseline BP and BPV by primary outcome

	Overall	Dead/Dependent	Independent
SBP, mmHg	155 (24)	163 (26)	153 (24)
DBP, mmHg	83 (14)	85 (14)	83 (14)
SBPV, mmHg	7.2 (4.1)	7.4 (4.4)	7.2 (4.1)
DBPV, mmHg	5.5 (3.9)	6.0 (4.1)	5.4 (3.9)

All values presented as mean (standard deviation).

Conclusion: Baseline BPV was not a significant predictor of short-term outcome in CHHIPS & COSSACS. Age and baseline NIH were confirmed as significant predictors of outcome; however baseline BP using a standardised set of multiple BP readings was not associated with outcome. Beat-to-beat BPV may have more relevance in acute stroke. Further prospective studies are required to establish the clinical relevance of BPV in acute stroke, and ist potential as a therapeutic target.

17 Acute stroke: emergency management, stroke units and complications B

RESULTS OF IMPLEMENTATION OF INTRAVENOUS THROMBOLYSIS IN STROKE PATIENTS IN THE RUSSIAN FEDERATION IN 2009-2010: DATA OF HOSPITAL REGISTRY

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Background: Intravenous (IV) rt-PA is the most effective treatment in acute ischemic stroke patients. Federal anti-stroke program was started in 38 regions of the Russian Federation (RF) since 2008 and by now 70 primary and 25 comprehensive stroke units (SU) were created with all possibilities for acute stroke care, available CT for 24 hs and neurorehabilitation. The aim of our study was to assess the rate, safety and efficacy of IV rt-PA using in SUs in the first 3 hours of stroke onset in comparison with Results of large multicenter trials.
Methods: A prospective, multicenter, observational study was conducted between 01Jan 2009 and 31Dec 2010 in 95 SUs. All consecutive patients (totally 49,688) who were hospitalized in SUs within 21 days after the IS onset were included in internet-based hospital registry (HP). We enrolled all patients treated with IV rt-PA in routing clinical practice according NINDS protocol that were registered in HP. Symptomatic hemorrhagic transformation (sHT) was defined according to NINDS criteria and calculated from CT scans done 22-36 hs after rt-PA. Mortality rate as well as number of patients with favorable outcome (mRs score 0-2) were also calculated.
Results: One thousand and sixty eight patients received IV rt-PA (2.15% of all ischemic stroke patients, ranging from 0 to 7.7% in different CUs, mean age 66.3; 70.4% male; mean NIHSS score at admission 13.8). At 22-36 hs the sHT rate was 7.1% (6.4% in NINDS trial and 7.3% in SITS-MOST). The mortality rate at 3 month was 16.4% (17% in NINDS and 11.3% in SITS-MOST). The favorable outcome was observed at 3 month in 52.5% patients (54.7% in SITS-MOST).
Conclusion: These data suggest that the first Results of implementation of IV rt-PA treatment in routing clinical practice in the RF are comparable with Results of large multicenter clinical trials in terms of safety and efficacy. Greater rate of mortality in comparison with SITS-MOST data can be explained more severe strokes at admission.

18 Acute stroke: emergency management, stroke units and complications B

URBAN STROKE CARE: HAMBURG AGAINST STROKE (HAGS)

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Background: Early intravenous thrombolysis with alteplase improves clinical outcomes in patients with ischemic stroke but only a minority of patients receives thrombolysis at all. We aimed at increasing the rate of thrombolysis in patients with ischemic stroke in the Hamburg metropolitan area and to shorten the delay from symptom onset to the beginning of thrombolysis.
Methods: In 2007, all 9 hospitals with dedicated stroke units in Hamburg together with local healthcare authorities initiated a stroke care quality project. The project included mandatory admission of all stroke patients in Hamburg exclusively to hospitals with stroke units, optimization of stroke emergency logistics in all stroke centers, a multimedial educational campaign using various mass and print media, and a mandatory stroke care quality monitoring system based on structured data assessment and quality indicators for procedural measures.
Results: From 2007 to 2009, a total of 22264 patients with acute stroke were registered. During that time, the proportion of expeditious neuroimaging (≤60 minutes) on admission in patients with symptom onset ≤3 hours increased from 53% in 2007 to 71% in 2009 (p<0.001). In parallel, the rate of thrombolysis in patients ≤3h with ischemic stroke increased from 53% to 65% (p<0.001), and the rate of expeditious thrombolysis (≤60 minutes from admission) increased from 65% to 82% (p<0.001).
Conclusion: Collaborative stroke care quality projects are suitable and effective for ameliorating acute stroke care and for enhancing rapid access to thrombolysis.

19 Acute stroke: emergency management, stroke units and complications B

NETWORKING IMPROVES ACCESSIBILITY OF STROKE FAST TRACK TREATMENT AT SRINAGARIND HOSPITAL, KHON KAEN, THAILAND

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Background: Stroke Fast Track has been established at Srinagarind Hospital since May 1, 2008. The treatment cost is supported by the National Health Security Office (NHSO). We launched the stroke fast track campaign to the community and local hospital around our hospital in October 2009.
Objective: To study the successfulness of stroke networking on stroke treatment and the outcome of the stroke fast track.
Results: Since 2008, there were 685 patients diagnosed as acute stroke. Out of those, 105 patients received rt-PA treatment (15.33%). The pre-networking era, there were 261 patients diagnosed with acute stroke. Seventy-nine patients were eligible for stroke fast track (30.27%) and 26 patients received rt-PA (9.96%) with the average door to needle time of 87 minutes. Two patients had intracerebral hemorrhage (7.69%). After the networking campaign, 424 patients were diagnosed as acute stroke. There were 202 patients (47.64%) were eligible for stroke fast track with the rt-PA treatment rate of 18.63% (79 patients). The average door to needle time was 54 minutes and two patients had intracerebral hemorrhage (2.53%).
Discussions: The overall outcome of stroke fast track may not be different from other reports. But the eligible rate is higher than other reports. The second year period after the stroke fast track service had better outcome and higher rate of participation. In addition to technical experience, the networking campaign may play an important role on the successful outcomes. These Results may support the importance of networking campaign to general public and hospitals under the catchment area of stroke center.
Conclusions: Networking may contribute to better outcomes in stroke fast track facilities and accessibility.

20 Acute stroke: emergency management, stroke units and complications B

TEMPORAL TRENDS IN STROKE EPIDEMIOLOGY AND QUALITY OF STROKE CARE. DATA FROM THE HAMBURG AGAINST STROKE (HAGS) PROJECT

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Background: Quality monitoring projects of acute stroke care provide unique data on regional stroke epidemiology and on stroke care quality within specified areas. We aimed at improving quality measures of stroke care across the Hamburg metropolitan area.
Methods: In 2007, all 9 hospitals with dedicated stroke units in Hamburg together with local healthcare authorities initiated a stroke care quality project. The project included a mandatory stroke care quality monitoring system based on structured data assessment and quality indicators for procedural measures.
Results: From 2007 to 2009, a total of 22264 patients with acute stroke were registered. 60% of patients had suffered an ischemic stroke, 33% a TIA, and 7% an intracerebral hemorrhage. 55% of patients were disabled (mRS 3-5) on admission. Within the observed period, the rates of patients with rapid access to physiotherapy and logopaedia steeply increased (p<0.001). Significantly more patients underwent neurosonography and screening for swallow disorders (p<0.001). Moreover, the proportion of patients who underwent neuroimaging and who rapidly received secondary prevention markedly increased (p<0.001). Results on emergency care including thrombolysis are reported separately.
Conclusion: Collaborative stroke care quality projects are suitable and effective for improving procedural measures of stroke care across larger areas.

21 Acute stroke: emergency management, stroke units and complications B

EVALUATING RATE OF ACUTE ISCHEMIC STROKE PATIENTS WHO ARE ELIGIBLE FOR INTRAVENOUS THROMBOLYTIC THERAPY IN NORTHWEST IRAN AND ITS LIMITATIONS

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Background: Intravenous thrombolysis is an approved therapy for acute ischemic stroke (AIS) patients and is recommended in multiple guidelines. Reports form developing countries shows its use is not as much as expected. The purpose of this study was to estimate how many of AIS patients in our hospital are eligible for intravenous thrombolytic therapy and what are the limitations.
Methods: Consecutive 515 AIS patients admitted in Imam Reza Medical Center, Tabriz, Northwest Iran, during September 2009-Agust 2010 enrolled in a observational study. Imam Reza Medical Center is a tertiary university hospital which has infrastructure for thrombolytic therapy. Neurological examinations, time between symptoms onset to hospital arrival, hospital arrival to performing brain computed tomography (CT) scanning and hospital arrival to complete investigations were recorded. Exclusion checklist for tissue Plasminogen Activator (tPA) administration was fulfilled by neurology residents. We didn't assess the patients capability to pay tPA expense, as in our country health insurance system dose not cover tPA.
Results: Mean time interval between hospital arrival to completing brain CT scanning was 91.3 min (ranged 20–378 min) and hospital arrival to complete investigations was 149.8 min (ranged 30–540 min). One hundred fifty nine (30.8%) patients were arrived to hospital in the first three hours of symptom onset. 82.3% of this early arrived patients (131/159) missed thrombolytic therapy due to delayed performance of brain CT scanning and laboratory tests and 7.5% (12/159) due to having other tPA

Oral Session
Acute stroke: emergency management, stroke
units and complications B

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49

contraindications. Remained sixteen patients were eligible for thrombolytic therapy which included 10.0% of early arrived patients and 3.1% of all cases.
Conclusion: Comparing with previous reports, in-hospital investigation delay is a more important barrier for implementation of thrombolytic therapy in our hospital.
Keywords: acute ischemic stroke, tissue Plasminogen Activator (tPA), eligible.

Stroke prognosis B

10 Stroke prognosis B

CEREBRAL EDEMA IN ACUTE ISCHEMIC STROKE PATIENTS TREATED WITH INTRAVENOUS THROMBOLYSIS

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Background: Cerebral edema (COED) deteriorates outcome in patients with large ischemic strokes. We analyzed the baseline characteristics and outcome of thrombolysis-treated patients with different types of COED and the effects of medical antiedema treatments.
Methods: Our study cohort included 943 ischemic stroke patients, with available information on both COED and outcome, treated with intravenous thrombolysis at the Helsinki University Central Hospital (1995-2008). COED on native control head CT scan was categorized according to the ECASS-II criteria: hypodensity on native head CT scan occupying less than (COED 1) or more than (COED 2) 1/3 of the hemisphere, or causing midline shift (COED 3). Univariate and multivariable Methods tested associa-tions of baseline parameters with development of COED, and association of COED with 3-month out-come (modified Rankin Scale, mRS).
Results: In control imaging, COED 1 was present in 167 (17.7%), COED 2 in 40 (4.2%), and COED 3 in 53 (5.6%) patients. Compared with patients without edema, patients with any type of COED had more severe admission symptoms (NIHSS), received thrombolysis later, and had more often hyperdense cerebral artery sign and early infarct signs on admission head CT scan. The number of patients with good 3-month outcome (mRS 0-2) was 77/167 (46%), 5/40 (13%), and 3/53 (6%) in COED groups, respectively. COED was independently associated with 3-month outcome. Medical antiedema treatment was considered necessary and given to 49/273 (18%) patients with COED; only five of them gained mRS 2, none mRS 0-1.
Conclusion: Cerebral edema is frequent (<28%) among thrombolysis-treated ischemic stroke patients, also in more severe forms (<10%). Higher baseline NIHSS, longer treatment delays, and admission head CT scan findings of developing infarct or visible clot are associated with edema development. Edema per se is a strong independent predictor of 3-month outcome. Antiedema treatment trials are warranted.

11 Stroke prognosis B

PROGNOSTIC IMPACT OF THE TP53 CODON 72 POLYMORPHISM IN STROKE

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Background: Accurate prediction of functional outcome after stroke is currently elusive although it is conceivable that poor prognosis may be related to neuronal apoptosis. The Tp53 Arg72Pro polymorphism occurs in a proline-rich domain involved in the pro-apoptotic function of the tumor suppressor protein p53. Here we studied whether the Arg72Pro polymorphism is a prognostic genetic marker of functional outcome after stroke.
Methods: Tp53 Arg72Pro and Ins16bp polymorphisms were genotyped in 408 patients with ischemic stroke and 128 patients with intracerebral hemorrhage (ICH) (exploratory cohort). The validation cohort included 103 patients with ischemic stroke and 47 with ICH from a different community. The main outcome variable was poor functional outcome (modified Rankin scale >2 at 3 months). Secondary outcome variables were early neurological deterioration (END) and infarct volume and residual ICH volume. In addition, the Arg72Pro polymorphic variants were expressed in rat cortical primary neurons, which were analyzed for the apoptotic phenotype.
Results: The Arg/Arg genotype was independently associated with poor functional outcome after either ischemic stroke (Exploratory cohort: OR 3.89 [95% CI 1.63 - 9.28], p=0.002; Validation cohort: OR 3.40 [95% CI 1.12 - 11.80], p=0.024) or ICH (Exploratory cohort: OR 360.7 [31.5 - 4132.1], p<0.0001; Validation cohort:

OR 4.73 [95% CI 1.17 - 29.78], p=0.013) after adjustment for confounding factors. This polymorphic variant was also associated with END (OR 7.77 [1.72 - 35.01], p=0.008) in ischemic stroke, and with increased residual lesion volume in ICH (B 15.40 [12.17 - 18.62], p<0.0001). Furthermore, the polymorphic variant p53-Arg triggered the intrinsic apoptotic pathway in rat cortical primary neurons and increased neuronal vulnerability to excitotoxicity.
Conclusion: The Tp53 Arg72Pro polymorphism might explain the inter-individual variability in the apoptotic response after stroke; the Arg/Arg genotype can be considered a genetic marker for poor functional outcome after stroke.

12 Stroke prognosis B

A PROGRAM OF RESEARCH INFORMING STROKE MANAGEMENT (THE PRISM STUDY): ONE YEAR OUTCOMES AFTER HOSPITAL TIA DIAGNOSIS

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Background: Few large-scale modern-day studies report outcomes of hospitalised transient ischaemic attack (TIA).
Methods: All patients with a TIA separation diagnosis (ICD-10 code G45.x) in New South Wales, Australia (population <7 million), were identified from administrative census of all hospitalisations 2005-7. Patients were followed for re-admission rates of stroke (ICD10 I60.x-I64), AMI (ICD-10 I21.x, I22.x, I25.2), and death at 7, 30, 90 and 365-days after discharge. Cumulative rates were estimated using competing risks survival analysis to account for competing effect of death. Cox-regression analyses estimated risks of a combined endpoint of stroke, AMI and death.
Results: 7,062 patients were discharged from hospital with TIA; median age=75.0. Within 7-days, 1.0% (95% CI=0.8-1.1%) were re-admitted to hospital with stroke; 1.6% (95% CI=1.4-1.9%) by 30-days, 2.6% (95% CI=2.3-2.9%) by 90-days and 5.3% (95% CI=4.8-5.8%) by 365-days. A combined triple endpoint of stroke and AMI admission or all-cause death was 2.8% (95% CI=2.5-3.3%), 5.6% (95% CI=5.0-6.2%) and 15.0% (95% CI=13.9-16.1%) 30, 90 and 365-days, respectively. Controlling for age, sex, year of separation and clustering effects by hospital, significant predictors of stroke re-admission included history of stroke in the previous five-years (Hazard Ratio (HR)=1.62, 95% CI 1.19-2.21), previous history of atrial fibrillation (AF) (HR=1.32, 95% CI=1.01-1.74), and smoking status (HR=1.59, 95% CI=1.12-2.26). Smoking status, COPD, dysphagia, AF and diabetes significantly and independently predicted a triple endpoint of stroke, AMI or death within 365-days.
Conclusion: Post-discharge stroke rates were low in this modern cohort of hospitalised TIA. However, TIA remains a predictor of serious outcomes with 15% having a stroke or AMI or dying in the first year. Stroke was predicted by previous stroke history, AF and smoking status; additionally COPD, dysphagia, and diabetes predicted the triple end-point.

13 Stroke prognosis B

MARRIED PERSONS SURVIVE STROKE BETTER THAN SINGLES

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Background: Married persons generally have lower mortality than persons living alone. We studied the potential influence of marital status (married/living with someone or single living) on survival in patients with first-ever-ischemic stroke.
Methods: A registry designed to register all hospitalized stroke patients in Denmark since 2001 holds 26 818 patients with first-ever ischemic stroke. Patients underwent evaluation including stroke severity (Scandinavian Stroke Scale, SSS), CT-scan and cardiovascular risk factors: hypertension, atrial fibrillation, diabetes mellitus, intermittent arterial claudication, previous myocardial infarction, smoking, and alcohol consumption. Marital status at time of stroke was registered. Survival was followed up to 1 year through the Danish Central Person Registry. Predictors of 1-month to 1-year case-fatality were identified using multiple regression analysis.
Results: Of the patients 48.5% were women; 51.5% were men. Mean age 71.2 (SD 13.4) years; mean SSS score 43.9 (SD 15.2). Single living at the time of stroke: women 54.0% and men 29.5%. Compared to patients married or living with someone at the time of stroke single living reduced the chance of survival within 3 months and within 1 year after stroke by 16% (OR 0.84; CI 0.70-1.00) and 15% (OR 0.85; CI 0.74-0.97) respectively, independent of age, sex, stroke severity and the cardiovascular risk factor profile. Marital status had no significant effect on survival within the first month after stroke (OR 0.92; CI 0.74-1.14).

Conclusion: Married persons survive stroke better than singles. Marital status does not influence survival from stroke by an effect on recovery from the initial infarct as survival within the first month was not affected by marital status. Marital status rather exerts an effect on post stroke deaths not directly related to the index stroke (such as recurrent cardiovascular events etc.). An effect on lifestyle may be involved.

14 Stroke prognosis B

PROGNOSIS OF CEREBRAL VEINS AND DURAL SINUS THROMBOSIS

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Background and purpose: Cerebral veins and dural sinus thrombosis (CVDST) is a rare condition occurring predominantly in young patients. In Mexico is of most interest for high frequency and presentation during pregnancy and postpartum. The objectives of this study were to evaluate the mortality rate, disability and recurrence in a short-term prognosis after an episode of CVDST.
Methods: We performed a prospective, observational study in a Neurological hospital in Mexico City. Data of patients with radiologically confirmed CVDST were collected during a 23 years period. The demographic, clinical, radiological data and outcome at the time of hospital discharge and 3 months follow-up were recorded and analyzed. Primary outcome was death or dependency as measured by the Modified Scale Rankin (mRs).
Results: From January 1987 to July 2010; 415 patients (mean age 31±12 years, 83% female) were included. The main causes of CVDS were; puerperium (40%), thrombophilia (25.8%), pregnancy (8.9%), oral contraceptives (7.5%). It was not possible to determine the cause in 17% of cases. During the acute phase 40 (10.5%) patients died (mRs 6) without finding at 3 months. At hospital discharge 140 patients (33.7%) had no symptom or signs (mRS 0), 40 (9.6%) had minor residual symptoms (mRS 1), and 117 (28.2%) had mild impairments (mRS 2). Fifty two (12.5%) were moderately impaired (mRS 3), 18 (4.3%) were severely handicapped (mRS 4 or 5). At 3 months follow-up three hundred sixty two (89.6%) were independent, forty three (10.4%) remain dependent (mRs > 2). Multivariate predictors of death or dependence were age > 29 years (hazard ratio (HR 2.6; 95% IC, 1.1 to 6.5), coma (HR 7.6; 95% IC, 2.1 to 26.5), intracerebral hemorrhagic lesion (HR 2.7; 95% IC, 1.1 to 6.8), lesion larger than 6 cm (HR 7.9; 95% CI, 3.2 to 19.1) and bilateral Babinski (HR 6.7; 95% CI, 2.6 to 17.3). Four patients (0.9%) had a recurrent sinus thrombosis, 5 (1.2%) had other thrombotic events.
Conclusions: Our Results suggest that different risk factors and predictors of mortality and dependence involved in the short term outcome in Hispanic patients with CVDST.

15 Stroke prognosis B

ISCHEMIC STROKE DURING SLEEP: ITS ASSOCIATION WITH WORSE FUNCTIONAL OUTCOME

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Background: Approximately one quarter of strokes occur during sleep. Despite the clinical and radiological similarities between wake-up stroke (WUS) and non-WUS, the functional outcomes of WUS are largely unknown.
Methods: This retrospective analysis reviewed 2,289 consecutive acute ischemic stroke or transient ischemic attack (TIA) patients who admitted between November 2002 and December 2009. WUS was defined as a stroke in which symptoms were recognized on awakening, and functional outcome was measured by modified Rankin Scale (mRS) score at discharge. We utilized three end-point analytic techniques to evaluate the association between WUS and functional outcomes in multivariable models: dichotomous analysis for "functional dependency" (a discharge mRS score≥2, regardless of initial stroke severity), severity-adjusted responder analysis for "unfavorable outcome" (mRS≥1 for an admission NIHSS score 0-7; mRS≥2 for NIHSS 8-14; or mRS≥3 for NIHSS≥15), and shift analysis for changes in overall distributions of mRS scores.
Results: WUS patients had higher initial NIHSS scores than non-WUS counterparts (median [IQR]; 4 [2, 7] vs. 3 [1, 6]; P<0.01), as well as mRS scores (Figure). WUS group showed delayed admission (P=0.02) with fewer reperfusion therapy (P<0.01), and higher proportion of TIA (P<0.01). The dichotomous analysis strategy failed to detect a significant association between WUS and functional dependency (adjusted OR, 0.99; 95% CI, 0.76-1.28). However, the responder analysis showed that WUS patients were more likely to have "unfavorable outcomes," (OR, 1.33; 95% CI, 1.02-1.72), and the shift analysis also detected significant effect of WUS on the mRS score distributions, toward increased dependency (OR, 1.22; 95% CI, 1.01-1.48).
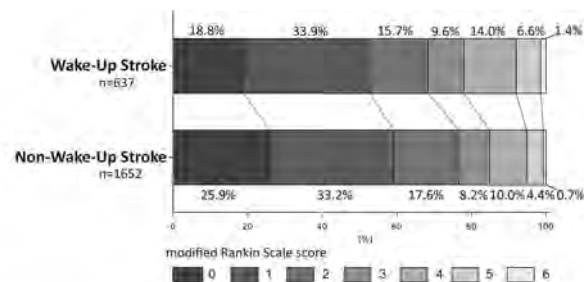
Figure. Distribution of modified Rankin Scale score according to the activity at the onset of stroke.

Conclusion: Our study showed that WUS was associated with worse functional outcomes in responder and shift analyses. Careful selection of appropriate analytic techniques may help to detect modest associations in observational studies.

16 Stroke prognosis B

HEALTH RELATED QUALITY OF LIFE IS RELATED TO OUTCOME AT ONE WEEK AND THREE MONTHS IN STROKE SURVIVORS: DATA FROM THE EFFICACY OF NITRIC OXIDE IN STROKE (ENOS) TRIAL

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Introduction: Consideration of health related quality of life (HRQOL) after stroke is becoming increasingly important, providing a patient's perspective on outcome. There is a need for a thorough and comprehensive analysis of the factors associated with HRQOL.
Methods: Data from 1,662 acute stroke patients in the Efficacy of Nitric Oxide in Stroke (ENOS) trial was used to explore HRQOL after stroke. HRQOL was measured at day 90, using the EuroQol questionnaire which assesses HRQOL across 5 domains (EQ 5D) and by a self-rated visual analogue scale (VAS). The relationship between baseline prognostic factors; outcome at day 7 (recurrent stroke, deterioration and dysphagia); and outcome at day 90 (modified Rankin Scale (mRS), Barthel Index (BI), mood (Zung depression score, ZDS) and disposition; were assessed by using Spearman's rank correlation coefficient for continuous data and ordinal logistic regression for ordinal or nominal data.
Results: HRQOL after stroke was significantly related to impairment (Scandinavian Stroke Scale) both at baseline (r=0.533; p<0.0001) and at day 7 (r=0.605; p<0.0001). At 90 days, HRQOL correlated strongly with dependency, mRS (r=-0.834; p<0.0001); disability, BI (r=0.834; p<0.0001); and mood, Zung (r=-0.727; p<0.0001). Correlation was stronger with EuroQoL domain scores rather than VAS. Neither age or side of affected hemisphere were related to HRQOL.
Independent predictors of a poor HRQOL were female sex (OR, 1.48; p<0.0001), pre-morbid mRS>0 (OR, 1.71; p<0.0001), previous TIA (OR 1.53; p=0.007), history of atrial fibrillation (OR 1.82; p=0.007), history of recurrent stroke (OR 5.03; p<0.0001), dysphagia (OR 5.18; p<0.0001), neurological deterioration (OR 4.21; p<0.0001) and being in an institution (OR, 0.53; p<0.0001).
Conclusions: After stroke, HRQOL was related to baseline impairment, and 90 day disability. Further work is needed to identify potentially modifiable factors that may be targeted to improve HRQOL after stroke.

17 Stroke prognosis B

INTRACRANIAL ARTERY CALCIFICATION AND OUTCOME IN ISCHEMIC STROKE PATIENTS AFTER HOSPITAL DISCHARGE: A COHORT STUDY

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Background and purpose: Although intracranial artery calcification (IAC) was reported as a risk factor for ischemic stroke, the prognostic implications of IAC in stroke outcome is unknown. The purpose of this study was to determine the association between IAC and risk of vascular events and death in stroke patients after hospital discharge.

Subjects and Methods: All patients with ischemic stroke during a one-year period were included (n=302). IAC, assessed by multi-detector computed tomography, were defined as hyperdense foci (peak density greater than 130 Hounsfield units) and assessed retrospectively in the seven major cerebral arteries. Patients were followed up regularly for up to two years for the occurrence of major clinical events (MCE), including fatal or nonfatal ischemic stroke, cardiac and peripheral artery events, and death from any cause.

Results: IAC was present in 260 patients (83%). During a mean follow-up period of 715 (±276) days, 88 (30%) MCE occurred in 67 patients: 45 (15%) new ischemic vascular events (ischemic stroke: n=22; cardiac event: n=15; vascular event: n=8) and 43 (14%) deaths of any cause. Kaplan Meier analysis showed that MCE were significantly greater in patients with IAC compared to those without (p=0.012, log-rank test). In the Cox-proportional-hazards regression model, the adjusted hazard ratios for MCE in the presence of IAC was 4.7 (95%CI: 1.06-21.34; p=0.04).

Conclusions: In ischemic stroke patients, the presence of IAC is a strong and independent predictor of MCE after hospital discharge, suggesting that careful attention should be given to the presence of IAC as a prognostic indicator in a simple head CT scan.

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18 Stroke prognosis B

STATINS AFTER CRYPTOGENIC ISCHEMIC STROKE IN YOUNG ADULTS IN CLINICAL PRACTICE

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Background: High-dose atorvastatin reduced the incidence of new vascular events after stroke or transient ischemic attack in a randomized trial. However, it is unknown whether very young individuals with cryptogenic stroke would benefit from statins.

Methods: We used a database of 1008 consecutive patients aged 15-49 with first-ever ischemic stroke to investigate (1) the practice of statin prescription and (2) whether statins would associate with subsequent vascular events (composite endpoint of stroke, myocardial infarction/other arterial thrombosis, revascularization, or vascular death). Four groups of statin users were identified: (1) never, (2) continuous, (3) early statin only, and (4) delayed start statin.

Results: Of the 300 patients included (mean age 40.5±8.3 years, mean follow-up in survivors 9.4±4.0 years), 100 (33.3%) patients used statin during the follow-up. These were likely to be older, have poorer lipid profile and hypertension. There were 41 (20.5%) events in patients never on statin (n=200), 1 (2.2%) in those with continuous statin (n=46), 1 (6.3%) in those with early statin only (n=16), and 4 (10.5%) in those with delayed start statin (n=38). After adjustment for age, sex, dyslipidemia, hypertension, antihypertensive medication, stroke year, and extent of evaluation, patients with continuous statin (hazard ratio [HR] 0.11, 95% confidence interval [CI] 0.02-0.84; P=0.033) and delayed statin (HR 0.11, 95% CI 0.02-0.78; P=0.027), but not with early statin only, were less likely to have endpoint events in a Cox proportional hazards analysis.

Conclusions: Young patients with cryptogenic ischemic stroke seem to benefit from statins in secondary prevention of vascular events.

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19 Stroke prognosis B

ELOQUENCE OF REGION AND EXTENT OF BRAIN ISCHEMIA DETECTED BY DWI PREDICTS DEGREE OF 24H NIHSS SCORE IMPROVEMENT AFTER ARTERIAL RECANALIZATION IN ISCHEMIC STROKE

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Introduction: Improvement in NIHSS score at 24 hrs or delta NIHSS change (ΔNIHSS) is an early measure of response to recanalization therapy and has been associated with good outcome. We hypothesized that ΔNIHSS achieved with recanalization may be influenced by eloquence of region and the extent of brain ischemia within a vascular territory on baseline imaging.

Methods: From the prospectively collected Keimyung University stroke database, patients with proximal anterior circulation occlusions who recanalized (TIMI 2/3) after IV/IV+IA therapy on DSA or MRA were analyzed. Two readers evaluated baseline DWI and graded ischemic infarcts to 16 anatomical regions as 7 cortical MCA (M1-M6, insula), 5 subcortical MCA (3 corona radiata, basal ganglia; posterior limb of internal capsule (IC)), 2 ACA and 2 PCA. Based on the number of infarct regions involved, patients were categorized into four groups: minimal (0-3 infarct regions), moderate (4-6), large (7-9) and extensive (>9). Median ΔNIHSS change with atleast 10 pts reported.

Results: Among 265 patients, subset of 101 patients who recanalized were studied. ΔNIHSS >10 was seen in 25 (25%) of subjects. Median ΔNIHSS was: 12 for minimal involvement, 10 for moderate, 0 for large and -1 for extensive (p=0.007). There was significant improvement in ΔNIHSS in patients with < 6 areas of involvement (p<0.001). The most eloquent regions where involvement predicted less ΔNIHSS were: basal ganglia (4/25, 16%) (OR 0.23 95%CI 0.07-0.75, p=0.01) and posterior limb of IC (1/25, 4%) (OR 0.09, 95%CI 0.01-0.7,p=0.006).The least eloquent region involved showing significant ΔNIHSS was M4 (14/25, 56%) (p=0.01, OR- 3.1 95% CI-1.22-7.93).

Conclusions: ΔNIHSS at 24 hours after recanalization is inversely proportional to the number of anatomical regions involved. Patients with more than six infarcted regions had marginal improvement in ΔNIHSS. Patients with involvement of basal ganglia and IC have least chance for a significant improvement in NIHSS score.

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20 Stroke prognosis B

KIDNEY FUNCTION AND ISCHEMIC STROKE IN YOUNG ADULTS

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Background: Kidney dysfunction is linked to poorer outcomes after ischemic stroke in the elderly, but data are lacking regarding young patients.

Methods: We investigated the kidney function based on admission estimated glomerular filtration rate (eGFR) in 958 patients aged 15-49 with first-ever ischemic stroke. Logistic regression adjusted for age, gender, and stroke risk factors was used to identify factors related to low (<60) and high (>120 mL/min/1.73 m^2) eGFR. In the follow-up study (mean follow-up in survivors 8.9±3.8 years), Cox proportional hazards analysis was used to investigate the association between eGFR and the following endpoints: (1) nonfatal/fatal ischemic stroke; (2) composite vascular event of any stroke, myocardial infarction, revascularization/other arterial occlusive event, or vascular death; and (3) death of any cause.

Results: Estimated GFR was normal (60-120 mL/min/1.73 m^2) in 809 (84.4%), low in 43 (4.5%), and high in 106 (11.1%) patients. Type 1 diabetes (odds ratio 18.84, 95% confidence interval [CI] 8.65-41.03), hypertension (4.29, 1.94-9.48), and cardiovascular disease (2.66, 1.19-5.96) were independently associated with low eGFR. Type 2 diabetes (3.82, 1.93-7.55), lower age (0.95 per year, 0.93-0.98), and male gender (1.74, 1.08-2.82), were associated with high eGFR. Both low (hazard ratio, 5.73, 95% CI 3.54-9.25) and high eGFR (1.78, 1.01-3.14) were associated with long-term mortality, when adjusted for age, gender, risk factors, stroke severity and subtype. No independent association between eGFR and vascular events appeared.

Conclusions: Despite their different associated risk factors, both low and high eGFR predicted long-term mortality after an ischemic stroke in the young.

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21 Stroke prognosis B

7 TO 29 YEAR FOLLOW-UP STUDY OF COGNITIVE OUTCOME AFTER YOUNG STROKE. THE FUTURE STUDY

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Background: There are no studies reporting on the long term follow-up of cognitive performance after a young stroke (18-50 years). In addition, existing studies do not report on possible confounding factors including measures on depressive symptoms and fatigue.

Objective: To investigate the long term post stroke cognitive performance, taking into account depressive symptoms and fatigue.

Methods: We investigated patients from the FUTURE study, a long term follow-up study on causes and consequences of young stroke including 777 patients. We here report on the first 50 patients who were recruited for follow-up examination 18.3 years (range 7-29) after stroke (mean current age 57.7 years, SD=8.4) compared with an age and education matched control group (mean age 55.0 years, SD=13.6). Cognitive functioning was investigated with a neuropsychological battery covering all major cognitive domains, mood and anxiety disorders and fatigue.

Results: The patient group consisted of 28 men and 22 women. Patients performed worse on tests of episodic memory (Auditory-Verbal Learning Test: p<0.001; Cohen's d=0.7-1.0), psychomotor-speed (Symbol-Digit Substitution Task; p<0.01;

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d=0.6) and executive function (Stroop interference p<0.01; d=0.7) than controls. Basic attention, language production and semantic memory were unimpaired (d=0.1-0.4). There were no differences between groups with respect to mood or anxiety disorders (d=0.1) and mental fatigue (d=0.2-0.3).

Conclusion: Even about 20 years after stroke, patients still suffer from episodic memory dysfunction, taking into account depressive symptoms or fatigue. Future studies will aim at the underlying substrate.

Etiology of stroke and risk factors B

10 Etiology of stroke and risk factors B

TIME COURSE OF N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE IN ACUTE ISCHEMIC STROKE

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Background: Studies suggest than N-terminal pro-brain natriuretic peptide (N-BNP) may be useful as a biomarker of cardioembolic stroke. However, there is scarce and contradictory data about the best time to determine it.
Objective: We aimed to determine the time course of N-BNP in patients with ischemic stroke.
Methods: Sample: consecutive acute ischemic stroke patients admitted over 10 months to a Stroke Unit. Stroke etiology was classified according to TOAST criteria. Patients with coronary disease, valve disease and renal failure (causes of N-BNP increase) were excluded. Blood samples were drawn within 24, 48 and 72 hours after stroke onset. Serum N-BNP concentration was measured using an electrochemiluminescence immunoassay. Friedman test was used to compare N-BNP values across the 3 times of blood sampling in patients with ischemic stroke in general, cardioembolic and noncardioembolic stroke. Post-hoc analysis with Wilcoxon Signed-Rank Tests was conducted with a Bonferroni correction. Mann-whitney test was used to compare the median values of N-BNP between groups of patients with cardioembolic stroke vs noncardioembolic stroke.
Results: 103 patients were included (36 cardioembolic stroke) with a mean age of 64.6±12.3 years. 61 (59.2%) were men. N-BNP values for cardioembolic stroke were significantly higher (p<0,001) than for noncardioembolic stroke in the 3 time points. There was a statistically significant difference of N-BNP values across the 3 time points in patients with stroke in general, cardioembolic and noncardioembolic stroke (p<0.001;0.002;0.001 respectively). In the 3 groups of patients, values of N-BNP were highest in the first 24-48h after ischemic stroke with no statistically significant difference (p=0.44; 0.84;0.20) and had a statistically significant reduction 72h after stroke onset (p<0.001;0.003;0.007).
Conclusion: N-BNP levels are highest 24-48 hours after ischemic stroke. These two time points are preferable for the determination of N-BNP.

11 Etiology of stroke and risk factors B

PLATELET MICROPARTICLES AS MARKER OF CEREBRAL EMBOLIC ACTIVITY/ISCHAEMIA IN SYMPTOMATIC CAROTID DISEASE

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Background: Microparticles are membranous phospholipid vesicles that are derived from activated platelets (PMP). PMP have been shown to be increased in stroke and TIA but it is unknown whether PMP are associated with risk markers of recurrent embolic events in patients with carotid artery disease, such as plaque haemorrhage, microembolic signals or multiple cerebral diffusion abnormalties (DWI).
Methods: Patients with recently symptomatic high grade carotid stenosis (60-99%, n=44, 33 men, mean age 75) and healthy volunteers (N=24, 10 men, mean age 65) were prospectively recruited. Patients were characterised by carotid MR imaging (presence of plaque haemorrhage, PH+), brain diffusion MRI (cerebral ischaemia, DWI+), and TCD (microemboli signals, MES+). Older healthy volunteers had a screening carotid ultrasound to exclude asymptomatic carotid disease. PMPs were identified as CD31+, CD45-, CD42a+ microparticles by flow cytometry. PMP s/ul was log transformed to improve normal distribution and ANCOVA was used to compare between groups.

Results: 2 patients were excluded due to claustrophobia, 3 controls for asymptomatic carotid disease and one for a previous stroke.
On controlling for age, there was no significant difference in PMP in patients versus the control group. (PMP: 11326 (±SD 8663) vs 5384 (±SD 3094); F=1.2 P=0.274).
In contrast, there were more PMP in patients with evidence of acute cerebral ischaemia (DWI+ patients 16493 (±SD 9876) vs. 7814 (±SD 5607); F=10.0 P=0.003) and with signs of on-going microembolisation (MES+: 17127 (±SD 9212) vs. 6976 (±SD 4998); F=19.0 p=0.0001) than in those without. These differences were independent of age and time from initial symptom. PH status did not affect PMP.
Conclusion: Elevated platelet microparticles in symptomatic carotid disease are associated with on-going microembolisation/cerebral ischaemia and have the potential to be used as a risk factor for recurrent stroke.

12 Etiology of stroke and risk factors B

LP(A) AND CAROTID ATHEROSCLEROSIS IN YOUNG STROKE PATIENTS

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Background: Elevated Lp(a) concentration is an independent risk factor for ischemic stroke. In middle-aged and older patients with ischemic stroke, the association of Lp(a) and carotid atherosclerosis (CA) is well established. This association has not been explored in young stroke patients.
Methods: Retrospective analysis of data from 196 patients aged 16-54 years consecutively treated for acute ischemic stroke in a tertiary stroke unit was performed. We assessed CA using carotid duplex. CA was graded as follows: group A: no CA; group B: patients with atherosclerotic plaques without stenosis (<50%); group C: carotid stenosis (> 50%). Lp(a), cholesterol and triglycerides were measured on fresh blood samples after an overnight fast. Statistical analysis was performed using univariate analysis and multinomial regression analysis adjusting for traditional risk factors including cholesterol and triglycerides.
Results: 196 patients were included (M/F: 119/77; mean age: 44.3±8.6). 115 patients had no atherosclerosis (group A); 67 patients had no significant stenosis (group B); 14 patients had carotid stenosis (group C).
There was a graded relationship between Lp(a) concentration and CA severity in univariate analysis (Lp(a) concentration: group A: 0.26 g/l ±0.33; group B: 0.44 g/l ±0.43; group C: 0.73 g/l ±0.69; p=0.001).
In multivariate analysis, patients with Lp(a) concentration >0.50 g/l (upper quartile) had an adjusted odds ratio (95% confidence interval) of 2.59 (1.15-5.87) (p=0.03) for carotid plaques, and of 9.13 (2.41-34.5) (p=0.001) for carotid stenosis. Lp(a) was the only lipid variable associated with CA in multivariate analysis.
Conclusion: We found a positive association of Lp(a) plasma concentration with carotid atherosclerosis in young adults with ischemic stroke. This association was strong, graded and independent of classical risk factors including cholesterol.

13 Etiology of stroke and risk factors B

CEREBRAL VASCULAR CALCIFICATION AS A PREDICTOR OF VASCULAR RECURRENCE IN PATIENTS WITH ISCHEMIC STROKE

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Background: The presence of calcification in coronary arteries is a strong predictor of cardiovascular risk. The existence of cerebral vascular calcification (CVC) has been associated with the presence of vascular risk factors. Our objective is to demonstrate that the presence of CVC predicts the recurrence of vascular events in patients with ischemic stroke.
Methods: We prospectively studied 240 patients (70.58±12.1 years, 58.3% male) with acute ischemic stroke (<12 h from stroke onset) with a follow-up period of 5 years. CT at admission was evaluated by a neurologist expert in blind to clinical data. CVC was considered by the presence of a hyperdensity (1000 UH) in any artery of the circle of Willis. Vascular recurrence (VR) was considered as the presence of vascular death, arterial revascularization, myocardial infarct, stroke or any combination of them.
Results: 64 patients (26.7%) showed VR. The presence of CVC was more common in patients with VR (26 (41.9%) vs 36 (21.7%), p = 0.002). In a logistic regression model including all significant variables in univariate model, we found that high levels

of LDL-cholesterol (OR: 0.98, CI 95%: 0-97-0.99), previous history of atrial fibrillation (OR: 6.39, CI 95%: 2.17-18.82), carotid atherosclerosis in ultrasound at admission (OR: 6.49; CI 95%: 2.36-17.84), endothelial dysfunction (determined by brachial arterial flow-mediated dilation (FMD) <4.5%) (OR: 3.36, CI 95%: 1.46-7.73) and the presence of CVC (OR: 2.52. CI 95%: 1.13-5.61) were independently associated with VR.
Conclusions: The presence of calcifications in any artery of the circle of Willis in basal CT during the acute phase of stroke predicts vascular recurrence during the following 5 years.

14 Etiology of stroke and risk factors B

AORTIC STIFFNESS AMONG ISCHEMIC STROKE SUBTYPES

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Background: Arterial stiffness is a known risk factor for stroke. Ischemic stroke has heterogeneous underlying etiologies. There is a paucity of data on aortic stiffening among ischemic stroke etiological subtypes, with some studies suggesting stronger association with small artery stroke. We compared aortic stiffness between stroke etiological subtypes.
Methods: We consecutively recruited 437 ischemic stroke patients admitted to the Singapore General Hospital from 2003-2007. Within 7 days of symptom onset, aortic stiffness was measured by the gold standard carotid-femoral pulse wave velocity (cPWV) by investigators masked to clinical data. Stroke was subtyped using the Trial of Org 10172 in Acute Stroke Trial (TOAST) classification.
Results: The baseline characteristics of the study cohort are median age of 63 years (IQR 55-71), 76% Chinese, 79% hypertensive, 50% diabetic, 78% hyperlipidemic and 36% current smoker. Stroke subtype distribution was 45% small artery stroke, 33% large artery, 6% cardioembolic, 2% other etiology and 10% unknown etiology. Median cPWV was 11.2 m/s (IQR 9.8- 13.0) among patients with small artery stroke, 12.3 m/s (9.9- 14.9) with large artery stroke, 11.0 m/s (9.0- 14.6) with cardioembolic stroke, 12.4 m/s (8.5- 15.9) with stroke of other etiology and 12.3 m/s (10.7- 14.5) with stroke of unknown etiology. Median mean arterial pressure (MAP) was 105 mmHg (IQR 92- 118) during cPWV assessment. The cPWV was lower in patients with small artery stroke compared to those with non-small artery stroke (12.2 m/s IQR 9.8- 14.8) (p=0.018) as well as to those with large artery stroke (p=0.006). There was no difference in cPWV between patients with cardioembolic stroke compared to non-cardioembolic stroke (11.6 m/s IQR 9.9- 13.8) (p=0.556).
Conclusion: In our cohort of acute stroke patients, the degree of aortic stiffening differed between stroke etiological subtypes. Contrary to some published data, the aortas of patients with small artery stroke were less stiff compared to those with large artery stroke.

15 Etiology of stroke and risk factors B

THE IMPORTANCE OF CANCER RELATED RISK FACTORS AS POSSIBLE STROKE ETIOLOGY

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Background: Coagulation disorders in cancer patients have been well described since the 19th century. Still their importance for stroke etiology in cancer patients has received little attention with different Conclusions being drawn. A recent study suggested that cancer related stroke mechanisms may be of special importance in patients with absence of conventional stroke mechanisms, indicated by elevated d-dimer levels and DWI lesion patterns.
Methods: To test this hypothesis we identified ischemic stroke patients with the additional diagnosis of active and malignant cancer admitted to our stroke unit from 2002-2010. Stroke etiology, types of cancer, d-dimer levels and DWI lesion patterns were obtained by using our prospectively collected stroke, MRI and laboratory databanks.
Results: 119 patients (66 male, 53 female) were included. D-dimer levels were available for 63 patients. 60 patients (50%) showed an unconventional or unclear stroke etiology (non-CSE), whereas 59 (50%) showed a cardioembolic, macro- or microangiopathic and therefore conventional stroke etiology (CSE). 24% were first

diagnosed with new or recurrent cancer, with metastatic disease (61/119) being a common feature. Breast-, prostate-, and colorectal cancer were most frequent, but cancer types traditionally associated with a higher rate of thrombembolic complications like gastric (8% vs. 5% in general population) or pancreatic cancer (8% vs. 3%) were significantly overrepresented (p<0.001). D-dimer levels in the non-CSE group tended to be higher than in the CSE group (11.1; SD 17.05 vs. 5; SD 7.94; p=0.085).
Conclusion: Cancer related stroke mechanisms like paraneoplastic hypercoagulability seem to play an important role in stroke etiology among cancer patients, especially in absence of conventional stroke mechanisms. Establishing accurate diagnostic criteria for cancer patients with unclear stroke etiology is needed, as therapeutic options and prognosis in this group may differ.

16 Etiology of stroke and risk factors B

ABO PHENOTYPES AND ISCHEMIC STROKE

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Background: There is evidence that ABO blood group affects the level of von Willebrand factor (VWF), since A and B antigens binds to the surface of VWF. Previous studies have shown that blood group non-O (i.e. phenotype A, B or AB) is associated with myocardial infarction. Studies on stroke and ABO are, however, more scarce. The aim of the present study was to investigate whether the ABO phenotypes are associated with ischemic stroke and/or ischemic stroke subtypes.
Methods: The study was performed in the Sahlgrenska Academy Study on Ischemic Stroke (SAHLSIS), which comprises 600 patients with ischemic stroke between the ages of 18 and 69 years, and 600 matched controls. Patients were classified according to TOAST criteria. ABO genotype was determined using restriction fragment length polymorphism polymerase chain reaction (RFLP-PCR). ABO was analysed as a dichotomized variable, i.e. O vs. non-O, A vs. non-A, and B vs. non-B.
Results: There was no significant association between ABO phenotype (blood group O vs. non-O) and overall ischemic stroke (odds ratio (OR) of 1.0, 95% confidence interval (CI) 0.9-1.2). This was also true for blood group A vs. non-A and B vs. non-B (ORs of 1.0 (95% CI 0.9-1.3), and 0.9 (95% CI 0.7-1.2), respectively). The ischemic stroke subtype analysis was confined to LVD, SVD, CE stroke and cryptogenic stroke. In this analysis, there was no significant association between any ischemic stroke subtype and ABO phenotype.
Conclusion: The findings in this study suggest that ABO phenotype does not have a major impact in the pathophysiologic mechanism of ischemic stroke or any of the ischemic stroke subtypes.

17 Etiology of stroke and risk factors B

TRIGGERS OF ISCHAEMIC STROKE: A CASE-CROSSOVER STUDY

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Background: Most potential triggers of ischaemic stroke (IS) have been identified in isolated and/or small studies and some factors, which are known to trigger myocardial infarction, have never been assessed. Using a case-crossover design, we investigated the precipitating effects of several potential triggers within 24 hours before IS onset.
Methods: 217 consecutive IS patients (mean age 61.4 years, 57% males) admitted to our stroke unit (03/2007-07/2009) were interviewed using a standardised questionnaire to seek for exposure to alcohol abuse (>36 g of ethanol), anger (very angry, furious or enraged), heavy physical exertion (>5 metabolic equivalents), heavy meal (larger or much larger than usual), illicit drug use and sexual intercourse before IS onset. We compared exposure to triggers within the day before IS onset (hazard period) to exposure during the same day one week earlier (control period) using conditional logistic regressions (odds ratios, OR; 95% confidence intervals, CI) or McNemar tests when OR could not be estimated.
Results: Interviews were done within a median time of 5 (IQR 3-7) days after IS onset. 51 (24%) patients reported exposure to at least one trigger during the hazard period compared to 9 (4%) during the control period (OR=15.0; 95% CI, 4.7-48.3). Patients were significantly more often exposed within hazard than within control periods to physical exertion (22 vs 1 patients, OR=22.0; 3.0-163.2), and anger (11 vs 0, p=0.001). There was a nonsignificant association with alcohol abuse [5 vs 1;

OR=5.0; 0.6-42.8], heavy meal [4 vs 1, OR=4.0; 0.5-35.8], sexual intercourse [6 vs 1, OR=6.0; 0.7-49.8] and illicit drug use (4 vs 0, p=0.125).

Conclusion: Our Results support the triggering effects of several factors within the hours preceding IS onset. Whether pathophysiological mechanisms leading to IS onset differ according to trigger remains to be determined.

18 Etiology of stroke and risk factors B

RISK OF VASCULAR EVENTS AFTER NON-DISABLING SMALL AND LARGE VESSEL CEREBRAL ISCHEMIA OF ARTERIAL ORIGIN

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Background: Small and large vessel disease (SVD and LVD) have a different pathogenesis and prognosis but the long-term risk of death and recurrent stroke appears to be similar in previous studies. Data on cardiac events are scarce.
Methods and Results: We included 971 patients with transient ischemic attack or non-disabling ischemic stroke of arterial origin referred to a university hospital in The Netherlands between 1995 and 2009 and followed them for the occurrence of vascular events or death. Primary outcome was a composite of fatal or non-fatal ischemic events. Classification of SVD/LVD was primarily based on brain imaging. During a mean follow-up of 6.3 years new vascular events occurred in 56 of 312 SVD patients (3.3%/year) and in 128 of 659 LVD patients (2.9%/year). The corresponding age and sex adjusted hazard ratio (HR) for LVD versus SVD was 0.76; 95%CI 0.56-1.05. Cardiac events occurred in 57 LVD patients (1.3%/year) and 15 SVD patients (0.9%/year); HR 1.18; 95%CI 0.66-2.09. Ischemic stroke recurred less in LVD patients (HR 0.60; 95%CI 0.39-0.94). Recurrent stroke was classified LVD in 43 patients (80%) after LVD and SVD in 20 patients (61%) after SVD.
Conclusion: In patients with non-disabling cerebrovascular disease we found for the first time a better long-term prognosis for patients with LVD for all vascular events, especially for recurrent strokes. Recurrent stroke tended to remain true to type. Our observations support a different pathogenesis in SVD and LVD.

19 Etiology of stroke and risk factors B

A SIGNIFICANT ASSOCIATION OF OBESITY WITH CEREBRAL MICROBLEEDS IN ASYMPTOMATIC ELDERLY SUBJECTS

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Background: Obesity is known to be associated with an increased risk of cardiovascular disease. However, few studies have investigated the effects of obesity on subclinical cerebrovascular disease. The presence of cerebral microbleeds (CMBs) is a radiological marker of small vessel disease and the location of CMBs has generally reflected two types of vasculopathies in cerebral small vessels: areteriosclerotic vasculopathy and cerebral amyloid angiopathy. In this context, we assessed whether obesity was related to CMBs and to CMB subtypes categorized by location.
Methods: Asymptomatic elderly subjects (n=1251; age ≥ 65 years) who visited for routine health check-ups were included in this study. CMBs were evaluated through T2*-weighted gradient-recalled echo MRI. The subjects were categorized into two groups depending on CMB location: strictly lobar and deep or infratentorial microbleeds. Body mass index was calculated, and obesity was defined using the World Health Organization Western Pacific Regional Office criteria.
Results: A total of 120 (9.6%) subjects were found to have CMBs. As the severity of obesity increased, the prevalence of CMBs increased (P for trend < 0.05), and in the obese group, 52 (11.1%) subjects had CMBs. Compared with the normal weight group, the risk of deep or infratentorial microbleeds was significantly increased in the overweight group [adjusted odds ratio (OR), 2.32; 95% confidence interval (CI), 1.19-4.53], and the obese group [adjusted OR, 2.17; 95% CI, 1.14-41.3] after controlling age, gender, hypertension, diabetes, hyperlipidemia, smoking, coronary artery disease, aspirin use, and the levels of total cholesterol, HDL-cholesterol, and triglyceride. However, the ORs for the strictly lobar microbleeds were not increased in either the overweight or obese groups.

Conclusion: Obesity was associated with deep or infratentorial microbleeds. This finding suggests that obesity affects cerebral small vessels through arteriosclerotic vasculopathy.

20 Etiology of stroke and risk factors B

ECHOCARDIOGRAPHIC FINDINGS IN PATIENTS WITH ACUTE ISCHEMIC STROKE AND ATRIAL FIBRILLATION

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Background: Paroxismal atrial fibrillation (Afib) may be the cause of a stroke and not be detected in the initial electrocardiogram (EKG). Transthoracic echocardiogram (TTE) has a low yield of thrombus detection in patients with acute ischemic stroke (AIS) and AFib. Echocardiographic findings that predict ischemic stroke in patients with atrial fibrillation (Afib) are not well defined, especially in acute stroke. Our objectives were to describe the echocardiographic findings of patients with AIS and AFib and to compare them to patients with AIS without AFib.
Methods: Case-control study of consecutive patients admitted to a tertiary hospital with AIS. Clinical, imaging, and echocardiographic findings were analyzed and compared between patients with and without Afib.
Results: A total of 321 patients were evaluated from May 2009 to October 2010 of which 52 (16.2%) had Afib. Patients with Afib were older (80.4±14.3 versus 69.9±9.6 yo, p<0.01), had higher NIHSS at presentation (11 [2-17] versus 2 [0-6], p<0.01), and were less frequently independent (modified Rankin scores ≤2) at discharge (60.8% versus 81.0%, p<0.01). A total of 304 patients were evaluated with an echocardiogram (32 patients had a TTE and transesophageal echocardiogram (TEE), 52 had a TEE only, and 220 patients had a TTE only). Patients with Afib more frequently had left atrial (LA) enlargement (>40mm) (AF 22.0% versus 7.9%, p<0.01), atrial septum aneurysm (ASA) (Afib 2.4% versus 0%, p=0.03) and mitral valve prolapse (Afib 2.4% versus 0%, p=0.03) and had a trend towards more wall motion abnormalities (Afib 7.3% versus 2.6%, p=0.1). Ejection fraction and the frequency of intramural thrombi were not different between groups.
Conclusion: Patients with AIS with LA enlargement, ASA, or mitral valve prolapse on echocardiographic examination should be monitored to identify those with Afib, even in the presence a normal EKG, so that appropriate measures can be taken to prevent a new stroke.

21 Etiology of stroke and risk factors B

PREVALENCE OF NON-DIPPING BLOOD PRESSURE PROFILE AND ITS RELATIONSHIP WITH IMPAIRED GLUCOSE METABOLISM IN PATIENTS WITH TIA OR ISCHEMIC STROKE

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Background: Non-dipping nocturnal blood pressure is associated with increased risk of cardiovascular events, and might be related to insulin resistance. Little is known about the prevalence of a non-dipping blood pressure pattern in patients with TIA or ischemic stroke. We aimed to assess the prevalence of such a nocturnal blood pressure pattern in patients with TIA or minor ischemic stroke and its association with impaired glucose metabolism.
Methods: We performed 24-hour ambulatory blood pressure measurement in 125 consecutive patients with TIA or minor ischemic stroke. Dipping percentage was calculated by: ((daytime mean arterial blood pressure (MAP) – nighttime MAP)/daytime MAP)*100. Extreme dippers were defined by a dipping percentage of ≥20, dippers ≥10 and <20, non-dippers ≥0 and <10 and reverse dippers <0. An oral glucose tolerance test was performed in patients (n=100) without a history of diabetes. Impaired glucose tolerance was defined as 2-hour post-load glucose levels between 7.8 and 11.1 mmol/L.
Results: Forty-six of the 125 patients (37%) were non-dippers and 12 (10%) were reverse dippers. The mean awake MAP in the dipping (94 mmHg) and the non-dipping (93 mmHg) groups were similar (p=0.68). Patients with a non-dipping or reverse dipping pattern were more likely to have diabetes compared with those with a dipping blood pressure pattern (21% versus 7%; p= 0.04). In the non-diabetics, patients with a non-dipping or reverse dipping blood pressure pattern tended to have higher mean 2-hour post-load glucose levels than those with a dipping or extreme dipping pattern (9.4 mmol/L versus 8.3 mmol/L; p = 0.13).
Conclusion: A non-dipping or reverse dipping blood pressure profile is often present in patients with TIA or minor ischemic stroke, and is associated with an

impaired glucose metabolism. Further studies should focus on the risk of recurrent stroke in these patients and the possibilities of subsequent secondary prevention.

Rehabilitation and reorganisation after stroke B

10 Rehabilitation and reorganisation after stroke B

NEURORESTORATION USING MONONUCLEAR AND MESENCHYMAL STEM CELLS IN CHRONIC STROKE

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Background: Stem cells promise to restore function in stroke and other chronic diseases. This study evaluates safety, feasibility and efficacy of autologous stem cells [naïve mononuclear (MNC) and expanded mesenchymal (MSC)] transplantation in patients with chronic stroke using clinical scores and functional imaging i.e., BOLD (blood oxygen level dependent and DTI (diffusion tensor imaging).
Methods: Thirty six (n=36) chronic stroke patients were recruited with inclusion criteria as 3 months-2years of stroke onset, motor strength of hand muscles of at least >2; NIHSS between 4-24,conscious and comprehendible. Fugl Meyer, modified Barthel index scales and functional imaging (BOLD and DTI) were used for assessment at baseline and 6 months follow up. The fMRI task used was fist making or extension of the wrist or MCP joints of the paretic hand. The mean culture time for mononuclear stem cells (MNC) was 120 ± 20 minutes which were administered to twelve patients (n=12), whereas the expansion of mesenchymal (MSC) took 23 ± 3 days in six patients (n=6). We used animal serum free media for expansion of MSC. Each patient was infused with 5×10^8 cells in 250 ml saline intravenously. Eighteen patients acted as controls.
Results and Discussion: The laboratory tests on day 1,3,5 & 7 were within normal limits in patients with stem cell therapy. mBI showed statistical significant improvements in MNC group when compared with the control group (p<0.05) (table 1). There was an increased laterality index and larger number of cluster activation of Brodmann areas BA 4, BA 6 post stem cell infusion (figure 1) compared to controls (p<0.05) indicating neural plasticity. Nine out of twelve patients in the MNC group recovered well with FA ratio >0.6. There was no statistical difference observed in the fiber number ratio (FN) between the groups.
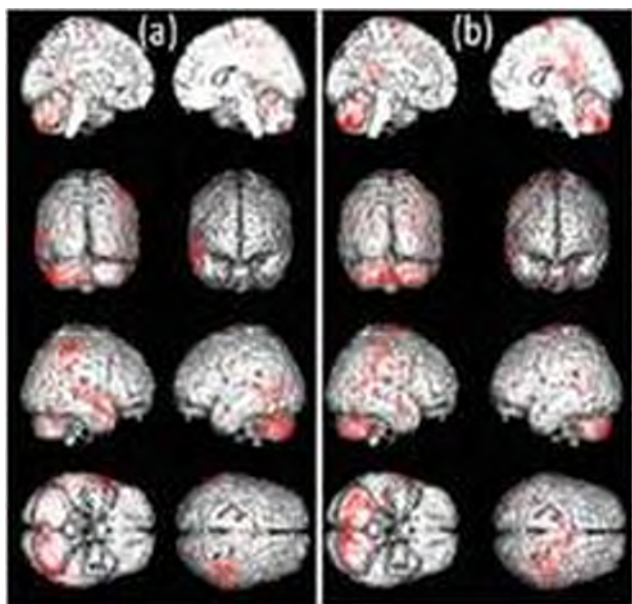
Conclusion: Autologous mononuclear and mesenchymal stem cell infusion is a safe and feasible in stroke patients. The serum free media was safe in expanding mesenchymal stem cells. Restoration of function and cortical reorganization was observed using stem cell therapy.

MECHANISMS, PREDICTION AND IMPACT OF LESION SITE IN STROKE MOTOR RECOVERY

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Background: The aim of this study was to assess the relationships between the pattern of activations induced by hand movement in stroke patients, level of recovery and site of lesion.
Material and Methods: Thirteen patients were prospectively included after a first event of sustentorial cerebral infarct. They underwent an fMRI session 21 ($\pm$ 7) days after stroke onset (E1), a DTI and anatomical sequences. The motor task consisted on a hand flexion-extension. They were clinically assessed on the motor score of NIHSS at 3 months. Seventeen healthy subjects followed the same protocol in one session. To evaluate the impact of primary motor cortex-M1 and corticospinal tract-CST lesions, we used the percentage of intersection between M1 and each infarct and the fractional anisotropy (FA) from DTI. First, we described activations in each group. Then, to predict recovery, we correlated activations with motor NIHSS at 3 months. Finally, to analyze the impact of lesion site, we correlated percentage of intersection M1-infarct and FA of the CST with activations at E1
Results: Mean motor NIHSS was 4 on admission and 2 at 3 months. The activation of M1 was more posterior and lateral in patient's group compared to healthy subjects. Activations of secondary cortical areas (contralesional premotor cortex-PMC, dorsolateral prefrontal cortex-DLPF and ipsilesional parietal areas-BA40) predicted poor recovery at 3 months. Inversely, well-recovered patients had a "normal" pattern of activations (ipsilesional primary sensory motor cortex-S1M1). When CST or M1 were damaged, we obtained the same abnormal pattern of activations (contralesional PMC and DLPF with ipsilesional BA40).
Conclusion: As previously published, well recovered patients had a "normal" pattern of activations at 3 weeks. Conversely, we showed activations of secondary motor areas when patients had a poor recovery. We highlight the important role of motor structures with the same abnormal pattern when there were damaged.

VIDEOTHERAPY IMPROVES OUTCOME AFTER STROKE – RCT COMBINED WITH FMRI

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Background: Evaluation of a home based videotherapy after stroke. fMRI before and after therapy to get insights into potential mechanisms of the therapy.
Methods: Subjects: Fifty six patients, first-ever stroke about 3.5 years ago. All of them had a hand paresis. Average NIH Stroke Scale 3.5
Intervention: Random assignment to one of three groups: "video", "text" and "usual care". In the "video group" patients trained using video clips displaying motor tasks re-quiring hand or arm function. The participants of the "text group" practiced the same tasks using written instructions. Both groups trained one hour per day for about six weeks. A third group, the "usual care"-group, didn't receive any specific "home work" or training.
Outcome parameter: Nine Hole Peg Test [NHPT], Wolf Motor Function Test [WMFT], Motor Activity Log [MAL] and Stroke Impact Scale [SIS] at PRE and follow-up (POST) examination. Quality of performance (WMFT-Quality) rated by the physiotherapist blinded to the allocation.
fMRI: fMRI was used in 39 study participants (13 per group) before and after the inter-vention/observation period: Observation of object related (right and left handed) hand interactions, either as pictures or as videos (action observation, AO). In a second condi-tion they had to imagine the observed movement from the 1st person perspective (action imagery, AI).
Results: NHPT and MAL improved significantly in the two intervention groups com-pared to controls. Clinical improvements are paralleled by differences in activations in the two intervention groups predominantly in premotor, prefrontal and parietal cortex. There were no alterations of activity within the usual care group.

Conclusion: Home based videotherapy has a benefit for stroke outcome. Plastic changes were observed in visual, sensorimotor and prefrontal areas.
References: 1. Ertelt D et al. (2007). Action observation has a positive impact on rehabilitation of motor deficits after stroke. Neuroimage, 36: 164-173.

13 Rehabilitation and reorganisation after stroke B

FOCAL BASAL GANGLIA STROKE LESIONS IMPAIR IDENTIFICATION OF FACIAL EMOTIONS CONVEYING SAFETY SIGNALS

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Background: Survival may depend on the ability to identify threats signaled by emotions in facial expressions. Although the importance of the basal ganglia in basic emotion processing had been suggested by studies of patients with neurodegenerative diseases, current neural models of emotion processing, largely based on evidence derived from functional imaging studies, do not include a prominent role for the basal ganglia.

Methods: To assess the specific role of the BG in processing emotions, we compared basic facial emotion identification in 23 young patients (mean age 44.9±11.6; 10 males) with a focal basal ganglia stroke to 68 matched healthy controls (43.8 years ±14.0; 27 males) after. We used quantitative MRI lesion analysis to assess the relationship between basal ganglia location and basic emotion identification. To assess whether facial emotion identification might be related to non-specific lesion effects, we also assessed a wide range of cognitive and motor abilities and screened participants for possible co-morbid conditions such as depression or anxiety. In addition, we assessed social behavior in terms of social adaptability and the ability to return to work after stroke.
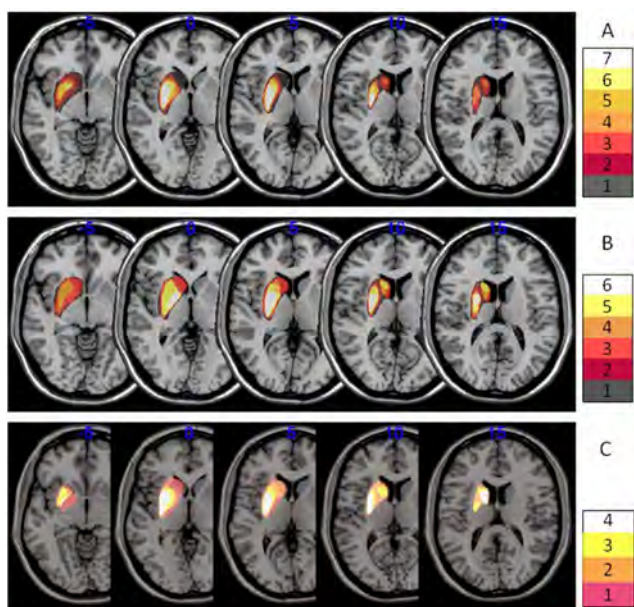
Figure 1. Lesion overlap in patients with emotion identification impairments for Anger (A), Fear (B) and Disgust (C).

Results: (1) The ability to identify basic emotions was impaired after focal lesions limited to the basal ganglia.
(2) This impairment was limited to anger, fear and disgust identification, that are threat-related emotions, suggesting a specific role for the basal ganglia in threat detection. These findings may reflect altered gating mechanisms for emotions conveying threat signals, with the basal ganglia selecting information relevant to individual safety.
(3) We found that the observed emotion identification impairments adversely affected social behavior suggesting that emotion identification skills may be of substantial practical importance, and should be considered in the clinical assessment and rehabilitation of patients with basal ganglia lesions.

14 Rehabilitation and reorganisation after stroke B

RIGHT CEREBRAL HEMISPHERE LESION IS AN INDEPENDENT PREDICTOR OF FALLS IN STROKE PATIENTS

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Background: Falls are a significant clinical concern in stroke patients. Our objective was to identify predictors of falls and its correlation with functional capacity and quality of life is stroke survivors.
Methods: Consecutive case series of stroke patients with independent gait. We prospectively collected demographic and clinical data, with application of the following scales: modified Barthel Index for functional capacity evaluation, Timed Up and Go Test (TUG), EuroQol for quality of life assessment and NIH Stroke Scale (NIHSS) for stroke severity quantification. After univariable analyses, variables with possible (P < 0.1) association with history of falls were included in a multivariable logistic regression model.
Results: From March 2009 to April 2010, 116 patients were studied, mean age 56±12 years, 50% female, median NIHSS of 2 (range 0 to 11). Falls occurred in 47 (41%) patients and were associated with worse functional capacity and quality of life (P<0.05). On univariable analyses, the following were associated with falls: time on TUG, female gender and right hemisphere lesion location. The TUG was higher in fallers when compared to non-fallers (23±13 vs. 17±10 seconds, P=0.011). Patients with right hemisphere lesion location more frequently fell when compared to other locations (54% vs 29%, P=0.010). In the multivariable analysis, only right hemisphere lesion location remained a significant predictor of falls.
Conclusions: Falls occur in an elevated proportion of stroke patients and are associated with significant burden to functional capacity and quality of life. Patients with right hemisphere lesions are at a particularly high risk of falls and probably deserve specific rehabilitation tailored to fall prevention.

15 Rehabilitation and reorganisation after stroke B

MOTOR CONSEQUENCES OF UNAFFECTED HEMISPHERE RTMS STIMULATIONS IN ACUTE STROKE: A PROSPECTIVE RANDOMIZED SIMPLE BLIND TRIAL

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Background: At the acute phase of stroke, the functional role of the unaffected hemisphere in motor recovery remains controversial. Increasing evidence suggests that stroke could alter the interhemispheric balance. During the subacute and chronic phase, activation of the ipsilesional cortex or inhibition of the controlesional cortex by rTMS slightly improves motor performance of the affected hand.
This prospective study aimed at elucidating the role of the unaffected hemisphere in the altered motor function using rTMS in the early phase of the stroke.
Methods: 16 patients (mean age 69±12, 5 females and 11 males) with acute ischemic (n=13) or haemorrhagic stroke (n=3) (5 cortical, 11 subcortical lesions) and mild deficits (mean NIH 4±2) were prospectively included in the first days following stroke onset (mean 4±2 days).
During 4 consecutive days, they received one rTMS session per day [1Hz (inhibitory), 5Hz (excitatory), and sham stimulation for each frequence] on the unaffected hemisphere in a crossover randomized simple blind design. Motor function of the affected hand was assessed by grip strength recordings (GT), Nine Peg Hole Test (NPHT) and Hand Tapping Test (HTT) before and after each rTMS session.
Results: Compared to sham stimulation, 1Hz rTMS stimulation significantly improved Hand Tapping Test of the affected hand (+2,24±3,06 after 1Hz rTMS; -0,77±2,28 after sham 1Hz rTMS; p=0,02, Student test). No significant effect was observed for 5 Hz stimulations.
Conclusion: Our study showed that rTMS applications over the contralesional hemisphere were feasible in acute stroke patients. Within the first days following stroke, the inhibition of the unaffected hemisphere by 1Hz rTMS improved motor function of the affected hand.

EARLY MOBILISATION AND THE RECOVERY OF MOBILITY IN ACUTE STROKE: RESULTS FROM A POOLED ANALYSIS OF TWO RANDOMISED CONTROLLED TRIALS

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Background: Very Early Mobilisation (VEM) is a distinctive characteristic of care in some stroke units. One recent pilot trial has indicated that patients who received a VEM protocol in addition to standard care (SC) were able to walk sooner than patients who received SC only. However to date, only two Phase II trials have compared VEM with standard care (SC): A Very Early Rehabilitation Trial (AVERT) in Australia and the recent Very Early Rehabilitation or Intensive Telemetry after Stroke (VERITAS) pilot trial in the UK. The aim of this analysis was to investigate the impact of VEM on the early recovery of mobility by pooling these two comparable trials.
Methods: Individual patient data from both trials were pooled and analysed. The primary outcome was early non-impaired mobility defined as Rivermead Mobility Index (RMI) of 10-13 at one week (day 5 to 7). The secondary outcomes were the early ability to walk (RMI) at one week (day 5 to 7) and independent walking at 3 months as measured by the Barthel Index (BI). Logistic regression was used to assess the effect of VEM on outcome with multivariate analysis used to adjust for known confounders including age, baseline stroke severity and pre-morbid mRS.
Results: All patients in AVERT (N=71) and VERITAS (N=32) were included. VEM patients had a greater odds of early non-impaired mobility (adjusted OR 7.81 (95% CI, 1.74, 35.01) and of early walking (OR 4.41; 1.30-15.13). The effect of VEM on independent walking at three months was not statistically significant (OR 2.30;0.71-7.37).
Conclusion: This analysis indicates that VEM has the potential to influence the early recovery of general mobility and ability to walk. This is important considering the ability to walk is a determinant of longer term functional recovery. Both studies are limited by small sample sizes so further larger trials are required.

COMBINING ONOBOTULINUMTOXIN A INJECTION AND WRIST ROBOTIC TREATMENT AFTER STROKE: A RANDOMIZED, PLACEBO-CONTROLLED PILOT STUDY

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Background: Although onobotulinumtoxinA (OBT-A) injection and robot-aided rehabilitation are both commonly used upper limb treatments in stroke survivors, there are few data on the efficacy of combining these two therapies. This randomized, controlled pilot study examined injection with OBT-A followed by a course of wrist robotic treatment (WRT.) We hypothesized that this combination would yield greater improvements in wrist movement than WRT alone.
Methods: Stroke subjects with motor strength>1/5 and Modified Ashworth Score (MAS) 1+ to 3 in both wrist flexion and pronation (target muscles of the WRT) were randomized to receive either 150 units of OBT-A or an equivalent volume of normal saline (SAL) to pronator teres and quadratus (25u OBT-A/.25cc each) and to flexor carpi radialis and ulnaris (50u OBT-A/.5cc each.) Electrical stimulation was used for muscle localization. Injections were followed by 18 sessions of WRT over 6 weeks using the In-Motion3. The primary outcome was Fugl-Meyer Assessment wrist/hand score (FMA-W/H) after 6 weeks of WRT. Secondary outcomes included the Arm Motor Ability Test and MAS.
Results: Of 63 subjects screened, 12 met criteria and were randomized - 6 to each group. Groups were similar demographically, but the OBT-A group had more severe wrist impairment. There were no statistically significant differences in adjusted, 6 week FMA-W/H scores (9.0 for OBT-A vs. 11.5 in SAL, difference=2.5 points. 95% CI for difference=-2.2, 7.3 using ANCOVA.) Other than pronator MAS (p<0.001), no differences were seen between groups for adjusted, secondary outcomes (all p>0.2.).
Conclusions: Although these data do not demonstrate a benefit to OBT-A injection prior to WRT, the study is limited by small sample size and greater impairment in the OBT-A group. The authors will offer insight into methodological issues for future combination studies including toxin dosing, muscle selection and possible outcome measures.

NEUROSTIMULATION TECHNIQUES BENEFIT STROKE PATIENTS WITH CHRONIC OROPHARYNGEAL DYSPHAGIA: PRELIMINARY RESULTS FROM A RANDOMISED CONTROLLED STUDY

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Chronic oropharyngeal dysphagia post stroke leads to increased risk of institutionalisation and early death. Pharyngeal Electrical Stimulation (PES)[Fraser et al. Neuron 2002], repetitive Transcranial Magnetic Stimulation (rTMS)[Jefferson et al. Gastroenterology 2009] and Paired Associative Stimulation (PAS)[Singh et al. Gastroenterology 2009] are neurostimulation techniques developed to increase excitability of the motor cortex (MI). Here we investigate the effects of these interventions when applied to cortical swallowing motor system in stroke patients with dysphagia persisting for more than 6 weeks.
In 14 dysphagic stroke patients (age: 69±2 years (mean ± SD), time post stroke: 69±21 weeks, 7 left hemispheric,1 undetermined), pharyngeal electromyographic responses were recorded with an intraluminal catheter after single TMS pulses over pharyngeal MI, to measure corticobulbar excitability before, and up to 30 minutes after randomisation to real and sham applications of one of three techniques. All patients underwent videofluoroscopic swallowing assessments (aspiration-penetration scores,APS) before and after real and sham.
Compared to sham, the application of all interventions showed a significant increase in cortical excitability in the unaffected hemisphere (max: 53±15%,mean±SEM) immediately post, not observed for the affected (rANOVA, Hemisphere*Time*Intervention=0.04). Also, real neurostimulation was associated with a reduced APS of -14±4% compared to sham (Wilcoxon's test, p=0.03). Comparison between the three real interventions showed no modality specific advantages.
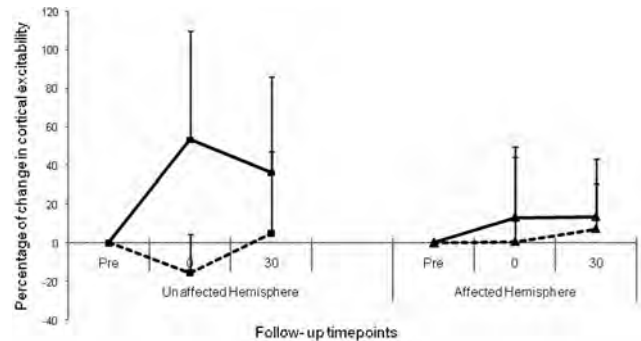
These preliminary Results of the randomised controlled trial show that neurostimulation interventions have beneficial neurophysiological and behavioural effects in dysphagic chronic stroke patients, increasing cortical excitability and improving swallowing safety. Further clinical trials are required in order to further support the use of neurostimulation as a useful adjunct in swallowing rehabilitation.

DIFFERENT PERSPECTIVES ON DISABILITY THREE MONTHS AFTER STROKE: A MIXED METHODS APPROACH

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Background: People who have suffered a stroke perceive to a large extent unmet needs of rehabilitation. Needs of health care services can be viewed from the perspective of the phenomena underlying the need i.e. the disability/problems and also from the perspective of the people with stroke as well as the health professionals. The aim was to describe disability/problems from the perspective of the people with stroke, represented by felt problems, reported by patients three months after stroke and to examine if there were differences between men and women. A further aim was to explore the concurrence between the perspective of the people with stroke (felt problems) and the perspective of the health professionals (assessed problems).

Methods: The patients (n=203) received care at the stroke units at Karolinska University Hospital, Sweden. Felt problems, collected using an open question, were categorized. Results from three established assessment tools: Katz Extended Index of ADL (KE); Barthel Index (BI) and Stroke Impact Scale (SIS) represented assessed problems. Items/domains in the assessment tools that corresponded to the categories with felt problems were identified and comparisons performed.

Results: Fatigue was the category in which the largest number of patients reported felt problems (n=58, 28%). More women than men had felt problems in the category Acquisition, meals and housework (p=0.01) whereas more men had felt problems in the categories Employment (p=0.02) and Driving (p=0.009). Fourteen out of the 28 categories of felt problems had corresponding items/domains in the KE/BI and the SIS. The KE/BI failed to capture 16-57% of the felt problems whereas the SIS failed to capture 0-33%.

Conclusion: There was a substantial lack of concurrence between felt and assessed problems indicating that the use of assessment tools has to be complemented with open questions if health services are to address the problems experienced by the patients.

20 Rehabilitation and reorganisation after stroke B

RISK FACTORS AND FREQUENCY OF SINKING SKIN FLAP SYNDROME IN PATIENTS UNDERGOING HEMICRANIECTOMY

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Background: Sinking Skin Flap Syndrome (SSFS) is characterised by decreased conciousness due to upright position, progression of paresis or other focal neurologic symptoms, orthostatic headache, epileptic seizures and dizziness, which occurs in patients after hemicraniectomy. SSFS may progress to "paradoxical" herniation as a consequence of atmospheric pressure exceeding intracranial pressure. Despite a growing rate of craniectomy in different diseases there are only few reports on small patient groups.

Methods: In our department of early rehabilitation including an intensive care unit we collected all patients with craniectomy from january 2009 until september 2010. CT scans of the admitting hospitals and those performed in our hospital and rehabilitation charts were reviewed retrospectively. In case of clinical deterioration CT scan has been done by routine. SSFS was diagnosed if there was a sinking skin flap on CT scan and a clincal deterioration. As possible risk factors age, kind of lesion, presence of cerebrospinal fluid (CSF) drainage (internal or external) were analysed.

Results: 32 patients with large craniectomy were identified. The underlying lesion was malignant hemispheric infarction in 10, subarachnoid hemorrhage complicated by infarction or spontaneous intracerebral hemorrhage in 6 and head trauma in 10 cases. In 7 (22%) patients a SSFS was diagnosed. All of them had CSF drainage, mainly a ventriculoperitoneal shunt. Only 3 of 25 patients without SSFS were treated by a ventriculoperitoneal shunt (p<0,001; fishers exact test). No association with SSFS was detected for kind of lesion or age.

Discussion: In our patients with different diseases leading to craniectomy SSFS is not a rare complication and was diagnosed in 22% of patients. Presence of CSF drainage is a significant risk factor of SSFS. Despite an adjustment of pressure of the shunt systems in most cases only immediate cranioplasty was effictive and showed a clinical improvement. Because of the delay of the rehabilitation process, CSF shunting should be discussed critically. If necessary cranioplasty should be performed as soon as possible to prevent persistent brain damage due to SSFS.

21 Rehabilitation and reorganisation after stroke B

VISION RESTORATION AFTER BRAIN DAMAGE: THE "RESIDUAL VISION ACTIVATION THEORY"

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Background: Visual field impairments after stroke or brain trauma are considered irreversible. However, there is considerable potential for vision restoration and plasticity even in older age, yet there is no theory to explain this restoration potential.
Methods: Literature review of peer-reviewed articles.
Results: Visual system damage is usually not complete but leaves (i) partially damaged tissue or "areas of residual vision" (ARVs) at the visual field border, (ii) alternate visual pathways unaffected by the damage, and (iii) residual functions in down-stream neuronal networks. Because patients tend to focus their attention on the "intact" visual field sectors, residual structures lack sufficient attentional resources, reducing their activation state. Thus, residual structures

have a triple handicap: fewer neurons, disturbances in temporal processing, and an inter- and intrahemispheric excitation/inhibition dysbalance. The resulting "non-use" impairs synaptic strength and network function even further. Residual structures can be reactivated by repetive actication through (i) visual experience, (ii) visual training, or (iii) non-invasive electrical current stimulation. This leads to strengthening of synaptic transmission of surviving cells in the damaged structure ("within-systems plasticity") or down-stream networks. Because post-lesion plasticity comprises mechanisms of normal perceptual learning, vision restoration can be induced at any time after the lesion and at all ages, irrespective of etiology (e.g. stroke, neurotrauma). Whereas acute activation of residual vision leads to only temporary vision improvements, permanent improvements require stimulation for many weeks or months, but eventually this will have lasting improvement in quality of life.

Conclusion: The "residual vision activation theory" provides a heuristic basis for further research and sets the stage for novel approaches to treat visual system dysfunctions after stroke or brain trauma.

Acute stroke: current treatment

1 Acute stroke: current treatment

ANTERIOR CHOROIDAL ARTERY INVOLVEMENT IS PREDICTOR OF POOR NEUROLOGICAL OUTCOMES IN DISTAL ICA OCCLUSIONS

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Introduction: Distal internal carotid occlusions with ischemic stroke has been shown to have poor outcomes despite recanalization therapy. We hypothesized that anterior choroidal artery involvement despite endovascular therapy may be one of the factors responsible for poor neurological outcomes in these patients.
Methods: The CT angiogram database of the Calgary stroke program was reviewed for patients with acute ischemic stroke with distal ICA occlusions (Tor L) were identified. Among these, patients within thrombolytic window period or selected on good scan occlusion paradigm who underwent endovascular intervention. CT or MRI done from day 1–7 after the procedure was evaluated for involvement of areas presumed to be supplied by anterior choroidal artery. Internal capsule with or without extension into paraventricular corona radiata was interpreted as the area supplied by anterior choroidal artery. MRS ≤2 at 3 months was used as good outcome. Recanalization was defined as TIMI 2-3 flow on angiography.
Results: Among 1454 patients in CTA database, 90 patients were identified to have distal ICA occlusions (T/L).41 (45.5%) patients underwent endovascular therapy with or without IV thrombolysis. Post-procedure, internal capsular involvement was seen in 29 (70%) patients. Of these,14 patients (48.27%) achieved recanalization (TIMI2/3) and good neurological outcome was seen in 5 (17%) patients. Among 12 (30%) patients with sparing of anterior choroidal artery territory, 8 (66.6%) patients had good neurological outcomes, with recanalization in all patients. Sparing of the anterior choroidal artery with recanalization post endovascular procedure was a strong predictor of good neurological outcomes (RR 3.9, 95% CI 1.5-9.3, p=0.004).
Conclusion: Anterior choroidal artery territory involvement is common among patients with carotid terminus occlusions. Ischemia to anterior choroidal artery territory is an important predictor of clinical outcome despite recanalization of the ICA.

2 Acute stroke: current treatment

INTRAVENOUS THROMBOLYSIS IN ACUTE ISCHEMIC STROKE PATIENTS WITH MILD SYMPTOMS

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Background: A controversy exists as to the management of acute ischemic stroke patients presenting with mild symptoms. No uniform definition of mild symptoms exists. We aimed to define mild stroke and report outcome of such patients undergoing iv thrombolysis in our large single-centre cohort.

Methods: The baseline cohort included 1427 consecutive ischemic stroke patients treated with intravenous thrombolysis at the Helsinki University Central Hospital between 1995 and 2010. We calculated observed/expected (O/E) ratio of good 3-month outcome (mRS 0-2) for each baseline NIHSS score after adjustment for age, onset-to-treatment time, baseline glucose level, mRS above 1 on admission, presence of hyperdense cerebral artery sign (HCAS) or early infarct signs on native head CT scan. A generalized linear model (GLM) was used to further assess the impact of increasing NIHSS scores on outcome.

Results: Twenty-seven (1.9%) patients were lost to follow-up. Patients with baseline NIHSS scores 0 to 4 had the lowest observed/expected (O/E) ratio < 0.5, followed by patients with NIHSS 5-10 (<1.0). Of 58 patients with baseline NIHSS 0-2 (all had at least one of the following: HCAS on native head CT scan, cerebral artery occlusion on CT angiography, or perfusion deficit on perfusion CT scan), 51 (88%) had good 3-month outcome. The corresponding number was 168/195 (86%) in patients with baseline NIHSS 3 and 4, whereas it was 422/575 (73%) in patients with baseline NIHSS 5-10. The risk of symptomatic intracerebral hemorrhage (sICH, ECASS II criteria) was 0%, 2.6% and 4.0%, respectively. The GLM analysis supported the Results of O/E ratio: first major drop in the Wald statistics was between NIHSS 4 and 5, and second between 10 and 11

Conclusion: Our findings suggest that only stroke patients with NIHSS≤4 should be regarded as "mild strokes". They should perhaps receive thrombolysis only when an artery occlusion or a perfusion deficit can be visualized.

3 Acute stroke: current treatment

UNVEILING AN EXCEPTIONAL ZYMOGEN: THE SINGLE-CHAIN FORM OF TPA IS A SELECTIVE ACTIVATOR OF NMDAR SIGNALING

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Objectives: Tissue plasminogen activator (tPA) is an ubiquitous and exceptional serine protease in that it displays low zymogenicity. Indeed, the single-chain tPA (sc-tPA) and two-chain tPA (tc-tPA) display similar activity in the presence of blood templates such as fibrin. Interestingly, tPA was also highlighted in the brain major functions and to modulate the N-methyl-D-aspartate receptor (NMDAR) signaling. Up to now, no difference has been underlined between the two forms of tPA regarding its neuromodulation. In the present study, we wonder whether sc-tPA and tc-tPA behave equally toward a non-fibrin substrate, the NMDAR, in the central nervous system.

Methods: tc-tPA was prepared by plasmin treatment from the commercial preparation of sc-tPA and conditioned in 0.5M bicarbonate ammonium buffer. Both forms were tested toward their modulation of NMDA-neurotoxicity and NMDAR signaling in vitro on cortical neurons and in vivo in the striatum and the hippocampus.

Results: Sc-tPA enhances NMDAR-mediated calcium influx (+34% vs. tc-tPA), promotes NMDA Erk(½) activation (+19% vs. tc-tPA) and NMDA neurotoxicity in cortical neurons (+51% vs. tc-tPA) and in the striatum (+100% vs. tc-tPA). We demonstrated that tPA mediates NMDA neurotoxicity through a plasminogen independent mechanism that requires its proteolytic activity. In the hippocampus only the sc-tPA is able to promote NMDAR-dependent long-term potentiation (LTP) in the CA1 network (+16% vs. control), whereas tc-tPA does not. Moreover, only the sc-tPA can reverse a mild long-term depression into LTP (excitatory post-synaptic potential slopes increased from 86% of the baseline to 107% in the presence of sc-tPA vs. 81% in the presence of tc-tPA).

Conclusions: We have demonstrated, both in vitro and in vivo, the first differential function between sc- and tc-tPA, for that sc-tPA is the selective modulator of NMDAR signaling, via its proteolytic activity and through a plasminogen-independent mechanism. This finding opens a new area of investigations into plasminogen-independent functions of tPA in the brain, including mechanisms controlling its expression, its secretion and its proteolytic processing.

STATIN THERAPY AND OUTCOME FOLLOWING ISCHAEMIC STROKE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Experimental data suggest that statin therapy may improve neurological outcome after acute cerebral ischaemia. However, findings from clinical studies are conflicting. Many studies may have been underpowered to detect a relationship between statins and outcome.

Methods: We performed a systematic review & meta-analysis of published & unpublished data, searching MEDLINE, SCOPUS, Cochrane, Web of Science, SciFinder Scholar, Embase, CINAHL & bibliographies. Statin use was analysed pre-stroke (at stroke onset) & acutely post-stroke (<72 hours). Outcomes were fatality & good functional outcome (mRS 0-2) at 30 days/hospital discharge, 90 days, 1 year.

Results: 22 studies were included (n=15866; 20 prospective). Mean age was 70.4 years; 7 studies reported NIHSS (median range 4-12). In individual studies, 4-48% of subjects received statins pre-stroke, 14-71% post-stroke. Pre-stroke statin was associated with lower fatality at 30 days/discharge (OR 0.64 [95% CI 0.49-0.83] p=0.001; 13 studies, n=9636, Figure 1) but not 90 days (OR 0.80 [0.50-1.28] n=2476) or 1 year (OR 1.78 [CI 0.43-7.31] 2 studies, n=1462). Post-stroke statin was associated with lower fatality at 30 days/discharge (OR 0.13 [0.08-0.20] p<0.001, 4 studies, n=2801, Figure 2) & 1 year (OR 0.17 [0.06-0.50] p=0.001, 2 studies, n=1462), but not 90 days (OR 0.69 [0.32-1.49] n=1131).

Pre-stroke statin use was associated with good functional outcome at 90 days (OR 1.32 [1.04-1.67] p=0.02, 4 studies, n=1611) but not 30 days/discharge (OR 1.68 [0.76-3.67] 5 studies, n=3408). Acute post-stroke statins were associated with good outcome at 30 days/discharge (OR 1.79 [1.21-2.65] p=0.004, 2 studies, n=528) & 90 days (OR 2.17 [1.46- 3.21] n=528). Only 1 study reported 1-year functional outcome.

Study	Odds ratio (95% CI)
Ní Chróinín et al	0.59 (0.29,1.16)
Stead et al	1.36 (0.35,5.20)
Pikija et al (2)	0.34 (0.12,0.97)
Pikija et al (1)	1.46 (0.07,30.97)
Arboix et al	0.42 (0.27,0.65)
Chitravas et al	1.21 (0.53,2.78)
Ois et al	0.86 (0.56,1.31)
Aslanyan et al	0.51 (0.23,1.14)
Elkind et al	0.14 (0.01,2.26)
Yoon et al	0.72 (0.29,1.78)
Reeves et al	0.33 (0.15,0.73)
Bushnell et al	1.03 (0.43,2.50)
Cuadrado-Godia et al	0.80 (0.39,1.65)
Overall (95% CI)	0.64 (0.49,0.83)
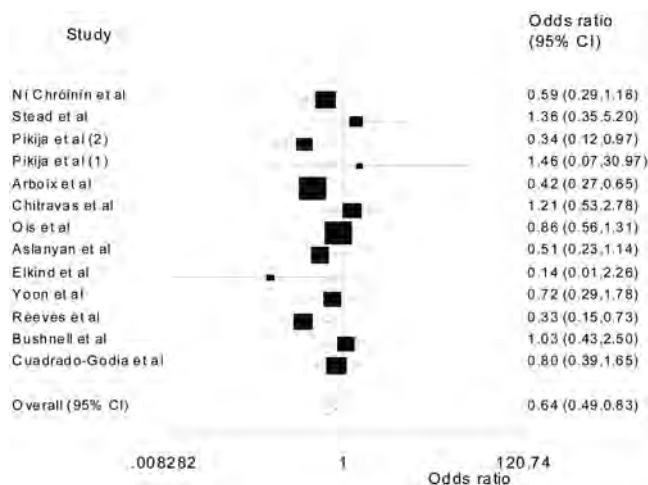
Figure 1. Unadjusted association between pre-stroke statin therapy and fatality at 30 days or discharge.
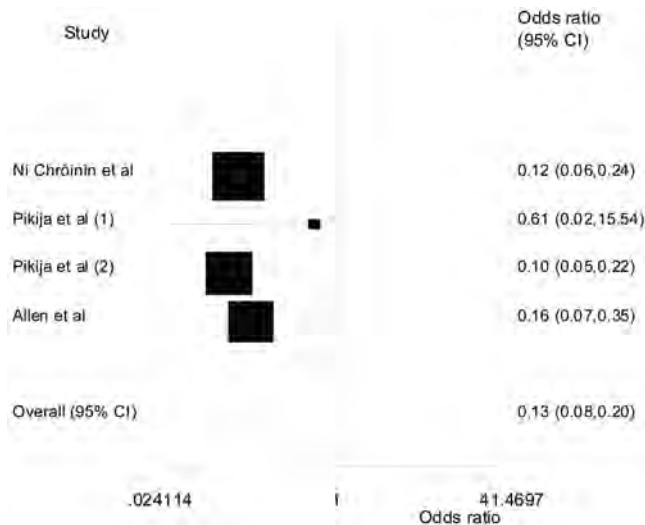
Figure 2. Unadjusted association between acute post-stroke statin therapy and fatality at 30 days or discharge.

Conclusion: Pre-stroke & post-stroke statin therapy were associated with survival & functional outcome at early & late time-points after ischaemic stroke. Randomised clinical trials of statin therapy for acute stroke are needed.

5   Acute stroke: current treatment

'PROPORTION OF PATIENTS TREATED WITH TPA IN A CENTRALISED VERSUS A DECENTRALISED ORGANISATIONAL MODEL OF ACUTE STROKE CARE'

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Background: Intravenous tissue plasminogen activator (tPA) treatment is the only proven effective treatment in acute ischemic stroke. Despite its efficacy only a small proportion of stroke patients receive this treatment. The aim of this study is to investigate differences in proportions of patients treated with tPA in a centralised versus a decentralised organisational model.

Methods: In this prospective study patients were recruited from 13 centers in the Netherlands over a six months period starting on February 2010. In the centralised model all thrombolytic therapy for four hospitals was carried out in a university hospital. The decentralised model consisted of nine general hospitals, all performing tPA treatment on a routine basis. The proportion of stroke patients treated with tPA was determined and the contribution of confounders for the rate of thrombolysis was evaluated in a logistic regression analysis. Also, favourable outcome at 3 months (modified Rankin score 0-2) and the occurrence of symptomatic intracranial haemorrhage (sICH), SITS-MOST definition were evaluated.

Results: 297 patients were enrolled in the central model, 910 in the decentralized model. Baseline characteristics were similar in both groups. In the centralised model 63 patients were treated with tPA (21.2%), and in the decentralised model 109 patients (12.0%). The likelihood of treatment with tPA increased considerably with the centralized model (adjusted OR 1.98, 95% CI 1.40–2.79). Other outcomes were not significantly different between groups; 3-month outcome (odds ratio 0.63, 95% CI 0.32–1.24); sICH (odds ratio 1.65, 95% CI 0.17–16.28).

Conclusion: In this study patients had a two times higher probability of treatment with tPA in a centralized model. No significant differences in efficacy and safety of tPA treatment could be established in routine practice. Further research on critical success factors of different organizational models for tPA treatment in acute stroke care is needed.

6   Acute stroke: current treatment

THE EFFECTIVENESS OF DUAL ANTIPLATELET TTREATMENT IN ACUTE ISCHEMIC STROKE PATIENTS WITH PURELY INTRACRANIAL STENOSIS: A SUBGROUP ANALYSIS OF CLAIR STUDY

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Background: Dual antiplatelet therapy of clopidogrel and aspirin reduces the presence and number of microembolic signals (MES) in patients with large artery disease including both intracranial and extracranial disease. We did a subgroup analysis of the CLAIR study (The CLopidogrel plus Aspirin for Infarction Reduction in acute stroke or transient ischemic attack patients with large artery stenosis and microembolic signals) to include only patients with intracranial occlusive disease assess the efficacy in this subgroup.

Methods: CLAIR was a randomized, multi-center clinical trial, which recruited patients with symptoms of ischemic stroke or transient ischemic attack onset within 7 days, with large artery stenosis (≥50%) detected by transcranial Doppler (TCD) and carotid ultrasound, and with MES detected by TCD recording. Patients were randomized into two groups: dual therapy of clopidogrel 300 mg for the first day and then 75 mg daily plus 75-160 mg aspirin daily for 7 days (dual therapy), or to receive 75-160 mg aspirin once daily for 7 days (monotherapy). TCD recordings for MES were done on day 2 and 7. This subgroup study only included patients with purely intracranial large artery disease.

Results: Seventy patients were included (dual therapy group 34 and monotherpay 36). MES presented in 19.4% patients in the dual therapy and 44.4% in the monotherapy group at day 7 (relative risk reduction 56.5%, 95% CI: 2.5-80.6; p=0.029). The mean and median number of MES were also significantly reduced in the dual therapy group at day 2 (p=0.042) and day 7 (p=0.018). After adjusting the presence or the number of MES at day 1, dual therapy remained an independent factor for the presence and number of MES at day 7.

Conclusion: Dual therapy with clopidogrel and aspirin is more effective than aspirin alone to reduce embolisation in patients with purely intracranial stenosis.

7   Acute stroke: current treatment

THERAPY IMPLICATIONS OF TRANSTHORACIC ECOCHARDIOGRAPHY IN TRANSIENT ISCHAEMIC ATTACK

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Background: The transient ischemic attack (TIA) requires an urgent evaluation to adapt secondary stroke prevention and thus to reduce the risk of early recurrence. Brain imaging, supra-aortic trunks ultrasound and the ECG are essential in an emergency. We are interested in the therapy implication of transthoracic echocardiography (TTE), since the hospital stay is often increased by the delay in receiving the TTE.

Methods: We conducted a retrospective cohort study, performing TTE on all patients admitted from two stroke's Parisian center with a TIA. Findings compatible with heart diseases (excluding heart rhythm detected on electrocardiogram) that would indicate anticoagulation as beneficial were identified: mitral valve stenosis, left ventricular hypertrophy >55mm, dilated cardiopathy, left ventricular systolic dysfunction (with an estimated ejection fraction <35%), previous myocardial infarction (with left ventricular wall dyskinesis), and intracardiac masses.

Results: Between February, 2006, and December, 2009, we identified 210 patients hospitalized with TIA. Transthoracic echocardiography was performed on all patients with a median lead time of 3 days. Of 6 patients (2.8%) transthoracic echocardiography found a previously known heart disease (3 with dilated cardiopathy, 1 with previous anterior wall myocardial infarction, and 2 with left ventricular systolic dysfunction with an ejection fraction <35%) and for which the patient was already anti –coagulated before TIA. Outside of these patients with a already known heart disease, Transthoracic echocardiography has found a indication for anticoagulation in only two patients (0.95%): One patient with left ventricular systolic dysfunction with an ejection fraction <35% and one patient with mitral valve stenosis.

Conclusions: In our study, transthoracic echocardiography had therapeutic involvement with implementation of anticoagulantion in only less than 1% of TIA. Transthoracic echocardiography can be performed outside the hospital and should not increase the length of stay in hospital. It is only justified as a matter of urgency in case of clinical signs or particular cardiological histories.

8 Acute stroke: current treatment

"NATURAL HISTORY" OF TPA-UNTREATED MINOR STROKE IN THE NORTH DUBLIN POPULATION STROKE STUDY

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Introduction: Current guidelines recommend caution when considering emergency tissue plasminogen activator (tPA) therapy for patients with minor neurological deficits. However few data exist regarding the "natural history" (without tPA) of stroke in unselected population-based cohorts. We sought to evaluate the risk of long term disability in "minor stroke" patients.

Methods: In the 294,529 residents of North Dublin we prospectively identified all transient ischaemic attacks (TIAs) and ischaemic strokes over a 1 year period in 2005-06, immediately before a regional stroke thrombolysis service was begun. National Institutes of Health Stroke Scale (NIHSS) at presentation and functional status (modified Rankin Score, mRS) at 90 days and 1 year were assigned by trained investigators.

Results: 478 patients were identified. 37.4% (179/478) had TIA or NIHSS=0 at presentation, 31.4% (150/478) had minor stroke (NIHSS=1-4), and 31.2% (149/478) had moderate/severe stroke (NIHSS=5-42). By 90 days, 34% of minor stroke patients had some disability (mRS≥2) (vs. 9.7% TIA/NIHSS=0, p<0.0001) and 16.7% had at least moderate disability (mRS≥3) (vs 6.4% TIA/NIHSS=0, p=0.005). At 1 year, 37.9% of minor stroke patients had mRS≥2 (vs 13.4% TIA/NIHSS=0, p<0.0001) and 26.2% had at least moderate disability (vs 9.9% TIA/NIHSS=0, p<0.0001). 9.7% of minor stroke patients were dead at 1 year. Disability was more likely in patients with NIHSS scores of 3-4 compared to 1-2, at 90 days (46.3% vs. 23.4%, p=0.004) and 1 year (47.1% vs. 29.9%, p=0.03).

Conclusions: In an unselected population-based cohort of TIA and ischaemic stroke patients nearly one third had NIHSS between 1-4 at presentation. Many, especially those with NIHSS scores of 3-4, had persistent stroke-related disability or were dead 1 year later. Routinely withholding thrombolytic therapy from such patients may represent a missed therapeutic opportunity.

9 Acute stroke: current treatment

WOMEN WITH ACUTE ISCHEMIC STROKE ARE TREATED LESS OFTEN WITH INTRAVENOUS ALTEPLASE THAN MEN

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Background: It is unknown whether men and women with acute ischemic stroke have equal opportunities for treatment with thrombolytics. We assessed the differences between men and women in treatment with intravenous alteplase and in hospital admission in an unselected observational cohort of 5515 patients.

Methods: We analysed data of consecutive patients with acute stroke, admitted within 24 hours from onset of symptoms during a two-year period in 12 representative hospitals in the Netherlands. All adult patients with acute stroke were included and time-paths were registered. The differences between men and women in mean onset to door time and in treatment with intravenous alteplase were analysed by means of multiple regression analysis. Associations were expressed as odds ratios (OR) with 95% confidence intervals (CI).

Results: Of all 5515 patients, 1657 (30%) were admitted to the hospital within 4 hours after stroke onset; 755 (45.6%) of these were women. Women admitted within

4 hours were treated just as often with intravenous alteplase as men (314 women (41.6%) versus 383 men (42.4%), OR 1.0; 95% CI: 0.8 to 1.3.

However, of all 5515 admitted patients, the 2778 women were treated less often with intravenous alteplase than men (314 women (11.3%), 382 men (14.0%), OR 0.8; 95% CI: 0.7 to 0.9). Adjustment for age did not affect this association (OR 0.9; 95% CI: 0.7 to 1.0). Fewer women were admitted to the hospital within 4 hours (755 women (27.2%), 902 men (33.0%), OR 0.8; 95% CI: 0.7 to 0.9) and women were admitted on average 36 minutes later than men (95% CI: 17 to 55 min). After adjustment for age this difference persisted (27 minutes, 95% CI: 9 to 47 minutes).

Conclusion: Women admitted to the hospital within 4 hours are treated just as often with thrombolytic agents as men. However, women are less often admitted within 4 hours than men and are therefore treated less often with intravenous alteplase.

10 Acute stroke: current treatment

HYPERTENSION AS A CO-MORBIDITY FACTOR IN A STROKE MODEL FOR CONSCIOUS ANIMALS: EFFECTS ON INFARCT SIZE, NEUROLOGICAL DEFICIT AND ACTIVATION OF GLIAL CELLS

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Background: IGF-I is a pleiotropic growth factor that stimulates the proliferation, differentiation and survival of neurons and glial cells. IGF-I has been shown to be neuroprotective in animal models of stroke. For successful translation to the clinic, drugs have to be administered in a clinically relevant way in conscious animals with a co morbidity factor, such as hypertension or diabetes (STAIR-criteria).

Material: A cerebral infarct was induced by application of 200†pmol Et-1 in the vicinity of the middle cerebral artery of conscious controls (WKY rats) and spontaneously hypertensive rats (SHRs). Motor/sensory functions were measured 1, 6 and 24 hours after the insult using the Neurological Deficit Score. The infarct size was assessed by cresylviolet staining. The activation of microglia and astrocytes was investigated by immunohistochemistry usingantibodies directed against ED-1 and glial fibrillary acidic protein (GFAP) 24 hours after Et-1 administration.

Results: First, we showed that subcutaneous administration of IGF-I in conscious rats with transient occlusion of the middle cerebral artery resulted in decreased infarct volumes in WKY rats. Second, induction of a cerebral infarct in SHRs resulted in a significantly larger infarct volume at 24 hr compared to controls. Accordingly, SHRs exhibited lower NDS at each time point, although these differences did not reach significance. Despite the larger infarct size in SHR, microglial activation in response to the insult was markedly reduced. Indeed, a reduced number of activated microglia in striatum and cortex was found. The activation of astrocytes, as assessed by GFAP expression, was the same in both animal models.

Conclusion: We conclude that subcutaneous administration of IGF-I after the insult can be neuroprotective in rats and that the SHR can be used to induce a clinically relevant ischemic infarct to further test therapeutic value of IGF-I.

11 Acute stroke: current treatment

DESTINY-S DECOMPRESSIVE SURGERY FOR THE TREATMENT OF MALIGNANT INFARCTION OF THE MIDDLE CEREBRAL ARTERY-SURVEY: ATTITUDE AMONG NEUROLOGISTS AND NEUROSURGEONS TOWARDS ACCEPTABLE DISABILITY AND CHOICE OF TREATMENT

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Background: Malignant middle cerebral artery (MCA) infarction cannot be survived without significant disability. The definition of "acceptable disability" is debatable and subject of ongoing Discussion. DESTINY-S is a survey on the attitude of neurologists and neurosurgeons towards the acceptable disability after malignant MCA infarction and therapeutic options for themselves.

Methods: Questionnaires where sent to 293 neurological and 129 neurosurgical departments. Participating physicians were asked about 1. demographic (age, gender, family status) and professional data (current position, qualification, experience in stroke treatment), 2. acceptable disability according to the modified Rankin Scale (mRS) and the therapy they would choose (surgical vs. medical vs. no therapy), depending on the side of the infarction (dominant vs. non-dominant). The survey was anonymous.

Results: A total of 1098 questionnaires were returned. Mean age of respondents was 36 years (31-44), 62% were male, 64% were neurologists. 44% regarded a mRS

score of 4 or better as acceptable for themselves (49% of neurologists vs. 35% of neurosurgeons (p<0.001)). Women were less likely to choose a mRS score of 4 or better (OR 0.62). 75% would choose decompressive surgery for non-dominant hemispheric infarction. Women (OR 0.48, <0.001) and respondents who were 51 and older (OR 0.53, p=0.018) were less likely to choose decompresive surgery. In infarctions of the dominant hemisphere 46% would choose decompressive surgery, 16% would choose medical treatment, and 35% would prefer no treatment. Neurosurgeons (39%, p=0.02) and respondents who were 51 and older (36%, p=0.038) were less likely to choose decompressive surgery. Other subgroups did not differ significantly.

Conclusion: The acceptance of severe disability after malignant MCA infarction among neurologists and neurosurgeons is unexpectedly high. The choice of treatment depends on dominant vs. Non-dominant infarction, medical speciality, gender, and age. The personal attitude of treating physicians towards may influence patients and relatives information, recommendation, the choice of therapy and, as a result, patients outcome.

12 Acute stroke: current treatment

GENDER DIFFERENCES IN PRESENTING SYMPTOMS OF ACUTE STROKE

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Background: We recently confirmed that women are treated less often with intravenous alteplase than men because their onset to door time is longer. The aim of this study was to assess differences in presenting symptoms between men and women that may be related to delayed admission of women with acute stroke.

Methods: We analyzed data of 1400 patients with acute stroke included in the PAIS study, a multi-center trial. Stroke symptoms were recorded by means of the NIH stroke scale (NIHSS). Risk factors and history were also recorded. Differences in frequency of presenting symptoms in relation to gender were analyzed with contingency tables. Associations were expressed as odds ratios (OR) with 95% confidence intervals (CI).

Results: Of all patients 616 (44.0%) were women. Mean age was 70 years, but women were on average 3 years older than men (95% CI: 2 to 5 years). Median NIHSS was 7 for women and 6 for men (p=0.01, rank-sum test). Women more often had atrial fibrillation (OR 1.6; 95% CI:1.2 to 2.2), more often presented with a lowered level of consciousness (OR 1.3; 95% CI: 1.0 to 1.7), a total gaze paresis (OR 1.3; 95% CI: 1.1 to 1.5), total paresis of the lower face (OR 1.2; 95% CI: 1.0 to 1.4) or mutism (OR 2.4; 95% CI: 1.5 to 3.7). Men on the other hand, presented more often with unilateral ataxia (OR 1.4, 95% CI 1.1-1.7). Adjustment for age did not affect these associations.

Conclusion: Our findings suggest that women with acute stroke present with different stroke symptoms than men. Women with acute stroke are generally older than men and suffer from atrial fibrillation more often, explaining why they had more severe strokes. Symptoms like lowered consciousness level and mutism may explain at least partly why women's experience longer delays in reaching the hospital than men.

Epidemiology of stroke

1 Epidemiology of stroke

EFFECTS OF PREHYPERTENSION AND HYPERTENSION SUBTYPE ON ISCHAEMIC AND HAEMORRHAGIC STROKE IN THE ASIA-PACIFIC REGION

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Background: The Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) defined blood pressure (BP) levels of 120-139/80-89 mmHg as prehypertension and those of ≥140/90 mmHg as hypertension. Hypertension is logically divided into three main categories: isolated diastolic (IDH: systolic BP <140 mmHg and diastolic BP ≥90 mmHg), isolated systolic (ISH: systolic BP ≥140 mmHg and diastolic BP <90 mmHg) and systolic-diastolic hypertension (SDH: systolic BP ≥140 mmHg and diastolic BP ≥90mmHg). While there is clear evidence that ISH and SDH increase the risks of stroke, there remains uncertainty about the effects of IDH. The objective was to determine the effects of prehypertension and hypertension subtypes (IDH, ISH and SDH) on the risks of ischaemic and haemorrhagic stroke in the Asia-Pacific Region.

Methods: The Asia Pacific Cohort Studies Collaboration is an individual participant data overview conducted by the principal investigators of cohort studies in the region. This analysis included a total of 346570 participants from 36 cohort studies. Outcomes were ischaemic and haemorrhagic stroke. The relationship between BP categories and stroke were explored using Cox proportional hazards models adjusted for age, sex, cholesterol and smoking.

Results: Compared with normal BP (<120/80mmHg), hazard ratios (95% confidence intervals [CI]) of ischaemic stroke were 1.60 (1.33-1.92) for prehypertension, 1.81 (1.37-2.39) for IDH, 2.86 (2.34-3.50) for ISH and 3.99 (3.32-4.80) for SDH. Those for haemorrhagic stroke were 2.17 (1.69-2.79) for prehypertension, 3.07 (2.19-4.30) for IDH, 4.04 (3.02-5.40) for ISH and 9.26 (7.25-11.82) for SDH.

Conclusion: In the Asia-Pacific region, prehypertension and all hypertension subtypes including IDH were clearly associated with increased risks of ischaemic and haemorrhagic stroke.

2 Epidemiology of stroke

DETERMINANTS OF HYPERTENSIVE RESPONSE IN ACUTE INTRACEREBRAL HAEMORRHAGE: DATA FROM 1000 INTERACT SUBJECTS

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Background: Various mechanisms may underlie the early hypertensive response in intracerebral haemorrhage (ICH). We investigated the determinants of baseline hypertension among subjects in the Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT).

Methods: The pilot (INTERACT1, completed August 2007) and main (INTERACT2, ongoing) trials are randomised controlled investigations of the effects of early intensive blood pressure (BP) lowering in patients within 6 hours of ICH and elevated systolic BP (150-220 mmHg). Associations between key demographic, clinical and ICH parameters and presenting (baseline) systolic BP were estimated using linear regression analyses on 1000 patients included in both trials by 6 March 2010.

Results: These patients (mean age 63 years; 64% male; 92% Asian) had a median time from onset to presentation of 1 hr 20 min (interquartile range 50 min to 2 hr 5 min) and mean baseline BP of 180/103 mmHg. Univariate predictors of higher baseline systolic BP including having a history of hypertension and higher NIHSS score (10 points or higher) at presentation, while those with haematomas located in basal ganglia/thalamus showed lower baseline systolic BP. These predictors remained significant in a multivariate model that included age, sex, ethnicity, time to presentation, history of hypertension, high NIHSS and haematoma location. Age, sex, ethnicity, time to presentation, prior ICH, ischemic stroke, diabetes, use of antihypertensive therapy, antiplatelet/warfarin therapy, intraventricular haematoma extension, and haematoma volume, were not related to baseline systolic BP.

Conclusions: History of hypertension, poor neurological state and haematoma location were the key determinants of BP elevation early after the onset of ICH. These Results do not support haematoma mass effect as a major determinant of the hypertensive response in ICH, but haematoma location may play a role.

3 Epidemiology of stroke

TIME-TRENDS IN CASE FATALITY AFTER STROKE: ANALYSES OF DATA FROM THE SOUTH LONDON STROKE REGISTER

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Background: Stroke mortality rates are reported to have declined in recent years but there is a lack of data from population-based studies examining the factors responsible for these trends including the impact of stroke unit care.

Methods: Trends in 90-day and 1-year case fatality of 3803 patients with first-ever stroke were estimated using data from a population-based register- the South London Stroke Register over the periods 1995-1997, 1998-2000, 2001-2004 and 2005-2008. The trends were compared by sex, age, ethnicity, stroke subtype and stroke unit care. Multivariate logistic regression analyses adjusting for case-mix variables were used to estimate the effect of time on case fatality.

Results: There was a significant decline in 90-day and 1-year case fatality (p-trend <0.001) between the years 1995-1997 to 2005-2008 (from 32.6% to 20.9% and from 40.7% to 27.3% respectively). The declining trends over this period remained consistent across gender, age, ethnicity and stroke subtype. The magnitude of the decline in 90-day and 1-year case fatality was greater for patients managed on a stroke unit (32.9% to 18.9%) and (37.1% to 25.6%) respectively compared to management on other wards

(36.8% to 33.7%) and (46.1% to 40.0%) respectively. The observed declining trends in 90-day (p<0.001) and 1-year (p<0.001) persisted in multivariate analyses after adjusting for age, sex, stroke subtype and level of consciousness. However, the trend observed with 90-day (p=0.67) and 1-year (p=0.26) were no longer significant after adjusting for stroke unit care indicating that changes in stroke unit admission over the years could possibly have accounted for most of the improved case fatality.

Conclusion: Case fatality at 90-days and 1-year after stroke decreased significantly in this population between 1995 and 2008. Stroke unit care may largely explain the declining case fatality in this population.

4   Epidemiology of stroke

PERCEIVED LIFE STRESSORS AND PREDICTION OF LONG-TERM STROKE MORTALITY AMONG MIDDLE-AGED MEN

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Background: To examine the association between perceived life stressors and long-term stroke mortality among a large cohort of middle-aged men.

Methods: A cohort of 10,059 men aged ≥40 years at study inclusion that were tenured civil servants or municipal employees were followed for mortality over 35-years. A composite perceived life stressor score was calculated based on a structured psychosocial questionnaire filled at baseline, assessing problems related to work, family and finance. The association between tertiles of perceived life stressors score and long-term stroke mortality or mortality from all other causes was assessed using Cox proportional hazard models, adjusted for traditional risks factors, socio-economic status and accounted for competing risk.

Results: During the 35-year follow-up 6,555 (65.2%) men died, 667 of stroke and 5,888 of all other causes. At baseline, subjects with higher perceived life stressor score were younger, had higher prevalence of smoking and coronary heart disease, and had less hypertension and lower socio-economic status (p<0.05 for all). Compared with the bottom tertile, the middle (HR 1.26, 95% CI 1.03-1.53) and top tertiles of perceived life stressors score (HR 1.34, 95% CI 1.08–1.66) exhibited higher risk of 35-year stroke mortality. The magnitude of the association was comparable to that of diabetes (HR 1.26, 95% CI 0.99–1.60). Calculated from directly adjusted survival curves (attached figure) the absolute risk difference of perceived life stressors tertiles (stroke mortality incident per 1000 participants) at 35-year was 13.7 for middle vs. bottom (P=0.02) and 17.9 for upper vs. bottom (P=0.01). No association was found between tertiles of perceived life stressors score and long-term mortality from all other cause (P>0.1 for all).
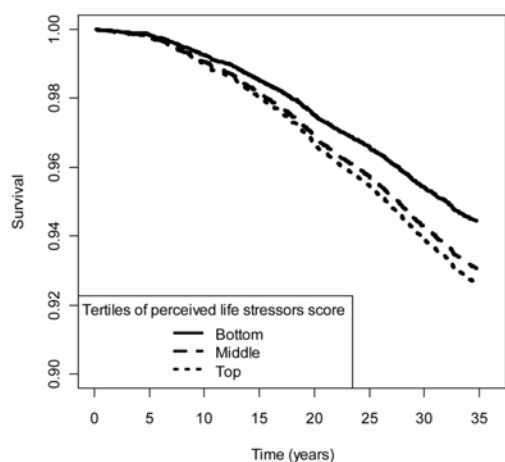
Conclusion: Perceived life stressors measured at baseline predict long-term stroke mortality over 35-year follow-up, but not mortality from all other causes.
Disclosure: None.

5   Epidemiology of stroke

PREVALENCE AND PREDICTORS OF DEMENTIA UP TO 15 YEARS AFTER STROKE: THE SOUTH LONDON STROKE REGISTER

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Background: Long-term follow-up studies assessing post-stroke dementia are rare. The aim of this study is to estimate prevalence and predictors of dementia up to 15 years after stroke.

Methods: Data were collected between 1995 and 2009 (n=4028) from the community-based South London Stroke Register covering an inner-city multi-ethnic source population of 271,817 inhabitants. Patients were assessed for cognition using Abbreviated Mental Test (AMT) or Mini Metal State Examination (MMSE) at 3 months and annually. Cognition was classified as impaired with a score of AMT<8 or MMSE<24. Baseline data included: age, sex, ethnicity, socioeconomic status, past medical history, case-mix severity and stroke subtype. Prevalence rates were estimated with 95% confidence intervals and inverse probability weighted regression was used to analyse the predictors of post-stroke dementia.

Results: Among stroke survivors, the prevalence of cognitive impairment ranged from 33% at 3 months to 42% at 14 years. Longitudinal analysis using inverse probability weighted regression showed that cognitive impairments was associated with the age of 65 and older (65-75 (OR= 1.8, 95%CI [1.29-1.48]), 75-85 (OR= 2.1, 95%CI [1.49-2.91]) and 85+ (OR= 6.7, 95%CI [4.46-10.12])), ethnicity (Black-Caribbean (OR= 1.8, 95%CI [1.25-2.73]) and Black-African (OR= 1.9, 95%CI [1.26-3.01])), socioeconomic status (OR= 2, 95%CI [1.5-2.59]), anti-hypertension medication (OR= 0.7, 95%CI [0.5-0.85]), smoking status (OR= 1.6, 95%CI [1.13-2.21]), urinary incontinence (OR= 2, 95%CI [1.39-2.86]), aphasia (OR= 1.6, 95%CI [1.01-2.56]), hemiparesis (OR= 1.5, 95%CI [1.11-1.98]) and stroke recurrence (OR= 2.2, 95%CI [1.26-4]).

Conclusions: The prevalence of cognitive impairment remains persistently high over time in stroke patients after their first stroke. Older age, ethnicity, socioeconomic status, smoking, urinary incontinence, aphasia, hemiparesis and stroke recurrence are predictors associated with post-stroke dementia. Hypertension management after stroke has a protective effect on cognition impairment. No difference in post-stroke cognition impairment was noted between stroke subtypes.

6   Epidemiology of stroke

ASSOCIATION OF COGNITIVE IMPAIRMENT AND HEALTH OUTCOME UP TO 3 YEARS AFTER STROKE: THE ERLANGEN STROKE PROJECT

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Background and purpose: Cognitive impairment (CI) is a frequent complication in stroke survivors. Data from population-based stroke cohorts on the impact of cognitive impairment on health outcome is limited. The purpose of this study was to determine association of cognitive impairment and different health outcomes up to 3 years after first-ever stroke.

Methods: Data was collected from the Erlangen Stroke Project, an ongoing population-based stroke registry covering a source of 103,000 inhabitants. The Mini-Mental State Examination (MMSE) for assessing global cognitive function was used; CI was defined as MMSE<24. Health outcome included limitations in extended activities of daily living (eADL, Frenchay Activities Index), activities of daily living (ADL, Barthel Index), depressive symptoms (Zung Self Rating Depression Scale), living conditions, and urinary incontinence. Using multivariate logistic regression analysis, association of CI with these health outcomes was investigated within distinct models at 12, 24 and 36 months after stroke.

Results: 705 patients with first ever stroke were included. Prevalence rates of CI at 12, 24 and 36 months were 15%, 13%, and 12.4%, respectively. In univariate analysis CI was associated with a lower ADL, lower eADL, depressive symptoms, living in an institution and urinary incontinence. In multivariable analysis an independent association of CI was found with institutionalization (OR 2.2 95% CI 1.7-4.2) and low eADL (OR 0.47 95% CI 0.3-0.7) at 12months, with depressive symptoms (OR 2.0 95% CI 1.0-4.1) and low ADL (OR 0.5 95%CI 0.4-0.7) at 24 months and with institutionalization (OR 2.5 95% CI 1.2-5.3) and low eADL (OR 0.25 95% CI 0.15-0.43) at 36 months.

Conclusion: CI among stroke survivors is associated with poor health outcome over the long term. These data provide evidence for the need of regular cognitive screening after stroke as well as development of effective interventions to improve long- term health outcome after stroke.

IMPACT OF CAROTID PLAQUE ON THE RISK OF STROKE AND ISCHEMIC HEART DISEASE IN A JAPANESE URBAN POPULATION: THE SUITA STUDY

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Background: Carotid atherosclerosis has been used increasingly as a subclinical marker for cardiovascular disease (CVD). However, few studies have examined the association of carotid atherosclerosis with CVD in Asian. We assessed the hypothesis that carotid plaque is a predictor of stroke and ischemic heart disease (IHD) events in a general urban Japanese population.

Methods: We studied 5,331 Japanese individuals (mean age 55.3 years, without stroke or IHD) who completed a baseline survey and carotid atherosclerosis in the Suita Study. Carotid atherosclerosis was evaluated by high-resolution ultrasonography with atherosclerotic indexes of intima-media thickness (IMT) in the common carotid artery (CCA), carotid artery bulb (Bulb), and internal and external carotid arteries. We defined plaque (PQ1 or PQ2), a focal IMT thickening, as an area where IMT≥1.1 mm or 1.4 mm, respectively. The risks of stroke and IHD across carotid atherosclerosis were compared by the use of multivariable-adjusted Cox proportional-hazards models.

Results: In 46,561 person-years of follow-up, we documented 124 cerebral infarctions, 49 hemorrhagic strokes, 12 unclassified strokes, and 125 IHD events. The hazard ratios (HRs; 95% confidence intervals, 95% CI) in subjects with PQ1 for all strokes and IHD were 1.6 (1.1-2.3) and 2.2 (1.4-3.5) in CCA and 1.1 (0.8-1.6) and 2.0 (1.3-3.0) in ICA, respectively, compared with subjects without PQ1. The HRs (95% CI) in subjects with PQ2 for all strokes and IHD were1.6 (1.1-2.2) and 2.6 (1.7-3.8) in CCA and 1.4 (1.0-2.0) and 2.6 (1.5-4.3) in Bulb, respectively. As for stroke subtypes, the HRs (95% CI) in subjects with PQ2 for cerebral infarction and atherothrombosis were 1.5 (1.0-2.4) and 2.1 (1.2-3.6) in CCA and 1.9 (1.2-3.0) and 3.3 (1.7-6.3) in Bulb, respectively.

	All CA		CCA		CA bulb	
	(-)	(+)	(-)	(+)	(-)	(+)
Person-years	14,633	31,929	29,932	16,629	18,082	28,120
Total strokes						
Cases	18	167	61	124	33	150
Adjusted HR	1	1.5 (0.9-2.5)	1	1.6 (1.1-2.3)	1	1.2 (0.8-1.8)
Cerebral infarction						
Cases	10	114	37	87	17	105
Adjusted HR	1	1.4 (0.7-2.7)	1	1.5 (1.0-2.3)	1	1.4 (0.8-2.4)
Atherothrombosis						
Cases	6	62	18	50	9	57
Adjusted HR	1	1.4 (0.6-3.4)	1	1.8 (1.0-3.2)	1	1.7 (0.8-3.5)
Hemorrhagic strokes						
Cases	6	43	20	29	13	36
Adjusted HR	1	2.2 (0.8-5.6)	1	1.9 (1.0-3.7)	1	1.2 (0.6-2.4)
Ischemic heart disease						
Cases	10	115	30	95	20	102
Adjusted HR	1	1.4 (0.7-2.7)	1	2.2 (1.4-3.5)	1	1.1 (0.7-1.9)

Multivariable-adjusting for age, sex, smoking, drinking, body mass index, blood pressure category (optimal, normal, and high-normal blood pressure and hypertension), total cholesterol, HDL cholesterol, blood glucose category (normoglycemia, impaired fasting glucose, and diabetes).

HR, hazard ratio; CA, carotid artery; CCA, common carotid artery

	All CA		CCA		CA bulb	
Plaque	(-)	(+)	(-)	(+)	(-)	(+)
Person-years	26,305	20,256	42,316	4,245	26,124	20,105
Total strokes						
Cases	57	128	140	45	54	126
Adjusted HR	1	1.4 (0.9-1.9)	1	1.6 (1.1-2.2)	1	1.4 (1.0-2.0)
Cerebral infarction						
Cases	30	94	91	33	28	93
Adjusted HR	1	1.8 (1.1-2.8)	1	1.5 (1.0-2.4)	1	1.9 (1.2-3.0)
Atherothrombosis						
Cases	14	54	47	21	12	54
Adjusted HR	1	2.4 (1.3-4.6)	1	2.1 (1.2-4.0)	1	3.3 (1.7-6.3)
Hemorrhagic strokes						
Cases	22	27	40	9	21	26
Adjusted HR	1	1.0 (0.6-2.0)	1	1.8 (0.8-4.0)	1	1.0 (0.5-1.9)
Ischemic heart disease						
Cases	19	106	81	44	20	104
Adjusted HR	1	2.8 (1.7-4.7)	1	2.6 (1.7-3.8)	1	2.6 (1.5-4.3)

Multivariable-adjusting for age, sex, smoking, drinking, body mass index, blood pressure category (optimal, normal, and high-normal blood pressure and hypertension), total cholesterol, HDL cholesterol, blood glucose category (normoglycemia, impaired fasting glucose, and diabetes).

HR, hazard ratio; CA, carotid artery; CCA, common carotid artery

Conclusion: Carotid plaque, especially when at least 1.4 mm thick, is a strong predictor of incidence of cerebral infarction and IHD in a Japanese general population.

PREVALENCE AND PROGNOSIS OF ASYMPTOMATIC VERTEBRAL ARTERY ORIGIN STENOSIS IN PATIENTS WITH CLINICALLY MANIFEST ARTERIAL DISEASE

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Background and Purpose: The risk of ischemic stroke in patients with asymptomatic vertebral artery (VA) stenosis is unknown. We examined the incidence of posterior circulation ischemic stroke in patients with an asymptomatic stenosis of the VA origin (VAo).

Methods: We used a hospital-based cohort study of 3717 patients with atherosclerotic arterial disease enrolled in the SMART (Secondary Manifestation of ARTerial disease) study in whom duplex ultrasound of the carotid artery (CA) and VA had been performed. Data were analyzed with Cox regression; hazard ratio's (HRs) were adjusted for age and vascular risk factors.

Results: In 282 patients (7.6%) asymptomatic VAo stenosis >50% was diagnosed with duplex ultrasound. During a mean follow-up of 4.6 years (SD, 3.0), posterior circulation ischemic stroke occurred in five of the 282 patients with an asymptomatic VAo stenosis at baseline (annual stroke rate, 0.4%) and in 12 of the 3435 patients without such a stenosis (annual stroke rate, <0.1%). The risk of posterior circulation ischemic stroke was higher in patients with VAo stenosis than in patients without VAo stenosis (HR, 4.2; 95% confidence interval (CI), 1.4-13.1) and was further increased in patients with both VAo and CA stenosis (HR, 10.5; 95% CI 3.0- 37.3). After adjustment for age and vascular risk factors, this risk remained essentially the same.

Conclusions: Patients with atherosclerotic arterial disease and an asymptomatic stenosis of the VAo have a higher risk of posterior circulation ischemic stroke than patients without such a stenosis, but the absolute risk remains low.

INTERACTION OF STROKE AND CHRONIC HEART FAILURE – REVERSE EPIDEMIOLOGY OF SOME CARDIOVASCULAR RISK FACTORS?

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Chronic heart failure (CHF) is a major risk factor for the development of stroke. We investigated the impact of clinical characteristics, of cardiovascular risk factors and of co-morbidities on the prevalence of stroke in CHF patients.

Methods: We analysed data from 4,746 patients from the patient cohort of the German Competence Network Heart Failure (age 65±13y mean ± SD, male 66.5%). Patients were in all stages of CHF severity (NYHA class I: n=474, II: 2652, III: 1515, IV: 105). Mean left ventricular ejection fraction (LVEF) was 40±16%

Results: At enrolment, 493 patients (10.4%) had suffered from prior cerebro-vascular event. These patients were older than those without stroke (68±12 vs. 65±13y, p<0.001). Stroke prevalence increased in parallel to CHF severity (NYHA class I,II,III,IV: 6.1%, 9.3%, 13.3%, 15.2%, p<0.0001) and to CHF duration (<1year, 1-5y, 5-10y, >10y: 8.7%, 10.9%, 11,4%, 12.2%, p=0.007). Stroke was more prevalent in patients with lower LVEF (LVEF<45%: 11.2%, vs LVEF≥45%: 8.8%, p=0.012) and in patients with atrial fibrillation (15.3% vs without AF: 9.3% p<0.001).

Patients with stroke had lower Hb (13.6±1.8 vs. 13.8±1.8 g/dL, p<0.001) and worse renal function (eGFR 70±24 vs. 63±23 mL/min/1.73m², p<0.001) vs non-stroke patients. However, a reverse epidemiology was observed for other risk factors:

Stroke prevalence was higher in patients with normal BMI ($<25kg/m^2$) than in overweight and obese patients (BMI>25kg/m^2; odds ratio (OR) 1.53, 95%CI 1.26-1.87). Also, patients with normal cholesterol (Chol <5,2mmol/L) had more often strokes than patients with cholesterol >5.2mmol/L (OR 1.45, 95%CI 1.18 - 1.78). Patients with stroke had lower systolic (127±21 vs 129±23mmHg, p=0.06) and diastolic blood pressure (74.7±12.9 vs. 76.5±12.5 mmHg, p=0.002) compared to non-stroke patients. Multiple adjustment did not alter the Results.

Conclusion: The prevalence of stroke increased in parallel to CHF severity and duration, and to co-morbidities such as renal impairment or anaemia. However, some cardiovascular risk factors such as BMI, cholesterol and blood pressure show reverse epidemiology for the association with stroke in CHF.

10 Epidemiology of stroke

BOTH REPORTED ADVERSITIES OF FAMILY LIFE AND PROCLAIMED MARITAL DISSATISFACTION PRECEDED INCREASED 32-YEAR FATAL STROKE RATES IN MIDDLE-AGED AND ELDERLY MEN

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Background: The potential role of different psychosocial factors in the pathogenesis of stroke raises increasing interest.

Patients and Methods: The Israeli Ischemic Heart Disease (IIHD) Project, a longitudinal investigation of cardiovascular disease among about 10,000 male civil servants and municipal employees in Israel aged 40-65, provided a wide range of occupations and socioeconomic levels in the male working population of Israel at the time of inclusion. Extensive appraisal of health and behavioral patterns in 1963 included a structured psychosocial questionnaire and 9333 men responded. Extent of marital satisfaction or dissatisfaction was queried upon the first follow-up examination (1965). Only 3.6% defined their marraoge as utterly unsuccessful. Underlying cause of death is available through 1997. Cox Proportional hazard regression with adjustment for age and established stroke risk factors (blood pressure, smoking, diabetes) was employed to estimate hazard ratios (HR) of fatal stroke. We compiled a summary index of family problems summing answers to all questions related to perceived family difficulties, support and coping.

Results: Fatal stroke occurred among 564 men of those (n=8591) with both family trouble score and marriage satisfaction report. Men with 1,2,3 or 4 "serious" or "very serious" answers to the above family problem questions, relative to none, revealed age-,Systolic BP-, smoking- and diabetes-adjusted, HRs of 1.07 (95%CI, 0.88-1.30), 1.23 (CI 0.95-1.59), 1.59 (CI 1.09-2.46) and 1.36 (CI 0.49-3.76, only 48 men) respectively, Ptrend<.0.05. Reportedly rather successful, not so successful and utterly unsuccessful marriage were associated with HRs of 1.12, 1.04 and 1.75 (CI 1.17-2.63) relative to reportedly successful marriage.

Conclusion: In this long-term follow-up study of working men perceived family problems, and disappointment with married life were independently associated with the risk of dying from stroke over a 32-year follow-up period. Traditional stroke risk factors did not confound these associations. The Results accentuate a possible bio-psychosocial Background for the development of stroke.

11 Epidemiology of stroke

CANCER DIAGNOSIS AMONG PATIENTS HOSPITALIZED WITH STROKE

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Background: As stroke rates have dropped over the last decade likely due to better traditional risk factor control, more attention is being paid to less conventional stroke risk factors. Presence of cancer can confer a hypercoagulable tendency thereby raising stroke risk, but there are very few large-scale epidemiologic studies on stroke in cancer-afflicted persons. Longer survival among cancer patients may be increasing the contribution of cancer to stroke incidence.

Objective: We evaluated the prevalence, patterns, and predictors of several cancers among patients hospitalized with an ischemic stroke in the United States.

Methods: The Nationwide Inpatient Sample was used to identify a subsample that included discharges with any International Classification of Diseases, ninth revision, and diagnosis codes for cancer and ischemic stroke from 1997 to 2006. Age-adjusted yearly acute ischemic stroke hospitalization rates in the US adult population with and without cancer were calculated.

Results: Prevalence of Cancer among hospitalized stroke patients increased from 1997 to 2006 (N= 31,075 (9.1% of all ischemic stroke hospitalizations) to 34,138 (10.6%), p<0.0001). The most common type of cancer among hospitalized stroke patients in 1997 and 2006 was prostate (21%, 19%), breast (19%, 19%), gastrointestinal (16%, 13%), and colorectal (13%, 13%). Over the decade there was a significant decrease in prevalence of stroke hospitalization (slope -3.02, 95% CI -3.89, -2.34) but not in the prevalence of stroke hospitalization among cancer patients (slope 1.35, -0.88, 3.35). Overall the percentage off stroke patients admitted with cancer comorbidity increased from 9.1% to 10.6% over the ten year period of observation (trend p<0.0001).

Conclusion: The proportion of stroke hospitalizations with a comorbid diagnosis of cancer has been steadily increasing, and in 2006 accounted for more than 1 in 10. As the population ages and cancer treatments improve, the proportion of ischemic stroke patients with cancer will continue to increase.

12 Epidemiology of stroke

CAREGIVERS STRESS IN STROKE SURVIVORS: INDIAN PERSPECTIVE

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Background: As life expectancy increases, India will face enormous socioeconomic burden to meet the costs of integrated rehabilitation of stroke patients. Caring for stroke patients leads to caregiver (CG) strain. The Aims of this study are to identify factors related to increased CG burden in stroke survivors in a census defined population, and to assess the relationship between patient characteristics and CG stress.

Methods: In a prospective population based study (Dec 2008-Dec 2009) 223 first ever stroke (FES) were identified. At 28 days, 127 (56.9%) were alive and 79 (35%) died and 17 were lost to follow-up. 111 CGs of 127 FES survivors, agreed to participate. The level of stress was assessed by two scales Oberst Caregiving Burden Scale (OCBS) and the Caregivers Strain Index (CSI) in CGs of survivors with mild stroke Modified Rankin Scale (MRS 1-2) and in those with significant disability (MRS 3-5).

Results: The mean age of CGs was 45.6 years approximately 22 years younger than that of patients (67.5 years). 89 (80%) of CGs were females and only 22 (19.8%) were males. Urinary incontinence (p=0.000008), morbidity at 28 days by Modified Rankin Scale (p=0.0051), female gender (p=0.0183), moderate to severe neurological deficit by National Institute of Health Stroke Scale (NIHSS) on admission (p=0.0254), were factors in FES cases leading to major CGs stress. CG factors responsible for major stress were long caregiving hours (p=<0.000001), anxiety (p=<0.000001), disturbed night sleep (p=<0.000001), financial stress (p=0.0000108), younger age (p=0.0021), and CGs being daughter-in-laws (p=0.012). However, CGs education, occupational status and marital status were not significantly related to CG stress.

Conclusion: In India, there are no organized stroke care delivery systems for the patient neither any support system for the CG. Integrated stroke rehabilitation services should also address CG issues to local situations, and include practical training in simple nursing skills and counseling sessions to help reduce CG burden.

Acute cerebrovascular events (ACE): TIA and minor strokes

1 Acute cerebrovascular events (ACE): TIA and minor strokes

EARLY RISK OF STROKE AND PERFORMANCE OF THE ABCD2 SCORE IN "TISSUE-DEFINED" VERSUS "TIME-DEFINED" TIA: AN INTERNATIONAL MULTI-CENTRE COLLABORATIVE STUDY

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Background: Stroke risk immediately after TIA, defined by time-based criteria, is high and clinical prediction tools (ABCD2, ABCD3-I scores) have been developed to assist management. The American Stroke Association has proposed changing the criteria for distinction between TIA and stroke from time-based to tissue-based, but prognostic research using these definitions is lacking. We have studied prognosis and performance of the ABCD2 score in TIA, sub-categorized as "tissue-positive" or "tissue-negative" on DWI or CT according to the newly proposed criteria.

Methods: 12 centres provided data on ABCD2 scores, DWI or CT brain imaging and follow-up in cohorts of TIA patients diagnosed by time-based criteria. Recurrent stroke rates at 7-days and 90-days were studied in relation to "tissue-positive" or "tissue-negative" sub-categorization, according to the presence or absence of brain infarction. Predictive power of the ABCD2 score was determined using area under ROC analyses.

Results: 4574 patients were included. Among DWI-imaged patients (n=3206), recurrent stroke rates at 7-days were 7.1% (95% CI 5.5- 9.1) after "tissue-positive" and 0.4% (0.2- 0.7) after "tissue-negative" events (p diff<0.0001). Corresponding rates in CT-imaged patients were 12.8% (9.3-17.4) and 3.0% (2.0- 4.2) respectively

(p diff<0.0001). ABCD2 score was predictive in both "tissue-positive" and "tissue-negative" events (AUC=0.68 (95% CI 0.63- 0.73) and 0.73 (0.67- 0.80) respectively, p sig <0.0001 for both Results, p diff=0.17). "Tissue-positive" events with low ABCD2 scores and "tissue-negative" events with high ABCD2 scores had similar stroke risks, especially after 90-day follow-up.

Conclusion: Our findings support the concept of a revised definition of TIA with subcategorization based on the presence or absence of infarction on grounds of prognosis.

2 Acute cerebrovascular events (ACE): TIA and minor strokes

PREDICTIVE VALUE OF BRAIN AND VASCULAR IMAGING IN TRANSIENT ISCHEMIC ATTACK PATIENTS. VALIDATION OF ABCD3-I SCORE

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Objective: Diffusion-weighted magnetic resonance imaging (DWI) is not only a sensitive diagnostic tool for detecting acute ischaemic lesions in patients with transient ischaemic attacks (TIAs) but also a prognostic tool. Morever, large-artery aterosclerosis (LAA) is a marker of poor prognosis. Recently, brain and vascular imaging have been added to a new prognostic score: ABCD(3)-I score.

Methods: We analyzed data from TIA patients of the PROMAPA study who underwent diffusion-weighted imaging (DWI) within 7 days of symptom onset. Items that contribute to the ABCD(3)-I score (age, blood pressure, clinical weakness, duration, diabetes, LAA, recurrence events and DWI), other clinical variables and stroke recurrence at seven- and 90-day follow-up were recorded.

Results: 462 TIA patients were included in the study. DWI abnormalities were identified in 117 (46.1%) patients. During follow-up, eight patients (1.7%) had a stroke within 7 days, and 14 (3.1%) had a stroke within 3 months. In cox proportional In the Cox logistic regression model, the combination of LAA and positive DWI remained as independent predictors of stroke recurrence at 90-day follow-up (HR 8.23, 95 CI 2.89-23.46, p<0.001). The area under the receiver operating characteristic curve was 0.79 (0.68-0.91, p=0.005) at 7 days and 0.67 (0.51-0.83, p=0.029) at 90 days. 0.004).

Conclusion: The combination of neuroimaging and vascular information improve prognostic accuracy in patients with TIA. ABCD3-I could select patients at high risk of very early recurrent stroke who need immediate evaluation and treatment.

3 Acute cerebrovascular events (ACE): TIA and minor strokes

EVOLUTION OF DWI SIGNAL ABNORMALITIES AFTER TRANSIENT ISCHEMIC ATTACK AND MINOR ISCHAEMIC STROKE

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Background: Diffusion weighted imaging (DWI) signal abnormality after transient ischaemic attack (TIA) predicts early stroke, independently of other risk markers included in the ABCD3-I score. Early stroke recurrence detected on follow-up DWI after the acute-phase DWI may identify patients at high risk for subsequent clinical

stroke, cognitive impairment, and seizures. We aimed to determine the evolution of acute DWI lesions and rate of new ischaemic lesion (NIL) occurrence on follow-up DWI after TIA and minor stroke.

Methods: Early DWI-detected stroke recurrence (defined as NILs on follow-up DWI one week after acute DWI) was identified in a prospective MRI study of TIA and minor stroke patients. Presence/absence of DWI lesion(s), topography, clinical variables, and clinical stroke recurrence by day 7 and 90 were recorded.

Results: 87 patients were included, 65 TIA and 22 minor stroke. Study patients' mean age was 68 years [Standard deviation 6], 64% male, mean ABCD2 score 4, mean ABCD3-I score 5 (TIA patients only). The median duration from symptom onset to acute (baseline) DWI was 2 days (Interquartile range 2-3) and to follow-up MRI was 10 days (IQR 8-12),with 7-day median interval between DWIs (IQR 5-9). 23/65 TIA patients (37.3% [95% CI 23.9-48.2]) had at least one DWI lesion at baseline. Early recurrent stroke occurred in 3.4% (3/87 patients) when defined clinically, compared to 6.9% [95% CI 2.6-14.4] (6/87) when defined by MRI (p<0.001). NILs were detected in 2/22 stroke patients 9.1% [95% CI 1.1-29.2] and 4/65 TIA patients 6.2% [95% CI 1.7-15.0]. In 60.9% [95% CI 38.5-80.3] TIA patients (14/23) with baseline DWI lesions, these were no longer detectable on early follow-up DWI.

Discussion: Early follow-up DWI increased the identification of recurrent ischaemia compared to clinical evaluation alone. Early resolution of initial DWI lesions after TIA indicates the dynamic nature of ischaemic changes and importance of early MRI for risk stratification in practice.

4 Acute cerebrovascular events (ACE): TIA and minor strokes

PERFUSION IMAGING PREDICTS OUTCOME IN TIA AND MINOR STROKE

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Background: Clinical progression occurs in many patients presenting initially with minor or transient ischemic symptoms. Identification of the patients at highest risk for progression may justify more aggressive acute treatment prior to deterioration. We tested the hypothesis that baseline perfusion (PWI)-diffusion weighted imaging (DWI) abnormalities predict infarct growth and clinical progression.

Methods: Patients with minor stroke (NIH Stroke Scale ≤ 3) and TIA presenting within 12 hours of symptom onset were prospectively enrolled and imaged. DWI and PWI (within 24 hours of symptom onset) and follow-up FLAIR (30 days) infarct volumes were measured with planimetric techniques. PWI-DWI mismatch volumes were calculated as Tmax+4s delay – DWI lesion. Infarct growth volume was measured as day30 FLAIR -DWI lesion.

Results: 137 patients were included; 54% had DWI lesions and 41.6% had PWI (Tmax+4s) deficits at baseline. Clinical deterioration occurred in 13 (9.5%) patients within 72 hours. 119 patients had follow-up imaging at day 30, 21 of whom developed infarct growth (17.6%). Patients with clinical worsening had significantly higher baseline mismatch volumes (median= 45 ml, IQR= 83.3) than those who did not progress (median=0 ml, IQR= 1, P<0.001). A mismatch volume of 10ml predicted clinical worsening with 77% sensitivity and 86% specificity (Area Under Curve (AUC)= 0.814, [0.66, 0.9]) and radiographic infarct growth with 81% sensitivity and 91.5% specificity (AUC=0.883, [0.78, 0.98]). Linear regression showed that for every 10ml of mismatch, there would be 2.5ml infarct growth on day 30 FLAIR [R=0.80, p<0.001].

Conclusion: In a population of patients with minor stroke and TIA, early MR perfusion-diffusion mismatch strongly predicts clinical deterioration and infarct growth. These findings suggest that there may be a group of patients with minor symptoms in whom reperfusion strategies may be beneficial.

5 Acute cerebrovascular events (ACE): TIA and minor strokes

YIELD OF AUTOMATED PERFUSION WEIGHTED IMAGING FOR THE EVALUATION OF TIA

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Background: Transient ischemic attack (TIA) is a major risk factor for stroke. Confirming the diagnosis of TIA is challenging. Perfusion weighted imaging (PWI) increase the yield of diffusion weighted imaging (DWI) to confirm the diagnosis of cerebral ischemic events. The RApid processing of PerfusIon and Diffusion (RAPID) software program performs rapid and fully automated processing of PWI

images. We investigate the yield of RAPID processed PWI for the assessment of TIA patients.

Methods: DWI and PWI were prospectively performed among consecutive patients referred for suspicion of TIA. DWI and two RAPID generated PWI maps (time to the maximum of the residue function [TMax] and the mean transit time [MTT]) were assessed by a vascular neurologist (JMO) who was blinded to the clinical data.

Results: 85 patients with suspected TIA were prospectively enrolled. MRI was performed within 1 day (IQR 0.5-3) after symptom onset. DWI imaging was positive for an acute ischemic lesion among 20% of patients. A Tmax lesion was detected among 27% while MTT was positive among 15% (p=0.021). Only 1 of the 13 patients with a MTT lesion did not have a TMax lesion. Both DWI and TMax were positive among 13% of patients, 14% had an isolated TMax lesion and 7% an isolated DWI lesion. The presumed location of clinical symptoms was ipsilateral to 94% of DWI and 87% of TMax lesions. Univariate analyses demonstrated that TMax lesions were associated with a history of prior stroke (p=0.017), and the presence of symptomatic vascular stenosis (p<0.0001). A symptomatic stenosis was found among 35% of patients with a Tmax lesion. Fifty six patients had a final diagnosis of TIA/Stroke. Using the final diagnosis of TIA/stroke as the gold standard, the combination of DWI and PWI had a specificity of 90% and a sensitivity of 46%.

Conclusion: Automatically processed PWI maps increased the yield of DWI for demonstrating ischemic lesions in patients with suspected TIA. The yield of the PWI TMax sequence was significantly higher than MTT. PWI lesions typically matched the presumed location of the clinical symptoms and most occurred in patients without symptomatic large vessel stenosis.

6 Acute cerebrovascular events (ACE): TIA and minor strokes

EARLY CT/CTA PREDICTS RECURRENT EVENTS IN MINOR STROKE/ TIA PATIENTS: MAIN RESULTS OF THE CT AND MRI IN THE TRIAGE OF TIA AND MINOR CEREBROVASCULAR EVENTS TO IDENTIFY HIGH RISK PATIENTS (CATCH) STUDY

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Background: Minor stroke and TIA patients are at high risk for recurrent events. Although MRI has been shown to predict recurrent stroke in this population, non contrast CT (CT) is the standard imaging modality used in most institutions. Arch to vertex CT Angiography (CTA) can quickly and accurately identify high-risk vascular lesions and can easily accompany CT. The main aim of this study was to assess the use of CT/CTA in the prediocion of recurrent events in minor stroke/TIA.

Methods: Consecutive patients presenting with TIA or minor stroke (NIHSS<4) at a single academic institution, were prospectively enrolled if a stroke neurologist assessed them and they had a CT/CTA (Aortic arch to vertex) completed within 24 hours of symptom onset. High risk CT/CTA phenotype was identified a priori as: new ischemic change on CT, intracranial or extracranial vessel occlusion or stenosis≥50% on CTA. Primary outcome was risk of clinical progression/recurrent stroke within 90 days. Predictors of the primary outcome were assessed using standard clinical variables.

Results: 510 patients were consented and prospectively enrolled. 302 were male with mean age 67 years (sd14). 428 also had MRI brain completed. Median time from symptom onset to CTA was 5.6 hours. There were 37 recurrent events in 36 patients (7%). In the univariate analysis, positive predictors of progression/recurrent stroke were: high risk CT/CTA phenotype; RR 3.8 (2-7.4, p=0.0001), symptoms ongoing in ED; RR 2.2 (1.02-4.7, p=0.049) and among the MR subset, acute DWI lesion on MRI: RR 3.5 (1.4- 9.0, p= 0.004). Overall CT/CTA identified 67% (95%CI: 49%-81%) of cases of clinical progression/recurrent stroke.

Conclusions: CT/CTA completed very early after symptom onset in TIA and minor stroke can predict clinical progression/recurrent events. These Results are exciting as they confirm CT/CTA as an imaging alternative in TIA and minor stroke risk stratification in institutions where acute MRI is not acutely available.

7 Acute cerebrovascular events (ACE): TIA and minor strokes

TRANSIENT ISOLATED "BRAINSTEM" SYMPTOMS: TIA OR TNA?

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Background: Transient isolated "brainstem" symptoms (e.g. isolated vertigo, dysarthria, diplopia, etc) are not TIAs by the NINDS Diagnostic Criteria. However, there are too few data on their prognosis to be confident of their nature. If some of these events are posterior circulation TIAs, then they should be common during the days and weeks prior to definite posterior circulation ischaemic events.

Methods: We prospectively studied all first TIA and ischaemic stroke in a population-based study in Oxfordshire, UK from 2002 to 2010 (Oxford Vascular Study). Definite posterior circulation events were defined as those with either a posterior circulation stroke or a NINDS-defined TIA with ≥50% symptomatic VB stenosis on MRA, CTA or angiography. Details of any TIA or TNA-like events within the preceding 90-days were recorded.

Results: Of 1927 definite TIA or ischaemic strokes, 299 were definite VB events. Of these, 72 (24.1%, 95% CI 19.2-29) had at least one TNA/TIA within the preceding 90 days (median=3.5 days) of which only 4 (6%) fulfilled the NINDS criteria for TIA. The other 68 cases were isolated vertigo (n=23), non-NINDS binocular visual disturbance (12); vertigo with non-focal symptoms (14), isolated slurred speech (6), isolated hemisensory tingling (5), transient confusion (3), transient total paralysis (2), isolated diplopia (2); and migraine variant (1). Among 178 patients with definite VB events who had VB arterial imaging, preceding transient isolated "brainstem" symptoms were particularly associated with the presence of ≥50% symptomatic stenosis (OR=3.1, 95% CI 1.6-5.9).

Conclusion: In patients with definite posterior circulation TIA or stroke, preceding transient isolated "brainstem" symptoms occurred in 24%. Despite this close temporal link and the association with ≥50% symptomatic VB stenosis, fewer than 10% of preceding events satisfied the NINDS definition of a TIA.

8 Acute cerebrovascular events (ACE): TIA and minor strokes

RECURRENT TIA AND EARLY RISK OF STROKE: DATA FROM THE PROMAPA STUDY

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Background: Many guidelines recommend urgent intervention for TIA patients with 2 or episodes within 7-days to reduce the early risk of stroke. However, whether all patients with multiple TIAs are at high early risk of stroke is unknown.

Methods: Between April 2008 and December 2009, we included 1255 consecutive TIA patients from 30 Spanish stroke centers (PROMAPA study). We prospectively recorded clinical characteristics. We also determined the early short-term risk of stroke (at seven and ninety days). Aetiology of TIA was categorised using the SSS-TOAST classification.

Results: Enough information was assessed in 1137 patients (90.6%). 7-day and 90-day stroke risk were 2.6% and 3.8% respectively. Atherosclerotic etiology (AE) was confirmed in 190 (16.7%) patients. Recurrent TIA was observed in 274 (24,1%) patients. Duration<1 hour (OR 2.94, 95% CI 2.18-3.96, p<0.001), AE (OR 1.97, 95% CI 1.39-2.78, p<0.001) and motor weakness (OR 1.37, 95% CI 1.03-1.82, p<0.029) were independent predictors of recurrent TIA. The subsequent risks of stroke in these patients at 7, and 90 days were significantly higher than those after a single TIA (5.8% versus 1.5%, p<0.001 and 6.8% versus 3.0%, respectively. HR 2.35, 95% CI 1.28-4.31 p=0.006). In the Cox logistic regression model, among patients with recurrent TIA, no variable remained remained as independent predictors of stroke recurrence at 90-day.

Conclusion: According to our Results, recurrent TIA within 7-days is associated with a greater subsequent stroke risk than after a single TIA. Nevertheless, we were not able to find any independent predictor of stroke recurrence among these patients.

9 Acute cerebrovascular events (ACE): TIA and minor strokes

MULTIPLE (>1) NEUROLOGICAL EPISODES AND THE RISK OF IPSILATERAL ISCHEMIC STROKE RECURRENCE IN PATIENTS WITH SYMPTOMATIC CAROTID STENOSIS

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Background: Carotid endarterectomy (CEA) reduces the risk of ipsilateral ischemic stroke in patients with symptomatic 50-99% carotid stenosis. We hypothesise that more than one recent focal neurological episode is a marker for a high risk of ipsilateral ischemic stroke recurrence before CEA.

Methods: This is a secondary analysis of the Additional Neurological SYmptoms before Surgery of the Carotid Arteries – a Prospective study (ANSYSCAP). We prospectively ascertained 230 consecutive patients with symptomatic 50-99% carotid stenosis who underwent evaluation before CEA. We followed the patients for 90 days or until CEA. The primary endpoint was ipsilateral ischemic stroke that occurred after the presenting event, but before CEA.

Results: Multiple (≥1) ipsilateral cerebrovascular events (TIA, amaurosis fugax, or minor ischemic stroke) occurred in 20% (46/230) of the patients within 7 days before the presenting event and in 33% (77/230) of the patients within 90 days before the presenting event. A recurrent ipsilateral TIA or amaurosis fugax occurred in 27% (63/230) of the patients within 90 days after the presenting event (not including events that occurred after an ipsilateral ischemic stroke recurrence or after CEA). The risk of ipsilateral ischemic stroke recurrence was not affected by the presence of multiple ipsilateral episodes within 7 or 90 days before the presenting event, and tended to be lower if the patients suffered a recurrent ipsilateral TIA or amaurosis fugax after the presenting event, see the table.

Table 1. Risk of ipsilateral ischemic stroke recurrence before CEA in patients with symptomatic 50-99% carotid stenosis

		Risk at 14 days (95%CI)	Risk at 90 days (95%CI)	Significance*
Multiple (≥1) ipsilateral cerebrovascular event within 7 days before the presenting event	Multiple	14.6%	22.9%	p=0.35
		(3.7-25.5%)	(8.2-37.7%)	
	Single	10.5%	17.8%	
		(6.0-15.0%)	(10.7-24.9%)	
Multiple (≥1) ipsilateral cerebrovascular event within 90 days before the presenting event	Multiple	11.2%	15.6%	p=0.77
		(3.9-18.6%)	(6.4-24.8%)	
	Single	11.3%	20.4%	
		(6.2-16.4%)	(11.9-29.0%)	
Multiple (≥1) ipsilateral TIA or amaurosis fugax within 90 days after the presenting event	Multiple	4.9%	14.4%	p=0.12
		(0.0-10.2%)	(0.4-28.3%)	
	Single	13.5%	20.3%	
		(8.2-18.7%)	(12.9-27.7%)	
Total		11.2%	18.7%	-
		(7.0-15.4%)	(12.2-25.2%)	

*At 90 days, log rank test.

Conclusions: Multiple ipsilateral cerebrovascular events before or after the presenting event were common but were not associated with an increased risk of ipsilateral ischemic stroke recurrence before CEA. The patients without multiple events before or after the presenting event had a high risk of ipsilateral stroke recurrence at 14 days and should therefore not undergo CEA at a slower pace than patients with multiple events.

10 Acute cerebrovascular events (ACE): TIA and minor strokes

PREDICTION OF EARLY ISCHEMIC RECURRENCE AFTER TIA

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Background: Previous studies have assessed the utility of ABCD2 score and imaging techniques to predict early ischemic recurrence after a TIA. These studies have not assessed the yield of detecting symptomatic arterial stenosis or occlusion (SASO) using transcranial color-coded sonography (TCCS) in addition to duplex ultrasonographic evaluation of cervical arteries. In this study we prospectively tested this variable (SASO) for the prediction of early recurrence in consecutive patients admitted to a TIA clinic.

Methods: Patients had in the 3 hours following admission cervical arterial Duplex, TCCS, brain MRI including Diffusion and FLAIR sequences, ECG and routine blood studies. We recorded stroke and TIA recurrence in the 48 hours following evaluation.

Results: 210 patients were included (M/F: 119/91; mean age: 60±17.7). Clinical diagnosis was: definite TIA in 120 patients (group 1); possible TIA in 12 patients (group 2); minor stroke in 11 patients (group 3), retinal ischemia in 10 patients, and other diagnoses in 57 patients. 7 patients had early recurrence: 5 TIAs and 2 strokes.

In patients from groups 1, 2 and 3, adjusted odds ratios for early recurrence were: 2.08 [95% CI: 1-4.34] for each supplementary point on ABCD2 score, 0.319 [CI: 0.04-2.3] for acute infarction on DWI, and 10.77 [CI: 1.82- 63.77] for SASO as detected by cervical Duplex or TCCS.

The ROC curve using the ABCD2 score showed an area under curve (AUC) of 0.761. We calculated a newer ABCD2S score adding 5 points to the ABCD2 score in patients with SASO. The ROC curve using ABCD2S score showed an AUC of 0.871 (p=0.001). The rate of early recurrence depending on ABCD2S was 0% for score 0 to 3; 6.6% for score 4 to 7 and 22.2% for score 8 to 12. Incorporating findings on DWI did not improve the predictive ability of ABCD2S score.

Conclusion: These findings suggest that TIA patients with SASO are at high risk of early ischemic recurrence. Consideration of this variable can help stratify risk in TIA patients.

11 Acute cerebrovascular events (ACE): TIA and minor strokes

EVIDENCE OF SUBACUTE REVERSIBLE COGNITIVE IMPAIRMENT AFTER FOCAL SYMPTOM RESOLUTION IN TIA AND MINOR STROKE: IMPLICATIONS FOR DEFINITIONS AND PROGNOSIS

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Background: Subacute reversible cognitive impairment (SRCI) occurs after major stroke. We did a population-based study to determine whether SRCI also occurs after TIA and minor stroke and whether it predicts long-term cognitive decline.

Methods: Mini-mental-state examination (MMSE) was done in consecutive testable patients with cerebral TIA or minor stroke (NIHSS<3) seen subacutely (24 hours to 7-days) in the Oxford Vascular Study (2002-2005) versus after 7 days, and in referrals seen subacutely with other diagnoses. We defined SRCI as improvement of >2 points on MMSE at 1-month follow-up, and identified cognitive impairment (Montreal Cognitive Assessment<26/30) and severe dementia (not testable) at 1, 2 and 5 years.

Results: SRCI was more frequent in cerebral TIA and minor stroke patients seen subacutely (80/206; 38.9%) versus later (14/74; 19%; p=0.002) or in those with other diagnoses (10/47; 21%; p=0.004). SRCI was associated with transient confusion at event onset (OR=5.5, 95%CI 2.5-11.7, p<0.0001), acute infarct on CT (OR=2.0,1.2-3.5, p=0.01) and with residual focal deficits at assessment [44/102 (43%) unresolved vs 50/178 (28%) resolved; OR=1.94, 1.13-3.34, p=0.01] although SRCI was still seen subacutely in those with no focal deficits at assessment (41/120 vs 9/58 in those seen after 7-days, OR=2.8,1.2-6.9, p=0.009). Although patients with SRCI had similar MMSE by 1-month to those without SRCI, their risks of cognitive impairment (OR=4.3,1.2-15.7,p=0.03) and severe dementia (OR=4.9, 1.0-25.8, p=0.05) were increased during follow-up.

Conclusion: Reversible cognitive dysfunction is a manifestation of TIA and minor stroke, may persist beyond resolution of focal symptoms and predicts long-term cognitive decline. Our findings have implications for diagnosis of transient confusion, for prognosis after TIA and minor stroke, and for deficit duration allowed in the time-based definition of TIA.

ATHEROGENIC DYSLIPIDEMIA IN PATIENTS WITH TRANSIENT ISCHAEMIC ATTACK

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Background: There is mounting evidence that atherogenic dyslipidaemia (ie, both low high-density lipoprotein cholesterol [HDL-C] and high triglyceride concentrations) is an independent predictor of high cardiovascular risk and possibly of stroke.

Methods: All patients included in the SOS-TIA cohort underwent an initial standardised evaluation, including medical history, physical examination, routine blood biochemistry, and diagnostic testing, and were followed for 1 year. Lipid profile was evaluated under fasting conditions. Atherogenic dyslipidaemia was defined as HDL-C blood concentration ≤40 mg/dL and triglycerides as ≥150 mg/dL.

Results: Among 1471 consecutive patients with transient ischaemic attack (TIA) or minor stroke, the overall prevalence of atherogenic dyslipidaemia was 5.8%, but varied from 4.6% to 11.1% according to the final diagnosis (possible TIA or TIA with a cerebral ischaemic lesion, respectively). Prevalence of atherogenic dyslipidaemia was independently associated with male sex, diabetes, and body mass index, but not with ABCD2score. Atherogenic dyslipidaemia also associated strongly with symptomatic intracranial stenosis ≥50% (adjusted odds ratio [OR] 2.86, 95% confidence interval [CI] 1.44–5.67), but not with symptomatic extracranial stenosis ≥50% (adjusted OR 1.15, 95% CI 0.62–2.14). Despite appropriate secondary prevention treatment, the 90-day stroke risk was greater in patients with versus without atherogenic dyslipidaemia (4.8% vs 1.7%, p=0.04).

Conclusion: The atherogenic dyslipidaemia phenotype in patients with TIA may be associated with intracranial artery stenosis and higher risk of early recurrent stroke. Further data are needed to confirm these findings and to assess the best way to reduce the important residual risk in such patients.

Stroke prevention

1 Stroke prevention

POPULATION-BASED STUDY OF TEMPORAL TRENDS IN ATRIAL FIBRILLATION RELATED INCIDENT ISCHAEMIC STROKE: EVIDENCE OF SUBSTANTIAL FAILURE OF PRIMARY PREVENTION

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Background: Atrial fibrillation (AF) is a major cause of severe, disabling stroke, especially in the elderly. Although there have been no population-based studies of time-trends in AF-related incident stroke, greater awareness of the importance of stroke prevention in AF, greater screening, and the availability of warfarin for primary prevention over the past two decades should have reduced the incidence of AF-related ischaemic stroke despite the aging population.

Methods: We studied all AF-related incident ischaemic strokes (IIS) from 2002-2008 in the Oxford Vascular Study (OXVASC) and compared our findings with Results from a previous population-based study in the same population in 1981-1986 (Oxford Community Stroke Project; OCSP).

Results: AF-related stroke (AF prior, at presentation, or within 1-month) accounted for 29.7% (212/715) of incident ischaemic strokes in OXVASC (mean/SD age = 80.5/9.9) versus 17.1% (93/545) in OCSP (77.0/8.7 years): relative rate =1.53 (1.24-1.89, p<0.0001). After adjustment for ageing of the underlying study population between the studies the excess of AF-related stroke in OXVASC remained (RR=1.32, 1.02-1.71, p=0.03), due entirely to an excess of known prior AF (153/715, 21.4% vs 60/545, 11.0%; adjusted RR=1.42, 1.02-1.98, p=0.03), with no difference in new AF (8.4% vs 6.1%, adjusted RR=0.96, 0.62-1.33). Of the 153

OXVASC patients with incident ischaemic stroke and known prior AF, 102 had a premorbid CHADS2 score of ≥2, of whom only 16 (15.7%) had been on warfarin for primary prevention.

Conclusions: The incidence of ischaemic stroke in patients with known prior AF was significantly higher in 2002-2008 than in 1981-1986, even after adjusting for aging of the population, despite the availability of a highly effective preventive treatment. Substantial underuse of anticoagulation in primary prevention in eligible patients is a major barrier to effective stroke prevention in the face of an aging population with high rates of AF.

2 Stroke prevention

ANTICOAGULANT AND ANTIPLATELET THERAPY IN 20,442 PATIENTS WITH ISCHEMIC STROKE AND ATRIAL FIBRILLATION – RESULTS OF AN OBSERVATIONAL NATIONWIDE STUDY

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Background: Even though most stroke patients with atrial fibrillation are recommended anticoagulant (AC) therapy, underuse is common in clinical practice. Using comprehensive national registers, we investigated the prescription of AC therapy and its influence on long-term mortality.

Methods: We studied a prospective cohort of 20,442 patients with ischemic stroke and atrial fibrillation who where registered in the Swedish Stroke Register in 2001 to 2005. Data on bleeding events and mortality were retrieved by linkage to other national registers. A propensity score for the likelihood of AC therapy was calculated and long-term mortality was estimated in a Cox regression model.

Results: Only 31% (n=6,399) of the patients were prescribed AC therapy. After adjustment for the propensity score, AC therapy was associated with reduced risk of death (HR=0.67; 95% CI 0.63 to 0.71). This reduction in mortality was found in most subgroups (including e.g. old and disabled patients). In addition, the rate of non-hemorrhagic fatal stroke was lower in the AC group (16%) compared to the antiplatelet (AP) group (25%). Rates of fatal and non-fatal hemorrhages per 100 person-years did not differ significantly between the AC (3.03; 95% CI 2.74 to 3.35) and the AP group (3.49; 95% CI 3.25 to 3.75).

Conclusions: In patients with atrial fibrillation, AC therapy reduced post-stroke mortality without increasing the risk of bleeding. The Results confirm the superiority of AC over AP therapy, as well as the need to facilitate the provision of AC therapy in secondary stroke prevention to patients with atrial fibrillation.

3 Stroke prevention

USE OF ANTITHROMBOTIC DRUGS IN PATIENTS WITH ATRIAL FIBRILLATION AND MICROBLEEDS: A DECISION-ANALYSIS

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Background: Many patients with atrial fibrillation (AF) have a high risk of thromboembolic stroke, but the risk of intracerebral haemorrhage on antithrombotic treatment may be greater if cerebral microbleeds are present. We aimed to determine whether the current evidence on risks and benefits of antithrombotic drugs is sufficient to guide decision-making.

Methods: We used a Markov state transition model to compare starting anticoagulation or antiplatelet agents or withholding antithrombotic treatment in a hypothetical 70-year old man with AF and microbleeds over a 5 year period. We assumed that warfarin would stop after intracerebral haemorrhage (ICH), and that anticoagulation would replace antiplatelet agents or no treatment after a thrombo-embolic stroke but no preceding ICH. Risks of bleeding complications and ischaemic stroke in each treatment arm were based on estimates from the literature and our own population-based data – Oxford Vascular Study. Confidence intervals on outcome estimates were derived using probabilistic sensitivity analyses.

Results: Estimates of stroke-free survival at 5 years were similar in each treatment group: 75% (95%CI 74-77%) using antiplatelet agents, 75% (70-81%) using warfarin, and 74% (73-76%) on no antithrombotic agents. However, clinically plausible variations in the baseline risks of ischaemic stroke and ICH produced qualitatively different Results in sensitivity analyses.

Conclusion: Current evidence is insufficient to recommend any particular primary stroke prevention strategy in patients with microbleeds and AF. It is possible that anticoagulation may not be of net benefit in this group of patients, and randomized controlled trials comparing this with alternative primary prevention therapies may therefore be necessary.

4   Stroke prevention

ANTIPLATELET THERAPY VERSUS ANTICOAGULATION FOR CERVICAL ARTERY DISSECTION; RESULTS OF THE NON-RANDOMISED ARM OF THE CADISS TRIAL

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Background: There is an early risk of recurrent stroke after carotid and vertebral dissection. Patients are treated with both anticoagulation and antiplatelets, but there is no randomized data to inform which is superior. The CADISS trial is randomizing patients with acute dissection between the two treatments. It included a non-randomised arm, which has now completed. We present these Results for the first time, and include them in an updated meta-analysis with previously published data.
Methods: 95 patients from 19 centres in the UK were recruited into the non-randomized arm between 2006 and 2010. All patients were recruited within 1 month of dissection. The primary endpoint was recurrent stroke at 3 months, when follow up data was available in 93. 61 were treated with antiplatelet therapy and 32 with anticoagulation. For the meta-analysis, Medline, Pubmed and the Cochrane Library were searched from 1966 until current. Reference lists were reviewed.
Results: At 3 month follow up, 1 patient in each group had recurrent ischaemic stroke (antiplatelet 1/61 (1.6%), anticoagulation 1/32 (3.1%)). 2 (6.3%) anticoagulation patients had recurrent TIA, compared with no patients in the antiplatelet group. There were no deaths in either group. For meta-analysis, including the CADISS study, there was data from 39 non-randomised studies including 1633 patients. There was no significant difference in risk of recurrent stroke [antiplatelet 13/498 (2.6%), anticoagulant 20/1135 (1.8%), Odds ratio 1.49 (95% CI 0.74 to 3.03) p=0.78], or stroke and death [antiplatelet 17/498 (3.4%), anticoagulant 31/1135 (2.7%), Odds ratio 1.26 (95% CI 0.69-2.30) p=0.90].
Conclusion: The non-randomised CADISS data shows a low rate of recurrent stroke, and no difference between antiplatelet and anticoagulation arms. This finding is supported by the Results of an updated meta-analysis. However all data is from non-randomised studies, and in the CADISS non-randomised arm many patients were recruited outside the higher risk first week. Data from randomized studies is required; the randomized arm of CADISS is randomizing patients within 1 week of onset between antiplatelet and anticoagulation therapy.

5   Stroke prevention

CAROTID ULTRASOUND IS MODESTLY USEFUL IN THE INDIVIDUAL ASSESSMENT OF STROKE RISK – RESULTS FROM THE 10-YEAR FOLLOW-UP OF THE CAROTID ATHEROSCLEROSIS PROGRESSION STUDY (CAPS)

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Aims: To predict the risk of stroke for individuals, score systems like the Framingham Stroke Risk Score (FSRS) have been developed, including 'classical' risk factors. Aim of the present study was to assess whether carotid ultrasound improves the individual stroke risk prediction in the context of primary prevention.
Methods: The 10-year follow-up of the Carotid Atherosclerosis Progression Study included the assessment of stroke, transient ischemic attack (TIA) and death of 4995 subjects without previous stroke. At baseline, conventional risk factors and carotid intima media thickness (cIMT), plaque and stenoses had been assessed. With reclassification statistics, we estimated the usefulness of carotid ultrasound to improve the risk stratification beyond the FSRS.
Results: In 40495 person years, we observed 106 strokes (68 ischemic), 64 TIAs and 163 deaths. Carotid stenoses were observed too rarely for further analysis (1 stenosis≥70%, 2 stenoses≥50%). IMT or plaque of the internal carotis arteries (ICA-IMT) were more useful for individual stroke prediction than common or bifurcational IMT. When all ultrasound parameters were included at once, the Framingham stroke risk model predicting the endpoint "any stroke or death" was improved significantly. Using the risk categories of <5%, 5-10%, 10-20% and >20% in 10 years, 337 subjects (7.2%) were reclassified to another risk category by carotid ultrasound.

122 were shifted to a higher, 217 to a lower risk category. Of these, 182 (54.0%) were correctly reclassified. The net reclassification improvement (NRI) was 7.74% (p=0.029), the integrated discrimination improvement (IDI) was 0.725% (p=0.023).
Conclusion: If the carotid ultrasound is not restricted to the common carotid artery but covers the internal carotid segments, the inclusion of ultrasound data into stroke risk models modestly improves the risk classification of individuals. Carotid ultrasound may improve targeting drug therapy for primary prevention of stroke.

6   Stroke prevention

CAROTID WALL THICKNESS AND PROGRESSION OF STENO-OCCLUSIVE DISEASE

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Background: Carotid atherosclerosis is a risk factor for vascular disease. Our aim in this study was to evaluate the possibility to individuate early markers of carotid stenosis progression in asymptomatic subjects.
Methods: Participants were 301 consecutive subjects with asymptomatic internal carotid artery plaques. Demographic characteristics, vascular risk factors, therapy, degree of carotid stenosis, surface and morphologic characteristics of plaque and carotid intima-media thickness (IMT) were detailed for all subjects. Subjects were prospectively evaluated for a 12-month period to assess the possible progression of stenosis.
Results: An increase of stenosis was detected in 90 subjects. Older age, diabetes, hypertension, surface irregularity and ulceration of plaques and carotid IMT were associated with an increased probability of carotid plaque growth. Age-stratified analyses showed that the association between high basal IMT values and plaque growth was stronger among subjects aged ≤ 65years (p=0.03). The use of antiplatelet drugs showed a significant protective effect against carotid stenosis progression (p=0.03).
Conclusions: Our data suggest that an integration of indicators of atherosclerosis evolution could provide further information in improving risk prediction. In this respect IMT could be an additional marker of risk, particularly in middle age patients, to better estimate the cerebrovascular risk profile and to plan a comprehensive prevention strategy.

7   Stroke prevention

EFFECTS OF TERUTROBAN ON PROGRESSION OF ATHEROSCLEROSIS: RESULTS OF THE PERFORM VASCULAR PROJECT

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Background: The PERFORM Vascular Project evaluated the effects of terutroban (30 mg o.d.) versus aspirin (100 mg o.d.) on progression of atherosclerosis, as assessed by change in ultrasonic carotid intima-media thickness (CIMT) in a subgroup of patients with a history of ischemic stroke or transient ischemic attack.
Methods: Patients from the PERFORM study were included in the vascular project - men and women participating in the main study were recruited, aged between 55 and 80 years, with validated baseline (M0) vascular evaluation. The primary endpoint was the annualized rate of change of the mean common CIMT. Secondary end points included the number of emergent carotid plaques in both carotid systems and the change in carotid stiffness from baseline to final visits. 1,100 patients had to be included in order to detect with a 90% statistical power treatment-related effect (CIMT difference of 0.025 mm). Analysis on the primary endpoint was performed using a linear mixed-effects model adjusted for baseline value on the full analysis set.
Results: A total of 1,141 patients were randomised from 52 centres in 16 countries. The mean follow-up was 28 months. At baseline the mean value of the CIMT was 0.87±0.16 mm, the mean number of plaques was 3.9±2.2 and the mean values of the carotid stiffness was 8.2±1.6 m/s. There was no difference between treatment groups for the mean rate of CIMT change per year: 0.011 (95% CI [-0.003;0.025])

nor did the rate of emergent plaques differ 0.91 (95% CI [0.77;1.07]) or the mean change in carotid stiffness 0.051 (95% CI [-0.143;0.244]).
Conclusion: In the PERFORM Vascular study, there was no evidence for a difference between terutroban and aspirin for any of the primary or secondary endpoints.

8 Stroke prevention

LONG TERM EVOLUTION OF CEREBRAL ATHEROTHROMBOTIC PROCESSES: PERFORM MAGNETIC RESONANCE IMAGING PROJECT

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Background: The aim of PERFORM Magnetic Resonance Imaging (MRI) Project, an ancillary study of the PERFORM trial was to investigate the potential effects of terutroban in comparison to aspirin on the evolution of MRI lesions in patients with atherothrombotic disorders after a ischemic stroke or transient ischemic attack.
Methods: Patients from the PERFORM study were included in the MRI project if they were men or women participating in the main study, aged between 55 and 80 years without MRI contraindication. The endpoints were: change in the total brain volume, hippocampal volume and in white matter lesions (combining hypointense and hyperintense lesions on the FLAIR sequence) from baseline (M1) to the final visit (M24) and were assessed globally and separately in the hemisphere ipsilateral and contralateral to the ischemic event. Safety criteria included the number of emergent microbleeds. Covariance analysis models were performed to estimate the treatment effect on the full analysis set.
Results: 1,056 patients were randomised. The mean follow-up was 28 months. At baseline total brain mean volume was 106.3 ± 12.42 cm^3, mean total hippocampal volume was 7.7 ± 1.1 cm^3 and mean values of FLAIR lesions in total brain was 6.1 ± 21.1 cm^3.
Between M24 and M1 the change in total brain volume was -4.8 ± 3.9 cm^3 (terutroban) versus -4.5 ± 4.0 cm^3 (aspirin) with no difference between treatment groups (- 205 (95% CI [-765; 353] p: 0.47). The change in total hippocampal volume was:-308±288 mm^3 (terutroban) versus -316±275 mm^3 (aspirin) with no difference between treatment group (7 (95% CI [-32; 47]; p: 0.71) as for the change in FLAIR lesions (total brain): (794±5263 mm^3, 975±7875 mm^3 for terutroban and aspirin respectively).The number of emergent microbleeds was 0.4 ± 1.1 (terutroban) and 0.2 ± 0.9 (aspirin), and difference was not significant.
Conclusion: PERFORM MRI study provides a large data base of brain changes after initial index. There was no evidence for a difference between terutroban and aspirin for any of the efficacy nor safety endpoints.

9 Stroke prevention

RANDOMISED COMPARISON OF BLOOD PRESSURE AFTER CAROTID ENDARTERECTOMY OR STENTING: RESULTS FROM THE INTERNATIONAL CAROTID STENTING STUDY (ICSS)

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Background: ICSS (ISRCTN25337470) is a randomised trial comparing carotid stenting (CAS) to endarterectomy (CEA) for patients with symptomatic carotid artery stenosis. Arterial hypotension is a frequent complication after CAS, but has been reported after CEA. We aimed to compare both early and long-term effects of CAS and CEA on blood pressure (BP).
Methods: Systolic and diastolic BP (SBP, DBP) were recorded in patients randomised in ICSS at baseline, at discharge after treatment, and at 1, 6, and 12 months. The use of any antihypertensive drug during follow-up was recorded. Patients with missing data were excluded. Analysis was on the basis of type of carotid intervention received. Within groups, changes in BP over time were compared with the paired t-test. The changes in BP were compared between the two groups and adjusted for baseline covariates with linear regression.
Results: 597 (CAS) and 644 (CEA) patients had sufficient data for analysis. Compared with baseline, BP was significantly lower at discharge in both groups, but the decrease was significantly greater after CAS than after CEA (mean

difference between groups in SBP, 10.5 mmHg; 95% confidence interval (CI),7.5 to 13.5; mean difference in DBP, 4.2 mmHg; 95% CI, 2.5 to 5.8). In both groups, SBP at 6 months was lower than at baseline; this persisted up to 12 months in patients after CEA (mean difference SBP within CEA, 4.4 mmHg; 95% CI: 2.2 to 6.4). No other changes in BP during long-term follow-up were observed. After discharge, there were no differences in BP changes between the groups. However, fewer CAS patients used antihypertensive medication during follow-up than CEA patients (relative risk at 12 months, 0.91; 95% CI, 0.85 to 0.97). Adjustment for determinants of BP did not affect our Results.
Conclusion: CAS leads to a larger early decrease in BP than CEA, but this effect does not persist after discharge from treatment. CAS has no advantages over CEA in terms of BP lowering, although drug use was less.

10 Stroke prevention

KNOW YOUR NUMBERS; CHECKING YOUR BLOOD PRESSURE IS EASY, LIVING WITH A STROKE ISN'T

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Background: The lack of awareness, detection and control of blood pressure (BP) remains a significant problem and is the most important modifiable risk factor for stroke. Since 2007, the National Stroke Foundation has undertaken a community-based awareness program for BP and other stroke risk factors called "Know your numbers (KYN)". Our objectives were to: a) determine whether individuals who were advised to see their GP following participation in KYN actually sought treatment; b) assess retention of participants' knowledge on risk factors and stroke; and c) engaged in behaviour change to modify risk.
Methods: Partner organisations volunteered to provide a "free" BP check and standardised educational resources via community "Pressure Stations". Evaluation Methods included: registration log and surveys of a "1 in 10" registrant sample at baseline and 3-month follow up.
Results: Between 2007-10 KYN captured 62, 558 registrants (62% female, 55% aged >55 years); 43% had BP ≥ 140/90 mmHg. Of those with high readings 32% reported they had not previously been told they had high BP; 55% were advised to see a doctor. Among the 909 who consented for 3 month follow-up, 64% returned surveys. Since KYN, 75% had rechecked their BP. Improved knowledge regarding high BP as risk factor for stroke and heart disease and lack of exercise as a cause of high BP were found. All 3-month respondents reported at least one action to change their risk.
Conclusion: The Australian KYN program is an effective and feasible community awareness program. It has provided an opportunity for people to have their BP measured, understand their readings and learn about stroke risk. KYN is a successful model for encouraging people with opportunistically high BP to be reviewed by their doctor and modify their cardiovascular risk.

11 Stroke prevention

BETA-1-SELECTIVITY OF BETA-BLOCKERS INFLUENCES EFFECTS ON BLOOD PRESSURE VARIABILITY AND RISK OF STROKE: A SYSTEMATIC REVIEW

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Background: Beta-blockers increase variability in systolic blood pressure (SBP), which probably explains their lesser effectiveness in preventing stroke versus myocardial infarction compared with other agents. This increase in variability in BP may be particularly marked on non-cardioselective agents, potentially calling into question the widespread first-line use of propranolol in migraine with aura, elderly patients with essential tremor or anxiety, and other groups at risk of stroke.
Methods: We determined beta-blocker subclass effects on variability in BP and stroke risk in a systematic review of randomised controlled trials (RCTs) comparing different types of beta-blocker with placebo or other agents. We determined pooled estimates of the effect of treatment on group variability in BP (ratio of the variances -VR) and on the risk of stroke versus myocardial infarction during follow-up.
Results: Compared with other antihypertensives, variability in SBP was increased more by non-selective beta-blockers (VR=1.34, 1.13-1.59, p=0.002, 25 comparisons, 9992 patients) than by beta-1-selective agents (VR=1.09, 95%CI 1.00-1.19, p=0.053, 68 comparisons, 40746 patients; difference-p=0.038). In direct comparisons, variability in SBP was also significantly lower with beta-1-selective versus non-selective beta-blockers (VR=0.81, 0.68-0.97, p=0.03, 18 comparisons,

954 patients). In comparisons with other antihypertensives, the increase in stroke risk with non-selective beta-blockers (OR=2.29, 1.32-3.96, p=0.002) was more marked than with beta-1-selective agents (OR=1.24, 1.08-1.42, p=0.003, difference-p=0.03), as was the risk of stroke relative to the risk of myocardial infarction: OR=1.50 (0.93-2.42) vs 0.99 (0.82-1.19).

Conclusions: Use of beta-1-selective rather than non-selective agents is advisable when beta-blockers are indicated for patients at risk of stroke.

12 Stroke prevention

SHUNT VOLUME DYNAMICS IN STROKE PATIENTS WITH PATENT FORAMEN OVALE

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Background: In patients with patent foramen ovale (PFO) there is evidence supporting the hypothesis of a change in right-to-left shunt (RLS) over time. Proven, this could have implications for the care of patients with PFO and a history of stroke. The following study addressed this hypothesis in a cohort of patients with stroke and PFO.

Methods: The RLS volume assessed during hospitalisation for stroke (index event/ T0) was compared with the RLS volume on follow-up (T1). In 102 patients with a history of stroke and PFO the RLS volume was re-assessed on follow-up using contrast-enhanced transcranial Doppler/duplex (ce-TCD) ultrasound. A change in RLS volume was defined as a difference of ≥20 microembolic signals (MES) or no evidence of RLS during ce-TCD ultrasound on follow-up. In case of shunt dynamics, the shunt volume was assessed while physical activity. In a complex cardiopulmonary monitoring setting the shunt volume was re-assessed in a phase of maximal physical activity. The study was approved by a local ethical committee.

Results: There was evidence of a marked reduction in RLS volume in 31/102 patients (T1 to T0 median 10 months); in 14/31 patients a PFO was no longer detectable. An index event classified as cryptogenic stroke (P<0.001; OD = 39.2, 95% confidence interval 6.0 to 258.2) and the time interval to the follow-up visit (P=0.03) were independently associated with a change in RLS volume over time. In 4 patients with an shunt reduction from curtain pattern to no further evidence for RLS on follow-up the shunt volume was re-assessed while maximal physical activity. In all 4 patients the RLS was thereby again evident; in 2 patients even a curtain pattern could be detected. All patients showed an increase of right atrial pressure.

Conclusions: RLS volume across a PFO decreases over time, especially in patients with cryptogenic stroke. Physical activity could facilitate a re-opening of a functional closed PFO.

Acute stroke: clinical patterns and practice A

1 Acute stroke: clinical patterns and practice A

FIELD NEUROPROTECTIVE THERAPY FOLLOWED BY ENDOVASCULAR RECANALIZATION TREATMENTS IN A PHASE 3 CLINICAL TRIAL

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Background: A promising treatment strategy for acute cerebral ischemia is neuroprotective therapy in the field to stabilize the penumbra, followed by intravenous and/or endovascular recanalization therapy to restore blood flow and rescue threatened tissue.

Objective: To characterize rates of utilization of endovascular recanalizatoin therapies (ERT) in ischemic stroke patients enrolled in a prehospital study.

Methods: FAST-MAG study is the first phase 3 RCT testing field initiation of neuroprotective therapy with magnesium sulfate vs. placebo initiated within 2 hours of last known well time. Enrollees are permitted to undergo FDA or national guideline approved recanalization therapies upon hospital arrival when clinically indicated.

Results: Among the first 1091 subjects enrolled in FAST-MAG there were 243 (24%) with intracerebral hemorrhage (ICH). Amongthe non-ICH cases, severe initial deficits in the ED (NIHSS ≥ 8) were present in 365. A total of 16 subjects received

endovascular recanalization therapy. Among these patients, mean age was 68 (SD 15), 50% were male, median prehospital LAMS motor deficit score was 5 (IQR 5-5), and median emergency department NIHSS of 18 (IQR 11-23). Prehospital neuroprotective study agent infusion was initiated a median of 46 minutes (IQR 40-55) after symptom onset. A total of 16 subjects received ERT, 8 in combination with intravenous (IV) tissue plasminogen activator (TPA), 2 in combination with intra-arterial (IA) TPA. Rate of interventional therapy utilization in 766 cases non-ICH cases was 2%, and in 365 with moderate-severe strokes was 4%. ERT in non-ICH cases presented with more severe stroke (NIHSS 18 vs. 9, p<0.0001).

Conclusions: The rate of endovascular recanalization therapy in FAST-MAG exceeds that in US administrative datasets (0.25%) and the trial will accrue sufficient patients for exploratory analyses of safety and benefit of field neuroprotection followed by endovascular rescue.

2 Acute stroke: clinical patterns and practice A

POPULATION-BASED STUDY OF ACUTE PHASE BLOOD PRESSURE IN RELATION TO PATHOLOGICAL SUBTYPE, SEVERITY AND AETIOLOGY OF TIA AND STROKE

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Background: It is uncertain whether high blood pressure (BP) after acute stroke is a specific response to cerebral injury, a non-specific response to stress, or even the remnant of a premorbid increase in BP.

Methods: We collected all acute phase post-event BP readings in a population based study (Oxford Vascular Study) of all patients with an acute stroke or TIA and related these to the most recent pre-morbid BP, clinical subtype, aetiology, vascular territory, and prior antihypertensive medication.

Results: Acute-phase BP and 17,474 premorbid BP readings were available from 1002/1024 (98%) consecutive eligible patients. Mean first acute-phase SBP was substantially higher after intracerebral haemorrhage than after ischaemic stroke, both in absolute terms (192.7 vs 160.2 mmHg, p<0.0001, in patients assessed within 3-hours) and in relation to the most recent premorbid reading (+43.1 vs +17.6 mmHg, p<0.0001). Mean first acute-phase SBP was no higher after cerebral versus ocular ischaemic events, and was inversely related to the severity of cerebral ischaemic events (165.1mmHg after TIA and minor ischaemic stroke vs 156.7mmHg after major stroke; p=0.015). Even after excluding patients assessed more than 3-hours after onset, the acute post-event SBP in patients with major ischaemic stroke was only 12.9mmHg higher on average than the most recent pre-morbid reading. Moreover, the first SBP in the acute phase only exceeded the maximum pre-morbid reading in 26.4% (23.7-29.2).

Conclusions: In contrast to intracerebral haemorrhage, acute-phase SBP in patients with ischaemic stroke was only moderately raised compared with premorbid levels, was similar after ocular and cerebral ischaemia, and was inversely related to severity of events, suggesting that cerebral ischaemia itself is not a major driver of acute phase SBP.

3 Acute stroke: clinical patterns and practice A

ELEVATED PREHOSPITAL BLOOD PRESSURE PREDICTS FURTHER WORSENING BEFORE HOSPITAL ARRIVAL IN INTRACEREBRAL HEMORRHAGE BUT NOT ISCHEMIC STROKE PATIENTS

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Background: Studies of BP and stroke progression have focused on the acute period, 2-24h after onset. Prehospital clinical trials have opened a potential new treatment window in the ultra-acute period 0-120 minutes after onset. The impact of BP on clinical course in the ultra-acute period has not previously been investigated.

Methods: FAST-MAG is a phase 3 clinical trial of prehospital magnesium sulfate vs. placebo initiated <2 hours from symptom onset. Data on first BP and Glasgow Coma Scale (GCS) obtained by paramedics in the field and GCS on arrival to the Emergency Department (ED) by study coordinators was collected. Early clinical deterioration (ECD) was defined as ≥ 2 point worsening on GCS from field to ED.

Results: Among 897 subjects enrolled 1/05 to 12/09, mean age was 70 (SD13), 42% were female, BP was measured in the field a median of 22 minutes (IQR 14 –40) after symptom onset. Initial imaging showed intracerebral hemorrhage (ICH) in 209 cases (23.4%). Field BP was higher among ICH than cerebral ischemia (CI) patients, SBP

176 (SD 25) vs. 156 (SD 28), p<0.001, DBP 100 (SD 18) vs. 87 (SD 17), p<0.0001. Initial GCS was slightly higher in ICH vs. CI patients, median 15 (IQR 15-15) vs 15 (IQR 14-15), p=0.018. ECD occurred more often among ICH than CI patients, 29% vs 6%, p<0.0001. Among ICH patients field SBP was higher in those who experienced ECD: SBP 182 vs. 173, p=0.022; DBP 102 vs. 99, p=0.211. Frequency of ECD in ICH increased with quartile SBP: 1st 20%, 2nd 27%, 3rd 28%, 4th 38%, p=0.045. The odds ratio for ECD was increased in each quartile relative to the 1st: OR 1.5 (95%CI 0.58, 3.7) for 2nd, 1.6 (0.63, 3.9) for 3rd, OR 2.5 (1.02, 6.09) for 4th. Among the CI patients, BP was not higher in those with ECD: SBP 158 vs. 156, DBP 87 vs. 86.

Conclusions: Elevated BP at time of first paramedic encounter is associated with ECD among ICH patients. Field initiation of BP moderating agents in likely ICH patients is a potential strategy to avert early deterioration.

4 Acute stroke: clinical patterns and practice A

RELATIONSHIP BETWEEN BLOOD PRESSURE VARIABILITY AND PROGNOSIS IN ACUTE ISCHEMIC STROKE PATIENTS WITH VASCULAR COMPRESSION ON THE ROSTRAL VENTROLATERAL MEDULLA (RVLM)

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Background: The rostral ventrolateral medulla (RVLM) has been investigated to play a pivotal role in cardiac and vasomotor regulation. One of the pathogenesis of hypertension is a vascular compression on the RVLM. However, it remains unclear whether RVLM vascular compression causes the significant variability in blood pressure observed during acute ischemic stroke. The purpose of this study is to evaluate differences in blood pressure variability and prognosis in acute ischemic stroke patients either with or without vascular compression on the RVLM.

Methods: We examined patients with acute ischemic stroke within 24 h of onset. Patients who received thrombolysis were excluded. Blood pressure was measured every 6 h for 72 h after admission and evaluated with successive variation (SV). The presence of RVLM vascular compression was evaluated using time-of-flight 3D MRI. Neurological impairment was evaluated using the National Institutes of Health Stroke Scale (NIHSS) at admission and 14 days after admission, and clinical improvement was determined by taking the difference in the NIHSS scores (decreased more than 4 points or recovered to 0) between at admission and at 14 days.

Results: We evaluated 56 patients (16 female; mean age 72.8±9.4 years). Vascular compression of the RVLM was identified in 15 patients (26.8%). The prevalence of hypertension was significantly higher in the compression group than the non-compression group (93.3% vs. 61.0%, P = 0.02). The SV value of the systolic blood pressure was significantly higher in the compression group (P < 0.0001). The proportion of patients showing clinical improvement was significantly lower in the compression group [odds ratio, 0.21 (95% CI = 0.06-0.78); P = 0.01].

Conclusion: The patients with RVLM vascular compression had shown a greater variability in blood pressure during the acute phase of ischemic stroke. Increased variability in blood pressure may lead to worse prognosis.

5 Acute stroke: clinical patterns and practice A

DOES THE IMPACT OF BLOOD PRESSURE VARIABILITY ON EARLY NEUROLOGICAL DETERIORATION AFTER ISCHEMIC STROKE DIFFER BY THE PRESENCE OF SYMPTOMATIC STENO-OCCLUSION?

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Background: Early neurological deterioration (END) after ischemic stroke is associated with poor stroke outcome and is more frequent in patients with symptomatic steno-occlusion (SYSO). However the pathophysiologic mechanisms involved in END are not well known, blood pressure (BP) and hemodynamic status may associated with END especially in patients with SYSO.

Methods: From a prospective stroke registry, a consecutive series of patients with acute ischemic stroke, who were hospitalized within 24 hours from onset between July 2007 and September 2010, were identified. BP during the first 72 hours and clinical information were obtained from the stroke registry and by reviewing electronic medical records. Differences of maximum and minimum (max-min), standard deviations (sd) and coefficients of variation (SBPcv and DBPcv) were selected as BP variability parameters. SYSO was defined as stenosis more than 50% or occlusion of cerebral arteries relevant to symptomatic ischemic lesions on diffusion-weighted MRI. END was defined as an increase of ≥2 points in the total NIHSS score, an increase of ≥1 point in the level of consciousness or motor items of NIHSS score, or any new neurologic deficits during the first 72 hours.

Results: Among 1052 (age, 67.7±13.2 years; male, 59.3%) patients, 548 (52.1%) had SYSO and 226 (21.5%) had END. END was more frequent in patients with SYSO (27.6% vs. 14.9%, p<0.001). SBPmax-min, SBPsd, SBPcv, DBPmax-min, DBPsd, and DBPcv were higher in patients with END than those without END. With adjustments for potential confounders, 1-SD increase of all BP variability parameters was significantly associated with increased odds of END (p's<0.01). Statistical significance of the association was left in patients with SYSO only after stratification by the presence of SYSO (p's<0.01).

Conclusion: BP variability is associated with END particularly in patients with SYSO.

6 Acute stroke: clinical patterns and practice A

ADMISSION HYPERGLYCEMIA AND PERFUSION DEFICITS IN ACUTE ISCHEMIC STROKE

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Introduction: Hyperglycemia (HG) after ischemic stroke is associated with larger infarct size and worse outcome. The underlying pathophysiology is unclear. We aimed to determine if patients with acute ischemic stroke and HG have larger perfusion deficits (ischemic penumbra and infarct core) or infarct cores on admission perfusion CT than normoglycemic (NG) patients.

Methods: In a prospectively established cohort (Jan 07-Jun 08) we identified 98 consecutive patients (mean age 64±14 years, 60% men) with acute supratentorial non-lacunar ischemic stroke who underwent a non-contrast CT and perfusion CT on admission. Clinical outcome (modified Rankin Score, good outcome mRS ≤ 2) was recorded after 6 months. The perfusion deficit area (mean transit time (MTT) >145% of the contralateral side values) and the infarct core area (MTT >145% and cerebral blood volume < 2 mL/100g) were measured at the caudate nucleus and the corona radiata level (ASPECTS level 1 and 2). Perfusion values were compared between patients with HG (admission glucose ≥ 7mmol/L) and NG with a MANOVA.

Results: Admission HG was present in 40 of the 98 patients (41%). A perfusion deficit was present in 82 (40% HG) patients at ASPECTS 1 and 77 (43% HG) at ASPECTS 2. The total area with a perfusion deficit (ASPECTS 1 HG 21.8 cm^2 ±11.2 and NG 22.5 cm^2 ±12.7; ASPECTS 2 HG 26.6 cm^2 ±12.5 and NG 25.0 cm^2 ±12.2) did not differ between the groups (MANOVA, p=0.2). The proportion ischemic core (ASPECTS 1 HG 30% ±30 and NG 26% ±23; ASPECTS 2 HG 33% ±27 and NG 25% ±23) was slightly, but not significantly, larger (p= 0.06) in the HG group. HG was associated with worse outcome at 6 months OR 2.9 (95% CI 0.8 – 10.4).

Conclusions: Patients with HG did not have larger perfusion deficits and only slightly larger infarct cores on admission. Worse outcome and larger final infarct size are therefore mainly due to reduced penumbral salvage. This offers a window of opportunity for glucose lowering therapy in HG patients.

7 Acute stroke: clinical patterns and practice A

HIGHER BASELINE TEMPERATURE IS ASSOCIATED WITH FAVORABLE CLINICAL RESPONSE, BUT EARLY INCREASE IN BODY TEMPERATURE PREDICTS POORER OUTCOME IN I.V. THROMBOLYSED ACUTE ISCHEMIC STROKE PATIENTS

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Background: Body temperature, inflammation, and infections may modify response to thrombolytic therapy. We studied the associations of body temperature and infection parameters recorded within 24 hours from symptom onset on clinical response to i.v. thrombolysis and 3-month outcome.

Methods: We included 985 consecutive patients with acute ischemic hemispheric stroke treated with i.v. thrombolysis in the Helsinki University Hospital during

1998-2008. Body temperature values on arrival, at 24 hours, and at 48 hours were recorded. Blood leukocyte count and C-reactive protein (CRP) levels were analyzed on arrival and at day 1. Favorable clinical response to thrombolysis was defined as National Institutes of Health Stroke Scale (NIHSS) score decrease of ≥4 points between 24 hours and baseline or a NIHSS score of 0 at 24 hours. Functional outcome was assessed at 3 months with modified Rankin Scale dichotomized at 0 to 2 (good) vs. 3 to 6 (poor). Associations between the study parameters were tested using multivariable logistic regression analysis.

Results: Of the baseline variables, higher leukocyte count (OR 1.10 per E9/L; 95% CI 1.03-1.17; p<0.01) and CRP (OR 1.01 per mg/L; CI 1.00-1.03; p=0.02), and less significantly lower temperature (OR 0.78 per °C; CI 0.58-1.06; p=0.10) were associated with poor outcome. Higher baseline temperature (OR 1.40; CI 1.06-1.87; p=0.02) and lower CRP (OR 0.99; CI 0.98-1.00; p=0.04) independently predicted favorable clinical response. Increasing body temperature over the first 24 hours was strongly associated with lack of favorable clinical response (OR 0.49; CI 0.37-0.65; p<0.001) and poor outcome (OR 1.63; CI 1.24-2.14; p<0.001).

Conclusion: Both baseline and 24-hour body temperature, leukocyte and CRP values were associated with clinical response to thrombolysis and outcome.

8 Acute stroke: clinical patterns and practice A

CHANGES IN CLINICAL SCORES FOLLOWING ACUTE ISCHEMIC STROKE DEPEND UPON LESION ANATOMY: A VOXEL-LESION SYMPTOM MAPPING ANALYSIS

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Introduction: Recent studies have shown that clinical scores e.g. NIHSS at a single time-point after stroke are dependent upon lesion site as well as size. In this study we investigated those stroke locations which significantly influence changes in clinical score – i.e. recovery rates, after correcting for lesion size.

Methods: We obtained retrospective clinical and acute-MRI data from 150 ischemic acute stroke patients cared for in our stroke unit. Clinical scores (National Institute of Health Stroke Scale (NIHSS) and Modified Rankin Scores (mRS)) were obtained from the clinical records at admission and discharge from the stroke unit, and a percentage-recovery rate calculated as: 100 x (Admission Score – Discharge Score)/(Admission Score x No. of Days). Acute lesions were delineated from DWI-MRI scans using a semi-automated algorithm, and subsequently co-registered and normalized into canonical space (Montreal Neurological Institute coordinates) within SPM8. Multiple linear regression was performed at every voxel with a minimum of 5 lesions, whereby lesion presence or absence, lesion size and age, acted as predictors of recovery rate. False-discovery rate correction for multiple comparisons was applied.

Results: Recovery rates were poorly predicted by lesion size alone. NIHSS recovery rates were significantly influenced by lesions in left corona radiata/operculum (higher than average), and medulla (lower than average). Right hemisphere lesions tended to be associated with a lower rate of recovery than left hemisphere lesions.

Conclusion: Recovery from stroke, as measured by standard clinical scales, depends upon lesion location. These Results may inform biological models of stroke recovery; assist in forming prognoses, and therapy planning; and can act as covariates in future stroke-therapy trials by accounting for some heterogeneity in stroke recovery.

9 Acute stroke: clinical patterns and practice A

ICF CORE SETS FOR STROKE – A PROFILE ANALYSIS OF STROKE PATIENTS DISCHARGED FROM HOSPITAL

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After being discharged from hospital, 60% of stroke patients become institution-alised (Beine and Coster, 2003). It imposes a negative impact on overall health costs (Patel et al., 2004). Laurence et al. (1982) confirmed that there are not standard criteria on discharging patients from hospital to home or to an institution (Hyde et al., 2001).

The Brief ICF Core Set identifies the fundamental aspects of stroke-related functioning (Geyh et al., 2006). It produces a functioning profile that could be a reference for follow-up on stroke patients (Lemberg et al., 2010).

The aim of this study is to characterise the sub-acute stroke patients on discharge using the Brief ICF Core Set for stroke and analyse its potential on discharge planning.

There were recruited 31 stroke patients admitted on Convalescence Unit (Anadia Hospital). It was filled in the Brief ICF Core Set for stroke on discharge. Results

were analysed according to ICF categories: body functions (BF), body structures (BS), environmental factors (EF) and activities and participation (AP) in three different groups of patients: Long-Care Group (LC), institutionalized patients; Home Assistance Group (HA), patients in need of home daily health assistance; Home Group (H), patients who go home with no daily health assistance. Descriptive statistical analysis was used to characterize the different profiles of each group (x ± SD), for each ICF category.

BF presented for LC, HA and H Groups respectively: 2,33±1,45; 1,17±1,10; 0,88±1,04. BS presented: 3,00±1,15; 1,75±0,91; 1,97±1,09. EF presented: 1,80±1,32; 1,57±0,68; 1,42±1,01. AP presented: 2,94±1,08; 1,44±1,14; 1,66±1,26 BF and EF categories might be capable of describing profiles on stroke patients at discharge, since the more independent groups presented lower average values. Further research is needed to prove the clinical potential of Brief ICF Core Set for stroke on helping health professionals on discharge decision-making.

10 Acute stroke: clinical patterns and practice A

BLOOD PRESSURE AND BLOOD GLUCOSE RESPONSE TO POSSIBLE REPERFUSION AFTER ACUTE ISCHAEMIC STROKE: EVIDENCE FROM THE VIRTUAL INTERNATIONAL STROKE TRIALS ARCHIVE (VISTA)

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Background: Elevations in blood pressure (BP) and blood glucose (BG) are common after stroke and are associated with poorer outcomes, though may simply represent a stress response reflecting severity and thus settle more rapidly with alteplase treatment. BP falls after recanalisation, but changes after iv alteplase are uncertain. No response of BG to alteplase has yet been described.

Methods: We compared BP and BG at 24 hours to baseline values in patients from VISTA, according to their exposure to alteplase as standard care, and early neurological change. We used Student's t-test for BP and for log transformed BG contrasts; we used linear regression to assess predictors of BP or BG responses.

Results: Despite a lower starting value, BP fell more in the alteplase patients than controls: Systolic BP fell by 10.9 (95%CI 9.9-12.0, n=2229) mmHg from 155 (154-156) to 144 (143-145) after alteplase versus 8.3 (7.4-9.2, n=3173) from 157 (156-158) to 148 (148-149) in controls, p<0.001. The fall was greater among patients who showed NIHSS improvement at 24h versus others (p=0.02). Diastolic BP fell by 7.3 (6.6-8.0) mmHg from 82 (82-83) after alteplase versus 5.8 (5.2-6.4) mmHg from 85 (84-85) in controls, p<0.001. Alteplase patients were younger with higher NIHSS (68 v 70y, 13 v 11 points); 70% v 76% had hypertension. However, multivariate analysis confirmed that alteplase predicted greater falls and lower final BP (all p<0.001).

Despite lower starting BG, 7.0 mM (6.9-7.1, n=1602) versus 7.3 (7.2-7.4, n=2686) p= 0.001, 24h fall in BG was greater in alteplase patients than controls. Ratios of 24h to baseline BG were 0.96 (0.94-0.97) versus 0.98 (0.97-0.99), p=0.02. In multivariate analysis alteplase treatment predicted greater BG falls (p=0.005) and lower 24h BG (p=0.003).

Conclusion: We provide new evidence that BG – and confirm that BP – each fall after thrombolysis, though both effects are small. A stress response reflecting stroke severity likely contributes to BP and BG elevations.

11 Acute stroke: clinical patterns and practice A

DOES EMR (ELECTRONIC MEDICAL RECORD) BASED REAL-TIME MONITORING SYSTEM IMPROVE QUALITY OF ACUTE STROKE CARE?

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Background: Accurate monitoring of quality of care will become crucial. Recently we developed the Electronic Medical Records (EMR) based Quality MeAsurement of Stroke care System (EQMASS) and applied it to daily practice. This study aimed to investigate whether there is a continuing trend of quality improvement over time with its application.

Methods: A total of 12 quality indicators and the corresponding performance measures were selected. Capturing the performance of the quality indicators in

each patient was integrated into our institution's EMR system and automatized. The performance measures were calculated at the point of discharge and reported automatically. Data of patients with acute ischemic stroke and transient ischemic attack, who were hospitalized within 7 days of onset, were collected. Significance for trend was determined using logistic or linear regression model with each indicator and global performance and time as the independent variable.

Results: Consecutive series of 997 patients were enrolled. The mean age was 66.5±13.2 years and 577 (57.9%) were male. The median NIHSS was 4 (IQR, 1 to 8). The patients who received thrombolysis were 129 (12.94%). Global performance and most of performance measures were improving over time of 18 months with statistical significance (P<0.01);neurologic examination, dysphagia screening, early antithrombotics, discharge antithrombotics, discharge anticoagulants with atrial fibrillation, lipid profile, discharge antihyperlipidemic agent, smoking cessation, considering rehabilitation. Indicators about brain imaging within 24 hours from arrival and administration of intravenous rt-PA, showed steady performance (≥90%) through study period and failed to show significant improvement.

Conclusions: Our study shows that the Introduction of EMR based real-time quality monitoring system into practice is feasible and may bring the continuing improvement in quality of stroke care with some saturation effects.

12 Acute stroke: clinical patterns and practice A

PHYSICIANS DELAY THROMBOLYSIS IF THERE IS MORE TIME TO THE END OF THE THROMBOLYTIC WINDOW

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Background: The earlier that thrombolysis is initiated, the greater the benefits of the treatment. We assess the hypothesis that the initiation of thrombolytic treatment is delayed if physicians have more time before the end of the thrombolytic time window.

Methods: Prospectively collected data from the SITS-EAST register on all patients treated with thrombolysis between Jan/2004 and Feb/2010 in 9 Central and Eastern European countries were analyzed. Patients were stratified according to the onset-to-door time into 6 groups (0-30, 31-60, 61-90, 91-120, 121-150, and >150minutes). Inter-group differences were assessed with Kruskal-Wallis test and Chi-square tests.

Results: Altogether, 5563 patients were treated with thrombolysis within 4.5 hours of symptom onset. The number of patients arriving at 0-30, 31-60, 61-90, 91-120, 121-150, and >150 minutes after symptom onset was 514 (9.7%), 1835 (34.6%), 1436 (27.1%), 861 (16.2%), 384 (7.2%), and 277 (5.2%), respectively. Patients arriving later after symptom onset had significantly lower NIHSS and also more frequently presence of old infarction on baseline CT/MRI. Other baseline parameters did not differ. Median door-to-needle time was 90, 80, 74, 60, 46, and 50 minutes (p< 0.001) in patients arriving at 0-30, 31-60, 61-90, 91-120, 121-150, and >150 minutes after symptom onset. Independently from other baseline variables, door-to-needle time was significantly (p< 0.001) associated with onset-to-door time ≤ 60 minutes in multiple logistic regression analysis.

Median of door-to-needle time and onset-to-treatment time by onset-to-door time
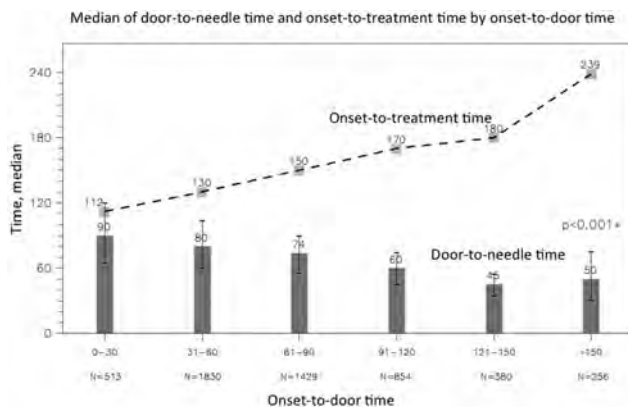
Conclusions: The benefit of thrombolysis is diminished for patients arriving early after symptom onset to hospital because physicians delay the treatment. It is necessary to improve adherence to guidelines and to treat patients within 60 minutes of arrival at the hospital regardless of the amount of time left to the end of thrombolytic window. This study was supported by a grant from IGA MH CR NS10106-4/2008.

Acute stroke: clinical patterns and practice B

13 Acute stroke: clinical patterns and practice B

IMPROVING STROKE PATIENTS' SATISFACTION WITH THEIR EDUCATION ABOUT THEIR DISEASE

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Background: Educating stroke patients about risk factors and natural course of the disease is perceived as an important component of health care quality. The aim of this study was to test whether the Introduction of a standardized information booklet in clinical routine improves patient satisfaction with the information received.

Methods: In this study, improvement of information provision for stroke patients by Introduction of a standardized information booklet in clinical routine was investigated. The booklet was created and evaluated by an interdisciplinary team including professionals, patients and other lay persons. The proportion of stroke patients reporting to be satisfied with the information received about their illness three months after stroke was measured by the stroke care questionnaire (SASC) before and after implementation of the booklet. Univariate and multivariable logistic regression analysis were performed to assess the impact of the Introduction of the booklet.

Results: Out of 1058 patients enrolled between June 2008 and August 2010, 813 answered the SASC (77%). Patients answering the SASC during a 14 month time period before (N=577) and a 12 month time period after (N=481) the implementation did not differ in age, gender, comorbidities, stroke severity (NIHSS), and level of education. The proportion of patients satisfied with the education was higher during the time period of distributing the booklet (88% vs. 83%; p=0.033). Factors independently associated with satisfaction with education were: having received the booklet [OR (95% CI); 1.6 (1.1-2.5)], intermediate level of education [OR (95% CI); 1.7 (1.0-2.8)], older age [OR (95% CI); 2.0 (1.1-3.6)], and better functional outcome three months after stroke [OR (95% CI); 2.5 (1.1-5.0)].

Conclusion: The Introduction of a standardized information booklet in clinical routine can improve stroke-patients' satisfaction with the information about the disease.

THE IMPACT OF PHASE ONE OF THE FAST NATIONAL STROKE AWARENESS CAMPAIGN: A TIME SERIES EVALUATION

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Background: In February 2009, the Department of Health in England launched the Face, Arm, Speech and Time (FAST) mass media campaign, to raise public awareness of stroke symptoms and the need for an emergency response in order to stimulate rapid access to thrombolysis.
Methods: Interrupted time series analysis assessed the impact of phase one of the FAST campaign on: service utilisation of a national stroke charity (The Stroke Association [TSA] website and information materials dispatched); emergency calls for suspected stroke to a regional ambulance service; emergency hospital admissions in England; and patients in England receiving thrombolytic treatment recorded in the Safe Implementation of Thrombolysis in Stroke database.
Results: Prior to the FAST campaign (May 2007 to January 2009) there were significant monthly increases in hits on the TSA website (702; 95% CI = 204 to 1,200); emergency calls (62; 95% CI = 44 to 81); hospital admissions (18, 95% CI = 7 to 28); and thrombolytic treatment rates (2; 95% CI = 1 to 3). In addition, there was an abrupt significant increase after the campaign for information materials dispatched by the TSA (January to February 2009, 123,751; 95% CI = 62,578 to 184,923) and hits on their website (February and March 2009, 34,088; 95% CI = 15,981 to 52,195). Emergency calls for suspected stroke and emergency admissions increased after the campaign, but these changes were not significant. Patients receiving thrombolysis also increased significantly between January and February 2009 (23; 95% CI = 4 to 42). Except for thrombolytic treatment rates, outcomes declined significantly over time after the campaign. Evidence of a differential impact of FAST campaign was found in terms of age, ethnicity and geographical area.
Conclusion: The FAST campaign had an initial positive, but transient, impact on public behaviour, with effects dissipating after campaign activity ceased. Such mass media campaigns may have only a limited and transient impact.

INTRAVENOUS ALTEPLASE IN ISCHAEMIC STROKE PATIENTS NOT FULLY ADHERING TO THE CURRENT DRUG LICENSE IN CENTRAL AND EASTERN EUROPE

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Background: The current European license for alteplase in acute ischaemic stroke excludes from treatment large groups of patients. Nevertheless, in everyday practice many patients receive thrombolysis off-label at the physician's discretion. Our aim was to evaluate safety and effectiveness of intravenous alteplase in patients not fully adhering to the drug license compared to those treated strictly according to the license in Central and Eastern Europe.
Methods: We analyzed the data contributed to Safe Implementation of Thrombolysis in Stroke (SITS-EAST) registry from 9 countries between February 2003 and February 2010. Our endpoints were: symptomatic intracranial haemorrhage (sICH), unfavorable outcome (mRS >2) and mortality at 3 months. Statistical analysis included multivariate logistic regression adjusted for all independent predictors.
Results: Of 5594 consecutive patients treated with intravenous thrombolysis, 1762 (31.5%) not fully adhered to the license. The most frequent deviations were: time-to-treatment >3 hours (13.1%), use of intravenous antihypertensives (8.3%), age >80 years (7.3%), oral anticoagulantion (4.2%), a previous stroke with concomitant diabetes (3.9%), previous stroke <3 months (2.7%). The non-protocol group showed a significantly higher rate of sICH, which was not confirmed in the multivariate analysis. License non-adherence significantly increased the risk of unfavorable outcome (OR 1.26; 95%CI: 1.08-1.48), with a strong trend for increased mortality

(OR 1.17; 95%CI: 0.97-1.42). Isolated time-to-treatment >3 hours was an independent predictor of unfavorable outcome (OR 1.32; 95%CI: 1.01-1.71).
Conclusion: Our findings show, that patients not fully adhering to the European license are not at increased risk of sICH, but achieve less favorable outcome. Some contraindications appear more redundant than others. However, the final Conclusions about safety and effectiveness should based on the Results of ongoing randomized trials.

VARIATIONS AND PREDICTORS OF ACUTE STROKE CARE FROM A EUROPEAN PERSPECTIVE: THE EUROPEAN REGISTERS OF STROKE (EROS) INVESTIGATORS

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Background: Stroke care utilises significant health care resources yet there are wide variations in the uptake of effective interventions across countries. We investigated these variations in acute stroke care in 6 populations and identify predictors of their receipt.
Methods: Data was collected between 2004 and 2006, from population-based stroke registers in France (Dijon), Italy (Sesto_Fiorentino), Lithuania (Kaunas), UK (London), Spain (Menorca) and Poland (Warsaw). All patients with first ever stroke from the source population were included. Predictors of uptake of various processes of care including time to hospital, stroke unit (SU) care, multidisciplinary team (MDT) management, and drug use, were investigated using univariate and multivariable Methods. Subarachnoid Haemorrhage cases were excluded.
Results: 1906 patients were studied, 579 of whom spent 50% or more of their time in hospital, on SU, 97.4% had a CT scan and 13.5% an MRI. Thrombolysis was received by 27 patients, antiplatelets by 79.4% of Ischemic stroke patients, and 10.4% were seen by (MDT). Key care indicators showed large variations across European populations that remained to be significant after adjustment for age, gender, employment, living conditions, and stroke severity. The percentage of patients spending 50% or more of their time in hospital, in a (SU) was highest in London (OR=1.0), while the ORs, and confidence intervals for the others were: 0.04 (0.02-0.06) Dijon; 0.08 (0.06-0.12) Kaunas; 0.18 (0.10-0.32) Warsaw; and 0.05 (0.03-0.09) for Sesto_Fiorentino. Seen by MDT was highest in London, and strongly associated with Stroke severity, and age (85+) was associated with less access to care.
Conclusions: Variations and inequalities in acute care for stoke patients were highlighted. The implementation of evidence based interventions is suboptimal and ways of understanding how to improve the diffusion of research evidence into practice in different healthcare settings is a priority for health systems.

WHAT MAKES A STROKE A MIMIC? SYSTEMATIC EVALUATION OF 33.865 PATIENTS FROM THE AUSTRIAN STROKE UNIT REGISTRY 2003–2009

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Background: Stroke is mainly a clinical diagnosis and imaging might be inconclusive within the first hours. Selecting stroke patients to receive thrombolytic therapy therefore is of utmost importance. False positive rates lie between 1.3 and more than 30% and are known to depend on accuracy of referral diagnosis and experience of the stroke physician. We therefore studied typical presentations of mimics in a large, nationwide cohort covering 32 acute stroke units.
Methods: Retrospective analysis of data from an ongoing national web-based stroke unit registry covering all admissions to acute stroke units in Austria between 2003 and 2009. We evaluated the demographic data, admission and discharge diagnosis,

referral procedures and clinical characteristics with respect to the differentiation of acute stroke vs. stroke mimic.

Results: 33865 (95.2%) of all patients had definite strokes vs. 1712 (4.8%) mimics. Stroke mimics were younger (68.0 vs. 73.0yrs), predominantly female (53.6 vs. 47.3%) and had a higher rate of prior disability as defined by the mRS. Stroke patients presented with worse mRS and a higher scores on the NIHSS on admission, more often showed normal level of consciousness, dysarthria, and more localizing signs such as gaze palsy, visual field defects, facial palsy or unilateral limb weakness, sensory loss and cortical signs such as aphasia and neglect symptoms. In contrast, bilateral limb weakness was significantly associated with stroke mimics. Multivariate regression analysis showed prior dependency (mRs 3-5) (OR 1.95; 95% CI 1.54-2.48), impaired level of consciousness (OR 1.94; 95%CI 1.49-2.52), unknown time of symptom onset (OR 1.47; 95%CI 1.22-1.77) and bilateral motor weakness (OR 1.49; 95%CI 1.11-2.00) as independent predictors for the diagnosis of stroke mimic.

Conclusion: Stroke mimics are typically lacking unilateral neurological deficits and present with less localizing clinical conditions.

18 Acute stroke: clinical patterns and practice B

HOW DOES THE TIME OF STROKE ADMISSION AFFECT QUALITY OF CARE?

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Background: Previous studies have shown that stroke patients who present outside of normal hours have an increased risk of dying in hospital (Reeves et al. Stroke 2009; 40: 569-576) as well as a reduction in direct admission to stroke units and brain imaging (Rudd et al. Age and Ageing 2007; 36: 247-255). We present data from the Stroke Improvement National Audit Programme (SINAP) comparing the quality of care for those patients who present within normal hours and outside of normal hours.

Methods: SINAP is a prospective database of acute stroke patients, documenting details of processes of care and outcomes over the first 72 hours. We compared several quality of care indicators (including the number of eligible patients thrombolysed) and 72-hour mortality, for patients who arrived within normal hours (Monday – Friday 8am to 6pm) and for those who arrived outside of normal hours.

Results: 4922 stroke patients were admitted to 44 hospitals between January and November 2010, and 233 were inpatients at the time of stroke. The 72-hour mortality rate was 2.2% (52/2354) for patients arriving within normal hours, and 3.0% (71/2345) for patients arriving outside of normal hours (P = 0.079). Further Results are shown in Table 1.

Table 1

	Arrival within hours (2354 patients)	Arrival out of hours (2345 patients)
Hospital arrival to first contact with stroke team: median delay (IQR)	116 minutes (15–878)	393 minutes (35–1240)
Hospital arrival to arrival on stroke bed: median delay (IQR)	228 minutes (125–532)	300 minutes (132–1240)
Hospital arrival to first brain scan: median delay (IQR)	140 minutes (55–330)	254 minutes (74–965)
Eligible patients thrombolysed	56% (136/241)	37% (108/293)

P<0.001 for all values.

Conclusions: Patients with acute stroke who arrive outside of normal hours wait longer to be seen by the stroke team, to get to a stroke bed and to have a brain scan. They are also less likely to be thrombolysed. It is possible that this may contribute to poorer outcomes.

Management and economics

1   Management and economics

ACUTE STROKE CODE PITFALLS: STROKE MIMICS AND THROMBOLYSIS CONTRAINDICATIONS

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Background: Acute stroke is a medical emergency. Understanding performance and pitfalls of acute stroke code activation could improve organization. We aimed to evaluate acute stroke protocol failure concerning diagnosis of stroke and contraindication for thrombolysis.

Methods: Consecutive data from our hospital stroke code activations in 2009 were analysed by patient gender, median age and initial NIHSS, symptom-to-door time (SDT), final diagnosis and reasons for thrombolysis exclusion. Protocol failure was measured in percentage of diagnosis other than acute stroke or transient ischaemic attack (stroke mimics) and percentage and motives of thrombolysis exclusion. Subanalysis was performed by type of stroke code activation, either by direct presentation (DP) at emergency department or by the pre-hospital emergency medical system (EMS).

Results: Data included 605 patients. Stroke mimics were 31% (n=188), more frequently females (61% and 51%, p=0.033), younger patients [58 (IQR 45-75) and 71 (60-78), p<0.0001], with lower NIHSS [0 (0-2) and 6 (2-14), p<0.0001] although similar median SDT [80 (48-128) and 80 (56-122), p=0.420]. Most frequently stroke mimics corresponded to psychiatric disorder (30%, n=56), seizures (16.5%; n=31), syncope (12.2%, n=23), migraine aura (6.9%, n=13) and non-recent neurological deficit (5.3%, n=10), accounting these reasons for two thirds of other diagnosis. Thrombolysis was not performed in 65% of acute ischaemic strokes, mainly due to minor or rapidly improving deficit (64%, n=115) and to more than 4.5 hours or unknown time from symptoms onset (15.1%).

Conclusion: Stroke mimics corresponded to almost one third of acute stroke code activations, and the most frequent reason was a psychiatric disorder. Stroke code allowed that 35% of activations in ischemic stroke patients could be selected for thrombolysis, but, apart from transient or resolving symptoms, time window was still an important exclusion factor.

2   Management and economics

RELIABILITY AND VALIDITY OF PROXY DERIVED MODIFIED RANKIN SCALE ASSESSMENT

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Background: The modified Rankin scale (mRS) is the most prevalent functional outcome measure in stroke trials. Cognitive or communication issues may preclude standard mRS interview; in these circumstances information is derived from interview with a proxy. The properties of proxy assessment have not been described.

Methods: Over a five week period, six undergraduate medical students (trained and certified in mRS) assessed a convenience sample of consenting stroke survivors at a University Hospital. Using a standard mRS approach, randomly paired researchers (blinded to each other's scores) performed independent interview of patients and proxies. Reliability was described using kappa statistics (with 95% confidence interval [CI]) and percentage agreement with chi-square testing.

Results: Seventy-nine stroke survivors were assessed (median age 79 years [IQR:72-85]). Proxies were family members, nurses or physiotherapists. Median mRS from patient derived interview was 3 (IQR:2-4); median mRS from proxy derived interview was 3 (IQR:2-4). Inter-observer variability for assessment of stroke survivors was moderate and similar to previous studies of mRS reliability (k=0.54, CI:0.65-0.75), [67% matched]. Inter-observer variability for paired assessment of proxies was moderate (k=0.40 CI:0.36-0.46), [52% matched], with greatest variability in therapist interviews but no difference in overall agreement rates (p=0.53). Comparing scores from patient and proxy interview, suggested no difference between groups in patient agreement (p=0.76); with overall agreement fair (k=0.28, CI:0.24-0.32) [45% matched].

Table 1. Reliability of paired assessments of mRS

	Patient	**Any proxy**	**Family**	**Nurse**	**Therapist**
	(n=79)	**(n=88)**	**(n=18)**	**(n=45)**	**(n=25)**
Patient	κ: 0.54 (0.45-0.65) 67%	κ: 0.28 (0.20-0.36) 45%	κ: 0.25 (0.16-0.34) 41%	κ: 0.32 (0.26-0.38) 48%	κ: 0.16 (0.07-0.25) 44%
Any proxy		κ: 0.40 (0.36-0.46) 52%			
Family			κ: 0.55 (0.22-0.87) 64%		
Nurse				κ: 0.33 (0.21-0.45) 48%	
Therapist					κ: 0.21 (0.00-0.41) 49%

Data are presented as kappa statistic (κ) with corresponding 95% confidence interval and percentage agreement (%).

Conclusions: Proxy derived mRS scores may differ from direct assessment and trialists should be cautious in their interpretation. Of the various parties that may be used for proxy assessment, no group was significantly more reliable or valid in their assessment, although there was a trend towards less variability with nurse derived scores.

3   Management and economics

STROKE MORTALITY IS CORRELATED WITH NATIONAL INCOME AND HEALTH FACILITY PROVISION: AN ECOLOGICAL STUDY

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Background: Stroke is a major cause of death globally. An inverse relationship between stroke burden and wealth has been previously proposed. However, other factors may also be responsible for these findings. This study explores the relationship between stroke mortality and income, health expenditure and healthcare services at the country level.

Methods: The World Health Organisation database was interrogated for country-specific data on age and sex-standardised death rate due to stroke (ASDR, /100 000), per-capita gross national income [GNI, adjusted for Purchasing Power Parity, International dollars (Int$)], total health expenses as a proportion of gross domestic product (HEG, %), government health expenses as a proportion of total health expenses of the country (GEH, %), government expenses on health as a proportion of total governmental expenses (GET, %), number of doctors (NoD, /10 000), number of nurses (NoN, /10 000), and number of hospital beds (NoB, /10 000). Data was analysed using SPSSv17.0; non-parametric tests were employed for non-normally distributed data.

Results: Data was available for all studied variables for 158 countries. Median GNI was Int$ 4960 (Int$ 210 - 47730), HEG 6.0% (1.7 - 7.9%), GEH 60.9% (10.8 - 99.8%), GET 10.8% (0 - 32.1%), NoD 11.5/10 000 (0.5 - 163.3/10 000), NoN 27.4/10 000 (0.5 - 163.3/10 000), NoB 25.5/10 000 (2.0 - 139.0/10 000). Median ASDR was 103.6/100 000 (25 – 249.4/100 000). On univariate analysis, ASDR was negatively correlated with GNI, HEG, GEH, GET, NoD, NoN, NoB. On multivariate analysis, it was negatively correlated with GNI (p<0.001) and positively with NoB (p=0.005), and not with HEG, GEH, GET, NoD, or NoN; r2 = 0.51, p < 0.001.

Conclusions: This study shows a significant negative relationship between ASDR and GNI, and positive relationship between ASDR and NoB. Higher GNI may be expected to translate to better population health and healthcare facilities with resultant reduced stroke mortality. The reason for the positive correlation between NoB and stroke mortality is unclear. More studies are needed to investigate this phenomenon.

4 Management and economics

STROKE TRIAL PATIENTS RECOGNIZED BY ALARM ON MOBILE PHONE (STREAM) - AUTOMATED REAL TIME SMS TEXT MESSAGING TO IMPROVE ACUTE STROKE CLINICAL TRIAL RECRUITING

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Background: Recruitment for acute stroke trials is often restricted by time and selective inclusion criteria. Most relevant first screening criteria usually are time of onset, NIHSS score and patient's age. Alertness of the physician in charge for clinical trial recruitment is often limited by the acute clinical ED-environment. Our aim was to implement an automated real time SMS text-messaging tool to improve identifying patients for clinical trials.

Methods: The Neurological department of Charité Berlin covers three hospital sites with four EDs, treating around 2500 stroke patients per year. Documentation of stroke patients in the clinical information system (SAP ish*med) is mandatory on a special standard stroke sheet (SSS). Saving of this document is obligatory linked to documentation of age, sex, stroke onset and of single NIHSS items. For the Stroke SMS-Alarm a remote data algorithm was developed. After first documentation, the data set (hospital site, date and time of admission, age, sex and NIHSS score) is send to a special filter-server via HL7. Then the text SMS is generated and sent to the receiver-group (study team and consultant neurologists).

Results: During the first two months test period 315 patients were identified on the three sites (age 72 years; 52% female; mean NIHSS 6.5). First analysis was performed in 107 patients (mean age 70 years; 63% female; mean NIHSS 5). Seventy-six percent of SMS messages were generated and sent within 60 minutes. No alarm was missed in patients with SSS. In 27 patients with no SSS-documentation due to different reasons no SMS was generated. Remote SMS-Stroke alarm was compliant to requirements of data protection.

Conclusion: SMS remote stroke alarm is feasible and reliable. It is a useful tool to support efforts in improving patient recruitment for acute clinical trials.

5 Management and economics

SAFETY AND FEASIBILITY OF OUTPATIENT MANAGEMENT OF MINOR STROKE: A POPULATION-BASED STUDY

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Background: Management of patients with TIA in specialist outpatient clinics is effective in preventing early recurrent stroke. Whether this approach is safe and effective for patients with minor stroke is less clear and has not previously been assessed.

Methods: We prospectively studied outcomes of clinic and hospital-managed patients with TIA and minor stroke (NIHSS ≤3 at time of assessment) in a population based study in Oxfordshire, UK, from 2002-2007 (Oxford Vascular Study - OXVASC).

Results: Of 877 patients with TIA and minor stroke, 554 (63%) were referred directly to the OXVASC clinic and 323 (37%) presented or were referred directly to inpatient services. Of the 234 clinic-referred minor strokes (mean age = 72.7 yrs), 6 were admitted to hospital directly from clinic (including 3 with ICH). The remaining 228 were sent home after investigation and treatment, of whom 14 (6.1%) were admitted to hospital within 30 days: 5 with recurrent stroke; 3 with sepsis; 3 with falls; 2 with GI bleeding; 1 for nursing care. The 183 patients (mean age = 74.5 years) with minor stroke initially referred and admitted directly to hospital for inpatient care (median length of stay = 8 days) had a similar readmission rate (11/183; 6.0%; p=1.0) within the 30 days after discharge. The 30-day risk of recurrent stroke was also similar in the two treatment settings (clinic - 5/230 vs inpatient - 3/183; OR 1.33, 0.3-5.1, p=0.70). However, at one month follow-up rates of use of secondary prevention medication were higher in clinic-managed patients: 97% vs 82% on antiplatelets or anticoagulants (p<0.001); 82% vs 66% on lipid lowering therapy (p<0.001); and 46% vs 28% on 2 or more antihypertensive drugs (p<0.001).

Conclusion: Outpatient management of minor stroke in a specialist clinic is feasible. Only 6% of patients subsequently had unplanned hospital admissions, rates of recurrent stroke were low, and uptake of secondary prevention was high.

6 Management and economics

EFFECTIVENESS AND EFFICIENCY OF A "FAST TRACK" TRANSIENT ISCHEMIC ATTACK CLINIC

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Introduction: efforts to promote the management of patients with transient ischemic attack (TIA) on an outpatient basis, quickly and safely, are underway. Our objective was to analyze the Results of the first 5 months of operation of a "Fast Track" Transient Ischemic Attack Clinic (FTTIAC) as well as its effectiveness and efficiency compared to the hospitalization-based management.

Methods: We analyzed the first 5 months (January-May 2010) of a FTTIAC, comparing its activity with the same period of 2009, when the TIA management involved it direct admission in a Stroke Unit (SU). Patients accessed the FTTIAC by three ways: primary care physician, neurologist and emergency department. Within the first 24 h from TIA onset the patient was evaluated by a neurologist experienced in stroke and a complete cerebrovascular basic study was carried out, including brain-CT, neurosonology, EKG and laboratory. In addition, the destination was decided: SU income (high risk TIA with ABCD2 score > 5) or outpatient FTTIAC (low and moderate risk).

Results: 119 patients treated in the HRTIAC: mean age 68 years, 50.4% male. Final diagnosis was TIA in 105 patients (88.23%). Of these, 39 (37.14%) had a high risk TIA and were transferred to the SU. In the same period of 2009 a total of 50 TIA were evaluated, and all of then were admitted to SU. The establishment of FTTIAC was associated to an increase of 110% in the number of patients with TIA treated. In addition, there was a 62.8% reduction in hospital admissions for TIA. Stroke recurrence at 3-months was similar in both groups.

Conclusion: The FTTIAC is an effective and efficient organization for TIA management, increasing the number of patients evaluated early and avoiding the hospitalization of more than a half of them.

7 Management and economics

EUROPEAN REGISTRY OF STROKE (EROS) PROJECT: COMPARING STROKE CARE IN EUROPE USING THE EQAT QUALITY ASSESSMENT TOOL TO PRODUCE QUALITY OF CARE SCORES

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Background: As part of a comparison of outcomes across contemporary population-based registers in 7 European centres in the EROS project, the EROS Quality Assessment Tool (EQAT) was developed to assess quality of stroke care

related to the available evidence base and European Stroke Guidelines. The original tool was lengthy (251 items) and we wanted to compare centres based on responses to subsets of the tool in 93 and 22 item formats.

Methods: The EQUAT was completed at semi-structured, face-to-face interviews delivered at a multidisciplinary site visit to centres in Dijon (France), Florence (Italy), Stockholm (Sweden), Mahon, Menorca (Spain), Kaunas (Lithuania), Warsaw (Poland) and South East London (UK). Interviews were conducted in English. Each centre's data were compared to the evidence-based guidelines and positive responses, indicating the presence of evidence-based features of stroke care, were summated for the different versions of the tool. Crude and weighted (according to the level of evidence supporting the item) scores were produced for each centre. Weighting was based on the hierarchy of evidence (scored 0 – absent, 1- expert opinion, 2-low quality evidence, 3- high quality evidence).

Results: Quality of stroke care varied considerably across the centres. Scores were calculated for each version (crude and weighted). For 93-item EQAT: Crude scores ranged from 41 – 78 (of possible 93). Weighted scores ranged from 73 – 149 (of possible 165). For 22-item EQAT: crude scores ranged from 10 – 21 (of possible 22). Weighted scores ranged from 18 to 42 (of possible 44). Upper and lower ranking of centres based on scores was consistent between versions.

Conclusion: Quality of stroke care measured by the EQAT varied considerably across the centres. By weighting the crude scores, some indication of the implementation of evidence is given. The abbreviated EQAT may be useful for assessing and categorising quality of stroke care but requires further testing and validation.

8 Management and economics

ASSOCIATION BETWEEN STAFFING LEVELS AND QUALITY STANDARDS ON STROKE UNITS

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Background: The performance and quality of stroke services may be influenced by the number of qualified nurses and therapists (physiotherapy, occupational therapy, speech and language therapy).

Methods: Data were obtained from the National Sentinel Stroke Audit 2010 of 201 NHS hospitals in England, Wales and Northern Ireland treating acute stroke patients. Nurse staffing levels (mean per 10 stroke unit beds) were correlated with quality standards of acute stroke care (continuous physiological monitoring, immediate access to scanning, direct admission to stroke unit from A&E, specialist ward rounds on seven days a week, acute stroke protocols/guidelines in place, nurses trained in swallow screening as well as stroke assessment and management) and other aspects of stroke service organisation.

Results: Units that have all quality standards for acute stroke care had more qualified nurses (10.2 whole time equivalents (wte) /10 beds) in place than units with less features (5.5 wte/10 beds; p<0.001). Hospitals where all patients were in stroke unit beds (or in intensive care) on the day of audit had 7.8 wte/10 beds whereas there were 7.0 wte/10 beds (p=0.038) if patients were also located on other wards. Hospitals offering thrombolysis were found to have more nurses available (7.8 wte/10 beds) compared to hospitals that do not have thrombolysis service (6.4 wte/10 beds; p=0.036). No such association has been observed for any of the therapists.

Conclusions: There is a clear association between the number of qualified nurses working on the stroke unit and better quality of stroke care in acute hospitals although this may not be the only factor for performance. The low variations in each therapist staffing levels may be a reason that no association has been found for these professions.

9 Management and economics

VARIATIONS IN PERFORMANCE MEASURES OF ACUTE STROKE CARE IN SIX EUROPEAN STROKE AUDITS: THE EUROPEAN IMPLEMENTATION SCORE (EIS) COLLABORATION

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Background: Quality of stroke care between different health care providers is often compared by performance measures. Although several regional or national audits focussing on monitoring acute stroke care are established, there is currently no consensus of performance measures for acute stroke care in Europe.

Methods: An up-to-date inventory on European stroke audits running in 2007 was provided within an EU funded FP7 project (European Implementation Score Collaboration). Between 11/2009 and 07/2010 two standardised surveys as well as a series of qualitative interviews were performed to determine the content, characteristics, reporting, feedback and benchmarking, development, selection and content of performance measures, and target values of the audits. For quality purposes all summarized information was validated by a representative of the respective audit.

Results: Six regional or national clinical audits on acute stroke care took part (Catalonia, Flanders, Germany, Scotland, Sweden, UK). Overall, 123 different parameters were defined to serve as quality indicators (91 process, 24 outcome, and 8 structural indicators). Anticoagulants in patients with atrial fibrillation was the only quality indicator used in all audits while five (stroke unit care, swallowing test, brain imaging, lipid lowering therapy, thrombolytic therapy) were used in all but one audit. Substantial variations were found across the audits in terms of used Methods in the developing process and selection of quality indicators, inclusion criteria, participation, population coverage, data documentation and collection Methods, available follow-up information and outcome measures.

Conclusion: There is a huge variety in measuring performance across European stroke audits hampering currently valid comparisons of stroke care between European countries. Common standards for definition of performance measures and for collection of information required for these measures should be defined in Europe.

Small vessel stroke and white matter disease

1 Small vessel stroke and white matter disease

THE CADASIL SCORE: A SCREENING TOOL TO SELECT PATIENTS FOR THE NOTCH3 GENE ANALYSIS

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Background: CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) is an inherited cerebrovascular disease caused by Notch3 gene mutations. The gold standard for diagnosis is the genetic test which is costly and time-consuming. To limit laboratory costs, a pregenetic screening procedure should be implemented because, although certain clinical and neuroimaging features are typical of CADASIL, none is pathognomonic.

Methods: We developed a score based on a pooled analysis of the largest international CADASIL series. The CADASIL score takes into account clinical, neuroimaging, and family history data and attributes weighted scores according to the frequency of the disease features pointed out in the pooled analysis. The total score ranges from 1 to 20. The score was applied to 61 consecutive genetically diagnosed CADASIL patients and 54 "Notch3-negative patients" (without pathogenic mutations in Notch3 gene exons 2-23); in both groups patients were probands who underwent genetic test for suspicion of CADASIL. We performed ROC (Receiver Operating Characteristic) analysis to evaluate the accuracy of the CADASIL score.

Results: At the ROC analysis area under curve was 0.74. The score of 14 had sensitivity=89% and specificity=48%. Positive and negative predictive values were respectively 66% and 79%. We did not find a significant correlation between score and age.

Conclusion: Applying the CADASIL score in two groups of probands with disease suspicion, we found that this score was a fairly accurate tool for selecting patients who should undergo genetic analysis for CADASIL. Since the CADASIL score is primarily intended as a screening tool, we propose a cut-off=14 despite a low specificity because a higher sensitivity is preferable in this screening context.

2 Small vessel stroke and white matter disease

NEUROPSYCHOLOGICAL PROFILE AND INFLUENCE ON FUNCTIONAL PERFORMANCES IN TWO SETTINGS OF MICROVASCULAR LEUKOENCEPHALOPATHY: CADASIL AND SPORADIC AGE-RELATED LEUKOENCEPHALOPATHY (ARL)

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Background: Microangiopathic leukoencephalopathy is frequently seen in the elderly with vascular risk factors (sporadic ARL). Similar white matter changes are found in CADASIL, a genetically-determined cerebral small vessel disease. Both conditions are characterized by progressive cognitive impairment and disability.
Objective: To assess the neuropsychological profile of 70 ARL and 55 CADASIL patients and the possible influence on functional performances.
Methods: In MILES (MIcrovascular LEukoencephalopathy Study), functional and neuropsychological performances were evaluated using a comprehensive battery [1]. For each test z scores were calculated considering age and education. To trace a neuropsychological profile of the two patient groups, compound measures were obtained using standard scores for the following domains: Memory, Speed and Executive Functions. Differences in the neuropsychological profile of the two patient groups were explored using t-test. The predictive value of neuropsychological indexes on functional performances was evaluated in each group using correlation and logistic regression analyses.
Results: No significant difference was found between the neuropsychological indexes of the two groups [Memory, $t(121)=1.3, p=0.19$; Speed, $t(115)=-1.1$, $p=0.29$; Executive Functions, $t(82)=0.2$, $p=0.85$]. In CADASIL, the only significant predictor of functional performance was the Memory index ($B=0.66$, $p<.01$), while in the ARL group, the only significant predictor was the Executive Functions index ($B=2.24$, $p<.05$).
Conclusions: Our study shows that the neuropsychological profile is similar in CADASIL and ARL patients, but there is a different relation with functional tests: memory seems to have a greater impact on functional performance in CADASIL, while executive functioning in ARL.
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3   Small vessel stroke and white matter disease

CEREBRAL SMALL VESSEL DISEASE INDICATORS AND PROGRESSION OF BRAIN ATROPHY AFTER 4 YEARS OF FOLLOW-UP. THE SMART-MR STUDY
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Introduction: White matter lesions (WMLs) and lacunar infarcts (LIs) are cross-sectionally associated with brain atrophy, but it is unclear whether they contribute to progression of atrophy. We investigated the prospective associations of presence and progression of WMLs and LIs with progression of global, subcortical and cortical atrophy.
Methods: Within the SMART-MR study, 540 patients (57 ± 9 years) without cortical, subcortical or infratentorial infarcts had brain MRI and other examinations at baseline and follow-up (mean interval 3.9 years). Brain segmentation was used to quantify volumes of brain tissue, cerebrospinal fluid and WMLs. Progression of WML was defined as the highest quintile of normalized WML volume change between baseline and follow-up and progression of LIs was defined as new LIs on the follow-up MRI. Volumes of total brain, ventricles, and cortical gray matter were divided by intracranial volume to obtain brain parenchymal fraction (BPF), ventricular fraction (VF) and cortical gray matter fraction (GMF) as indicators of global, subcortical and cortical atrophy. Linear regression analysis was used to estimate prospective associations of measures of WMLs and LIs with brain volume at follow-up adjusted for age, sex, baseline brain volume, vascular risk factors and severity and type of atherosclerosis.
Results: Every 1% more WML volume at baseline corresponded with a 0.12% higher VF at follow-up (95% CI 0.04 to 0.21, p=0.005). Progression of WML corresponded with a 0.1% higher VF (95% CI 0.05 to 0.16, p<0.001) and a 0.39% (95% CI -0.8 to 0.03, p=0.07) lower GMF at follow-up. Progression of LIs corresponded with a 0.6% lower GMF at follow-up (95% CI -1.2 to -0.01, p=0.03) and a 0.29% lower BPF at follow-up (95% CI -0.58 to 0.01, p=0.06).
Conclusion: In patients with atherosclerotic disease, presence of WMLs at baseline and progression of WMLs and Lis are associated with progression of brain atrophy independent of vascular risk factors.

NO EVIDENCE FOR INCREASED IRON DEPOSITION IN DEEP GRAY MATTER REGIONS IN SUBJECTS WITH MRI FINDINGS SUGGESTIVE OF CEREBRAL SMALL VESSEL DISEASE
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Background: Recent investigations have shown increased iron deposition in the deep grey matter of patients with multiple sclerosis (MS) which is an immune mediated inflammatory demyelinating disorder of the white matter. Small vessel diseases (SVD) are a further cause of white matter damage and are also frequently associated with microbleeds, i.e. hemosiderin deposition in the brain parenchyma. We therefore speculated that iron concentrations might also be increased in patients with severe white matter hyperintensities (WMH) as a hallmark of SVD.
Methods: A cohort of 61 patients (mean age: 71 ± 8 yrs) with some degree of WMH was dichotomized according to WMH severity according to the Fazekas scale into a group A with minor changes (n=25, age=68 ± 9 yrs) and a group B with early confluent to confluent lesions (n=36, age=74 ± 7 yrs). R2* imaging was performed on a 3 T magnet and maps were calculated for several deep gray matter structures (thalamus, caudate, putamen, pallidum, hippocampus, amygdala, nucleus accumbens) and the brainstem (segmented using FIRST, as part of FSL). WMH volume was assessed using DispImage and brain tissue volume was estimated using SIENAX, as part of FSL.
Results: The two groups significantly differed in age, WMH and cerebrospinal fluid volume. Regarding iron concentrations, group comparisons (controlled for these three covariates) did not yield significant differences between subjects with minor and more severe WMH, except for the globus pallidum with a higher concentration in group A (34.96 ± 4.88) rather than group B (32.68 ± 3.88; F1=4.410; p<0.04).
Conclusion: Using a sensitive MRI method to quantitatively map iron deposition, we could not substantiate the speculation of increased iron deposition in deep gray matter in SVD. This indicates that not white matter damage per se but rather its aetiology is linked with such observations in MS.
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The authors report no conflicts of interest.

5   Small vessel stroke and white matter disease

MICROBLEEDS ARE ASSOCIATED WITH SUBJECTIVE COGNITIVE FAILURES. THE RUN DMC STUDY
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Background: Cerebral small vessel disease (SVD), including white matter lesions (WML) and lacunar infarcts, is related to cognitive impairment but also to subjective cognitive failures (SCF). SCF have been reported to be an early predictor for dementia. Cerebral microbleeds (CMB) are another manifestation of SVD and have been related to cognitive impairment, but the role of CMB in SCF has never been studied. We therefore wanted to investigate whether CMB are related to SCF among non-demented elderly with cerebral SVD, independent of WML and lacunar infarcts.
Methods: The RUN DMC study is a prospective cohort study among 503 non-demented elderly with cerebral SVD aged between 50-85years. All subjects underwent FLAIR and T2* scanning. The number of SCF, subjective memory (SMF) and subjective executive failures (SEF) was assessed by the Cognitive Failure Questionnaire. The relation between SCF and the number and location CMB was assessed by linear regression analyses adjusted for age, sex, education, depressive symptoms, cognitive function, total brain volume, WML and lacunar infarcts.
Results: Mean age was 65.6 (SD 8.8) and mean MMSE was 28.1 (SD 1.6). CMB were present in 11% of the subjects. We found a relation between the total number

of CMB and SCF (β 0.10; p 0.02) and SEF (β 0.11; p 0.02), we also found a relation between the number of lobar CMB and SCF (β 0.10; p 0.03), SMF (β 0.10; p 0.03) and SEF (β 0.12; p 0.02), we did not find any relation between the number of deep SMB and subjective failures.

Conclusion: The number and the lobar location of CMB is related with SCF in non-demented elderly independent of coexisting SVD. These Results suggest that CMB are associated with the earliest manifestations of cognitive impairment. This knowledge may have important clinical implications in understanding the role of the ever expanding spectrum of small vessel disease in cognitive impairment.

6 Small vessel stroke and white matter disease

DO MICROBLEEDS RESULT IN COGNITIVE IMPAIRMENT IN SMALL VESSEL DISEASE AND WHAT IS THEIR EFFECT ON TISSUE ULTRASTRUCTURE?

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Cerebral microbleeds (MB), seen on gradient echo T2*-weighted (GE) MRI, are common in small vessel disease (SVD). They have been associated with cognitive decline but whether they are causal, or merely a marker of disease severity, is unclear.

In the prospective SCANS cohort of 121 subjects with lacunar stroke and leukoaraiosis we determined the relationship between MB and cognition and the effect of MB on local tissue ultrastructure. MB were graded by a neuroradiologist using the Brain Observer Microbleed Scale (BOMBS). A standard neuropsychological battery was administered. MB effect on tissue ultrastructure was assessed using DTI. We co-registered DTI images with GE and T1 images and determined DTI values in regions-of-interest (ROI) containing MB. This was compared with DTI values in lacunar infarct (LI) ROI. We also assessed a concentric "shell" of tissue around MB and LI to see if there was evidence of white matter tract disruption.

MB number correlated with lesion volume (LV) (rho=0.28, p<0.001). In the complete sample (n=121) neither the presence, nor number, of MB was associated with cognitive function (p-values>0.35). Restricting analysis to those with MB (n=49), the number of MB was associated with cognitive function (Global, Executive and Working Memory factors; p<0.03, p<0.04, p<0.05), but this was not significant after controlling for brain volume (BV) and LV (all p-values>0.7). MB appeared not to be associated with any change in DTI parameters in the MB ROI or in surrounding voxels. In contrast LI were associated with an increase in MD and a reduction in FA (p<0.03 vs. MB), a pattern indicating tissue damage.

We found no evidence that MB were associated with cognitive dysfunction in SVD independent of BV and LV. Consistent with this we found no evidence of white matter tract damage associated with MB. This suggests that whilst MB are a marker of vascular damage, they do not seem to disrupt white matter tracts or independently reduce cognitive function.

7 Small vessel stroke and white matter disease

MICROBLEEDS ARE INDEPENDENTLY RELATED TO GAIT DISTURBANCES IN ELDERLY WITH CEREBRAL SMALL VESSEL DISEASE

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Background: Cerebral small vessel disease (SVD), including white matter lesions (WMLs) and lacunar infarcts, is related to gait disturbances. Microbleeds are another manifestation of SVD, but their clinical impact remains unclear. We therefore investigated the relation between the number and location of microbleeds and gait, independently of WMLs and lacunar infarcts.

Methods: 485 elderly with cerebral SVD, aged 50-85 years, without dementia or parkinsonism, underwent MRI scanning. The number and location of microbleeds were rated. Gait was assessed with a GAITRite system and the Tinetti and Timed-Up-and-Go (TUG) test. Microbleeds were related to gait parameters by age, height, total brain volume, WMLs and number of lacunar infarcts adjusted linear regression.

Results: The subjects had a mean age of 65.6 years (SD 8.8), and 43.1% were female. A higher number of microbleeds was independently related to a shorter

stride length (standardized β=-0.09; p=0.016), and poorer performance on the Tinetti and TUG-test (standardized β=-0.17; p<0.001 and standardized β=0.14; p=0.001). These relations seemed to be explained by microbleeds in the temporal and frontal lobe and basal ganglia, including the thalamus.

Conclusions: This study offers the first indication that microbleeds are associated with gait disturbances in elderly with cerebral SVD, independently of other coexisting markers of SVD. A preplanned follow-up of our study will assess the effect on gait deterioration and parkinsonism.

8 Small vessel stroke and white matter disease

PROGRESSION OF BRAIN MICROBLEEDS IN ESSENTIAL HYPERTENSIVE PATIENTS - A TWO YEAR FOLLOW UP STUDY

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Background: Brain microbleeds (BMBs) are common in hypertensive patients and are associated with higher blood pressure (BP) levels. However, little is known about risk factors for progression of BMBs, in particular the contribution of BP levels. The aim of our study was to explore in a cohort of essential hypertensive patients the degree of BMB progression and the association with BP levels.

Methods: In 193 participants from the HYpertension and BRainDamage (HYBRiD) study, a longitudinal cohort-study of hypertensive patients, we performed brain MRI and 24 hour ambulatory BP measurement at baseline (off medication) and after 2 years of follow up (on medication). BMB progression was defined as the presence of any new BMB on T2* GE MRI. The relation between progression and 24h BP was tested in logistic regression analyses.

Results: Progression of BMBs on follow-up MRI was seen in 12 (6,2%) participants. Patients with progression of BMBs were significantly older and had more often BMBs and higher number of BMBs at baseline. Also, 24h systolic (SBP) and diastolic BP (DBP) at baseline were significantly higher in patients with progression. Baseline 24h SBP and DBP were significantly associated with progression of BMBs, after correction for age and sex (OR 1.55; 95%CI 1.10-2.18 and OR 1.88; 95%CI 1.07-3.31 per 10 mmHg respectively), and after additional correction for degree of BP control at follow-up (OR 1.55; 95%CI 1.09–2.20 and OR 1.88; 95%CI 1.06–3.33 per 10 mmHg respectively). However, when additionally corrected for the presence of BMBs at baseline, only 24h SBP remained significantly associated (OR 1.44; 95%CI 1.01-2.04 per 10 mmHg).

Conclusion: We found, in 6.2% of patients with essential hypertension progression of BMBs after two years follow-up. 24 h SBP at baseline seems to be the most important predictor for progression of BMBs. High blood pressure seems to be an important modifiable risk factor for progression of BMBs.

9 Small vessel stroke and white matter disease

LEUKOARAIOSIS AND STROKE SEVERITY AS INDEPENDENT PREDICTORS OF ACUTE POST-STROKE DYSPHAGIA

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Background and purpose: Dysphagia is an important negative prognostic factor for stroke outcome. It occurs in 30-50% of patients with acute stroke. It has been demonstrated that disruption of cortical subcortical connectivity may result in dysphagia. However, the impact of these alterations on clinical and cognitive stroke outcome is still to be elucidated. The aim of this observational study is to identify clinical and neuroanatomical correlates of post-stroke dysphagia and to assess its impact on cognitive outcome.

Materials and Methods: We prospectively examined consecutive patients admitted for ischaemic or haemorrhagic stroke within 72 hours of symptom onset. Demographic data and vascular risk factors were recorded on admission. All the patients underwent to neurological examination, IQ-CODE and brain MRI. Dysphagia was be assessed using Water Swallow Test. The patients were followed up at 14 days, 3 and 6 months after stroke to assess the persistence of dysphagia, the clinical and cognitive outcome.

Results: Up to date, we recruited 143 patients (70M/73F; mean age 73 yrs ±12). 40 had a hemorrhagic stroke. At admission, dysphagia occurred in 48.3% of the patients. No differences were evidenced for the demographic and common vascular risk factors between dysphagic and non dysphagic patients. Dysphagia was more frequent in patients with hemorrhagic stroke (p=0.004), lesion size >3 cm (p<0.001), leukoaraiosis (p<0.001), insular stroke (p<0.001) and higher stroke severity (p<0.001). Logistic regression analysis revealed that stroke severity

assessed using NIHSS [OR 1.35 (95% CI 1.21 – 1.51)] and leukoaraiosis [OR 6.71 (95% CI 2.23-20.22)] independently predicts the occurrence of dysphagia after an acute stroke. Follow-up evaluations are ongoing.

Conclusion: In our study, we confirmed the correlation between the stroke severity and post-stroke dysphagia. Interestingly, an independent correlation was observed with leukoaraiosis. This datum suggests that dysphagia might be not a pure motor disturbance but the consequence of an impairment of executive functions due to the disruption of cortical subcortical connectivity.

Vascular imaging

1 Vascular imaging

ISCHAEMIC HEART DISEASE AND SMOKING ARE ASSOCIATED WITH LOWER PREVALENCE OF PLAQUE HAEMORRHAGE: A CAROTID MRI STUDY

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Introduction: Carotid plaque haemorrhage (PH) is a main feature of plaque instability, can be readily detected by carotid MRI and predicts ipsilateral ischaemic events. Risk factors for developing PH other than male sex are less well studied. Recently, a lower prevalence of PH was reported in current smokers compared to non-smokers in histological study from endarterectomy. We aimed to analyse associations between PH in vivo and known vascular risk factors.

Methods: 176 symptomatic patients (mean age 71.8±9.9, range 41-91 yrs) with ipsilateral significant (>50%) carotid artery stenosis from 3 prospective studies undergone 3D carotid MRI to classify presence of PH. Chi square and binary logistic regression analysis were used.

Results: 112 (63.6%) patients had PH. Current smokers were less likely to have PH than non-smokers (39/73 [53.4%] vs. 45/64 [70.3%], p=0.043). PH frequency in ex-smokers was not different from current smokers (71.8%, ns). Patients with ischaemic heart disease (n=47) had lower prevalence of PH (53.2 vs. 67.4%, p=0.082). Multiple binary regression model showed significant independent predictive value for presence of PH for: IHD (Odd's ratio [OR] 0.344, 95% CI 0.155-0.763, p=0.009), current smoking (OR 0.367, CI 0.164-0.821) with sex as only other significant factor.

Discussion: The lower prevalence of PH seen in current smokers confirms a recent histopathological study. To our knowledge, the finding of a negative association between IHD and PH is novel. While a protective effect from e.g. hypercoagulable state cannot be excluded, inclusion of patients with already symptomatic carotid disease suggests that negative associations between risk factors point to their partial independence and potential additive effects.

Conclusion: Current smokers and a history of IHD predict a lower prevalence of PH in patients with symptomatic carotid disease. This supports independence of IHD, smoking and PH with potential additive effects for stroke prediction.

2 Vascular imaging

PLAQUE HAEMORRHAGE INDEPENDENTLY PREDICTS RECURRENT TIA AND STROKE IN SYMPTOMATIC CAROTID ARTERY STENOSIS

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Introduction: Histopathological evidence indicates that carotid intraplaque haemorrhage (PH) is associated with plaque instability. PH is a common feature in symptomatic carotid disease and can be detected by non-invasive MRI. Prospective studies suggest that MR detected PH predicts ischaemic events in asymptomatic and symptomatic patients. Those studies were limited by low number of events. In this pooled single-centre study, we assessed whether PH predicts recurrent TIA and stroke in symptomatic significant carotid artery disease.

Methods: A total of 176 symptomatic patients (mean age 71.8±9.9) with ipsilateral (50%-99%) carotid artery stenosis from three prospectively recruited studies had

undergone 3D carotid MRI and were followed up until carotid endarterectomy or at least 60 days Survival analysis was performed using multiple Cox regression and log rank test.

Results and Discussion: 112 patients (63.6%) were classified as PH+ (MRI hyperintense plaque), 70 patients (39.8%) had 50-69% stenosis. During follow-up 30 recurrent events were noted (20 TIA, 10 stroke), all of which were seen in PH+ patients. Multiple Cox regression showed that PH and degree of stenosis predicted TIA or stroke during f-u (PH: HR 7.39 CI 1.62-33.80, p=0.01, < vs. > 70% stenosis: HR, 4.72, CI 1.18- 18. 92, p=0.028) with no effect from age, smoking, ischaemic heart disease, time from initial event. Log rank test showed a significant prediction of stroke alone by PH (p=0.009), but due to very high number of censored data this has to be considered preliminary.

Conclusion:. This study confirms and extends previous reports that PH independently predicts recurrent hemispheric events in patients with symptomatic carotid disease. Preliminary analysis further suggests that PH may also predict stroke alone.

3 Vascular imaging

PREDICTORS OF PROGRESSION OF CAROTID ATHEROSCLEROSIS AFTER 13 YEARS OF FOLLOW-UP. THE TROMSØ STUDY

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Background: The purpose of the study was to explore predictors of progression of carotid atherosclerosis after 13 years follow-up.

Methods: Subjects were 1442 men and 1533 women who participated in a longitudinal population-based study with ultrasound examination of the right carotid artery at baseline and after 13 years of follow-up. Total cholesterol, HDL cholesterol, fibrinogen, blood pressure, body mass index (BMI) and waist-hip ratio and information about smoking habits, prevalent diabetes were obtained at baseline. Carotid atherosclerosis was assessed as total plaque area (TPA) and mean intima-media thickness (IMT). Associations between risk factors and carotid atherosclerosis were assessed in linear regression models stratified by sex.

Results: In multivariable models, age, total cholesterol, daily smoking and systolic blood pressure were independent predictors of total plaque area and IMT after 13 years follow-up in both men and women. In men, fibrinogen was significantly associated with both TPA and IMT, and showed borderline association with progression of TPA and IMT (p=0.05). Diabetes and waist-hip ratio were associated with IMT in men, but not in women. BMI was associated with IMT in women, but not with progression of IMT. Age, smoking and systolic blood pressure were predictive of progression of TPA in both men and women. Total cholesterol was predictive in women, and of borderline significance in men. In women, but not in men, age, total cholesterol and daily smoking were independent risk factors for progression of IMT. None of the risk factors were significantly associated with progression of IMT in men.

Conclusions: Age, daily smoking and systolic blood pressure were the most consistent predictors for progression of carotid atherosclerosis in both men and women. Associations between risk factors and carotid atherosclerosis differed depending on type of measure used to assess atherosclerosis.

4 Vascular imaging

AUTOMATED EVALUATION OF LEPTOMENINGEAL COLLATERALIZATION IN ISCHEMIC STROKE: FEASIBILITY AND PROOF OF CONCEPT

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Background: Collateral status in acute ischemic stroke significantly correlates with clinical outcome but so far there is no standardized method of collateral rating based on CT angiography (CTA). User independent automated collateral rating would be valuable for fast decision-making. The purpose of this study is proof of concept that reliable automated collateral (AC) assessment can be obtained in acute stroke CTA images using analysis software.

Methods: Collaterals were rated in CTA maximum projections (MIP) images of 35 acute stroke cases with proximal MCA occlusion. In consensus, two raters scored abundance of collaterals in the ischemic hemisphere compared to the unaffected side using the following score: 0- virtually absent; 1- less; 2- equal or more than unaffected side. For AC scoring, CTA MIP images were skull stripped, co-registered to MNI-152 standard space and thresholded (70-370HU) to define vessel-specific voxels (Analyze 10.0). Templates with masking of the saggital and transversal sinus were used to calculate the relative vessel-abundance (VA) per hemisphere: [mean vessel-HU] x [vessel-volume] (FSL4.1, FMRIB). The collateral index (CI) was calculated as the ratio of relative VA in the ischemic hemisphere to the other side. Optimal cut-off values of CI for predicting collateral scores (CS) were determined by CART (TIBCO Spotfire S+ 8.1). Agreement between rater-based and automated CS was assessed by weighted kappa (SAS 9.2).

Results: The correlation between CI and CS was significant (Spearman 0,742). CI range was 0,61 to 1,23 with optimal cut-offs at 0.74 and 0.97 for classification of CI into CS. Agreement between CI and predicted CS was significant (kappa 0.661).
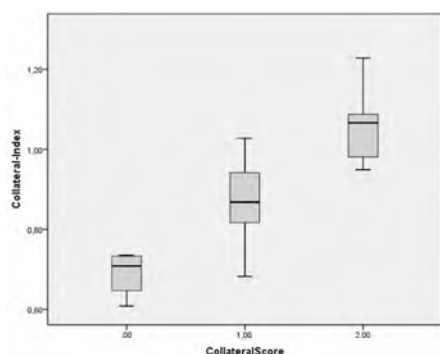
CI

	Cut-off	Median	St. dev.	Range	N
CS 0		0,71	0,059	0,13	4
	0,71				
CS 1		0,87	0,090	0,35	25
	0,97				
CS 2		1,06	0,095	0,28	6

Conclusion: Proof of concept for automated assessment of collateral vessels is presented: software-based CI in acute stroke CTA images highly correlated with reference CS. The CI can be classified to generate rater-based CS. The Results encourage further development of software for AC scoring.

5 Vascular imaging

CORRELATION BETWEEN APPARENT DIFFUSION COEFFICIENT AND CEREBROVASCULAR RESERVE IN EUROPEAN ADULTS WITH MOYAMOYA DISEASE

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Background and purpose: Impairment of frontal cerebrovascular reserve (fCVR) has been associated with the risk of stroke and cognitive dysfunction in adults with Moyamoya disease (MMD). Raising of apparent diffusion coefficient (ADC) calculated using diffusion-weighted MRI may be related to subtle structural changes in normal-appearing white matter (WM). ADC may be an alternative to determine patients with hemodynamic compromise. The aim of this study was to assess the association between ADC and fCVR in adults with MMD.
Method: Cerebral blood volume (CBV) ratio was measured with perfusion MRI in frontal regions using the cerebellum as a reference region in 14 European adults with MMD (5 men, 10 with bilateral arterial impairment). Each hemisphere was studied independently. We calculated the CVR using the CBV ratio and the acetazolamide challenge. Impairment of fCVR was defined as a negative CVR. ADC was calculated from regions of interest located in normal-appearing centrum semi ovale WM. ADC were compared between hemispheres with reduced fCVR and hemisphere with positive fCVR. Then, we determined the best ADC value predictive of reduced fCVR using ROC curve.
Results: Twenty eight hemispheres were studied. Thirteen had a reduced fCVR. ADC in centrum semi ovale was higher in hemispheres with fCVR impairment compared with those with positive fCVR (p= 0.008; Mann-Whitney test). There was a significant negative correlation between ADC and fCVR values (- 0.5; p = 0.008; Spearman Rho). The ADC with the best Youden index (sensitivity: 84.6%; and specificity:73.3%) to detect reduced fCVR was 800.5 (AUC = 0.8; p = 0.008).
Conclusion: Reduced fCVR was strongly correlated with increased ADC in normal-appearing WM of centrum semi ovale. Thus, ADC may be used instead of acetazolamide challenge to detect patients with impaired cerebral perfusion at risk of cognitive disorders or stroke.

6 Vascular imaging

DIAGNOSIS OF CEREBRAL CIRCULATORY ARREST BY TRANSCRANIAL DOPPLER IN BRAIN DEATH

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Background: The diagnosis Brain Death (BD) can be made based on neurologic examination, apnea test, ancillary studies such as EEG, arteriography, or radionuclide scan. The accurate diagnosis of brain death is necessary for decision making in the critically ill patient, including assessing the need for continued mechanical ventilation and identifying candidates for organ donation. The use of Trancranial Doppler (TCD) to determine BD seems uncommon in most countries. The use of TCD to confirm BD has a sensitivity of 91-100% and specificity 97-100%. The diagnosis of cerebral circulatory arrest by TCD required the demonstration of no arterial or venous intracranial blood flow in the setting of reverberating flow and normal systemic hemodynamic status.
Aim: To evaluate the role of TCD in established BD.
Methods and Materials: TCD was used to confirm cerebral circulatory arrest, once BD was established clinically.TCD requires the presence of optimal bone windows and experienced operators. 152 consecutive cases clinically diagnosed as BD were evaluated by TCD during the period 2000-2010. TCD were performed within 2-24 hours from the clinical diagnosis of BD. The mean age was 62.8 years and there were 94 men and 58 women. The orbital, temporal and foraminal windows were insonated and both the depth and spectral pattern were obtained using a power M Mode TCD machine (Spencer Technologoies, USA).
Results: 143 patients showed features such as small systolic flow, absence of diastolic filling, reversal of flow during diastole and reverberating flow pattern in the major arterial trunks of the Circle of Willis. In 136 patients, the above pattern was consistently noted in the siphon, middle cerebral and Basilar arteries.
Conclusions: The positive predictive value was very high from the siphon, middle cerebral and basilar artery. TCD should be a first-line measure in the diagnosis of BD. TCD is a relatively inexpensive, rapid, bedside test to confirm the diagnosis of brain death. Decision making by relatives to declare patients BD, is enabled by TCD.

7 Vascular imaging

INCREASED LYMPHOCYTE-PLATELET COMPLEX FORMATION AS A MEASURE OF ENHANCED PLATELET ACTIVATION IN RECENTLY SYMPTOMATIC VERSUS ASYMPTOMATIC 'MICROEMBOLIC SIGNAL NEGATIVE' CAROTID STENOSIS PATIENTS-RESULTS FROM THE PLATELETS AND CAROTID STENOSIS (PACS) STUDY

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Introduction: Cerebral microembolic signals (MES) may predict increased stroke risk in carotid stenosis patients. However, the relationship between MES and

platelet activation status in symptomatic vs asymptomatic carotid stenosis has not been comprehensively assessed.

Methods: This pilot, observational analytical study compared MES and platelet activation status in early (≤4 weeks after TIA/stroke) and late phase (≥3 months) symptomatic versus asymptomatic moderate or severe (≥50%) carotid stenosis patients. Whole blood flow cytometry was used to quantify platelet surface activation marker expression (CD62P & CD63) and circulating leucocyte-platelet complexes. Bilateral simultaneous transcranial Doppler ultrasound monitoring of the middle cerebral arteries was performed for 1 hour to classify patients as MES+ve or MES-ve.

Results: Complete data were available in 31 early phase symptomatic, 27 late phase symptomatic (19 post-carotid intervention), and 25 asymptomatic carotid stenosis patients. 32% of early phase and 19% of late phase symptomatic patients vs 12% of asymptomatic patients were MES+ve (p ≥ 0.07). Early symptomatic MES-ve patients had higher % lymphocyte-platelet complexes than asymptomatic MES-ve patients (2.8 vs 2.3%; p=0.0085). Within the symptomatic subgroup, CD63 expression was lower in early phase MES+ve than MES-ve patients (5.88 vs 14.5%; p=0.0028), but higher in late phase MES+ve than MES-ve patients (12.8 vs 10.0%; p=0.023).

Discussion: Increased lymphocyte-platelet complex formation in recently symptomatic compared with asymptomatic MES-ve patients indicates enhanced platelet activation status in this early symptomatic subgroup. The lack of statistically significant differences in "MES positivity" between early symptomatic and asymptomatic patients may reflect a type II error. Larger longitudinal studies are needed to determine whether platelet biomarkers aid risk-stratification in patients with symptomatic and asymptomatic carotid stenosis

8 Vascular imaging

ROLE OF BIOLOGICAL MARKERS IN PREDICTING FINDINGS OF MULTIMODAL THROMBUS IMAGING: IMPLICATIONS FOR AETIOLOGY AND RECANALIZATION

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Background: Thrombi exhibit different characteristics on CT (hyperdense MCA "HDMCA" sign), CT angiogram (clot burden score) and gradient echo MR (susceptibility vessel sign "SVS"). These features may predict recanalization and underlying stroke aetiology. Their association with serum bio-markers is also unknown.

Methods: The study population was a cohort of patients with acute ischemic strokes included in the Keimyung Stroke Registry, Korea (2005-2009). Detailed clinical and biochemical data was collected prospectively. Imaging analysis was done at the University of Calgary.

Results: We included 264 patients with anterior circulation strokes (46% females, median age 68 years) who underwent intra-arterial "IA" stroke therapy (combined IV/IA in 115). All had NCCT, 94% had CTA and 92.4% had MRI before IA therapy. HDMCA was seen in 44.4% and SVS in 60%. Median clot burden score was 6. Compared to CTA, sensitivity and specificity of HDMCA sign was 47.2 and 81% and of SVS sign 65.5 and 75% in detecting thrombus. Correlation between HDMCA and SVS was fair (kappa 0.29, p 0.0001). In univariate analysis of potential source of thrombus, the presence of the SVS sign was associated with cardio-embolic source (OR 2, p 0.03) and its absence with underlying large artery disease (OR 0.34, p 0.011) whereas the presence of the HDMCA sign did not correlate with source of thrombus. In a multivariable analysis of biological markers, only platelet count > 250,000/uL (p=0.049) and WBC count>10,000/uL (p=0.014) predicted the presence of HDMCA sign. Only ESR>15 mm/hr (p=0.02) and decreasing stroke symptom onset to MR time (p=0.04) predicted SVS sign. Only small clot burden (score>5) predicted recanalization (TIMI 2-3) post IA procedure (OR 3.3, p 0.026).

Conclusion: Thrombi show diverse characteristics on different imaging modalities. The HDMCA sign may suggest a cellular platelet and WBC rich thrombus. The SVS sign may suggest a fibrin rich thrombus forming in an inflammatory milieu (raised ESR). Larger studies are needed to understand the clinical utility of multimodal thrombus imaging in acute ischemic stroke.

9 Vascular imaging

ASSESSMENT OF CEREBRAL PERFUSION BY MULTICHANNEL NEAR-INFRARED SPECTROSCOPY IN PATIENTS WITH SEVERE MIDDLE CEREBRAL ARTERY STENOSIS

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Background: In case of insufficient collateral circulation high-grade stenosis can result in hemodynamic instability and hypoperfusion-related cerebral ischemia in the anterior borderzone region between the anterior and middle cerebral artery. We investigated the cortical perfusion of this area utilizing multichannel near-infrared spectroscopy (NIRS) after injection of indocyanine green (ICG).

Methods: Twenty patients (mean age 52.3 years; 55% male) suffering from unilateral severe middle cerebral artery stenosis with a clinically asymptomatic course under antithrombotic medication at time of investigation were enrolled. Non-invasive NIRS examination (Hitachi ETG 4000) was performed using a 24-channel probe per hemisphere corresponding to the 10-20 EEG system. After application of an ICG bolus a semiquantitative analyses of the concentration was performed and its kinetics were compared to the unaffected hemisphere.

Results: We found a confined cortical area represented by 6 contiguous channels covering parts of the dorsolateral prefrontal cortex and frontopolar area to show a delayed transit of the ICG bolus. In this area, ipsilateral to the MCA-stenosis the bolus peak time (BPT, 95% CI 0.34-0.51, p<0.001), time to peak (TTP, 95% CI 0.28-0.44, p<0.001), rise time (p<0.042), and the maximal rise time (p<0.037) were significantly increased as compared to the contralateral hemisphere. In addition the slope (max ICG/TTP) and blood flow index (max ICG/rise time) showed interhemispheric differences (p<0.001). In contrast, in channels covering exclusively the anterior or middle cerebral artery distribution territory no significant differences were observed.

Summary: Our study suggests that spatial variations in cortical perfusion can be assessed by multichannel NIRS to an extent that might be of clinical relevance. Here ICG kinetics in patients with severe unilateral MCA-stenosis were found to be significantly delayed in an area associated to the anterior borderzone.

Clinical trials B

1 Clinical trials B

TENECTEPLASE VERSUS ALTEPLASE FOR ACUTE ISCHAEMIC STROKE: AN IMAGING BASED EFFICACY TRIAL

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Background: Alteplase (tPA) is of proven benefit for ischaemic stroke but has only around a 50% early recanalisation rate with proximal intracranial occlusions. Tenecteplase (TNK) is a genetically modified plasminogen activator that is more fibrin specific and has the potential to be a more effective lytic agent.

Methods: Acute ischaemic stroke patients with symptom onset<6 hours were randomised 1:1:1 to standard dose intravenous tPA (0.9 mg/kg) or 0.1 mg/kg TNK or 0.25 mg/kg TNK. TNK was given as a single bolus. Randomisation was in blocks of 15 patients with equal numbers in each group to allow (blinded) data safety monitoring every 15 patients with clearly defined stopping rules for excess symptomatic intracranial haemorrhage (sICH), parenchymal haematoma (PH), and death in any one group. Apart from the usual clinical inclusion/exclusion criteria for thrombolysis, all patients underwent advacned CT imaging with CT angiography (CTA) and CT perfusion (CTP) before randomisation. Advanced CT imaging criteria included an intracranial occlusion on CTA (anterior, middle or posterior cerebral artery), the presence of a perfusion lesion of at least 20†mL with>20% mismatch between mean transit time (MTT) lesion and CBV lesion, with a CBV infarct core<1/3 of middle cerebral artery territory. All patients had follow-up angiographic and perfusion imaging at 24 hours with the primary outcome being blinded measurement extent of reperfusion of the MTT lesion at 24 hours. Secondary outcomes included vessel recanalisation at 24 hours, early clinical improvement from acute to 24 hour National Institutes of Health Stroke Scale (NIHSS), and 3 month modified Rankin Scale, as well as the aforementioned safety outcomes. All outcomes were measured on de-identified data (imaging) or by observers blind to treatment (clinical).

Results: There were no safety concerns at each of the 15 patient recruitment points. Recruitment is now complete with 75 patients randomised at three Australian University Hospitals. Three month follow-up is ongoing. Final results will be presented at the European Stroke Conference May 2011.

2 Clinical trials B

IMPACT OF STROKE, MYOCARDIAL INFARCTION, CRANIAL NERVE PALSY AND ACCESS SITE HAEMATOMA, ON SHORT-TERM DISABILITY IN THE INTERNATIONAL CAROTID STENTING STUDY (ICSS)

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Background: ICSS (ISRCTN25337470) is a randomised trial comparing carotid stenting (CAS) to endarterectomy (CEA) for symptomatic carotid stenosis. On the outcome measure of stroke, myocardial infarction (MI) or death within 30 days of treatment, CEA was safer than CAS, mainly due to an excess of non-disabling strokes after CAS. There was no significant difference in the rate of disabling stroke or death. We hypothesised that the impact on disability at one month of non-disabling stroke after CAS would be counterbalanced by a greater incidence of non-stroke complications after CEA.
Methods: Disability in ICSS was measured using scores on the modified Rankin Scale (mRS) at randomisation and at 30 days after the procedure. Non-disabling stroke was defined by mRS<3 at 30 days. We performed a per-protocol analysis of the proportion of patients experiencing "minor" outcome events (non-disabling stroke, MI, cranial nerve palsy and access site haematoma) comparing CEA with CAS. We also compared the overall proportions of patients showing an increase in Rankin score (indicating worsening of disability) at 30 days.
Results: 821 patients underwent CEA and 828 CAS, per-protocol. Significantly more patients receiving CEA (93, 11.6%) had a minor outcome event than those receiving CAS (63, 7.9%, P<0.05, Chi square test). Of these, 23 (2.8%) CEA and 17 (2.1%) CAS patients had an increase in mRS at 30 days (NS). Among all the patients receiving treatment, 41 (5.0%) of CEA patients and 43 (5.2%) of CAS patients had a disabling stroke, died or had a minor event with an increase in Rankin score (NS).
Conclusion: The impact of an increased rate of stroke after CAS was balanced by an increased rate of minor outcome events after CEA. The number of patients in ICSS with an event leading to death or worsening of disability one month after treatment did not differ between CEA and CAS. Measures of disability should play a greater part in the comparison of CAS with CEA.

3 Clinical trials B

EFFECTS OF SYSTOLIC BLOOD PRESSURE AND ITS VARIATION ON SUBSEQUENT STROKE IN PATIENTS WITH ISCHAEMIC STROKE DURING ANTIPLATELET THERAPY: A SUB-ANALYSIS OF THE J-ASAP STUDY

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Background: The Japanese Aggrenox Stroke Prevention vs. Aspirin Programme (JASAP) study was a double blind randomised clinical trial to compare the efficacy and safety of extended-release dipyridamole plus aspirin versus aspirin alone over 1 year in 1294 patients with non-cardioembolic ischaemic stroke. We analysed the effect of blood pressure and its variation on recurrence of ischemic stroke and occurence of intracranial hemorrhage (ICH) in patients enrolled in the J-ASAP study.
Methods: We analysed individual blood pressure at all visits including baseline, weeks 0, 1 and then every 4 weeks to a maximum of 124 weeks to compare mean systolic blood pressure (SBP) and standard deviation (SD) of variations of individual SBP measurements between patients with and without recurrence of ischaemic stroke or ICH.
Results: Mean SBP was significantly higher in patients with than without ischaemic stroke (141.08 mmHg vs. 137.29 mmHg, p=0.0079), while SD of variation of individual SBP measurements was significantly larger in patients with than without ICH (14.46 mmHg vs. 12.20 mmHg, p=0.0024). There was no significant difference in mean SBP between patients with and without ICH (139.38 mmHg vs. 137.47 mmHg, p=0.4280) or in SD of variations of individual SBPs between patients with and without ischaemic stroke (12.82 mmHg vs. 12.21 mmHg, p=0.1653).
Conclusion: Mean SBP was higher in patients with than without recurrence of ischaemic stroke, while SD of variation of individual SBPs was larger in patients with than without ICH among the J-SAP population.

4 Clinical trials B

THE RISK OF OCCLUSION AND ASSOCIATED EVENTS IN THE ASYMPTOMATIC CAROTID SURGERY TRIAL: 10 YEAR FOLLOW-UP ANALYSIS

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Objective: This study analyzes the risk of occlusion and associated neurological events in patients with severe asymptomatic carotid artery stenosis included in the Asymptomatic Carotid Surgery Trial-1 (ACST-1) trial.
Methods: In ACST-1, 3120 patients were randomised between immediate carotid endarterectomy (CEA) or deferral. During the study period (1993-2008), we studied patients who developed a new occlusion of their internal carotid artery and we evaluated the associated neurological events. Patients with contralateral occlusion at baseline were excluded from analysis. Kaplan-Meier analysis was performed to estimate freedom from occlusion and occlusion related stroke-free survival. Cox proportional hazard regression models were used to determine risk factors for the development of occlusion and related stroke.
Results: Mean follow-up in ACST-1 was 80.8 months (range 0 -165 months). During follow-up the mean time to occlusion was 32.9 months (SD 30.2). The likelihood of occlusion was significantly greater (log rank: p<0.01) in the deferred group. Risk of symptomatic occlusion after 5 and 10 years was lower in the immediate versus deferred groups.
Conclusion: Occlusion was commoner and overall stroke-free survival significantly lower in the group of patients allocated deferral of CEA. Occlusion itself is not an independent risk factor for stroke.

5 Clinical trials B

THE QASC CLUSTER RANDOMISED CONTROLLED TRIAL OF A TEAM-BASED INTERVENTION TO IMPROVE MANAGEMENT OF FEVER, HYPERGLYCAEMIA AND SWALLOWING DYSFUNCTION IN ACUTE STROKE: PATIENT 90-DAY OUTCOMES

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Background: The Quality in Acute Stroke Care (QASC) study, a cluster randomized controlled trial examined the effect on death, disability and dependency of a multidisciplinary intervention to improve management of fever, hyperglycaemia and swallowing dysfunction following acute stroke in NSW, Australia.
Methods: Patients from 19 Australian acute stroke units (ASUs) were recruited; pre and post intervention. ASU's were randomised to intervention (n=10) or control (n=9). Intervention ASUs received evidence-based clinical treatment protocols for the management of fever, hyperglycaemia and swallowing dysfunction, in conjunction with multidisciplinary team building workshops, a standardised staff education program and engagement of local stroke unit coordinators. Control ASUs received an abridged copy of the Australian acute stroke guidelines relevant to fever, hyperglycaemia and swallowing management. Patient outcome data were obtained via a 20 minute computerized assisted telephone interview 90-days post-admission. Intention to treat analysis was used adjusting for baseline data and clustering.
Results: A total of 1699 patients participated; 690 pre-intervention and 1009 post-intervention. Patients from control-group ASUs were significantly more likely to be dead or disabled at 90-days (mRS>2) than patients from intervention ASUs (58% vs 42%; P=0.006) and to have lower SF-36 physical health scores (mean 42.5 vs 45.6; P=0.002).
Conclusion: This is a landmark study demonstrating a 16% absolute improvement in death or disability at 90-days for patients who received care in ASUs delivering the multidisciplinary intervention. It provides compelling evidence that multidisciplinary care to manage fever, hyperglycaemia and swallowing dysfunction can decrease death, disability and improve health status.

THE QASC CLUSTER RANDOMISED CONTROLLED TRIAL OF AN INTERVENTION TO IMPROVE MANAGEMENT OF FEVER, HYPERGLYCAEMIA AND SWALLOWING DYSFUNCTION IN ACUTE STROKE: DID CLINICIAN BEHAVIOUR CHANGE?

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Background: Fever, hyperglycaemia and swallowing dysfunction post-stroke are associated with poor outcomes. Using a cluster randomized control trial design we evaluated the effect of a behaviour change intervention to improve management of these factors after acute stroke.

Method: 19 acute stroke units (ASUs) in NSW, Australia were randomized. Intervention ASUs received 3 evidence-based clinical treatment protocols for the management of fever (temperature$\geq$37.5 C), hyperglycaemia (glucose>11mmol/L) and swallowing dysfunction for the first 72 hours; multidisciplinary team building workshops; a standardised education program; and engagement of local stroke coordinators. Control ASUs received an abridged copy of the Australian acute stroke guidelines relevant to fever, hyperglycaemia and swallowing management. Participants were those with ischaemic stroke or intracerebral haemorrhage prospectively admitted to within 48 hours of symptom onset. Patients' medical records were audited for all instances of fever, hyperglycaemia and swallow screen. Intention to treat analysis was conducted adjusting for baseline data and clustering.

Results: Data were collected for 1,817 patients. At baseline, over three quarters of febrile patients (79%) did not receive paracetamol at first febrile event; two thirds (67%) of hyperglycaemic patients did not receive insulin and three quarters (76%) did not receive a swallow screen. Non-diabetic patients were significantly more likely to have no glucose readings within the first 72 hours when compared with diabetic patients (P<0.05). Final analysis of the effectiveness of the intervention on clinician behaviour currently is being undertaken and will be presented.

Conclusion: Identification of an effective behaviour change intervention to improve the management of fever, hyperglycaemia and swallowing dysfunction in acute stroke is warranted. We provide robust trial evidence of the effectiveness of an intervention to address this priority.

THE MISTIE TRIAL: SURGICAL PERFORMANCE RESULTS FROM TIER I AND TIER II

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Background: We report results of safety, efficacy, and surgical performance for the "Minimally Invasive Surgery plus t-PA for Intracerebral Hemorrhage Evacuation" (MISTIE) trial, which has completed the first two surgical tiers.

Methods: The protocol assessed safety, efficacy and surgical performance, including accuracy of catheter placement and volume reduction at the end of treatment.

Results: 40 subjects were randomized to minimally invasive surgery (MIS) plus t-PA (n=29) or medical therapy (n=11). This population was 53% male, average age 62 ± 11 yrs, with 58% basal ganglia/42% lobar locations. At presentation, the clot size was: ICH, 45†mL ± 20; IVH, 3†mL ± 6; with functional levels of Glasgow Coma Scale 11 ± 3 and NIH Stoke Scale 23 ± 7. The safety profile for the surgical group was within specified thresholds. Mortality levels at 7 days and 30 days were 0% and 10.5%, respectively. Rebleeding was observed in 10.5% of subjects, and there were no instances of brain infection. Clot removal rates were 19%/day for subjects receiving 0.3 mg, and 16%/day for 1.0 mg. Removal rates for the treatment groups were significantly higher than in medical subjects (1%/day). A strong correlation between accuracy of catheter placement and resulting residual clot volume at the end of treatment was demonstrated (R2=0.61). Subject demographics, clot location, and duration of treatment do not appear to affect this relationship. Logistic regression revealed baseline factors (GCS and NIHSS) and ICH/IVH clot volumes at presentation and end of treatment were predictors of good functional outcome (modified Rankin 0-3) at 180 days. Surgical extraction of clot was associated with mRS 0-3 (Odds Ratio 2.2 /10 cc remaining; p=0.03).

Conclusions: MIS appears safe compared to medical therapy and provides for removal of clot without craniotomy. Excellent neurosurgical performance for catheter localization is critical to optimizing removal of intracerebral hemorrhage. Removal of clot may benefit MISITE ICH patients. Trials of MIS will require close monitoring of procedural process and variation of surgical performance, if the effect of clot removal on outcome is to be fully tested.

Brain imaging

46 Brain imaging

AMYLOID DEPOSITION REVEALED BY 11CPIB–PET FOLLOWING ACUTE ISCHAEMIC STROKE

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Background: Stroke increases the risk of cognitive impairment. The exact mechanism remains uncertain. Alzheimer's disease (AD) and Vascular Cognitive Impairment (VCI) are the commonest forms of cognitive impairment. They share risk factors and have considerable clinical and pathological overlap. There is also evidence that vascular pathology may have a causative and additive effect on amyloid deposition, the pathological hallmark of AD. Using 11CPiB-PET enables assessment of amyloid deposition. We hypothesised that an acute ischemic stroke may trigger amyloid deposition and cause an increase in 11CPiB retention.
Method: Eligible patients admitted with stroke underwent an MRI scan to determine stroke characteristics and for anatomical co-registration. This was followed by an 11CPiB-PET scan within 21 days of the stroke. Where possible, repeat scans were performed at intervals ranging from 2 weeks to one year. Analysis of scans was based on standard uptake value ratio (SUVR) of regions of interest using the cerebellar cortex as reference region. A ratio exceeding 1.4 was considered high.
Results: 50 patients underwent PET scans. 34 were male; mean age was 69.9 years (range 42-87). On initial scan 16 patients showed high PiB retention in the region of the stroke. 15 of these patients showed varying degrees of haemorrhagic transformation in the same region. Follow-up scans in 6 of these patients showed no sign of regional 11CPiB retention. Follow up scans were also performed in 9 patients whose initial scan was normal. The repeat scans showed no significant change compared to baseline.
Conclusion: After acute ischaemic stroke there may be focal increase in 11CPiB retention. The normalisation of the phenomenon on repeat scan suggests that this was likely due to extravasation of 11CPiB secondary to reduced blood brain barrier integrity rather than the triggering of amyloid deposition.

47 Brain imaging

MRI BIOMARKERS AND THEIR PREDICTION OF MORTALITY IN A HEALTHY ELDERLY POPULATION

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Background: Brain atrophy and vascular brain lesions are common in older people evaluated by cerebral MRI. The aim of the present study was to evaluate the predictive value of MRI abnormalities frequently found in elderly subjects with respect to all-cause mortality.
Methods: MRI was performed in 268 participants of the MEMO Study. Silent stroke was defined dichotomously as the presence of a hypointense (T1) or hyperintense (T2, proton density) lesion of 3mm. White matter hyperintensities were measured semiquantitatively as the number of hyperintense lesions in the deep white matter summarized over all brain lobes assessed by proton density-weighted and T2-weighted images. Cortical atrophy was assessed on a semiquantitative scale with 4 categories of increasing atrophy (0-3) applied to each lobe and to the Sylvian fissure. The lobar scores were summarized to a total cortical atrophy score with a range from 0 (no atrophy) to 15 (maximal atrophy). Biventricular atrophy was assessed as the ratio of the biventricular width divided by the width of the brain at the level of the frontal horns. Vital status of the participants and causes of death of those who had died during the 10-year follow-up (1997-2007) were documented.
Results: The median age of participants was 72 years (69-76) with 48% being female. Among the participants, 77 (29%) died. The cumulative survival time was 2305 person years with a median survival of 9.8 (8.5 – 10.06) years. On performing Cox proportional hazard analyses for the 4 predictors of interest, only atrophy was significantly associated with mortality with a hazard ratio of 1.15 (1.04 – 1.27, p=0.0087), before and after adjustment for age, sex, and cardiovascular risk factors and morbidity.
Conclusion: Cortical atrophy assessed by MRI is a marker of all-cause mortality in an elderly German population adding to the predictive value of traditional cardiovascular risk factors. There was no significant effect of the other MRI measures on mortality.

48 Brain imaging

ESTIMATION OF ISCHEMIC LESION AGE BY MAGNETIC RESONANCE IMAGING: DOES DWI HAVE FLAIR?

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Background: In stroke patients with hyperintense lesions in diffusion weighted imaging (DWI), negative fluid-attenuated-inversion recovery (FLAIR) imaging may allow for the estimation of an early ischemic lesion age (i.e. <4.5 h). However, visual and automated analysis of FLAIR images is challenging compared to DWI. We tested the hypothesis that hyperintense lesions in FLAIR imaging can be predicted by an intensity threshold in DWI.
Methods: In a retrospective analysis we included DW and FLAIR images of ischemic stroke patients with a symptom onset <9 hours and a proven DWI lesion. After coregistration, the slice representing the largest extent of the DWI lesion was identified. In the corresponding FLAIR image the hyperintense area was defined by a region of interest (ROI). This FLAIR-ROI was mirrored to the DWI image. 7 mm circular ROIs were placed in the DWI lesion (DWI-ROIs) and labeled according to the FLAIR pattern (FLAIR-positive or FLAIR–negative). The ability of relative DWI intensity values (compared to a ROI of the unaffected MCA territory) to predict FLAIR hyperintensity was tested by receiver-operating-characteristic (ROC) analysis.
Results: In 12 patients (mean age 57 a, mean time stroke-to-MRI: 176 min) 45 DWI-ROIs were classified as FLAIR+ and 52 as FLAIR-. ROC analysis identified the DWI threshold of 160% to predict FLAIR hyperintensity with a sensitivity of 88%, a specificity of 77%, a positive-predictive-value of 77% and a negative-predictive-value of 87% (area-under-the-curve: 0.82).
Conclusion: In this pilot study we found that low DWI intensities may predict the absence of FLAIR lesions, possibly allowing for the identification of an early lesion age by DWI alone. These Results are promising and lay the groundwork for the analysis of a larger multicenter sample using a voxel based semiautomated approach.

49 Brain imaging

MAGNETIZATION TRANSFER IMAGING AND POST-STROKE FUNCTIONAL DISABILITY

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Introduction: Correlation between post-stroke disability evaluated one month post-stroke and final cerebral infarct volume measured on T2/FLAIR MRI sequences at

the same time is moderate. The aim of the present study was to assess a possible association between the intensity of cerebro-vascular microstructural lesions identified on magnetization transfer imaging and functional handicap measured at one month post-stroke.

Methods: Patients with mild to moderate first ever stroke recruited in the VIRAGE multicenter study were included. In these patients a brain MRI was performed before the twelfth hour after symptoms onset (T1), between day 3 and 5 (T2) and between day 30 and 45 (T3) after stroke. At T3 magnetisation transfer imaging sequences were acquired in 58 patients. Magnetization transfer ratio was measured in the area abnormal on initial T1 diffusion imaging. Correlation between different MTR parameters (mean, standard deviation, peak and variation coefficient) and functional prognosis evaluated on modified rankin scale (mRS) were calculated using univariate and multivariate logistic regression.

Results: On univariate analysis, mRS > 2 measured 30 to 45 days after stroke was found to be correlated to initial NIHSS severity, thrombolysis, MTR peak, MTR standard deviation and MTR variation coefficient. In a model including sex, thrombolysis, initial NIHSS severity, diffusion volume measured at T1, final infarct volume measured at T3 on FLAIR and MTR parameters, multiple regression analysis identified initial NIHSS severity (OR = 1.23 CI95% 1.07-1.41; p = 0.01) and MTR peak (OR = 0.86 CI95% 0.75-0.98; p = 0.02) as the only variables independently associated to disability.

Conclusion: Brain microstructural evaluation following stroke could improve the correlation between imaging data and functional handicap 30 to 45 days post-stroke. Magnetization transfer imaging could be used as a surrogate marker in the evaluation of acute stroke treatments efficacy.

50 Brain imaging

INVERSE PWI/DWI MISMATCH IN SUBCORTICAL ISCHEMIC STROKE

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Background: Perfusion weighted imaging (PWI) and diffusion weighted imaging (DWI) are the basis of stroke MRI. In acute territorial infarcts the mismatch region (PWI-DWI) has been used as an operational definition of the ischemic penumbra. In small subcortical ischemic stroke, however, we have previously shown (Doege et al. AJNR 2003, Fiebach et al. Eur Radiol 2010) that the area of diffusion disturbance can be larger than the area of perfusion drop ("Inverse Mismatch"). These reports were based on relatively few patients examined at 1.5 T. Here, we aimed at clarifying the occurrence of different pathophysiological patterns in acute subcortical stroke in a prospectively recruited larger sample.

Methods: In 112 patients (median age: 71 y, range 21 – 95 y, 40 females) with subcortical ischemic stroke, MRI was performed within 24 h of symptom onset. MRI protocol (Siemens 3 T, TIM Trio) included DWI (TR 7600 ms, TE 93 ms, b 1000,0), bolus track PWI (TR 1390 ms, TE 29 ms, FA 60°), FLAIR. In 60 patients follow-up examination within 24 h was performed. We classified as "Mismatch" when the PWI was by 20% larger than the DWI, as "Inverse Mismatch" when the PWI was by 20% smaller than the PWI, other patients were classified as "Match".

Results: Infarctions were located in the thalamus (45), in the ACHA territory (43), lenticulostriate arteries (15), deep penetrating arteries of white matter (9). Of 112 patients, 94 showed an IM on admission MRI (84%), a mismatch was seen in 7 subjects, 11 were classified as "match". Findings for 60 subjects with follow-up scans are given in Table 1.

Table 1

	Inverse Mismatch	Match	Mismatch
Admission	53	5	2
Day 1	57	1	2

Conclusion: 84% of patients with small subcortical ischemic stroke showed an "Inverse Mismatch" pattern on admission. We hypothesize that this may be due to the lack of collaterals in small subcortical stroke. However, other patterns also occur. It seems likely that different pathophysiological patterns have different therapeutic and prognostic implications.

ANALYSIS OF CEREBRAL VASOREACTIVITY OF PATIENTS WITH SEVERE UNILATERAL CAROTID STENOSIS USING FUNCTIONAL MAGNETIC RESONANCE IMAGING

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Background and purpose: Previous transcranial Doppler studies have suggested that, in patients with severe carotid stenosis, an exhausted hemodynamic reserve (HR) is an independent predictor of stroke. Otherwise functional magnetic resonance imaging can assess the HR on the microvascular vessels by comparing the BOLD (Blood Oxygen Level Dependent) contrast signal in cerebral cortex during hypercapnia and normal condition. The purpose of this study is to quantify the parameters from the BOLD signal induced by auditory stimulus, during normo and hypercapnia in patients with severe unilateral carotid stenosis and to compare the BOLD signal from the ipsilateral hemispheres (IH) and contralateral hemispheres (CH).

Methods: The images were obtained from 12 patients with severe carotid stenosis. Patients were submitted to an auditory stimulus (3s) in three different conditions: normocapnia and EtCO2 increase of 5 and 10mmHg. The images were acquired with a 3T Philips MR, preprocessed and analyzed using an autoregressive method.

Results: The BOLD signal from the IH was different from the CH during the basal condition and at 5mmHg (p<0.0001), but not at the 10mmHg ETCO2 increase. For each BOLD parameter, the major differences between the hemispheres were the onset time (p<0.0001) and amplitude of BOLD signal (p<0.0001). Hence, in both parameters the IH presented no significant variations with the CO2 increment. However, the BOLD signal for CH showed an increase on the time-to- onset and amplitude decrease (p<0.0001). The width and time to peak parameters of the BOLD signal showed no differences between the hemispheres and at hypercapnic conditions.

Conclusion: The Results demonstrate that, among patients with severe carotid stenosis, BOLD fMRI can reliably identify some that have an exhausted ipsilateral hemisphere HR, which cannot respond to a vasodilatory stress like hypercapnia. Future studies should address if those patients also have an additional risk of stroke.

52 Brain imaging

VALUE OF MTT TO PREDICT INFARCTION WITHIN THE DWI LESION: IMPACT OF PRE-SCAN REPERFUSION

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Introduction: In the mismatch model, the DWI lesion is assumed to represent the irreversible core, yet may permanently revert after reperfusion. Whether PWI helps determine infarction risk within DWI lesions is therefore a key issue. Recently we found that MTT adds significantly to infarct prediction within DWI lesions (Carrera, Stroke in press). Since part or whole of the DWI lesion may have already reperfused at time of DWI/PWI (Olivot, RADAR), here we determined the impact of pre-scan reperfusion on the predictive value of MTT.

Methods: Patients from the I-KNOW database had DWI/PWI <12hrs of stroke onset and structural MR <1mo later to map the infarct. Eligibility for this voxel-based study also required infarct and DWI lesion ≥1 8x8x8 mm Voxel-of-Interest (VOI). Among DWI positive (DWI+) VOIs, prescan reperfusion was defined as MTT < mean contralateral MTT + 2SDs. ROC curves were used to determine the predictive value of MTT for infarction separately for reperfused and non-reperfused DWI+ VOIs using AUCs and standard Optimal threshold (OT).

Results: 42 pts were eligible (68±12yrs; NIHSS 12±3; MRI <6hrs in 36/42). Across pts, there were 844 and 1164 reperfused and non-reperfused DWI+ VOIs, respectively, of which 57% and 67% infarcted (p<0.001). There was no significant difference in mean AUC between reperfused and non-reperfused VOIs (0.604 vs 0.615, respectively; p= 0.34), and both AUCs were significantly greater than neutral 0.5 As expected, the OT across pts was shorter among reperfused vs non-reperfused VOIs (7.4s±2.5 vs 13.6s±3.2; p<0.001).

Conclusion: These Results show that MTT is a significant, albeit only fair, predictor of final infarction within the DWI lesion, regardless of prior reperfusion. Thus, incorporating information from PWI improves prediction of tissue outcome within DWI lesions, whether already reperfused or not. That distinct MTT thresholds prevailed will have to be taken into account in future probabilistic voxel-based multilinear models.

53 Brain imaging

ADVANCED NEUROIMAGING AND COGNITION IN PATIENTS AFTER CAROTID ENDARTERECTOMY

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Background: Carotid endarterectomy artery (CEA) decreases the risk of suffering a stroke. However, the effects of CEA on cognition, brain methabolism and perfussion continue to be controversial. Our aim was to evaluate these items with functional neuroimaging and neuropsychological tests.
Methods: We included 17 patients, 10 men and 7 women, scheduled for CEA, mean age of 65, with severe unilateral asymptomatic carotid stenosis, or symptomatic stenosis but with no acute lesion in MRI (TIA, amaurosis fugax). We performed regular neurological studies, adding 18-FDG PET, HMPAO-SPECT and neuropsychological evaluation before and three months after surgery. We performed a voxel-by-voxel analysis and regions of interest (ROI) analysis using SPM5 and WFU-Pickatlas toolbox software for SPM version to analyse image studies and to compare basal and post-CEA images. The SPM maps were obtained using a cluster and voxel level threshold of p<0.05 corrected by False Discovery Rate. We analysed neuropsychological studies by t-paired test (p<0.05, SPSS v.15.0).
Results: 10 patients were underwent CEA of left carotid stenosis and 7 of right carotid stenosis. All patients presented with several vascular risk factors. A statistically significant improvement in 18FDG uptake was found on voxel-by-voxel and ROI analysis in occipital lobes, left cerebellum and right inferior temporal lobe of patients scheduled for left CEA in PET study. A statistically significant improvement in cerebral perfusion was found on voxel-by-voxel and ROI analysis in contralateral occipital lobe in the same group. Neuropsychological studies showed a significant improvement in verbal domains caused by proactive interference between newly learned tasks with old material in patients undergoing left CEA. Differences were maintained after excluding patients with recent TIA.
Conclusion: There was a mild improvement in metabolism and perfusion in posterior regions, and in verbal domains after CEA.

54 Brain imaging

METHOD FOR DETERMINING INFARCT GROWTH SIGNIFICANTLY INFLUENCES THE MEASUREMENT OBTAINED

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Background: Putative infarct core can be measured using CT perfusion (CTP) according to proposed viability thresholds. Limited brain coverage means not all of the final infarct volume will be covered by CTP. Image co-registration permits growth of putative infarct core to be measured in corresponding slices on follow-up imaging.
Methods: Acute CTP was obtained in a series of suspected stroke patients. Core was defined as cerebral blood volume (CBV) pixels <2.0ml/100g. Follow-up imaging was manually co-registered to baseline CTP images using commercially available software. Infarct growth was measured first by subtracting total putative core volume from final infarct volume in the corresponding co-registered slices (termed "simple growth"). Growth was also measured for each slice of the perfusion scan individually, where only those core pixels that appeared within the final infarct volume were subtracted from the coregistered slices infarct volume (co-reg growth). False positive core volume, representing pixels below a CBV threshold of 2.0ml/100g that did not subsequently proceed to infarction was also

recorded. Differences in infarct growth measurement method were compared with a paired t test.
Results: 52 patients with suspected acute stroke had non-jog CTP at baseline and follow up imaging with CT or MRI (n=13 and 39 respectively). 2 patients had intracerebral haemorrhage precluding infarct volume measurement. Infarct growth was significantly greater when measured slice by slice (mean simple growth =4.5ml, SD 20.3, mean co-reg growth 10.8ml SD 19.2 p= <0.05). Mean false positive "core" volume was 6.3 ml SD 10.2.
Conclusion: Thresholded perfusion lesions which represent putative infarct core can be reversible. Accounting for this reversibility requires more complex image post-processing. As lesion growth has been used as an outcome measure in clinical trials, the method employed could crucially influence measured outcomes.

55 Brain imaging

EVALUATION FOR 'SILENT' NEURONAL LOSS USING 3T MR SPECTROSCOPY IN PATIENTS WITH CHRONIC OBSTRUCTION OF INTRACEREBRAL MAIN ARTERY

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Background: In general most of patients with chronic obstruction of an intracerebral main artery do not express any neurological symptoms, however, it has been recently verified that incomplete "silent" neuronal loss due to chronic ischemia can exist even if there is not any change in neuroradiological images. Thus we have tried whether that incomplete neuronal loss can be diagnosed or not using 3T MR spectroscopy.
Methods: Twelve patients with the obstruction of internal carotid or middle cerebral artery who underwent MR spectroscopy using 3T MRI (SIGNA HDxt: GE) were enrolled in this study, where mean age was 72.1±8.1 years old and sex ratio was male 6 to female 6. On a metabolic map obtained from MR spectroscopy 2 ROIs (region of interest) were put on the coronal radiation in both lesion and healty sides, in which each absolute value of NAA (N-Acetyl-Aspartate), Creatine (Cr), and Choline (Cho) were measured. As a candidate indicative of neuronal loss 3 parameters of NAA absolute value, NAA/Cr, and NAA/Cho were set out and compared between lesion and healthy side. Moreover, value of cerebral blood flow (CBF) in MCA territory was measured in both sides.
Results: There was not any significant difference between both sides in NAA absolute value and NAA/Cr, meanwhile the value of NAA/Cho in lesion side was significantly lower than that in healthy side (p<0.05), besides no significant difference was observed between both sides of CBF value.
Conclusion: Data from this study may imply that 3T MR spectroscopy can diagnose a "silent" neuronal loss in patients with chronic obstruction of an intracerebral main artery.

56 Brain imaging

PERFUSION CT PREDICTS SUBSEQUENT TISSUE AND CLINICAL OUTCOME IN HYPERACUTE ISCHEMIC STROKE

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Background: The clinical utility of acute stroke Computed Tomography Perfusion (CTP) is still under investigation.
Methods: Acute ischemic stroke patients who were admitted to hospital within 6 hours of symptom onset were scanned using multimodal CT. Patients were reimaged with diffusion MR at 24 hours. Acute and 24 hour NIHSS scores as well as a 90 day mRS were recorded and correlated with CTP measures of tissue pathophysiology. CTP defined the acute perfusion lesion using a threshold of Tmax >2seconds, and the acute infarct core defined within this Tmax>2s lesion using a threshold of CBF <50% (and using a delay correction algorithm).
Results: 314 stroke patients admitted to hospital within 6 hours of symptom onset were studied. Patients with major reperfusion at 24 hours (defined as >80%) had a median acute and follow-up NIHSS of 13 and 6 respectively, and a median 90 day mRS of 2. Patients without reperfusion (defined as <20% at 24 hours) had a median and follow-up NIHSS of 16 and 12 respectively and a median 90 day mRS of 5 (p=0.049).
Acute NIHSS was strongly correlated with CTP-defined perfusion lesion (Tmax >2sec; r2 0.71, p=0.001). Additionally, the volume of the CTP penumbra (Tmax >2 secs, CBF >50%) not progressing to infarction at 24 hours was also correlated with

acute to 24 hour NIHSS improvement (r2=0.59 p=0.04), as well as with 90 day mRS (r2=0.62, p=0.06). Using the CTP-defined penumbral and infarct core thresholds, patients with a large (>25mL) acute infarct core showed less improvement in acute to 24 hour NIHSS (median improvement 4, IQR 1-6, p=0.048), than those with core <25 mL (median improvement 8, IQR 5-11, p=0.031). Those with a baseline infarct core >25 mL also had poorer recovery at day 90 than those with baseline core <25 mL (median mRS =5 and 2 respectively, p=0.039).

Conclusion: CTP can be reliably used to predict likely tissue and patient outcome with and without subsequent reperfusion. Further, this study provides strong clinical validation of CTP, as salvage of CTP defined penumbra from progression to infarction predicts clinical recovery and a large CTP-defined infarct core predicts poor patient outcome.

57 Brain imaging

T2-ARTERIAL SPIN LABELING (ASL) PERMEABILITY IMAGING IN A PATIENT WITH ACUTE TERRITORIAL BRAIN ISCHEMIA

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Background: Knowledge about water permeability in acute ischemic brain areas is scarce. The common assumption is that permeability of the capillaries is increased in these areas due to ischemic cell death. However quantification of such water exchanges between capillary and extra-capillary space with routine magnetic resonance imaging (MRI) is not established.

Methods: Three healthy volunteers and one patient with acute cerebral ischemia were investigated with a new T2-ASL sequence to measure cerebral water permeability, additional conventional T1 imaging with contrast agent (T1-gad) was performed on a 3-Tesla scanner. After verification of the method in the healthy subjects, the patient with acute infarction in the PCA territory was further evaluated: a visual analysis of the T1-gad and the T2-ASL images was performed evaluating the congruence of contrast-agent signal and hypointense areas on T2-ASL. In a second step a region of interest (ROI) was fitted on the hypointense T2-ASL area and the corresponding contralateral intact brain area. The water transit-time was calculated for both regions.

Results: Comparison of T1-gad signal and T2-ASL hypointense signals in the stroke patient showed a high congruence defining the affected area. A significant decrease of the water-transit-time was found for the ischemic area (intact side 790±190ms (mean ± SD); ischemic area 30±10ms; p<0.05) reflecting an increased permeability (figure).
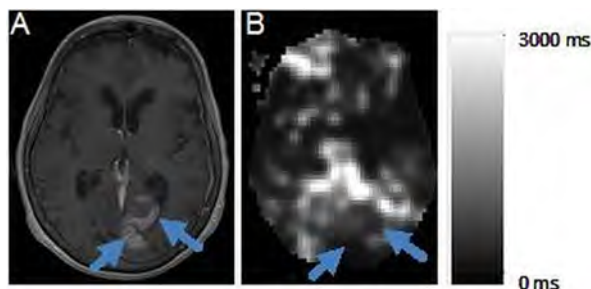
Figure: (A) Conventional T1-weighted imaging with contrast agent illustrating a disrupted blood-brain barrier im the ischemic left PCA-territory. (B) The corresponding T2-ASL imaging shows a hypointense signal in projection of the ischemic area reflecting a faster water-transit time (and therefore a higher permeability).

Discussion: We present a new T2-ASL sequence which can be used to detect and quantify the water permeability in ischemic brain areas. Detection and quantification of water permeability at different time points after ischemic stroke might help to better understand the ongoing mechanisms of blood-brain-barrier disruption and restorage. This might be of interest to evaluate the risk for hemorrhagic transformation depending on an increased permeability.

58 Brain imaging

SPATIAL DISTRIBUTION OF MTT VALUES IN ACUTE ISCHEMIC STROKE

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Background: MR diffusion-(DWI) and perfusion-weighted imaging (PWI) are commonly used in acute ischemic stroke to identify the infarct core and penumbra, based on different perfusion impairment levels. Anyhow, severity of perfusion impairment is not consistent within the penumbra. The aim of this work was to analyze the centripetal evolution of perfusion impairment from infarct core to the periphery of the ischemic region using the mean transit time (MTT) parameter.

Methods: 25 datasets of acute stroke patients with an MRI examination within the first 6 hours after symptom onset and after 24-36h including DWI, Time-of-flight (TOF) angiography and PWI images were analyzed. MTT maps were calculated from the PWI data and coregistered to the DWI images, in which the infarct core was segmented. Using this segmentation, 15 increasing concentric 3D shells with a thickness of 7mm, were computed and used to determine the mean MTT in each shell. The patients were dichotomized due to recanalization information derived from TOF images.

Results: A significant difference (p=0.02) in skewness of curves describing the distribution of the mean MTT values from infarct core to periphery between patients with (s=0.65) and without (s=-0.21) recanalization was found. There was no significant difference in absolute MTT values in any shells. Nevertheless, MTT values in patients with recanalization tend to be higher in all shells surrounding the infarct core as in those that did not recanalize.

Conclusion: Our Results suggest that patients with and without recanalization exhibit different evolutions of MTT values from infarct core to periphery. Therefore propensity for macrovascular rekanalisation seems to be dependent not only on the clot properties but also on perfusion conditions in the distal microvascular bed. This 3D approach might enable a characterization of acute ischemic strokes by different perfusion parameters on a more pathophysiological basis.

59 Brain imaging

DEFINITIONS OF ISCHEMIC TISSUE REGIONS IN CT AND MT PERFUSION IMAGING STUDIES ARE VERY INCONSISTENT

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Background: Magnetic resonance (MR) and computed tomography (CT) perfusion imaging is widely used in studies of acute ischaemic stroke to identify tissue at risk of infarction, but the reported perfusion values for at risk tissue vary between studies. Differences in definitions of tissue at risk might be contributing to this uncertainty.

Methods: We systematically reviewed studies of perfusion weighted imaging (PWI) and perfusion CT (CTP) that assessed perfusion thresholds, mean perfusion parameter values or lesion volumes in patients with acute stroke. We used electronic and manual literature searching, cross-checked papers and extracted data. We condensed descriptions of tissue regions into 3 categories: non-viable tissue; at risk tissue; and not at risk/normal tissue. We noted the timing of follow up imaging, assessment of recanalisation and summarised the definitions for the three tissue regions.

Results: We identified 7152 papers of which 69 were included (49 MR and 20 CT) from 29 individual centres or collaborative groups. Many studies did not describe how tissue regions had been defined. Where given, there were 8:4 (MR:CT) definitions of non-viable tissue, 10:8 definitions of at risk tissue and 6:2 definitions of not at risk/ normal tissue, with little overlap between MR and CT definitions. For example, at risk tissue was defined as infarct tissue on follow up MR or CT which had not been abnormal in either the acute DWI or the acute ADC map in 14/49 MR studies and as the final infarct on DWI, MR or CT in 12/20 CT studies. Recanalisation after stroke was assessed in 19:11 studies but reported in only 9:9 studies.

Conclusion: There is substantial variation in the definition of tissue status in acute stroke perfusion imaging. 12 different definitions of non-viable and 18 different definitions of tissue at risk are unlikely to be helpful. Standardisation of definitions is required.

DYNAMICS OF WATER DIFFUSION CHANGES IN ACUTE ISCHEMIC STROKE

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Background: Diffusion-weighted imaging (DWI) is a reliable tool to identify acute ischemic stroke lesions by a decrease of the apparent diffusion coefficient (ADC) within minutes of stroke onset. However, normalization of the ADC has been reported. Diffusion-tensor imaging (DTI) adding additional parameters such as fractional anisotropy (FA) and may offer the opportunity to better identify irreversibly damaged tissue within the area of ischemia in hyperacute stroke. We aimed to determine acute diffusion changes during the first hours of acute ischemic stroke.
Methods: In a prospective, multicenter, observational cohort study, patients with acute ischemic stroke were studied by DTI on admission, within 3 hours and after 3 days. ADC, FA, axial and radial diffusivity were measured in the acute ischemic lesion at each time point.
Results: A sample of 21 patients was studied on admission after stroke onset (t1) and 3 hours (t2) and 3 days (t3) after the initial examination. ADC values were reduced as expected and remained stable (mean t1: 0.000599; t2: 0.000610; t3: 0.000601 mm^2/s). FA slightly decreased during the first three days (t1:0.290; t2: 0.278; t3: 0.251). Axial diffusivity decreased between t2 and t3 (t1: 0,000786; t2 0,000792; t3 0,000760 mm^2/s) while radial diffusivity increased between t1 and t2 (t1: 0,000505; t2 0,000519; t3 0,000522 mm^2/s).
Conclusion: Diffusion parameters derived from DTI display dynamic changes with a typical course during the first days of acute ischemic stroke. The analysis of water diffusion changes may enhance the understanding of the dynamics of tissue damage in acute stroke.

T2' AND CBV IN ACUTE STROKE PATIENTS

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Background: T2prime (T2') is sensitive to an increased Deoxy-Hemoglobin concentration in brain parenchyma indicating tissue at risk of infarction and a good predictor of lesion growth in acute stroke. However, its pathophysiological basis and relation to other perfusion parameters such as CBV is poorly understood. We hypothesized that T2' values are independent of CBV and therefore might add additional information to understanding stroke pathophysiology.
Methods: 18 datasets of acute stroke patients with an MRI examination within the first 6 hours after symptom onset, after 24-36h and after 5-8 days including diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) along with quantitative T2 and T2* (qT2, qT2*) imaging for calculation of T2' maps were analyzed. In addition relative CBV maps were derived from perfusion raw data. Images were coregistered and regions of decreased ADC and prolonged time-to-peak (TTP) as well as final infarct size in FLAIR were defined. Regions of interest including TTP>ADC mismatch, lesion growth (LG=FLAIR-ADC) and surviving tissue (ST=TTP-FLAIR) were defined and superimposed onto the corresponding T2' and CBV maps. In addition recanalization information was derived from TOF-angiography.
Results: p-values for correlation of T2' and CBV in different ROIs were 0.9087 in ADCroi, 0.2065 in TTProi, 0.2141 in mismatch, 0.5013 in ST and 0.1809 in LG. Also when dividing patients into subgroups regarding recanalization information (recanalization = 11 and no recanalization = 7), no significant correlation between T2prime and CBV was found in any ROI localization.
Discussion: No correlation was found between CBV and T2' in different stroke regions. Accordingly, T2' values seem to be independent of perfusion parameters

such as CBV and therefore might contribute independent information to understanding stroke pathophysiology.

ARE AUTOMATED PROTOCOLS FOR MAGNETIC RESONANCE PERFUSION IMAGING READY FOR CLINICAL USE?

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Background: Due to rater bias and time intensive operator input, in magnetic resonance perfusion imaging, an automated approach to delineation of regions of interest would be preferred to a manual one. We have tested the hypothesis that existing software solutions would, when automated, and due to numerous artifacts, exaggerate volumes of hypoperfused tissue in acute stroke patients and even produce perfusion deficits in a cohort of patients with no ischemia.
Methods: Using three software packages: Stroketool, PMA and Perfscape/Neuroscape, perfusion maps of cerebral blood flow, mean transit time and Tmax were created for 145 patients with acute ischemic stroke and 39 control patients. Volumes of hypoperfused tissue were calculated using two different protocols: the manual and the automated protocol, and the Results were then compared between Methods.
Results: The median difference between the automatically and manually derived volumes was up to 210 ml in Perfscape/Neuroscape, 123 ml in PMA and 135 ml in Stroketool. Correlation coefficients between the perfusion volumes and radiological and clinical outcome were much lower for the automatic volumes than for the manual ones. In control patients the median volume of hypoperfused tissue was 92.9 ml (IQR 13.3-323.4 ml) when calculated with Perfscape/Neuroscape, 30.42 ml (IQR 13.9-71.4 ml) when calculated with PMA and 78.71 ml (IQR 40.3-140.8 ml) when calculated with Stroketool.
Conclusions: Automated use of the here evaluated software packages produced falsely exaggerated volumes of hypoperfused tissue. Software improvements such as successful filtering and implementation of algorithms for judging asymmetry between hemispheres but also human input in selecting the vessel territory of expected hypoperfusion might enable highly automated protocols to credibly assess perfusion deficits and identify mismatch patients suitable for thrombolysis.

3T HIGH B-VALUE DIFFUSION-WEIGHTED MR IMAGING IN HYPERACUTE ISCHEMIC STROKE IN THE VERTEBROBASILAR TERRITORY

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Background: Diffusion-weighted MR imaging (DWI) is the key method for detecting ischemic lesions within the first hours after stroke onset. B values applied in stroke diffusion studies are usually in the range of 800-1500 s/mm^2, but progress in MR technology permits higher b values. High b-value DW sequences have already been used for imaging acute ischemic stroke at 1.5T and 3T, but it is still uncertain whether high b-value DW sequences improve detection of acute and hyperacute ischemic lesions.
Methods: At 3T, DWI was performed in patients referred with a clinical diagnosis of hyperacute cerebral infarction using conventional MR sequences as well as echo planar DW sequences. The examination included a usual DW sequence (b = 1000 s/mm^2, TR = 3100 ms, TE = 79 ms) and two high b-value DW sequences (b = 3000 s/mm^2, TR = 4100 ms, TE = 108 ms and b = 5000 s/mm^2, TR = 4300 ms, TE = 118 ms) with 5 mm section thickness in all DW sequences.
Results: We present case reports of 6 patients with hyperacute ischemic stroke in brainstem and thalamus. In all 6 patients, all hyperacute ischemic lesions in brainstem and thalamus were clearly visualized at high b-value DWI using b values of b = 3000 s/mm^2 and b = 5000 s/mm^2, but were not visible or only suggested at usual DW imaging. With increasing b value, DW images appeared noisier.
Conclusion: At 3T, high b-value DW sequences may be beneficial in diagnosing hyperacute ischemic lesions in the vertebrobasilar territory, but further studies are necessary to improve this MR technique in imaging hyperacute ischemic lesions in the vertebrobasilar territory.

COMPARISON OF CT PERFUSION LESION VOLUMES FROM DIFFERENT SOFTWARE PROCESSING

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Background: CT perfusion (CTP) is increasingly used in clinical decision making and may be used to select subjects for clinical trials. Perfusion thresholds for ischemic core and penumbra have been proposed but different mathematical algorithms are used, yield different threshold values, and are not standardised.
Methods: Raw CTP data (non-jog) from a series of patients with suspected acute stroke was processed using two different software packages (Philips Brilliance Workspace, The Netherlands and MIStar, Apollo Medical imaging Technology, Australia). The contralateral ACA and superior sagittal sinus were chosen as the arterial input and venous outflow function respectively. Identical thresholds to define infarct core (absolute cerebral blood volume [CBV] <2.0ml/100g) and penumbra (Mean transit time [MTT] ≥145% of contralateral hemisphere) were applied using each software package. Volumes of putative core, penumbra and total thresholded perfusion lesion were measured.
Results: Data were processed for 55/56 acute stroke referrals (one excluded due to movement artefact). Mean difference in overall perfusion lesion volume was 1.6ml, (95% limits of agreement -46 to +49.2ml).
Mean difference in penumbra volume was 6.4ml (95% limits of agreement -33 to +45.8), while mean difference in core volume was 4.7ml (95% limits of agreement -24.1 to +33.8).
Conclusion: Although overall perfusion lesion volume was similar, significant differences in measured infarct core and ischemic penumbra were found when CTP is processed with different software packages. Different mathematical assumptions including correction for arterial delay and bolus dispersion may account for the differences. Viability thresholds may vary depending on post processing method. Clinicians should be aware of the different scan appearances and volumes generated by different processing algorithms.

Figure 1: MRI of a 84 year old man with left MCA and right ACA ischemia (*a*: DWI, *b*: FLAIR) due to 90% left ICA stenosis, right ACA is supplied from left. While there is no BBB dysfunction detectable on post-contrast T1w (*c*), post-contrast FLAIR (*d*) reveals leakage of contrast agent and sulcal hyperintensity and increased parenchymal hyperintensity in acute ischemia (green arrowheads) and in remote areas (yellow arrows).

EARLY DETECTION AND DIFFERENT PATTERNS OF A HARM SIGN AS SURROGATES FOR POSTISCHEMIC BLOOD-BRAIN-BARRIER DYSFUNCTION

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Background: As the time window and age range of thrombolysis has been gradually extended in recent years patient safety in regard to cerebral hemorrhage is of high importance and ischemic blood-brain-barrier (BBB) dysfunction is an important aspect. The hyperintense acute reperfusion marker (HARM) in follow-up magnetic resonance imaging (MRI) 1-3 days after an MR contrast agent application has been shown to be a marker for BBB dysfunction. Its value predicting hemorrhagic transformation (HT) is currently still explored. We investigated, whether a HARM sign might already be detectable earlier, minutes after contrast agent application and specified different patterns of a BBB dysfunction.
Methods: To date 7 patients with acute ischemic stroke were imaged within 72 hours after systemic thrombolytic therapy on a 3T MR scanner (Siemens Skyra): diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR), MR-angiography, T2*-, T2- and T1-and susceptibility-weighted imaging (SWI), contrast-enhanced perfusion-weighted imaging (PWI), followed by T1w and FLAIR. Signs of HT in SWI and of a BBB-dysfunction in contrast-enhanced T1w and FLAIR were analysed.
Results: A HARM sign was present in 4/7 patients, in 3 directly adjacent to the acute DWI lesion, in 2 in remote areas. A parenchymal BBB disruption was present in 1 patient. Figure 1 displays the patient with both focal and remote HARM sign; figure 2 a patient with parenchymal BBB disruption. HT was detectable in 2 patients (1 patient with and 1 without HARM, respectively).

Figure 2: MRI of a 75 year old man with left MCA ischemia (*a*: T1, *b*: FLAIR, both without contrast agent) due to cardiac embolus. While there is evidence of some mild parenchymal BBB dysfunction on contrast-enhanced T1 (*c*, yellow arrow), this is more prominent on post-contrast FLAIR (*d*) that reveals additional sulcal hyperintensity and leakage of contrast agent to subarachnoid space adjacent to the acute ischemia (green arrowheads).

Conclusions: A HARM sign is already detectable minutes after contrast agent application providing information of BBB dysfunction on post-contrast FLAIR not visible on T1w images. Beyond the index lesion remote areas may be visualised on post contrast FLAIR completing the picture on the extent of parenchymal and vascular injury. This offers new avenues to investigate pathophysiology and safety related questions in acute stroke patients.

66 Brain imaging

SHORT ACQUISITION TIMES FOR MULTIMODAL CT EXAMINATION IN ACUTE STROKE

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Background: Multimodal CT imaging in stroke comprising CT perfusion and CT angiography can provide additional information beyond that obtained with non contrast brain CT, may aid clinical decision making and could represent a widely accessible imaging modality for recruitment to clinical trials in stroke. The additional time required to acquire CTP and CTA was assessed in a series of acute stroke patients within a multicentre collaborative study.

Methods: Patients with suspected acute ischemic stroke (<6hr from ictus) in 3 stroke centres were recruited prospectively. Non contrast brain CT was obtained acutely at the discretion of the treating physicians. Additional imaging with CTP/CTA or acute stroke MRI was obtained after obtaining informed written consent/assent. Symptom onset time was recorded in addition to time of CT, CTP and CTA. The additional time taken for acquisition of CTP/CTA was calculated.

Results: Acute CT imaging was undertaken in 61 of 81 patients recruited to the study. One CT examination was terminated early due to pulmonary oedema. Two subjects had CTP/CTA after treatment with rt-PA whose scan times were not assessed. Median onset to CT time in the remaining 58 subjects was 155 mins, IQR 130.5-196.5 Onset to CTP was 168 mins (141-235), onset to CTA was 171 mins IQR 139-240). Median time from beginning to end of CT imaging was 14 minutes (IQR 10-19 mins).

Conclusion: Multimodal CT Imaging acquisition adds relatively little time to imaging protocols. As routine multimodal CT was not routinely performed in our institutions for acute stroke the additional time needed could likely be reduced should CTP/CTA be incorporated into routine imaging protocols. The short amount of time needed for additional imaging makes CT an attractive modality for imaging-based trial recruitment.

67 Brain imaging

AUTOMATED PERFUSION-DIFFUSION LESION ASSESSMENT IN ACUTE ISCHEMIC STROKE: A VALIDATION STUDY

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Background: Penumbral imaging with perfusion (PWI) and diffusion-weighted (DWI) MRI in the clinical setting is qualitative, but this is inaccurate relative to quantitative measurements. Manual planimetric measurements are accurate but are prohibitively time intensive in the emergent setting.

Methods: Customized software was used to generate Tmax maps thresholded to +4s using a deconvolution algorithm and a manually selected arterial input function. Planimetric measurements of the Tmax+4s maps and DWI lesion volumes were made using Analyze software. The Perfscape software package was used to generate Tmax+4s maps, using an automated AIF selection algorithm. This software calculated Tmax+4s deficit, DWI lesion and penumbral (Tmax+4s-DWI) volumes automatically. Bivariate Correlation and Bland-Altman analyses were used to calculate the accuracy of automated measurements.

Results: A total of 76 patients were included. DWI volumes calculated automatically (17.3±41.0 ml) were correlated with manually determined volumes (29.1±57.9 ml); (Spearman's Rho 0.929). Automated DWI lesion volumes were smaller than manually measured volumes (mean difference -11.8 ml, 95% limits of agreement -51.6, 28.0 ml). Automated (31.7±42.8 ml) and manual Tmax+4s perfusion deficit (52.6±68.2 ml) volumes were correlated (Spearman's Rho 0.908). Automated Tmax+4s PWI deficit volumes were smaller than manually measured volumes (mean difference -20.9, 95% limits of agreement -88.7, 46.9 ml). Automated (14.3±26.4 ml) and manual mismatch volumes (23.5±51.3 ml) were correlated (Spearman's Rho 0.631). Mismatch ratios assessed automatically (7.0±17.1) were correlated with those derived from manually calculated volumes (6.88±22.6); (Spearman's Rho 0.755). The automated software detected the presence of a mismatch ratio of >1.2 with sensitivity of 81.6% and specificity of 78.9%. Sensitivity and specificity increased to 92.3% and 84.0% respectively for a mismatch ratio of >2.0.

Conclusions: The Perfscape tool generally underestimates both DWI and PWI volumes, relative to manual planimetric measurements. This automated tool may facilitate treatment decisions based on penumbral imaging patterns.

68 Brain imaging

ENHANCING ASPECTS INTERPRETATION ON CT THROUGH USE OF AN ONLINE INTERACTIVE TRAINING TOOL (ASPECTSINSTROKE.COM)

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Purpose: The Alberta Stroke Program Early CT Score (ASPECTS) is 10-point scale that grades the extent of ischemic change within the territory of the middle cerebral artery. ASPECTS is a well-validated, reliable scoring system. It has been used as a prognostic and treatment stratifying tool in acute ischemic stroke. We have developed an online teaching tool (ASPECTSINSTROKE. COM), which helps in understanding ASPECTS by providing interactive training (figure 1).

Methods: We did a survey to determine the barriers to ASPECTS use by the residents, nursing staff and physicians involved in acute stoke patient care. We found that providing interactive training through a website would improve understanding of the scoring system. The website training section consists of interactive examples with brief clinical history, early and follow-up NCCT scans. Expert interpretation is provided at the end of scoring. A feedback system through email is included within the website to further facilitate learning.

Results: The website was launched in month of September 2010. We have collected information on the use of this teaching tool from "Google analytics". A total of 657 visits from September 15, 2010 to January 14, 2011 was recorded with average website usage time per user of 5 minutes. The highest visits were recorded from North America followed by Europe and Asia (figure 2). A trend towards increasing usage over time was noted.

www.aspectsinstroke.com
Map Overlay
Sep 15, 2010 - Jan 14, 2011
Comparing to: Site

Visits
1 █████ 134

657 visits came from 212 cities

Site Usage

Visits	Pages/Visit	Avg. Time on Site	% New Visits	Bounce Rate
657	**5.56**	**00:05:48**	**71.69%**	**38.96%**
% of Site Total: 100.00%	Site Avg: 5.56 (0.00%)	Site Avg: 00:05:48 (0.00%)	Site Avg: 71.39% (0.43%)	Site Avg: 38.96% (0.00%)

Conclusion: An interactive web approach is an efficient and effective alternative method for teaching interpretation of early ischemic changes on non-contrast CT using ASPECTS. We plan to validate the usefulness of this approach through an ongoing study.

69 Brain imaging

CAN MRI PATTERNS PREDICT ETIOLOGY IN TIA PATIENTS?

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Background: DWI-positive and DWI-negative TIAs are clinically indistinguishable. We investigated whether MRI-positive TIAs have radiological patterns that point towards underlying pathology and if their etiological distribution resembles stroke's TOAST criteria.
Method: Images were acquired at Copenhagen University Hospital Bispebjerg March-December 2010. Emergency doctors referred patients clinically suspect of TIA to MRI performed within 72 hours of symptom debut on 1,5T (GE Healthcare) and 3T (Siemens) scanners with a protocol consisting of T2-FLAIR, gradient echo and diffusion weighted sequences. MRI patterns distinguished between single and multiple lesions, cortical or deep location, and the presence or absence of old infarcts. Outcome of etiological work-up was ascertained retrospectively through electronic health records by an independent, blinded senior consultant neurologist. The study was approved by the Danish Data Protection agency; file no. 2010-41-4789.
Results: 143 patients were included, 38 patients (27%) had DWI-positive lesions characterized as shown in table 1. The etiological work-up showed cardioembolism 21%, small vessel disease 16%, large artery atherosclerosis 11%, cryptogenic 45% and 8% other/unknown. Small vessel disease was characterized by deep lesion location and presence of old infarcts with 100% sensitivity, 94% specificity, 75% PPV and 100% NPV. Cardioembolism was characterized by multiple cortical lesions with 75% sensitivity, 83% specificity, 55% PPV and 93% NPV. Large artery atherosclerosis was characterized by single cortical lesions with 75% sensitivity, 71% specificity, 23% PPV and 96% NPV.

Table 1. Lesion characteristics on DWI and T2-FLAIR (N=38)

Single	26 (68%)
Multiple	12 (32%)
Cortical	24 (63%)
Deep	14 (37%)
Old infarcts	18 (47%)

Conclusion: MRI lesion pattern is a strong indicator towards underlying etiology, and acute MRI can contribute to the acute management of patients with TIA.

70 Brain imaging

BENEFITS OF STROKE NEURO-RADIOLOGY MDT IN A DISTRICT GENERAL HOSPITAL SETTING

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Introduction: Little evidence is available on who should report the brain scan following stroke. Many district general hospitals do not have neuro-radiology services, most CT Brain scans are reported by the on-call radiologist and in some hospitals by the stroke physicians: British Association of Stroke Physicians (BASP) Guidance recommends Neuro- Radiology MDT (NRMDT) meetings in all Acute Stroke Services. We undertook an audit project on Stroke NRMDT meetings in Non-thrombolysis patients in a District General Hospital setting.
Method: A prospective audit of all patients with clinical diagnosis of acute stroke from March 2010 – August 2010 which were managed on the acute stroke unit was conducted. Patients who were initially managed at a tertiary hyper acute stroke centre were excluded. All cases were clinically presented and brain imaging reviewed by a radiology consultant with specialist interest in Neuro-radiology.
Results: A total of 80 CT Brain scans (45 males, 35 female) were included. Average age was 73 years (range 53-93). Initial reports showed no acute changes in 49 cases, acute stroke in 26 cases and stroke mimic in 5 cases. 8 reports advised further imaging.
Following the NRMDT the initial CT report was modified on 28 occasions. Previous stroke related changes were identified in 18 cases, a new mass lesion was detected on 2 cases, and new acute stroke was identified in 8 cases.
Further MRI scans were advised in 20 cases, previously requested MRI scan were cancelled in 3 cases and other investigations (e.g. lumbar puncture) were advised in 5 cases.
Conclusions: The NR-MDT has a significant impact on managing stroke patients both clinically and from governance point of view. The audit was presented in the internal Clinical Audit meetings of both Medicine and Radiology departments. Following recommendations were accepted:

– All brain imaging of stroke patients should be discussed at the NR-MDT.
– The meeting would take twice weekly.
– Improve clinical information provided on CT request card.
– Amend the radiology report if significant changes are found.

71 Brain imaging

TABLESIDE FLAT PANEL PARENCHYMAL BLOOD VOLUME MEASUREMENT IN NEUROVASCULAR INTERVENTIONS: PRELIMINARY EXPERIENCE

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Background: Cerebral blood volume is an important perfusion parameter in estimating the viability of brain parenchyma, e.g. in cases of ischemic stroke. Recent technological advances allow parenchymal blood volume (PBV) imaging in the angiography suite just before, during or after an interventional procedure. The aim of this work is to share our preliminary clinical experience in different neurovascular interventions.
Methods: Flat panel CT PBV measurement was performed on a biplane flat detector angiographic system (Axiom Artis Zee, Siemens, Erlangen, Germany). Fifteen patients (10 women, 5 men) were examined; age range 40-86 (median 61.5) years. Presenting symptoms included: acute stroke or stroke-like symptoms in 7 patients, subacute stroke in 3 patients, headache and nausea in 5 patients. In the 10 stroke patients an arterial stenosis or occlusion was confirmed. The remaining 5 patients suffered an intracranial hemorrhage, 3 of them suffered a subarachnoid hemorrhage due to aneurysmal rupture.
Results: In the 15 cases studied, 18 PBV measurements were performed. 14 acquisitions were of good diagnostic quality. The remaining 4 acquisitions failed technically (one due to motion artifacts, one due to selective intra-arterial contrast agent injection and the other two due to injection technique and/or hardware failure). In an acute stroke case with occlusion of the left internal carotid artery treated by endovascular recanalization techniques, the pre-interventional PBV acquisition depicted the hypoperfusion on the left side, which normalized after successful intervention.
Conclusion: Flat-panel PBV measurement in the angiography suite provides an attractive and feasible tool for peri-interventional neuroimaging. The technique suffers some technical limitations and potential errors, which should be optimized in the recent future.

55% DETECTION RATE OF THROMBI OR EMBOLI IN PATIENTS WHOM RECEIVED INTRAVENOUS THROMBOLYSIS IN A COHORT IN SITS MOST, STOCKHOLM, SWEDEN

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Background and purpose: In modern acut stroke investigation there are more and more written about the bridgning therapy when discussing acute ischemic stroke within a proper time window. If a thrombi or emboli can be detected – the Discussion of intraarterial therapy are an uprising issue. In general the knowledge for the rating of the chance to locate a thrombi or emboli are underestimated which will reduce possibilities for so called bridging therapy. Bridging therapy is to start out with the intravenous thrombolysis and then let a interventionist try to remove or treat the thrombi or emboli as soon as possible.

Materials and Methods: In the SITS MOST database for the primary uptake area mainly served by our departement of Neuroradiology in Karolinska University Hospital Solna there were 99 pat during 4 years (2007-2010) which have been given intravenous thrombolysis. 21 of them had only a unenhanced CT brain done. (9 of these 21 during 2007). Of the remaining 78 it was also done a CT-angiography (CTA). The reports from these investigations were read. The presence and where a thrombi or emboli was localized was recorded.

Results: 78 CTA were performed. 35 (45%) were without detection of any thrombus or emboli and 43 (55%) with thrombi or emboli. 25 (32%) of the latter were in the segment M1, ICA-terminus/T-occlusion or BA which are generally concidered to have a worse prognosis and less effect if only treated with intravenous thrombolysis than more distal and thrombi in smaller vessels.

Conclusions: In patients whom gets intravenous thrombolysis it is common to find thrombi or emboli. The possibilities to find patients whom can potentially benefit of bridging therapy are good.

IMPORTANCE OF IMAGE CO-REGISTRATION WITH LIMITED BRAIN COVERAGE OF CT PERFUSION

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Background: Imaging acute stroke patients with CT perfusion (CTP) improves sensitivity for detecting brain ischemia and may permit visualisation of the ischemic penumbra. A potential drawback of CTP is the limited brain coverage available for perfusion analysis which varies between different scanners.

Methods: CTP with 24 or 40 mm coverage was obtained within 6 hrs of symptom onset in suspected stroke patients. Follow-up MRI or CT scans were coregistered to baseline CTP frames to obtain a matching spatial position. Infarct volume was determined from the coregistered follow up scan. Volumes were compared across those slices which matched original CTP positioning ("co-reg volume") and all slices, including those not covered by the original CTP slab (total volume).

Results: 56 patients with suspected ischemic stroke underwent non-jog mode CTP <6hours from symptom onset. 30 had visualised arterial occlusions on CTA. Infarct volume was determined on follow up MRI or CT in 36 subjects (14 had no visualised infarct, 4 had no further imaging, 2 had space occupying haemorrhage precluding infarct measurement). Total volume was significantly greater than the co-reg volume which matched the original CTP slices (Mean total volume=45.3ml, SD 76.6, mean co-reg volume= 25.1 SD 35.2, p=0.01). The difference in total and co-reg infarct volume was not significant when scans with 40mm slab coverage were analyzed separately (n=18, mean coreg volume = 24.1 ml, SD 33.0, mean total volume =41.4 SD 72.3 p=0.166).

Conclusion: Differences in perfusion scan brain coverage means that varying amounts of final infarct volume could potentially be predicted by CTP. Increasing coverage to 40 mm resulted in insignificant differences in final infarct volume measurement. When limited brain coverage is available with CTP, image co-registration is an important part of accurately quantifying relevant final infarct volume.

T2 INCREASE DOES NOT RELIABLY PREDICT LATER INFARCTION

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Background: Distinct from signal alterations in diffusion weighted images T2 values are also dependent on tissue water content and known to increase with time from symptom onset in acute ischemic stroke. The purpose of this study was to evaluate whether the increase of T2 values in different regions in acute ischemic stroke is reversible or above a certain threshold indicates irreversible damaged brain tissue.

Methods: Twenty patients with acute ischemic stroke in the territory of the MCA underwent MRI including DWI, perfusion weighted imaging (PWI), fluid-attenuated inversion recovery (FLAIR) to determine final infact size (FI), TOF-angiography (acute and on day 1/2) and a triple-echo-T2-sequence (calculation of T2 maps) within 6 hours after symptom onset. Images were coregistered and regions of decreased ADC and prolonged time-to-peak (TTP) as well as surviving tissue (ST=TTP-FI) and lesion growth (LG=FI-ADC) were defined and superimposed onto the qT2 map. In addition patients were dichotomized according to recanalization information. Mean qT2 values were derived for each patient within each region of interest.

Results: Mean T2 values for patients with recanalization (n=12) in ST-ROI were 114.7±6.8ms (mean ± sd) and in LG-ROI 114.0±6.2 ms respectively. T2 values for patients without recanalization (n=8) were 117.0±10.7 ms in ST-ROI and 117.1±11.2ms in LG-ROI respectively. There was no significant difference between T2 values measured in LG and ST ROI for patients with or without recanalization.

Conclusions: Even though it has been shown that T2 values increase with time from symptom onset within the infact core, increased T2 values in areas of perfusion impairment do not identify irreversible damaged brain tissue and high T2 values are even found in tissue that is not part of the final infarct lesion and can therefore normalize.

CEREBROVASCULAR EFFECTS OF STATINS IN PATIENTS WITH LEUKOARAIOSIS – AN MRI STUDY

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Background and purpose: Currently, there is no specific treatment for patients with leukoaraiosis. We investigated the effects of statins on regional cerebral blood flow (rCBF) and L-arginine induced vasoreactivity (CVR) in patients with moderate to severe leukoaraiosis.

Methods: We included 8 statin-naïve patients (2 female; mean age 56±11 years) with moderate to severe leukoaraiosis (Fazekas score >1). They received MRI scans prior to and after L-arginine infusions. Extend of leukoaraiosis was assessed using the Wahlund score on T2-weighted images of the first scan. MRI scans including L-arginine infusions were repeated after treatment with simvastatin (80 mg/d for 8 weeks). White and grey matter were segmented allowing for separate analysis of tissue specific perfusion parameters. For the arterial input function six regions (three on each hemisphere) supplied by distal segments of the middle cerebral artery were selected. rCBF and CVR were determined before and after treatment with simvastatin.

Results: Median Wahlund score was 13 (IQR 10-16). Wahlund scores negatively correlated with baseline rCBF in white matter (Spearman's rho -0.8, p=0.022). Simvastatin treatment led to an increase of rCBF by 17.5% (IQR 12.0-24.2%; p=0.049) in white matter and a median change of L-arginine induced CVR in grey matter by 15.7% (IQR 12.3-18.2%; p=0.012). CVR in white matter after treatment with simvastatin correlated negatively with L-arginine induced changes in diastolic blood pressure (median -10 mmHg, IQR 4 to 14 mmHg, Spearman's rho -0.8, p=0.040).

Conclusion: For the first time, we have provided MRI evidence of an improved cerebral perfusion in patients with leukoaraiosis after treatment with simvastatin.

3T VS. 1.5T: WHAT ARE THE DIFFERENCES IN INFARCT VOLUME MEASUREMENTS AND ADC VALUES?

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Background: Although increasing magnetic field strength increases SNR, we recently reported that 1.5T is superior to 3T for early MCA stroke diagnosis. Here we compare acute and follow-up infarct volumes in two populations of acute stroke patients imaged at 1.5T and 3T.

Methods: Patients with acute carotid stroke were included if they have a MRI with DWI (b=1000 s/mm²) in the first six hours of stroke onset and a control MRI in the next three days. They were imaged on a 1.5T MRI unit for n=72 and on a 3T MRI unit for n=125. Quantitative ADC maps were generated. The infarct volume was delineated by manual outlining as the hyperintense DWI area on initial (V1) and control (V2) MRI. ADC values were measured within V1 (ischemic tissue) and in healthy tissue (lenticular nucleus). Comparison between volumes and ADC measurements were performed between patients imaged at 1.5- and 3T by running a Mann-Whitney test for volumes and t-Student test for ADC values.

Results: Patients at 1.5 and 3T had similar median NIHSS (15 vs. 16, p=0.27), time to initial MRI (128 vs.135 min, p=0.67), and treatment with rtPa (78% vs. 75%, p=0.81). Median V1 was significantly smaller at 3T than at 1.5T (9.3 vs. 23.4 cm³, p<0.0001) whereas median V2 was similar in both groups (42 at 3T vs. 53 cm³ at 1.5T, p=0.6). The ADC value within V1 was similar at 3T and 1.5T (642 vs. 647×10⁻⁶ mm²/s, p=0.61) whereas the ADC value in the healthy tissue was higher at 3T (842 vs. 747×10⁻⁶ mm²/s, p<0.0001).

Conclusion: The finding of a smaller apparent infarct volume with similar ADC value in the 3T group on the initial MRI (<6 hours) but not in the control MRI (> 24 h) in patients with similar clinical severity and imaging delay is consistent with the lower diagnosis value of 3T MRI early after stroke. One putative explanation for this unexpected finding is that potentially reversible early ADC changes are more detectable at 1.5T than at 3T whereas later irreversible ADC changes are equally detected at both fields.

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78 Brain imaging

CT ATTENUATION CHANGE IN HYPERACUTE ISCHEMIC TISSUE DIFFERS WITH TISSUE TYPE - INITIAL QUANTIFICATION RESULTS

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Background: Computed tomography (CT) is used to detect early ischemic signs - hypoattenuation and focal swelling - in stroke. Few studies have explored attenuation changes accompanying early ischemic signs on CT in different tissues or their associations, eg with perfusion. We tested Methods to measure CT attenuation change in acute ischemic tissue.

Methods: We used data from 2 multicentre stroke studies, selected as examplars for this pilot. We included patients with acute ischemic stroke who had CT <6 hrs of stroke and MR diffusion imaging (DWI) at 24–72hrs. We devised a template of small regions of interest to sample standardised areas of cortical grey, subcortical grey and white matter of both hemispheres. We outlined the visible infarct on the 24-72hr DWI and transposed the outline onto the <6hr CT scan. We compared mean attenuation (in Hounsfield Units, HU) extracted from the standard regions in ischemic tissue within the DWI-derived outline with the value for non-ischemic tissue.

Results: We used data from 20 patients (mean age 75.5 SD 12.5years) scanned 174 (range 75-330) mins after stroke onset. In subcortical grey matter, we found mean attenuation of ischemic tissue (30.3 SD 3.0) was lower than in contralateral subcortical grey (33.3 SD 2.1) matter (p=0.0001). The attenuation of ischemic white (26.4 SD 2.4) and cortical grey matter (30.7 SD 1.8) was also lower than in contralateral white (27.5 SD 2.3) and subcortical grey (32.1 SD 1.6) matter, but the difference was not significant (p=0.19 and p=0.08 respectively). Non-ischemic ipsilateral and contralateral tissues had the same attenuation.

Conclusion: CT attenuation in ischemic tissue differs with tissue type at a given time after stroke. A larger sample is required to explore the effect of time to scanning, stroke severity, perfusion, artery occlusion, patient age, leukoaraiosis, etc on changes in CT attenuation in ischemic tissue, and whether relative HU could be used to determine tissue viability.

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80 Brain imaging

ASSOCIATION BETWEEN CEREBRAL ARTERY CALCIFICATION AND MICROBLEEDS IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Objective: The aim of the present study was to investigate the association between cerebral artery calcification and cerebral microbleeds (CMB).

Background: We previously reported that cerebral artery calcification was associated with white matter hyperintensities and lacunes. Since these small vessel-associated conditions were reported to be related with microbleeds, cerebral artery calcification might show association with microbleeds.

Design/Methods: We identified 110 consecutive patients with acute ischemic stroke who underwent CT angiography within seven days of symptom onset. Calcifications of the intracranial internal carotid artery (I-ICA) were graded and CMBs were also counted according to their location. Correlation between I-ICA calcification and CMB was tested by using Pearson's correlation and multiple linear regression analysis.

Results: The stroke patients ranged in age from 26 to 95 years (67±13 years). I-ICA calcification was found in 162 arteries (73.6%) and CMB was detected in 26 patients (23.6%). Univariate analysis revealed that I-ICA calcification was correlated with total CMB (correlation coefficient r = 0.41, p < 0.001) and CMB in deep gray matter (r= 0.339, p < 0.001), but not with CMB in lobar region (r=0.139, p = 0.053). Multiple linear regression showed that I-ICA calcification was independent determinants of CMB in deep gray matter (B = 0.291, p = 0.043), but not total CMB (B = 0.313, p = 0.466) and CMB in lobar region (B = -0.377, p = 0.363).

Conclusions: I-ICA calcification is common in patients with acute ischemic stroke and is an independent predictor for CMB in the deep gray matter rather than total CMB or CMB in lobar region.

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81 Brain imaging

INTER-RATER RELIABILITY OF MODIFIED ALBERTA STROKE PROGRAM EARLY COMPUTERIZED TOMOGRAPHY SCORE

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Background: The Alberta Stroke Program Early CT Score (ASPECTS) was used to detect significant early ischemic changes on brain CT of acute stroke patients. We designed the modified ASPECTS and compared it to the above system.

Methods: The CT images were chosen from the stroke data bank of Ghaem hospital, Mashhad in 2010. The inclusion criteria were the presence of MCA territory infarction and performance of CT within 6 hours after stroke onset. Axial CT scans were performed on a third-generation CT scanner (Siemens, ARTX, Germany). Section thickness above posterior fossa was 10 mm (130 kV, 150 mAs). Films were made at window level 35 HU. The brain CTs were scored by four independent radiologists based on the ASPECTS and modified ASPECTS. The readers were blind to clinical information except symptom side. Cochrane Q and Kappa tests served for statistical analysis.

Results: 24 CT scans were available and of sufficient quality. Difference in distribution of dichotomized ≤7 and >7 ASPECT scores between four raters was significant; Q=13.071, df=3, p=0.04. Distribution of dichotomized <6 and ≥6 scores based on modified ASPECT system between 4 raters was not significantly different; Q=6.349, df=3, p=0.096.

Conclusion: Modified ASPECT method is more reliable than ASPECTS in detecting major early ischemic changes in stroke patients candidated to tPA thrombolysis.

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82 Brain imaging

CEREBRAL LESION TOPOGRAPHY AS CLINICAL INDICATOR OF SPASTICITY AFTER ISCHEMIC STROKE

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Background: From a health policy and economic perspective the development of spasticity is one of the main complications of stroke. Currently objective data of clinical indicators for the likelihood of spasticity development is not available. The present study examined whether the topographical distribution of ischemic brain

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areas influences the development of spasticity. The occurrence of spastic tone was determined and the lesion topography from the acute phase was analysed by MRI.

Methods: In a prospective cohort study, a collective of 211 patients with clinical signs of central paresis due to a first-ever ischemic stroke were examined in the acute stage and 6 months later. 98 patients could be included in the MRI analysis in acute phase. At both examination times the degree and distribution of paralysis and muscle tone in the upper and lower limb were evaluated. Spasticity was assessed on the Modified Ashworth Scale (MAS) and defined as MAS >1 in any of the examined joints.

Results: 42.6% of the subjects showed spastic tone. In 8.5% spasticity was found in the upper limb, 7.1% of the patients had spastic tone in the lower limb while in 27% both the upper and lower limb were affected. No infarcted brain area could be identified as the causing structure concerning the development of spasticity. Although the lesions' volume is not the causing factor in the development of spasticity it still has an influence on its severity. We found a significant correlation (Kendall Tau-b =0.59) between the volumina and the degree of spasticity. Due to optophenographic analysis we assume an influence of a putamen lesion on the severity of spasticity.

Conclusion: There is evidence that putamen lesions influence the development of spasticity. Further analyses of existing data by means of new algorithmic procedures are needed to confirm this assumption. Changes in functional and neurotransmitter levels that are beyond the morphologic evidence must also be taken into account.

83 Brain imaging

COMPARISON OF FOUR-DIMENSIONAL CT ANGIOGRAPHY (4D-CTA) WITH MRA IN ACUTE ISCHEMIC STROKE PATIENTS WITH PROBABLE INTERNAL CAROTID ARTERY OCCLUSION

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Background and purpose: Emergency MR angiography (MRA) can provide useful information to find the internal carotid artery (ICA) occlusion in an acute stroke setting. However, the usefulness of four-dimensional CT angiography (4D-CTA) using 320 detector rows remains uncertain for emergency diagnosis of cerebral vasculature in acute ischemic stroke. The aim of our retrospective study was to investigate whether or not there were some differences between 4D-CTA and MRA findings in acute ischemic stroke patients with probable internal carotid artery occlusion.

Materials and Methods: Included for analysis were acute ischemic stroke patients 1) who were admitted to our institution within 72 hrs of stroke onset from September 2010 to January 2011, 2) who underwent 4D-CTA within 24 hrs following emergency MRA on admission and 3) in whom the affected ICA was absolutely not visualized in MRA. We compared 4D-CTA findings with MRA findings.

Result: During study period, 185 acute stroke patients were admitted and emergency MRA showed no visualization of the affected ICA in 19 of them. Among the 19 patients, 5 patients underwent 4D-CTA following MRA. Four-dimensional CTA demonstrated antegrade flow of the affected ICAs as time-sequence dynamic images in 4 of the 5 patients and the affected ICAs were not occluded at their origin, although in the rest 4D-CTA could not visualize the affected ICA at all.

Conclusion: In an acute stroke setting, 4D-CTA can provide more accurate information of the affected ICA which is absolutely not visualized in MRA.

84 Brain imaging

AUTOMATIC DETECTION AND QUANTIFICATION OF WHITE MATTER LESIONS IN WHOLE-BRAIN MRI OF ACUTE ISCHEMIC STROKE PATIENTS

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Background: The presence of white matter lesions (WMLs) in patients with acute cerebro-vascular disease is common and the volume has been reported to be associated with mental impairment and the hemorrhagic risk with antithrombotic agents. The current method of semi-automated segmentation of WMLs is time-consuming and with significant interrater difference. The aim of this study is to establish Methods of computer-assisted segmentation of MRI images to provide real-time measurement of WMLs for clinical use and to avoid interrater bias.

Methods: We adopted retrospectively four patients with acute ischemic stroke in Landseed Hospital with multi-parametric MRI sequences, including T1-weighted

(T1-w) and fluid attenuation inversion recovery (FLAIR)-weighted MR sequence (512*512*23). The semi-automated segmentation of WMLs was performed by MRIcro® software by an experienced neurologist. The proposed automated method was performed first by using T1-w to extract the gray and white matter by using statistical parametric mapping (SPM) software. The FLAIR imagings were then used to detect WMLs by using the fuzzy C-means method. We can choose different cluster numbers with brain volumes difference of WMLs and calculate brain volume by equation: Brain Volume (c.c.) = (Pixel Count × (FOV/512)^2 × Section Thickness)/1000. Kappa statistics was utilized to assess the agreement between the newly-developed computer-assisted diagnosis (CAD) and manual segmentation in WMLs detection. Correlation between two measurements in 8 hemispheres was calculated with Pearson correlation coefficient.

Results: The average kappa in 8 hemispheres is 0.85 (0.79-0.91). The Pearson correlation coefficient of the WMLs volume between examiner and our algorithm was 0.97.
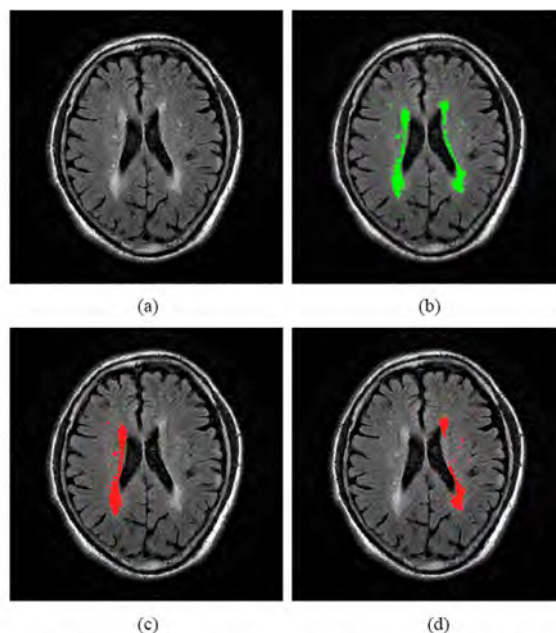
Fig (a) Original FLAIR weighted image (b) White matter lesions detection automatically (c, d) WMLs detection of right and left side by single experienced physician (YWC)

Conclusion: Our study provides a novel application of CAD in whole brain WMLs detection in (FLAIR)-weighted sequence. It may serve an automated tool for analyzing WMLs to facilitate its clinical application and the related stroke study.

85 Brain imaging

NEUROIMAGING CHARACTERISTICS OF PATIENTS WITH HEMORRHAGIC TRANSFORMATION OF BRAIN INFARCTION

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Background: Hemorrhagic Transformation of Brain Infarction (HTBI) is frequent in neuroimaging of stroke patients and makes influence in thrombolysis therapy with rTPA and anticoagulation therapy.

Methods: Consecutive patients with HTBI admitted in Ghaem hospital, Mashhad during 2010 enrolled an observational study. Presence of intraventricular hemorrhage, heterogenous patchy or punctuate hemorrhage within infarct zone, territorial involvement, cardioembolic etiology and confirmation of HTBI in serial neuroimaging was evaluated. All of the patients underwent brain CT with a third generation Ziemens, Germany equipment within 48 hours post event.

Results: 34 patients (16 males, 18 females) with mean age 71.5 years and HTBI were investigated. Cardiac source of embolism was found in 73.5% and atrial fibrillation was present in 50% of the HTBI. MCA, PCA and ICA constituted 76.5%, 14.7% and 5.9% of infarct territories in HTBI. Extensive infarction, > 1/3 of

brain hemisphere was found in 29.4% of HTBI. Heterogenous patchy or punctuate hemorrhage within infarct zone and intraventricular hemorrhage was found in 47% and 11.7% of HTBI respectively. Serial CT confirmed HTBI in 64.7%.

Conclusion: Serial neuroimaging is the most reliable detector of HTBI and more than two-third of HTBI patients have cardioembolic stroke.

86 Brain imaging

DETECTION OF BASILAR ARTERY PLAQUES BY CONVENTIONAL MRI IN PARAMEDIAN PONTINE INFARCTION

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Background: Paramedian pontine infarction probably Results from an occlusion of a penetrating branch from the basilar artery at their origin known as basilar branch disease. The cause of basilar artery branch occlusion is usually atherosclerosis and differs from lipohyalinosis that typically leads to lacunar infarct, which is an isolated "island" infarction far from the basal surface of the pons. The occlusion at the penetrating branch at its origin likely explains infarct extension to the surface. High resolution MRI is a useful method to detect arterial plaques. However, conventional MRI might be also able to identify basilar artery plaque at the origin of basilar artery branch in patients with paramedian pontine infarction.

Methods: The conventional MRI of patients who presented with paramedian pontine infarction within 3 months onset at two hospitals between January 2008 and December 2010 was reviewed by two radiologists. Presence of basilar artery plaques needed to be consensus by both radiologists.

Results: 39 patients with paremedian pontine infarction were found during period of the study. 18 of them were men. Conventional MRI was able to identify basilar artery plaques in only 5 of 39 patients with paramedian pontine infarction. MRA of basilar artery showed significant abnormalities in 3 of 5 patients whose basilar artery plaques detected by conventional MRI.

Conclusions: Basilar artery plaques sometimes are able to detect by conventional MRI in patients with paramedian pontine infarction. However, the profit of this method is significantly low as compared to high resolution MRI.

87 Brain imaging

CT PERFUSION AND CT ANGIOGRAPHY BEFORE THROMBOLYSIS IN ACUTE STROKE

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Military Hospital - National Health Center, Budapest, Hungary Background: Clinical treatment decision in stroke depends on accurately assessing damaged tissue versus tissue at risk. CT perfusion (CTP) and CT angiography (CTA) can be obtained rapidly, it is useful in busy emergency departments. The CT technology helps physicians to identify patients who are suitable for treatment and shows probable efficiency of thombolytic therapy.

Methods: In our study we have shown the Results of 22 patients who had undergone CTP and CTA within 3 hours after onset of symptoms. We calculated MTT, CBF and CBV maps. The patient divided in 3 groups depending on the location of occlusion (occlusion of ICA, occlusion of main branch of MCA and occlusion of secondary branch of MCA). After intravenous thrombolysis we calculated the size of the lesion in the follow up CT identical slice to perfusion images. We compared the size of the lesion to the CBV lesion and the calculated penumbra region.

Results: The average size of MTT was 33,01±10,14 cm², the size of CBV was 14,06±9.08cm², the calculated penumbra region was 18,95±9,87 cm² volt. In the follow up CT the average lesion size was 16,34±8,09 cm². The survivor bran tissue (MTT minus ischemic lesion size) was 16,67±9,97 cm². There was an association between the different clinical outcomes and the Results of CTP and CTA.

Conclusion: In most of the cases the CTP and CTA can be used and evaluated in the diagnosis of stroke and in predicting the final tissue damage. There is a good correlation between the Results of the CTP and the probable efficiency of the therapy.

88 Brain imaging

CLINICAL EVALUATION FOR REVERSIBLE AND IRREVERSIBLE BRAIN LESIONS IN MELAS PATIENT

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Background & Significance: The presumed pathogenesis of the stroke-like episodes in patients with MELAS (mitochondrial, encephalomyopathy, lactic acidosis, and stroke-like episodes) were either a mismatch between perfusion and metabolism or the impaired autoregulation of cerebral blood flow but remains controversial. To explain the pathogenesis of the stroke-like episodes in patients with MELAS syndrome, we performed the brain MRI, MR spectroscopy and acetazolamide challenge SPECT.

Case: A 22-year-old man presented recurrent episodes of generalized seizure, hemiparesis and visual perception disturbance. The diagnosis of MELAS was confirmed by molecular genetic analysis showing 3243 mt DNA point mutation. The T-2 weighted MR imaging demonstrated high signal intensities in both occipital regions and subcortical white matter of left frontoparietal area. After 50 days follow up brain MRI presented resolution of subcortical white matter lesions of left frontoparietal area but no changes of both occipital lobe lesions. The 1H-MR spectroscopy showed elevation of lactate and decrease of N-acetylaspartate contents in the involved area. The SPECT revealed perfusion defects of bilateral temporooccipital area. After IV injection of acetazolamide, perfusion defect of right occipitoparietal area was recovered but no interval change of the corresponding contralateral area.

Conclusion: These findings demonstrates that coexistence of the mismatch between perfusion and increased metabolic demand and the impaired autoregulation of cerebral blood flow may be responsible for the pathogenesis of stroke-like episodes in MELAS syndrome.

89 Brain imaging

CEREBRAL HEMODYNAMICS IN PATIENTS WITH SYMPTOMATIC DISTAL AND PROXIMAL INTERNAL CAROTID ARTERY STENOSIS: EVALUATION WITH DYNAMIC CT PERFUSION IMAGING WITH ACETAZOLAMIDE CHALLENGE

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Background: Ischemic symptoms in patients with carotid artery steno-occlusion are most closely related to disturbed cerebral hemodynamics, and evaluation of abnormal cerebral perfusion in these patients is therefore clinically important. We aimed to evaluate the difference in cerebral hemodynamics measured by acetazolamide challenged CT perfusion (CTP) imaging between patients with distal and proximal internal carotid artery (ICA) stenosis.

Methods: Fourteen patients with symptomatic moderate to severe unilateral stenosis at the distal (n=7) or proximal (n=7) ICA underwent CTP imaging and transfemoral cerebral angiography. CT examination was performed using a multidetector helical scanner (Light Speed 16, GE Healthcare, USA). The regional cerebral blood flow (rCBF), cerebral blood volume (rCBV), and mean transit time (rMTT) were measured in the ipsilesional vascular territory of the distribution of the anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA) in the patients and compared with those of the contralateral side and three normal controls. The Cerebral vascular reserve (CVR) capacity was measured using acetazolamide.

Results: The mean stenosis rate was 81.9±16.2% in proximal ICA stenosis patients and 65.4±17% in distal ICA stenosis patients. The resting rCBF in the ipsilesional ACA and MCA was significantly decreased in the proximal ICA stenosis patients than in the distal ICA stenosis patients or normal controls (P<0.05). The rCBF and rCBV were significantly increased in the ipsilesional ACA territories in the proximal ICA stenosis patients after acetazolamide challenge (P<0.05). The CVR capacity changes were not significantly different distal and proximal ICA stenosis patients.

Conclusion: These findings suggest that the patients with proximal ICA stenosis have resting misery perfusion state than those of distal ICA stenosis with preserved vasomotor reactivity.

DIFFUSION TENSOR IMAGING AND DIFFUSION TENSOR IMAGING-FIBRE TRACTOGRAPH DEPICT THE MECHANISMS OF BROCA-LIKE AND WERNICKE-LIKE CONDUCTION APHASIA

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Objectives: Conduction aphasia is usually considered to be arcuate fasciculus (AF) damaged. It is important to underline many features of conduction aphasia relate more to a cortical deficit than a pure disconnection mechanism. In this study, we tried to explore the mechanisms of Broa-like and Wernicke-like conduction aphasia using diffusion tensor imaging (DTI) and DTI-fibre tractograph (DT-FT).

Methods: We enrolled five Broca-like, five Wernicke-like conduction aphasia and ten volunteers, we analyzed AF, Broca's and Wernicke's area by DTI, measured fractional anisotrogy (FA), compared the Results of left hemisphere with that of right hemisphere (conduction aphasia cases and volunteers, respectively), then compared the Results of conduction aphasia cases with those of volunteers, we also compared the fiber construction of Broca's and Wernicke's areas by using DT-FT.

Results: The FA occupied by the identified connective pathways in the left hemisphere was larger than in the right in control group (P<0.05). Among Broca-like aphasia, the FA of left Broca's area was smaller than that of right mirror side (P<0.05) while the FA Wernicke's area just like the control group, and the FA of left anterior segment of AF was smaller than that of right mirror side (P<0.05). On the other hand, among Wernicke-like conduction aphasia, the FA of left Wernicke's area was smaller than that of right mirror side (P<0.05) while the FA Broca's area just like the control group, and the FA of left posterior segment of AF was smaller than that of right mirror side (P< 0.05).

Conclusions: Some conduction aphasia occurred due to a cortical lesion. The different damaged areas of AF, the different features of language disorders of conduction aphasia. A lesion involved Broca's area and the anterior segments of AF would lead to Broca-like conduction aphasia, whereas a lesion involved Wernicke's are and posterior segments of AF would lead to Wernicke-like conduction aphasia.

Interesting and challenging cases

168 Interesting and challenging cases

NEUROSARCOIDOSIS PRESENTING WITH STROKE AND CRANIAL NEUROPATHY: CASE REPORT AND NEURORADIOLOGIC FINDINGS
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Background: Sarcoidosis involves the nervous system in approximately 5% of cases. Neurosarcoidosis has a wide variety of clinical presentations such as cranial neuropathy, encephalopathy, meningitis, intracranial mass lesions, and others. Stroke in neurosarcoidosis is extremely rare.
Methods: Case report, clinical, neuroradiologic and laboratory findings.
Results: We report on a 26-year-old woman, who presented with acute vestibulopathy and visual field loss two weeks after the diagnosis of acute sarcoidosis (Löfgren's syndrome) had been made. Cranial MRI-scan showed multiple infarcts in the diffusion-weighted sequences in both hemispheres, the largest lesion affecting the left occipital lobe (fig. 1). In the time-of-flight-(TOF) angiography a proximal stenosis of the left posterior cerebral artery was seen (fig. 2). Additionally there was gadolinium enhancement in the pituitary stalk and the right side of the cavernous sinus. Transcranial Doppler's sonography confirmed a high-grade stenosis of the left posterior cerebral artery and a stenosis of the right middle cerebral artery. Transesophageal echocardiography was normal. CSF showed lympho-monocytic pleocytosis, oligoclonal bands were negative. High-dose i.v.-methylprednisolone was given with a fast remission of the vestibular dysfunction but not improving the visual field-loss.
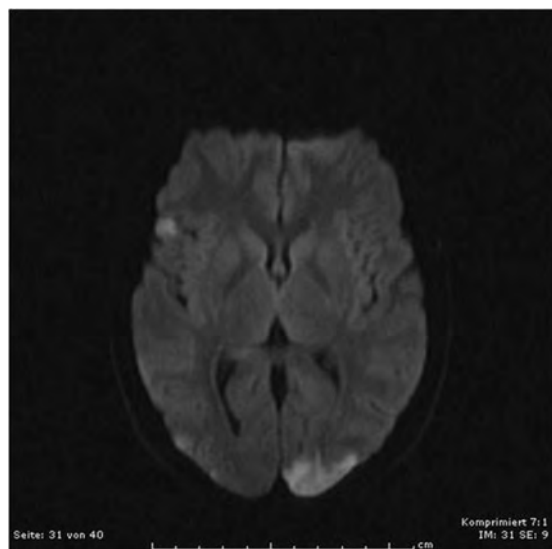
Conclusion: Granulomatous vasculitis typically involving perforating arteries is found in neurosarcoidosis and usually causes a slowly progressive encephalopathy. In the present case vasculitic involvement of the arterial circle of Willis is to be presumed due to the evidence of cerebral artery stenosis in Doppler's sonography and TOF-angiography. The present case proves that stroke is a rare but severe manifestation of neurosarcoidosis presumably due to granulomatous vasculitis of large brain arteries. Neurosarcoidosis is to be taken into account in the differential diagnosis of cerebral infarction in younger age.

169 Interesting and challenging cases

BILATERAL INFARCTION OF THE GENU OF THE CORPUS CALLOSUM AND FORNIX: AN INTERESTING CAUSE OF GLOBAL AMNESIA AND A REVIEW OF THE LITERATURE
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Background: Infarction of the corpus callosum is uncommon. Memory disturbance due to ischaemic stroke may be misdiagnosed as one of the more common causes of acute memory deficit. We present a case of global amnesia following bilateral infarction of the genu of the corpus callosum and fornix and a review of case reports in the literature.
Methods: Description of a case report and a MEDLINE search (1990-2010) for case reports using the key words fornix, genu, corpus callosum and infarction.
Case: A 71 year old male vasculopath was referred to the neurovascular clinic 6 days following abrupt onset of memory disturbance. The following day he was able to drive to the seaside but was unable to recollect events of the past year. He ate 4 ice-creams having not remembered eating ones earlier. He had profound anterograde and retrograde amnesia. He had no focal neurological deficits. Magnetic resonance (MR) imaging with diffusion weighted sequences revealed restricted diffusion in the genu of the corpus callosum and fornix bilaterally (images 1 and 2) consistent with acute infarction. He had no carotid disease on MR angiography and echocardiography was normal.

Results: 12 case reports exist, 5 of which involve the retrosplenium, 1 the fornix and retrosplenium, 3 the fornix in isolation and 3 involving the genu and fornix in combination.
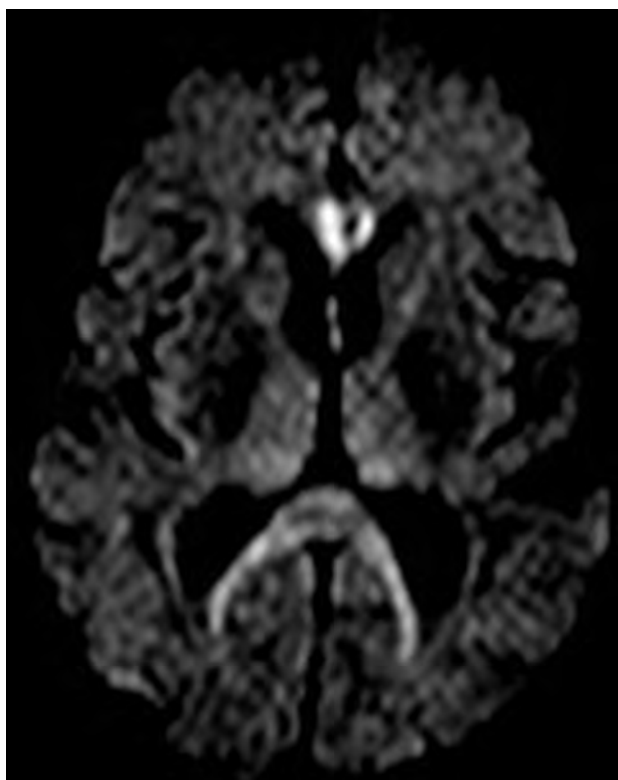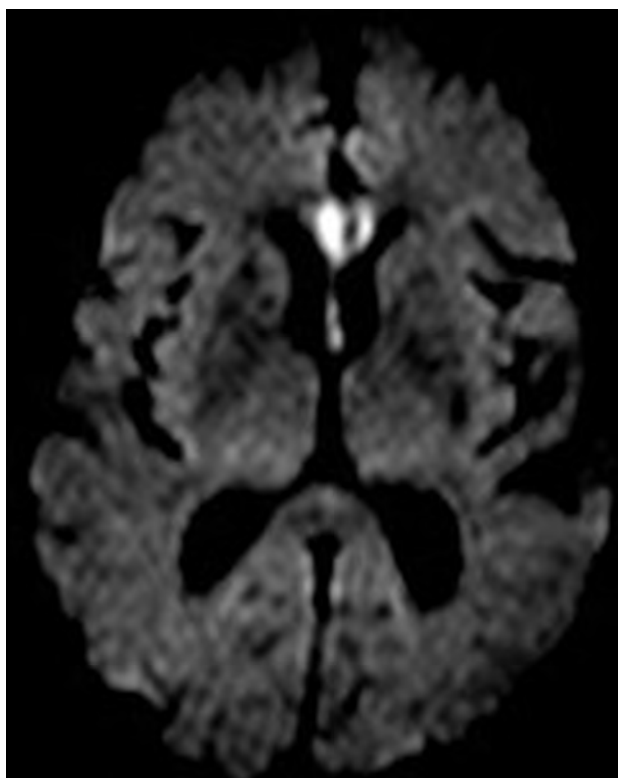
Conclusion: Memory disturbance as a result of corpus callosum infarction is very uncommon. The retrosplenium and in particular the fornix appear to be important components of the memory tracts. Ischaemic stroke remains an important cause of acute amnesic syndromes and can be misdiagnosed leading to delay in appropriate investigation and secondary prevention. To our knowledge this is one of only 4 cases in the literature to present with this pattern of genu and fornix infarction with isolated amnesia.

170 Interesting and challenging cases

EXTERNAL DECOMPRESSIVE SURGERY IN EXTENSIVE CEREBRAL VENOUS THROMBOSIS WITHOUT HEMORRHAGIC PARENCHYMAL LESION: A CASE REPORT

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Purpose: The most frequent cause of death in patients with Cerebral Venous or Sinus Thrombosis remains trans-tentorial brain herniation. In malignant cases, decompressive surgery may be the ultimate chance to avoid a fatal issue.

Case Report: A 20-years old woman was admitted in our institution with unusual and severe headache. Nausea with iterative vomiting were present but neurological examination showed no focalization sign. The initial Computed Tomo-Venography showed extensive thrombosis of the all sinuses, cerebellar veins and deep veins system. Intra venous heparin was initiated immediately but she deteriorates in the early hours (Glasgow Score Scale 9). A mechanical local thrombectomy was decided during the first day, just before her admission in the intensive neurological care unit. Despite aggressive therapy including pentobarbital coma, hypertonic saline, diuretics and secondary ventriculostomy during a brief interruption of the anti-coagulant treatment, the patient continues to have refractory intracranial pressure. A new computed tomography showed no hemorrhagic infarct but the persistence of the venous thrombosis and a mild sub-arachnoid hemorrhage in the inter-pedoncular cistern. External decompressive craniotomy was decided 48 hours after the onset of the hospitalization with progressive normalization of the intracranial pressure levels.

The clinical status improved then dramatically and the patient was discharged to her home after 5 weeks with a modified Rankin Scale 1.

Conclusion: External decompressive craniectomy should be considered in patients with malignant cerebral venous thrombosis. Reviewing the recent literature, we found several uncontrolled case series where this procedure can be life-saving with an excellent outcome.

171 Interesting and challenging cases

THE RISKS OF BLOWING UP BALLOONS

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Background: Non traumatic cervical artery dissections (CAD) have been related with different recreational activities (not with balloon inflation) and mild mechanical injuries. Proposed mechanisms include minor/non detected cervical trauma, jerky head movements, forced neck hyper-flexion and hyper-extension movements that would rupture the arterial wall.

Case Report: 35 year-old woman admitted with diplopia and intense cervical pain of sudden onset, which started abruptly in her son's birthday.

At emergency room she showed vertical upgaze paresis, affecting saccades and pursuit, convergence nystagmus, accommodative insufficiency and pseudoabducens left palsy. Cervical pain started while she was preparing the party, after blowing up balloons for more than thirty minutes. Despite the pain, she kept on blowing balloons, until so intense that she had to give up. Later on she started noticing double vision.

With normal brain plain CT, diagnosis of posterior circulation ischemic stroke of unknown origin was established and treatment with antiplatelet therapy (Aspirin300mgr/day) and analgesia was initiated. Brain Magnetic Resonance (MR) two days after symptoms onset revealed subacute ischemic infarction affecting left thalamus and pretectum and some non-diagnostic irregularity of left vertebral artery at V3. Angio-CT (ACT) showed focal narrowing and irregularity of both vertebral arteries. Digital substraction angiography (DSA) confirmed the ACT findings.

Neurologically stable, she was discharged five days later with mild residual diplopia.
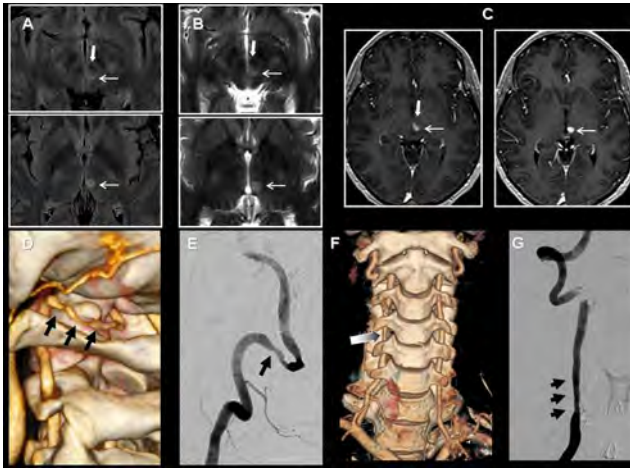
Figure 1. A, B. Axial FLAIR (A) and axial T2-weigthed images (B): hiperintense lesion (white thin arrows) in left midbrain pretectum and medial inferior part of the left thalamus. (red nucleus=white thick arrow). C. Axial 3D-spoiled gradient-recalled (SPGR) T1-WI post-contrast: homogeneous enhancement of the lesion. D. 3D Volume-Rendered (VR) post-contrast CT angiography (CTA): focal narrowing and irregularity of the lumen (black arrows-V3 segment). E. Digital Substraction Angiography (DSA). Lateral projection of left vertebral artery: The image correlates with CTA (black arrow). F. 3D VR post-contrast CTA: Narrowing of intraforaminal segment (V2) of right vertebral artery (thick grey arrow). G. DSA. Antero-posterior projection of right vertebral artery: smooth focal tapered narrowing of V2 segment.

Conclusions: We describe a new possible mechanism for CAD. Dissection symptoms started after continuous balloon blowing up for more than 45 minutes. In this activity, repeated increases of intrathoracic pressure happen. During these Valsalva manoeuvres, secondary increases in the pressure in the cervical region and neck compartments occur, due to decreased central venous return and cervical muscles contraction. This repetitive pressure increases in the neck may lead to disruption of the wall of the cervical vessels.
In some cases, blowing up balloons can be a risky business.

172 Interesting and challenging cases

APHEMIA: TO BE OR NOT TO BE TREATED WITH INTRAVENOUS THROMBOLYSIS

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Background: Aphemia is a disorder of speech with disruption of a specific network in the motor system that is responsible for articulation. The most common cause is an ischemic infarct usually seated in the inferior frontal gyrus. We report two patients with aphemia due to acute stroke resolved successfully with intravenous thrombolysis.
Methods: The first patient is a 78 years old man with history of hypertension and atrial fibrillation and the second one is a 77 years old man with history of dilated myocardiopathy. Both patients were attended in the Emergency Department after sudden develop of speech difficulty. On examination they made sounds but could not produce words. They kept intact written language expression and had also full comprehension. Oro-bucco-facial apraxia was no present. They were able to move tongue on command. All other neurological examinations were normal. Both cases scored 4 in NIH stroke scale (NIHSS).
Results: In the first patient the brain CT scan did not show any acute ischemic lesion. In the second case a perfusion brain CT showed an ischemic zone in the left frontal cortex with marked decrease in the cerebral brain flow and slightly reduced in the cerebral brain volume suggesting the presence of ischemic penumbra. A transcranial and cervical duplex ultrasound study was performed showing no signs of significant cervical stenosis or relevant asymmetry in the intracranial arteries. They received 0.9 mg/kg recombinant human tissue plasminogen activator (rt-PA) intravenously at 130 and 190 minutes from symptoms onset respectively. 2 hours later both patients were full recovery. CT brain at 24 hours was normal in the two cases.
Conclusion: rt-PA should be considered in stroke patients with aphemia. Although the NIHSS in most cases of aphemia, as ours, are likely to be relatively low, the

decision could be guided by likehood of disability as any stroke causing difficulty in oral communication.

173 Interesting and challenging cases

RECURRENT STROKE LIKE EPISODES DUE TO INNOMINATE VEIN OCCLUSION

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Background: Retrograde jugular venous flow is reported as a unique sonographical or radiological finding without clinical complains. Occlusion of innominate vein is a rare clinical condition, associated with Paget von Schroetter syndrome or thoracic compression. Clinical presentation is typical due to acute venous thrombosis e.g. edema, cyanosis, paresis, paraesthesia and occurrence of collateral veins. Severe neurological deficits due to these have not been reported yet.
Methods: We present a case with three episodes with dysphasia, hemiparesis and facial palsy, agitation and confusion for more than 24 hours strictly associated to territory of left middle cerebral artery. There was no evidence for cerebral infarction in MRI or thrombosis of sinus veins at any time. Seizures were ruled out. Arterial sonography showed regular findings. Prolonged ischemic neurological deficits of cardioembolic origin caused by known artrial fibrillation were discussed. Then special attention was paid on complete retrograde flow of left jugular vein.
Results: There was an unusual hyperintensive signal presenting to left transverse sinus in arterial "Time of flight" MR- angiography. Arterial Angiography was performed and showed normal filling of extra- and intracranial arteries and no evidence for supposed arterio- venous fistula. In venous phase left transverse sinus did not fill with contrast media. Right jugular vein presented with regular orthograde flow. Left jugular vein showed complete retrograde flow. Proceeded phlebography shows total occlusion of left innominate vein. Whole venous drainage from the left arm occurred by retrograde jugular venous flow and crossflow through transverse sinus to the right. Surgical construction of jugulo- jugular bypass was done. After this the patient could discharge without pathologic clinical finding.
Conclusion: Impaired venous drainage from left cerebral hemisphere caused by retrograde left jugular venous flow and crossflow through transverse sinus leads to accumulation of venous blood which maid cause hypoxic conditions with functional deficits without morphologic changes.

174 Interesting and challenging cases

CASE REPORT OF A RARE BUT CHALENGING STROKE MIMIC - SPONTANEOUS SPINAL EPIDURAL HAEMATOMA

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Introduction: With the modern reorganisation of stroke services, pre-hospital systems are being designed to prioritise selection and transfer of patients with sudden onset of neurological deficits to acute stroke units that provide a thrombolysis service. This creates new problems in making a prompt diagnosis of stroke mimics.
Spontaneous spinal epidural haematoma (SSEH) is a rare condition. It represents a neurosurgical emergency, and swift diagnosis and referral are paramount. The usual clinical presentation is sudden neck or back pain followed by limb weakness – usually paraparesis or quadriparesis, but there have been case reports of cervical Brown Sequard syndrome with hemiparesis [1].
Methods: We present the case of a 53 year old male patient who was brought in by ambulance to our stroke unit, one hour after developing sudden onset neck pain, with left arm and leg weakness. On examination there was dense left arm and leg weakness, but also 4/5 right leg weakness and a C4-C5 sensory level. Previous medical history included atrial fibrillation for which he was on warfarin treatment – INR on admission 3.1. Head CT scan was normal so MRI head and cervical spine was performed. This demonstrated a large acute left dorsal epidural haematoma extending from the level of C2 to T1. The cord compression was more prominent from C5 to T1.
Results: The patient was referred to neurosurgery and underwent C6-T1 laminectomy with evacuation of epidural haematoma. Subsequently there was significant improvement of his neurological deficits.
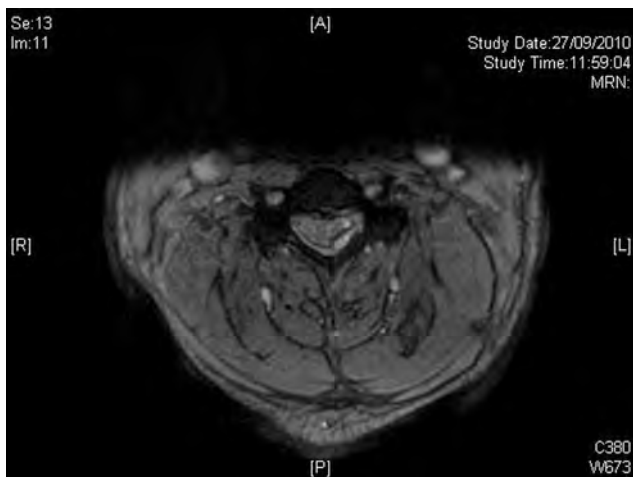
Discussion: This case report emphasizes the necessity of prompt diagnosis of a rare stroke mimic like SSEH in the context of acute presentations to the stroke units. It also highlights the clinical varieties and management options for this rare condition.

175 Interesting and challenging cases

ISOLATED LEFT VENTRICULAR NONCOMPACTATION: AN UNCOMMON CAUSE OF EMBOLIC STROKE

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Isolated left ventricular noncompactation: an uncommon cause of embolic stroke.

Background: Isolated left ventricular noncompactation (LVNC) is a rare disorder of endomyocardial morphogenesis that Results in multiple trabeculations in the left ventricular myocardium. Main clinical manifestations are heart failure, embolic events, cardiac arrythmias and sudden death. Diagnosis is made by echocardiography and cardiac MRI, fulfilling following criteria: 1. Absence of coexisting cardiac structural abnormalities. 2. Numerous, excessively prominent trabeculations and deep intratrabecular recesses in left ventricle. 3. Recesses are supplied by intraventricular blood on colour Doppler. 4. Two-layer structure with thin compacted layer (C) and thick noncompacted layer (N), with a N/C rate >2. Oral anticoagulation is recommended after embolic events. Other therapies are heart failure therapy, implantation of an automated defibrillator/cardioverter and heart transplantation, depending on risk stratification.

Case Report: A 36-year-old patient with no relevant past medical history presented with dizziness, multidirectional nystagmus and ataxia. MRI showed two ischemic lesions involving right cerebellar hemisphere and left posterolateral medulla. Digital angiography did not show any finding suggesting arterial dissection. Echocardiography showed lack of compaction in apical and lateral walls of the left ventricle, which was confirmed by MRI (N/C rate 16/5), leading to the diagnosis of LVNC.

Conclusions:

– LVNC is a rare type of myocardiopathy.

– Mortality and morbidity are high, including heart failure, thromboembolic events and ventricular arrythmias and sudden death.

– Development of high definition image tests has increased the frequency of diagnosis.

176 Interesting and challenging cases

SUSAC'S SYNDROME – AN UNDERDIAGNOSED ENTITY

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Introduction: Susac's syndrome is a rare disease with unknown pathogenesis caused by a micro angiopathy affecting arterioles of the brain, retina and cochlea giving the classic clinical triad of subacute encephelopathy, visual loss and sensorineural hearing loss. We describe a young patient with initial diagnostic dilemma, later diagnosed with this syndrome due to characteristic clinical and radiological features.

Case report: 23 year old male university student presented to stroke unit on early October 2010 with acute patchy visual loss in his left eye and progressive personality changes for few days noted by friends. His neurological examination was unremarkable except for patchy loss in visual fields in left eye. Fundus examination showed branch retinal artery occlusion in his left eye confirmed by further flourescin angiogram of retina (Fig 1). Blood tests including autoantibody & thrombophilia screen,ESR and viral serology were negative. T2 weighted MRI brain showed multiple small foci of high signal intensities in periventricular white matter and central corpus callosum (Fig 2). MRA brain showed significant narrowing and beaded appearance of intracranial arteries suggestive of vasculitis. He was started on oral high dose steroids with initial diagnosis of Cerebral Vasculitis.After 3 weeks he continued to deteriorate with personality changes and on questioning complained of reduced hearing both ears which on further audiological examination showed bilateral low frequency sensorineural hearing loss. A diagnosis of Susac's syndrome was made and started on IV methyl prednisolone & cyclophosphamide.There was marked improvement in short term memory and concentration on psychometric testing and he continues to make good progress.

Figure 1. Fundus examination showing branch retinal artery occlusion confirmed by retinal flourescin angiography.
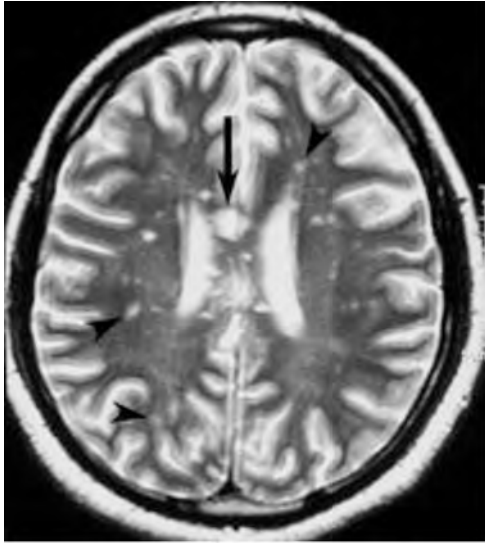
Figure 2. MRI T2 weighted image showing mulitple small high signal intensity lesions in periventricular white matter and corpus callosum.

Conclusion: Susac's syndrome is a rare commonly under diagnosed disease and a high index of suspicion is necessary when dealing with young patients with classic features as early treatment may prevent further cognitive sequelae.

177 Interesting and challenging cases

INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHAEMIC STROKE IN A PATIENT WITH VENTRICULO-PERITONEAL SHUNT

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Case description: A 75 year old male was admitted with sudden onset of left sided weakness involving face, upper and lower limbs. There was no history of headache, vomiting. He has had a ventriculo-peritoneal (VP) shunt inserted in 2005 for normal pressure hydrocephalus.

He had signs of left hemiparesis and NIHSS was 14. CT brain showed a VP shunt and no early ischaemic changes or any signs of intracerebral bleed. Though NIHSS improved to 8, thrombolysis was considered in view of persistent neurological deficit. Previous neurosurgery and VP shunt is considered a contraindication for thrombolysis. Patient and her family were keen for it. He was thrombolysed with intravenous Alteplase. 24 hours NIHSS was 0 and post thrombolysis CT scan showed no intracerebral bleed (Figs. 1 and 2).
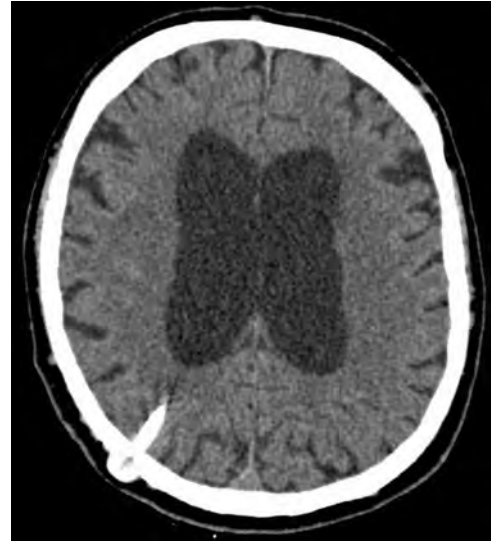
Discussion: Thrombolysis for acute ischaemic stroke is well established but only a small proportion is eligible due to delayed presentation and a long list of contraindications. Most of contraindications are based on expert opinion, rather than scientific evidence. European license [1] is more restrictive than the American one and states any history of CNS damage as a contraindication.

Many case reports of thrombolysis performed outside license have been published and in a recent large series, 51% of thrombolysed patients had one or more license contraindications and off-license thrombolysis was not associated with poorer clinical outcome, except for age >80 years, nor with increased rates of symptomatic intracerebral hemorrhage [2].

In a review of 273 cases of off-label thrombolysis, Aleu et al. [3] could not find any report of history of VP shunt and thrombolysis. We also searched PUBMED and did not find any case report. To our knowledge, this is the first reported case of a VP shunt thrombolysed with a good outcome.

References:
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2. Meretoja et al. Stroke. 2010;41:1450-1458.
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178 Interesting and challenging cases

THREE ATTACKS OF TRANSIENT GLOBAL AMNESIA WITHIN TWO DAYS: A CASE REPORT

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Transient Global Amnesia (TGA) is a classical disease. It presents with an abrupt onset of anterograde amnesia. An attack is lasting most of the time less than 10h and recedes gradually. The recurrence rate is estimated to be low. We report a case of patient with 3 attacks of TGA within 2 days.

Mrs. M., aged 68 years, after an altercation with her neighbor, starts at 9 am aTGA: she asks repetitive questions about time and date and is not able to form new memories. At hospital (2 hours later), the patient has all recovered. Few minutes later, during the consultation, the patient presents another memory disorder with an anxious perplexity: "But where am I here? Where am I here?" One explains it to her, but she goes on asking. This state of amnesia lasts 8 hours and she comes back to her normal state. The next morning, the patient starts another typical TGA with recovery in 3 hours. For each of the episodes neurological examination is normal.

The key differential diagnoses to be considered are: Temporal Partial Seizure (TPS), Transient Ischaemic Attack (TIA). In this patient, High-resolution MRI with thin slices hippocampus and two Diffusion-weighted MR imaging (realized in the first minutes of the attack and 6 hours after onset) are also completely normal. To detect a TPS, 2 EEG are performing. The first pattern recorded during the attack and the second realised after TGA are strictly normal. No abnormality is finding on the PL. Given the normality tests, a complete clinical recovery, the diagnosis of TGA is retained.

Many reports confirm that attacks are solitary with infrequent recurrences in the year following. This presentation with multiple attacks in less than 2 days is to know after removal of differential diagnoses.

VERTEBRAL ARTERY DISSECTION PRESENTING WITH 5TH AND 6TH CERVICAL ROOT LESION WITHOUT CEREBRAL ISCHEMIA

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Background: Vertebral artery dissection (VAD) is rarely associated with cervical compressive radiculopathy (1-3%) (e.g. Stroke 2006;37:2499), and then also Results in posterior circulation ischemia. In the presence of neck pain, isolated arm paresis due to radiculopathy as the sole manifestation of VAD is exceedingly rare.

Case report: A 52 year-old man presented with a history of neck pain for 9 days, that was severely exacerbated under chiropractic therapy during the last 6 days, eventually radiating to the left shoulder region. He had noticed a paresis of the upper arm for 2 days prior to admission.

On admission, clinical examination revealed paresis of C5 and C6 muscles of the left arm with the following MRC grades: upper arm abduction and elevation 2, upper arm external rotation 4-, elbow flexion 4. The deep tendon reflexes (DTR) of the left biceps brachii and brachioradialis muscles were absent, while DTRs of the left triceps brachii and all other muscles were normal. Only a small area of sensory impairment was found in the left lateral proximal upper arm. Coordination and cranial nerves were normal. Colour-coded duplex sonography of the cervical arteries did not show signs of stenosis; however, the vessel wall in the left V1-/V2-segment seemed thickened by echolucent material.

Magnetic resonance (MR) imaging showed a circular hematoma of the left vertebral artery in the V2 segment compressing the nearby C5 and C6 nerve roots. MR angiography of the cervical vessels and MR imaging of the brain were completely normal.

Conclusion: The diagnosis of VAD can be very tricky in case of missing signs of cerebral ischemia and negative ultrasound findings of stenosis. Radiculopathy as the only neurological manifestation of VAD may be easily confused with cervical disk prolapse, plexopathy of Parsonage-Turner-Syndrome, etc. To diagnose VAD in this setting is important, as one would want to avoid steroids for their thrombogenic potential and initiate antithrombotic therapy.

PERCHERON INFARCT: TWO ANGIOGRAPHICALLY PROVEN CASES AND INTERVENTION

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Background: An artery of Percheron (PA) is a rare vascular variation arising from the unilateral posterior cerebral artery (PCA) that sends perforators to the bilateral thalami. Its occlusion leads to a Percheron infarct (PI). Recent advances in neuroimaging have shed light on this uncommon pathology.

Methods: Patients with PI were retrospectively studied from a series of 569 patients with ischemic strokes.

Results: We found two cases with PI: Case 1: A 60-year-old healthy female abruptly became somnolent. They found BTI without major artery involvement. Abulia, stereotype behavior and diplopia persisted as she became conscious. We assumed that a cryptogenic embolus that had migrated into the basilar tip had transiently disrupted the perforators from bilateral PCA. However, a conventional angiogram revealed a recanalized PA. Case 2: A 64-year-old female who had recently had a myocardial infarction suddenly became comatose and developed tetraparesis. Urgent CT/CTA in the ER was normal, but proximal perforators from the PCA were absent on an emergency conventional angiogram. Selective intraarterial fibrinolysis dramatically diminished her symptoms, as the PA from the left PCA emerged. MRI after the intervention showed incomplete BTI.

Conclusion: Although the PA is a smaller artery, PI presents with BTI that often is accompanied by critical states with disturbance of consciousness. As other pathologies such as basilar tip thrombus may show similar features and lesions, direct confirmation of PA by means of vascular imaging with higher resolution is necessary for the diagnosis of PI. While a rapid and precise diagnosis is still challenging, experimental treatment with ultraselective fbrinolysis against PI seems promising. In light of this fact, an emergency conventional angiogram and subsequent intervention may contribute to both diagnosis and treatment in cases of suspected PI. Ultra high field MRA or multislice CTA with iv rt-PA may replace these in the near future.

SAFETY AND EFFECTIVENESS OF EMERGENCY CAROTID ARTERY STENTING FOR A HIGH-GRADE CAROTID STENOSIS WITH INTRALUMINAL THROMBUS UNDER PROXIMAL FLOW CONTROL IN HYPER-ACUTE AND ACUTE STROKE SETTING

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Background and purpose: The purpose was to investigate the feasibility, safety, and effectiveness of emergency carotid artery stenting (eCAS) for high-grade carotid stenosis with intraluminal thrombus (ILT) under or without proximal flow control (PFC).

Material and Methods: Included for the analysis were acute ischemic stroke patients 1) who were admitted between 2001 and 2009, 2) who had serious neurological symptoms, 3) without large diffusion-weighted imaging lesions, 4) high-grade carotid stenosis with ILT and 5) who underwent eCAS. Patients had undergone eCAS without PFC until 2004 (group C) and have undergone eCAS under PFC since 2004 (group P). National Institutes of Health Stroke Scale (NIHSS) on admission, NIHSS just before CAS, 7-day NIHSS after CAS, and 3-month modified Rankin Scale (mRS) were investigated between two groups.

Results: Forty-nine patients underwent eCAS, and eight of the forty-nine patients had high-grade stenosis with ILT. Four of the eight patients belonged to group C, and four of the eight patients belonged to group P. Probable distal embolism associated with eCAS occurred in two cases of group C, however did not occur in group P. In group C and P, 7-day NIHSS (median) was 15 and 5 (p<0.05), 3-month mRS (median) was 4 and 2 (p<0.05), respectively, although there were no significant differences in NIHSS on admission and just before CAS between two groups.

Conclusion: In acute stroke patients suffering from high-grade carotid stenosis with ILT, eCAS under PFC is safer and more effective in achieving favorable clinical outcome than eCAS without PFC.

LUXURY PERFUSION IN EARLY POST-STROKE PERIOD DESPITE PERSISTENT ARTERIAL OCCLUSION

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Background: Cerebral autoregulation (CA) maintains uniform blood flow. In acute ischemic stroke (AIS), CA is usually impaired &, owing to impaired vasomotor response, rapid recanalization of an occluded artery might result in abnormally increased regional blood flow- "Luxury perfusion" (LP). We describe LP and its hemodynamic consequences in a patient with persistent arterial occlusion.

Methods: We present the clinical course and salient radiological findings in a young AIS patient due to carotid dissection.

Result: A 49-years old man presented with 1-day history of multiple transient episodes of right-sided weakness. The episodes were precipitated by exertion and each lasted 5-10 minutes. Brain MRI revealed multiple acute infarcts in left middle cerebral artery (MCA) territory. Catheter angiography suggested left internal carotid artery (ICA) dissection. Considerable neurological fluctuations occured during first few days, related to change in blood-pressure and body position. CT perfusion imaging demonstrated prolonged Mean transit-time in left MCA territory with elevated cerebral blood-volume and blood-flow, representing LP (despite occluded ICA). Perfusion and vasodilatory reserve evaluated by HMPAO-SPECT confirmed LP in the left hemisphere (55% counts versus 45% on right on baseline scan. Interestingly, vasodilatory challenge with acetazolamide induced paradoxical reduction in perfusion in left hemisphere (counts 47% versus 53% on right). Intracranial steal phenomenon (reversed Robin Hood syndrome) was observed during vasomotor reactivity (VMR) assessments with transcranial Doppler. Anti-thrombotics, statins and "head-down" position with liberal intravenous fluids for 2-week resulted in good clinical recovery. No intracranial steal phenomenon was noted on TCD-VMR evaluations at 3 months. He has remained symptom-free during 11 months of follow up.

Conclusion: Luxury perfusion can occur in patients with persistent arterial occlusion & appears protective. However, it may not withstand vasodilatory challenges & contribute towards neurological fluctuations during early phase of AIS. Early recognition & appropriate measures can prevent further tissue injury.

INTRAVENOUS THROMBOLYSIS IN HANDL MIMICKING ISCHEMIC STROKE WITH FRONTOPARIETAL HYPOPERFUSION IN CT SCAN

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Background: Headache with neurologic deficits and CSF lymphocytosis syndrome (HaNDL) is an entity of unknown physiopathology that can present as a stroke mimic. Routine brain CT and MRI scan performed in HaNDL cases are usually normal. We present a patient with a HaNDL syndrome mimicking a stroke treated with intravenous thrombolysis due to fronto-parietal hypoperfusion detected in perfusion computed topography (CT).
Methods: A 38-year-old woman was admitted to the emergency department referring acute motor aphasia, mental confusion and mild right hemiparesis that had started abruptly two hours before. Blood tests, EKG and CT scan were normal. A perfusion CT scan revealed a left frontal and parietal hypoperfusion area without arterial occlusions in CT-angiography. A left cerebral media artery stroke was suspected and thrombolysis with intravenous tPA was administered. After 5 hours she completely recovered of her neurological deficits, and could talk, she referred moderate headache which lasted 10 hours. Cranial multiparametric magnetic resonance imaging performed at 24 hours was normal.
Results: 3 days later she had a new episode of aphasia and right hemiparesis with headache. This time a lumbar puncture was performed which revealed mononuclear pleocytosis and a high protein level (1.3 g/l). Microbiological tests ruled out infectious disease and a diagnosis of HaNDL syndrome was performed. The patient experienced other 7 episodes of neurological focal deficit with headache during the following 2 months. After 6 months of follow up, she has had no more focal neurological deficits or headache.
Conclusion: HaNDL can present as a stroke mimic with perfusion CT abnormalities.

CEREBRAL CAVERNOUS MALFORMATIONS AND SYMPTOMS OF TRANSIENT ISCHEMIC ATTACK AND STROKE – CASE STUDY

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Background: Cerebral cavernous malformations (CCMs) are developmental malformations of the vascular bed within the brain and/or spinal cord. These malformations are made up of immature blood vessels that are prone to rupture and repeated haemorrhage. Patients may be asymptomatic or present with focal neurological deficits or seizures depending on the location of the lesion, which often become clinically apparent between the ages of 20-40 years. Recently, genetic studies have shown that patients with multiple CCMs may be due to a familial autosomal dominant form of the disease, most common in the Hispanic population. Although neurosurgeons have been aware of large CCMs, there is very little information in medical literature regarding this condition causing transient ischemic attacks (TIA) and stroke symptoms. As MR imaging is becoming more frequently used for diagnosing TIA, more of these lesions are picked up in routine practice.
Case presentation: A 39 year old lady presented with acute onset of total right hemiparesthesia associated with occipital headaches that were dull in nature. She had also suffered multiple episodes of dizziness in the previous month and complained of unsteadiness on her feet. On examination she had a GCS of 15/15 with no focal neurological deficit. Initial differential diagnoses included TIA and migraine. An MRI brain scan showed multiple CCMs, widespread throughout the cerebral cortex. There was also evidence of haemorrhage in cavernomas located in the left temporal lobe and pons. Her symptoms gradually improved and a repeat MRI showed that the haemorrhage had resolved. No neurosurgical intervention was offered at that time.
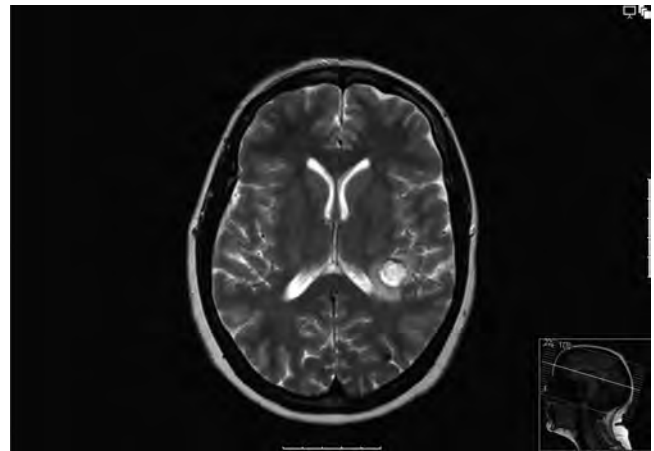
Image 1. MRI T2 axial flare image showing left temporal lobe CCM with haemorrhage.
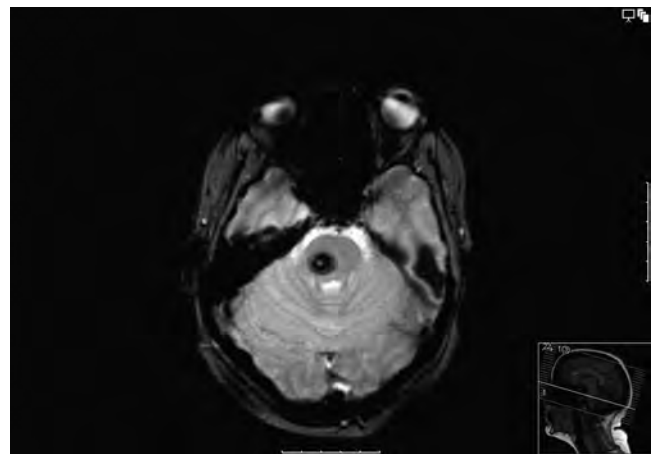
Image 2. MRI Gradient Echo im5age showing pontine CCM with haemorrhage.

Conclusion: The diagnosis of CCM should be considered in younger patients presenting with acute stroke/TIA symptoms. Neurosurgical intervention may be needed for those developing recurrent symptoms, depending on the site and size of the lesion.

ISOLATED WEAKNESS OF INDEX, MIDDLE AND RING FINGERS DUE TO CENTRAL PRECENTRAL CORTICAL INFARCTION

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Background: Small cortical strokes can produce isolated motor paresis that mimics peripheral neuropathy in the upper extremity. Several cases of isolated fingers weakness caused by small cortical infarctions have been reported. However,

isolated weakness of index, middle, and ring fingers has not been reported to be caused by precentral cortical infarction.

Case: A 79-year-old woman noted difficulty in using her chopsticks one morning. She complained of weakness in her index, middle, and ring fingers. Neurological examination revealed the following muscle weakness: flexion (MRC 2/5), extension (2/5), abduction (3/5), and adduction (3/5) of the right index, middle, and ring fingers. Strength was normal for other fingers, wrist, elbow and shoulder movements. She had no sensory deficits. Nerve conduction studies in the upper limb were unremarkable. Brain MRI showed acute cortical infarction on the left central precortical gyrus. MRA revealed stenosis of the right posterior cerebral artery and atherosclerosis in the intracranial arteries.

Conclusion: We report a case of isolated weakness in index, middle, and ring fingers due to central precentral cortical infarction. To our knowledge, this is the first report of isolated weakness in index, middle, and ring fingers caused by a small cortical infarction.

186 Interesting and challenging cases

SPONTANEOUS CONVEXITY SUBARACHNOID HEMORRHAGE: CLINICAL PRESENTATIONS, RADIOLOGICAL FINDINGS AND ETIOLOGIES

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Introduction: Acute non traumatic convexity subarachnoid hemorrhage (cSAH) is a rare type of cerebro-vascular disease with various etiologies. The aim of this monocentric study was to identify clinical presentations, imaging pattern and etiologies in a large case series of such patients.

Methods: We retrospectively analysed clinical and radiological data of consecutive patients with a diagnosis of isolated cSAH on CT scan, admitted to our institution between 2009 and 2011. All patients had brain magnetic resonance imaging (MRI) as a part of their initial evaluation.

Results: 18 patients (13 women and 5 men, mean age: 61 years) were identified. The main clinical symptoms at presentation were focal transient neurological deficit (n = 11) and thunderclap headache (n = 5). Two patients had progressive headache and two other had partial epileptic seizure. MRI abnormalities associated to cSAH were prior hemorrhage, microbleeds, severe leukoencephalopathy and hemosiderosis in favour of probable amyloid angiopathy (AA) (n=5), or vasogenic edema in parieto-occipital areas compatible with a posterior reversible encephalopathy syndrome (PRES) (n=3). Other underlying causes of cSAH were: reversible cerebral vasoconstriction syndrome (RCVS) (n=3), vasculitis (n=1) and excessive dose of anticoagulant (n=1). Three cases remained unresolved.

Conclusion: This study confirms that cSAH is a rare condition possibly related to a wide spectrum of etiologies. Combination of brain MRI and MRA and eventually digital subtraction angiography allow identification of AA, RCVS and PRES which represent more than 50% of the underlying mechanisms. Among older patients, cSAH was mainly related to AA while in younger patients, RCVS represented the most frequent etiologie.

187 Interesting and challenging cases

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME CAUSED BY INTRACRANIAL HYPOTENSION

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Background: Posterior reversible encephalopathy syndrome (PRES) is meanwhile a well-recognized syndrome since its initial description by Hinchey et al. in 1996. Endothelium cell dysfunction resulting in vasogenic edema preferably in the occipital lobes is thought to be the main mechanism. A number of conditions (arterial hypertension, preeclampsia/eclampsia, allogeneic bone marrow transplantation, organ transplantation, autoimmune disease and high dose chemotherapy) may lead to PRES. Intracranial hypotension (IH) has been previously reported as possible cause in a single case by Pugliese et al. in 2010.

Methods: We hereby present a case of a 68-years-old female patient with IH and PRES.

Results: The lady received lumbar liquor drainage for 14 days for treatment of a dural tear following lumbar disc operation. After successful closure of the tear she was send to a rehabilitation centre. The next day she was severely disorientated and presented mild left sided hemisyndrome. Under the suspicion of posterior cerebral

infarction she was transferred to a stroke unit. Moderate arterial hypertension and type-2 diabetes were known vascular risk factors. Normal values were registered during her hospital stay. Considering CT and MRI finally a PRES was diagnosed. No other potential cause other than the lumbar liquor drainage was found. During rehabilitation treatment over three months the symptoms significantly regressed. Finally, only moderate deficits in attention, concentration and short-term memory were detectable. Follow-up MRI shows a nearly complete remission of the hyperintense lesions in the occipital lobes. Beside that a prominent leucoaraiosis and a partial infarction of the anterior cerebral artery was visible.

Conclusion: Our observation indicates that IH can lead to PRES.

188 Interesting and challenging cases

TRANSIENT FLOATING THROMBUS OF THE INTERNAL CAROTID ARTERY ASSOCIATED WITH THE JAK2V617F MUTATION

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Background: Essential thrombocythemia (ET) is a mieloproliferative disorder (MPD) characterized by sustained elevated platelet count. ET is an uncommon cause of cerebrovascular disorders and, if it occurs, thromboses of cerebral veins are more frequent than of arteries.

Case: A 33-year-old woman with a medical history of infertility and sudden hypoacusia one month earlier, was admitted for acute speech difficulty and right facial-arm-leg weakness, with a NIHSS score of 10. The carotid duplex showed a free-floating thrombus (FFT) in the left internal carotid artery that was not producing flow aceleration. However, the thrombus dissapeared two hours later, as shown by a second carotid duplex and arteriography, without any clinical deterioration. The MRI showed a brain infarction in the left middle cerebral artery territory. Peripheral blood showed a platelet count of 505×10^9/L. Other causes of stroke, including thrombophilias and cardiac source of emboli were ruled out after a complete cerebrovascular study.The JAK2V617F mutation was detected in peripheral blood samples by a multiple allele-specific PCR. The BCR-ABL1 translocation study (Philadelphia chromosome) was negative. The bone marrow aspiration showed clustered hyperlobulated megakaryocytes. She was diagnosed with MPD and specifically ET. Antiplatelet treatment was initiated with progressive neurological improvement. The 3-month mRS score was 2.

Conclusion: the JAK2 mutation may cause thrombosis in large arterial vessels with subsequent stroke production, even in the presence of a mild thrombocytosis. Thus, this entity should be considered in young patients with ischemic stroke and any degree of thrombocytosis.

189 Interesting and challenging cases

HORNER SYNDROME ASSOCIATED WITH HYPOCHROMIA IRIDUM REVEALING A CONGENITAL AGENESIS OF THE INTERNAL CAROTID ARTERY

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Internal carotid artery (ICA) agenesis is a rare developmental anomaly and most frequently asymptomatic, but it may also present as cerebrovascular accidents (CVA). The association with Horner's syndrome is exceptional. We present three cases of agenesis of ICA associated with a Horner's syndrome and hypochromia iridum presenting as focal neurological symptoms.

A system of collaterals develops as a consequence of agenesis of the ICA making the majority of cases asymptomatic. Three types of collateral circulations have been described. These collaterals increase the risk of aneurysm formation and the occurrence of life threatening subarachnoid hemorrhages.

The association of congenital Horner's syndrome and hypochromia iridum without anhidrosis are highly suggestive of sympathetic pathway injury early in life. Such signs should prompt further diagnostic evaluation to demonstrate the presence of the agenesis of the carotid canal. Early diagnosis is essential to rule out potentially life threatening associated vascular anomalies.

190 Interesting and challenging cases

STROKE IN YOUNG MAN SECONDARY TO PAROXYSMAL AF AND THYROTOXICOSIS

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Background: Thyrotoxicosis is a rare thyroid dysfunction, with annual incidence of 0.5 to 1.4 cases/1000 individuals, being more frequent in females. It is characterized by a series of adrenergic demonstrations, which can affect all organs and body systems, and particularly the heart. Atrial fibrillation (AF) is the most common arrhythmia observed in patients with thyrotoxicosis. We report a case which a stroke occurred in a male patient caused by paroxysmal atrial fibrillation due to thyrotoxicosis.

Clinical Case: Male, 41 years, caucasian, 45 days ago developed sweating, palpitations and anxiety, then 10 days ago evolved with left paresthesias and left hemiparesis. There was no relevant medical history. At the admission to the hospital, presented mild hypertension and the cardiac rhythm of AF was detected. During the physical examination a slight increase in thyroid was noted. The cranial resonance confirmed the ischemic area, and duplex carotid and angioresonance were normal Patient underwent anticoagulation, and was investigated for the stroke etiology. Tests of inflammatory activity, lipid profile, serology for HIV, syphilis, Chagas disease, as well as the cerebrospinal fluid were normal. After one month the thyrotoxicosis was confirmed by thyroid function and thyroid scintigraphy that showed goiter with diffuse hypercaptation. Initially, the patient was treated with tapazole and after underwent to total thyroidectomy which the patological findings confirmed the linphocitic thyroiditis. The patient partially recovered the motor and sensitive deficits with a Rankim scale 2/3. After the surgical procedure, he needs continuous hormone replacement.

Conclusion: In the Framingham study AF in the absence of rheumatic heart disease was associated with more than fivefold increase in stroke incidence. Hyperthyroidism is associated with increased supraventricular ectopic activity in patients with normal hearts, the activation of arrhythmogenic foci by elevated thyroid hormones may be an important causal link between hyperthyroidism and AF. This report Aims to emphasize the importance of thyropathy screening exams even in young people and male sex.

191 Interesting and challenging cases

SPONTANEOUS MULTIPLE CERVICAL ARTERY DISSECTIONS IN THE PUERPERIUM

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Background: Spontaneous cervical artery dissection (sCAD) has rarely been reported as a cause of stroke in pregancy/puerperium. We report a case of a young woman with a four vessel sCAD in the puerperium.

Case report: A 31-year-old female with past history of migraine, bifid spine and orthopaedic surgery that contraindicated MRI, presented with a 90-minute episode of anosognosia, dysarthria and left hemiparesis. Eighteen days before she had an uncomplicated c-section with general anaesthesia. On the fifth day after childbirth she complained of sudden onset of posterior neck pain that persisted until admission day. Emergency Department observation, brain CT and laboratory tests were unremarkable. Cervical ultrasonography, revealed proximal occlusion of right internal carotid artery (ICA), high left ICA occlusion and left vertebral artery (VA) stenosis. Digital-subtraction angiography (DSA) confirmed a right ICA dissection with suprabulbar occlusion, left ICA dissection; both VAs with irregular walls ("string-of-beads" appearance and pseudoaneurysm formation). Anticoagulation was started. Follow-up cerebral and renal DSA performed 4 months later showed persistent right ICA occlusion but all other arteries were normal.

Discussion: In a series of seven sCAD in the puerperium diagnosis was made 10 days after delivery, head/neck pain was present 3 days after delivery and delivery was vaginal in most of the cases. Dissections were bilateral in 4 cases and a diagnosis of fibromuscular dysplasia was suggested in 5 cases. In our patient delivery was not vaginal and fibromuscular dysplasia was not confirmed on follow up DSA. Four vessel sCAD in this setting was only reported once until now. Transient wall abnormalities and/or increases in blood pressure induced by postpartum hormonal changes have been suggested as explanations. In our case a minor trauma induced by hyperextension of the neck during general anaesthesia could have also contributed.

192 Interesting and challenging cases

HYPOGLOSSAL NERVE PALSY AS THE PRESENTATION OF CAROTID ARTERY DISSECTION

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Introduction: Dissection of internal carotid artery is an uncommon but known cause of stroke in young adults, accounting for about 2% of ischemic strokes. There is an association with risk factors as hypertension, diabetes, dyslipidemia, antiphospholipid syndrome, thrombophilia, minor cervical trauma and some genetic diseases. Dissection of the carotid extracranial portion most commonly presents with symptoms of cerebral ischaemia in association with fronto-temporal headache, pain in the side of the neck and referred pain to the face, ipsilateral to the affected artery. Other manifestations include Horner's syndrome and cranial neuropathies. The lower cranial nerves involvement is described in only 12% of the cases and usually occurs by direct compression.

Case report: 45 year old, previously healthy male. Admitted at the Emergency Department because of difficulty in chewing, in the articulation of words, feeling "tongue-tie", limitation of tongue movements to the left side, associated with unilateral headache in the left frontal region since 1 week ago. With history of minor trauma in the context of a traffic accident about three weeks before the onset of the symptoms. He was avaliated by otolaryngologist and a palsy of the XII left pair was found. During hospitalization were performed Cerebral CT and neck vessels Doppler that were normal and Cerebral Angio-MRI that showed image suggestive of dissection of the terminal segment of the cervical portion of the left internal carotid artery, adjacent to the skull base. Treated with antiplatelet and statins, presented good clinical evolution, only with very mild palsy of the left hypoglossal nerve.

Conclusion: It's a common assertion that the spontaneous carotid artery dissection occurs in otherwise healthy individuals. There are described cases in association with trivial activities. We emphasize the need to consider carotid artery dissection in the differential diagnosis of isolated lower cranial nerves palsy.

193 Interesting and challenging cases

STARFRUIT NEUROTOXICITY MIMICKING AN ACUTE BRAINSTEM STROKE

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Background: Starfruit is commonly used as cough and diuretic medicine in Western countries. Patients with renal impairment are at risk of central nervous system damage following its ingestion, for starfruit contains toxins that may accumulate in the brain and result in stroke-like episodes.

Methods: Case report of a 52 year-old male admitted at our emergency with a possible brainstem stroke.

Results: A patient with history of high blood pressure and ongoing hemodialysis developed hiccups, confusion, and convulsions. Upon admission, bilateral ophtalmoparesis, hyperreflexia, facial central paresis, and ataxia were present and he evolved with tetraparesis and loss of gag reflex. The computed tomography had no signs of ischemia and IV TPA was considered. A stroke mimic was suspected after lab Results showed severe disturbance of renal function, electrolytes imbalance, and metabolic acidosis. TPA protocol was suspended and patient started on anti-epileptic drug and urgent hemodialysis. After eighteen hours, symptoms improved and neurological exam was completely normal. Once awake he reported ingestion of large amount of starfruit twelve hours before admission. Magnetic resonance imaging did not show signs of ischemia.

Conclusion: Starfruit neurotoxicity was discovered in 1980, when its extract was injected in mice and triggered seizures. Since then, multiple researches have confirmed this toxic effect that has been attributed to a dramatic increase of serum oxalate, among other substances. The main findings may mimic stroke: hiccups, vomiting, distal paresthesias, as well as convulsions and hemodynamic instability, with elevated risk of death. Immediate assessment with computed tomography and magnetic resonance imaging help differentiate both hypotheses. Uraemic patients must be alerted about the risk of intoxication and physicians must be aware of this differential diagnosis. Future studies should address the screening for the respective neurotoxin and its treatment.

194 Interesting and challenging cases

BILATERAL INTERNAL CAROTID ARTERY THROMBOSIS WITH CEREBRAL INFARCTION FOLLOWING CHEMOTHERAPY FOR BLADDER MALIGNANCY

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Introduction: Bilateral simultaneous thrombotic internal carotid artery occlusion is an uncommon cause of non-fatal stroke. We report an unusual case of spontaneously

resolving bilateral internal carotid artery thrombosis with cerebral infarction following gemcitabine and cisplatin chemotherapy for transitional cell carcinoma. We have encountered only a few previous reports of spontaneous resolution of bilateral carotid thromboses but none, as far as we are aware, in this clinical context.

Case report: A 43 year old right handed lady had completed a second cycle of gemcitabine and cisplatin for transitional cell carcinoma three days prior to presentation with stuttering onset right sided numbness, weakness, and global aphasia. She had smoked 20 cigarettes daily for 25 years. Examination was remarkable for global aphasia, right upper motor neurone facial weakness, flaccid right hemiplegia and sensory loss.

Full blood count showed a thrombocytosis of $1000×10^9$/litre (normal range 150-400). MRI brain scan with diffusion weighting showed right occipital infarction and extensive left cerebral infarction involving the frontal, parietal and occipital lobes. CT angiogram showed proximal bilateral internal carotid artery filling defects causing 60-70% stenosis. Carotid Doppler ultrasound showed similar appearances. Repeat vascular imaging 11 days later, while on anti-platelet therapy, showed resolution of the filling defects suggesting thrombosis as the cause. Echocardiogram was normal. Initial lupus anticoagulant screen was positive.

Discussion: A combination of thrombocytosis, chemotherapy and malignant state may account for the thrombogenic/procoagulant state in this patient. Gemcitabine has been associated with thrombocytosis while cerebral infarction has been reported following cisplatin treatment. Although we have not demonstrated persistence, a possible role for lupus anticoagulant cannot be excluded. The mechanism of spontaneous thrombus resolution is unclear.

195 Interesting and challenging cases

ALEXIA WITHOUT AGRAPHIA - AN INTERESTING CASE

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Background: We present a rare case of Alexia without agaphia due to an infarction in the splenium of corpus callosum. Alexia (difficulty in reading) without agraphia (difficulty in writing) is one of the classic disconnection syndromes. Disconnection syndromes are the result of interruption of inter or intrahemispheric white matter tracts.

Case report: A 70 year old right handed man presented with right homonymous hemianopia.(HH) He had a past medical history of Type II diabetes mellitus. He was in atrial fibrillation. Examination revealed right HH. He was unable to read. He was able to write spontaneously and on dictation but unable to read his own writing. He was able to trace the letters with his finger and discern the meaning of simple words. There was no dysphasia or difficulties with repetition. He was able to name objects and identify colours normally. This is characteristic of alexia without agraphia.

MRI revealed an acute infarction involving the left occipital cortex (DWI sequence - Panel A) and splenium of the corpus callosum (Panel B) resulting in right HH and alexia without agraphia respectively.

There was no significant recovery.
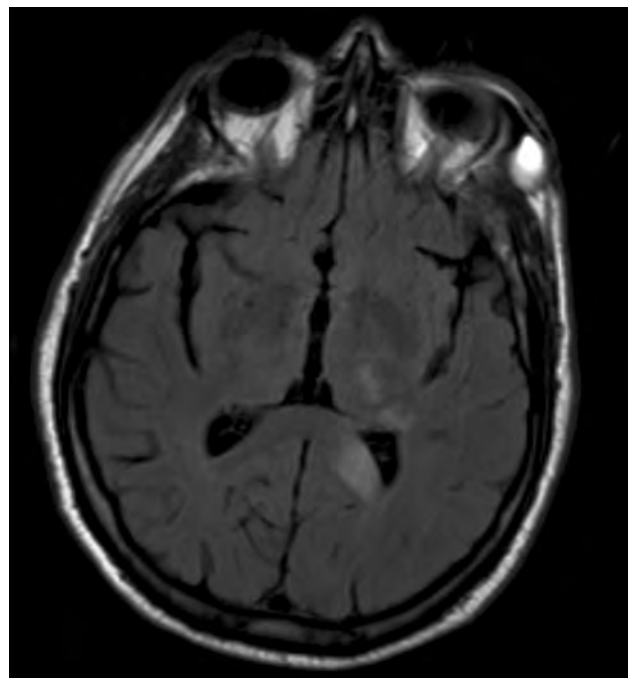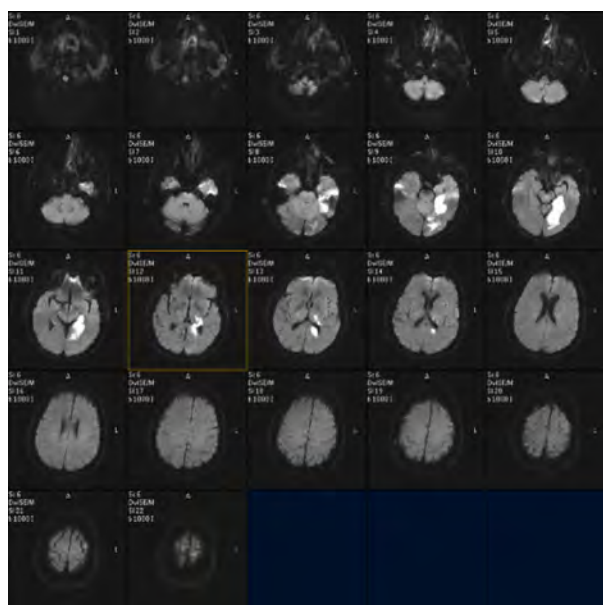
Discussion: Alexia without agraphia is a rare classic disconnection syndrome.

In the presence of right HH due to damage of left occipital cortex, the ability to read depends on visual input from unaffected right visual cortex reaching the language area in the left hemisphere. Fibres which connect these two areas pass through the splenium of corpus callosum and hence the infarction of dominant splenium Results in Alexia. As the angular gyrus is spared, there is no agraphia. However, letters can be physically traced by fingers as the intact sensorimotor system can decode lexical stimuli.

Alternatively, a single lesion proximal to the language area affecting the tracts from both Visual cortices might also cause alexia without agraphia and without homonymous hemianopia [1]

Reference:

1. Neuroradiology (1992) 34:210-214.

196 Interesting and challenging cases

RECURRENT ISCHAEMIC EVENTS FROM A PERSISTING PSEUDOANEURYSM: A RARE COMPLICATION OF EXTRACRANIAL VERTEBRAL ARTERY DISSECTION

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Background: Pseudoaneurysms are a recognised complication of cervical artery dissection. While carotid pseudoaneurysms often persist, the majority of vertebral pseudoaneurysms resolve. Ischaemic events due to embolisation from a persisting pseudoaneurysm are rare, and to our knowledge so far have only been reported in the anterior circulation.

Case report: A 35 year old man presented with three attacks of transient ataxia and left sensory-motor hemiparesis, which had occurred over the preceding 6 months. All attacks were set off by a paroxysm of sneezing, and all were followed by a unilateral headache. MRI-brain showed no ischaemic lesions, but MR-angiography showed a right proximal vertebral (VA) dissection with stenosis and a distal pseudoaneurysm. Although a diagnosis of migraine was considered, recurrent embolic events from the pseudoaneurysm were suspected and the patient was started on aspirin. Follow-up imaging failed to show ischaemic lesions and suggested some regression of the aneurysm. However, the patient's attacks continued, and further MRI eventually showed an acute cerebellar infarct, which confirmed the diagnosis of recurrent embolism. The patient declined long-term anticoagulation, and stenting of the aneurysm was not considered technically feasible. The patient therefore underwent coil occlusion of his right vertebral artery, which he tolerated well. 8 months post-procedure he has not had any further events.

Conclusion: Recurrent embolisation from a persisting pseudoaneurysm is a very rare complication of VA-dissection. Treatment decisions have to be made on an individual basis. In this patient, given that he had recurrent attacks despite being on antiplatelet drugs, intervention was indicated. While coil occlusion of the VA involved sacrificing the parent vessel, it was the most technically feasible and definitive treatment, and it led to a good outcome.

197 Interesting and challenging cases

TRANSIENT ISCHAEMIC ATTACK PRESENTING AS MONOCULAR VISUAL LOSS IN A WOMAN WITH MRI ABNORMALITIES – WHAT MAY LIE IN STORE?

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Background: Identifying rare causes of stroke and transient ischaemic attack in young and middle aged adults is challenging, given the broad differential diagnosis, but important as many have specific treatments.
Case: A 51 year old woman presented with sudden transient painless visual loss in her left eye. 2 years previously she described similar transient visual loss in the same eye. At age 39 she had sudden persistent near complete loss of vision in her right eye, attributed to anterior ischaemic optic neuropathy. Vascular risk factors included smoking, hypertension and hyperlipidaemia. One sister had an ischemic stroke aged 44. A second sister had a history of seizures, depression and a stroke-like episode aged 44, with CT imaging showing bilateral white matter hypoattenuation.
Results: MRI brain showed bihemispheric subcortical white matter hyperintensities with normal intracranial vessels. Carotid duplex ultrasound, cardiac monitoring, echocardiography and cerebrospinal fluid analysis were normal. Serological tests for thrombophilia, autoimmune, inflammatory and infective aetiologies were negative. Alphagalactosidase enzyme levels were 5.4umol/l/hr (normal range 3-20umol/l/hr). On sequencing the alpha-GAL gene (locus Xq22.1), she was found to be heterozygous for c.1021delg mutation found in exon 7, which Results in early termination of the alphagalactosidase protein, the glycoside hydrolase deficient in Fabry's disease.
Discussion: Fabry's is an X-linked lysosomal storage disease. It can manifest a variable phenotype including cerebrovascular disease in heterozygous females, possibly due to skewed X chromosome Lyonisation. Enzyme replacement therapy may have a role in symptomatic females. Diagnosis in female heterozygotes is challenging, as it may mimic atherosclerotic disease, and alpha-galactosidase levels may be normal. Alpha-GAL genetic analysis should be considered in women with atypical presentations of cerebrovascular disease, and suggestive family history.

198 Interesting and challenging cases

PITFALLS IN DIAGNOSING CORTICAL VEIN THROMBOSIS

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Background: Thrombosis of cerebral sinus veins as an important cause for headache or intracerebral hemorrhage can easily be diagnosed by modern angiographical techniques of CT or MRI. In contrast, diagnosing cortical vein thrombosis is much more difficult. We present 2 cases where cerebral vein thrombosis manifested as space-occupying lesion or as progressive intracerebral hemorrhage, with initially normal CT angiography.
Case Report 1: A 70 ys old man developed generalized seizures, mild left brachio-facial hemiparesis and slowly progressive edema in the right fronto-precentral region, with polycyclic marginal contrast enhancement. As he improved clinically under oral steroids, the diagnosis of glioblastoma was suspected. Although CT angiography revealed hypervascularization of the lesion, there was no evidence for a vascular malformation in transfemoral angiography (DSA) of cerebral arteries and veins. A few weeks later, FLAIR-weighted MRI revealed hyperintense vascular structures in the upper right fronto-parietal region, indicating thrombotic cortical veins ("cord sign"). This was confirmed by dynamic MRI angiography with 1 image per second, where hypervascularization could be attributed to congested, serpentine-like veins.
Case Report 2: A 73 ys old man acutely developed headache, mild left brachio-facial hemiparesis and left visual neglect. Brain CT showed intracerebral

hemorrhage of 4.6 cm diameter, with normal CT angiography. Hemiparesis and the hemorrhage worsened during the next days. An arterial DSA was labeled as normal. Only 10 days later, CT scan showed a "cord sign" in the right frontal region, and MRI unveiled several thrombotic cortical veins in the right more than the left cerebral hemisphere. Antithrombotic medication lead to rapid absorption of the bleeding and to regression of symptoms.
Conclusions: Diagnosis of cortical vein thrombosis may become evident only later in the course of the disease, when the "cord sign" shows up in CT or MRI. Progressive edema and marginal contrast enhancement may falsely indicate a brain tumor, congested veins and collaterals may simulate an AVM.

199 Interesting and challenging cases

ACUTE ISCHEMIC STROKE, CEREBRAL VENOUS THROMBOSIS, THYROTOXICOSIS AND ANTIPHOSPHOLIPID ANTIBODIES: A FORTUITUS ASSOCIATION?

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Background: Arterial cerebral ischemia has been described in different diseases of the thyroid. A possible association between thyrotoxicosis and cerebral venous thrombosis (CVT) was also already reported. The association of arterial and venous cerebral ischemic events in patients with hyperthyroidism has not been previously described. We report the case of a patient with thyrotoxicosis who presented initially with an arterial ischemic stroke complicated by a concomitant CVT.
Case report: A 21 yo woman was admitted to our hospital 7 days after the acute onset of expression aphasia and right arm weakness. On physical examination she was alert, tachycardic (heart rate 150 bpm, sinus tachycardia on ECG) and had an enlarged thyroid gland. A brain MRI/MRA showed a left frontal infarct and an occlusion of the left middle cerebral artery. Transthoracic echocardiogram, CSF analysis, and carotid Doppler ultrasonography were unremarkable. Laboratory investigation confirmed biochemical hyperthyroidism. She was treated with aspirin, a beta blocker and antithyroid drugs. Six days after admission, she had a sudden decrease in the level of consciousness. A new brain MRI/MRA showed thrombosis of the sagittal, left transverse and sigmoid sinuses. Laboratory Results showed an elevated factor VIII coagulant activity and a positive lupus anticoagulant IgG. She developed refractory intracranial hypertension and was treated with bilateral frontal craniectomy. She presented progressive improvement and was discharged home after 3 weeks, with a modified Rankin scale score of 2, using oral anticoagulation.
Conclusion: CVT and arterial ischemic events can happen concomitantly in patients with hyperthyroidism. Although there is insufficient evidence to prove that a hypercoagulability state in hyperthyroidism predisposes to cerebral ischemia, the presence of antiphospholipid antibodies and other hypercoagulability studies should be performed in patients with thyrotoxicosis and ischemic events.

200 Interesting and challenging cases

ACUTE STROKE 24 HOURS AFTER AGGRESSIVE ANTICOAGULATION AND ANTIPLATELET THERAPY - WOULD YOU THROMBOLYSE?!

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Introduction: With the expansion of stroke thrombolysis worldwide, clinicians are increasingly faced with situations where the evidence base for thrombolysis is unclear. This is a particularly challenging example.
Case report: A 75-year-old man with a Background of hypertension and myocardial infarction 10 years previously presented to the emergency department with chest pain without ECG changes (subsequently troponin negative).
Treated as an Acute Coronary Syndrome, he was loaded with Aspirin 300mg, Clopidogrel 600mg, and Fondaparinux (low molecular weight heparin) 2.5 mg subcutaneously.
He collapsed 24 hours later with left visual neglect, left facial droop, slurred speech and reduced power in his left arm. An urgent CT head within half an hour was normal.
As the onset of symptoms was less than one hour, NIHSS score 18 with no absolute contraindications to thrombolysis, intravenous thrombolysis was administered.
He died 48 hours later, having developed dramatic haemorrhage on CT.
Discussion: Diedler et al (Stroke 2010) analysed the SITS-MOST data retrospectively to look at the risk of haemorrhage in patients already taking antiplatelets. They showed that patients already taking aspirin and clopidogrel at stroke onset suf-

fered more spontaneous intracranial haemorrhage (13.4%) following thrombolysis than those on aspirin alone (5.9%) but no increased mortality or poor functional outcome (p=0.003).

Our patient developed a likely ischaemic stroke despite loading with aspirin, clopidogrel as well as low molecular weight heparin 24 hours beforehand.

On questioning 30 stroke physicians at UK thrombolysis centres, 47% supported thrombolysis, 7% were uncertain and 46% were against thrombolysis in a case such as ours.

This highlights the need for further studies to assess the safety of thrombolysis for stroke in patients taking dual antiplatelet therapy and for clarity on when it is safe to thrombolyse after anticoagulation with low molecular weight heparin.

201 Interesting and challenging cases

"VASCULOPATHY" IN SNEDDON'S SYNDROME: A DOUBLE-EDGED SWORD

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Background: Sneddon's syndrome, the association of livedo reticularis and stroke is a rare cause of cerebral infarction in young people. The vascular pathology in the dermal arterioles is characteristic, while cerebral vascular abnormalities are rarely demonstrable. While a few isolated cases of haemorrhage have been reported, the underlying mechanism remains elusive. We report, for the first time to our knowledge, a case of sporadic Sneddon's syndrome declaring itself as a lobar haemorrhage followed by recurrent ischaemic events.

Case: A 33 year old Caucasian woman presented with headache and right homonymous hemianopia. She had a history of psoriasis and Raynaud's syndrome, but no conventional vascular risk factors and no family history of vascular disease. She was mildly hypertensive at presentation. Skin examination revealed florid livedo reticularis confirmed histologically. MR imaging revealed an occipital haematoma with significant small vessel disease. Intra-arterial angiography revealed irregularity of small caliber arteries, with a prominent and widespread blush of dural and leptomeningeal vessels. Autoantibodies including anti-phospholipid antibodies and thrombophilia investigations were negative.

3 years later, she re-presented with recurrent focal cerebral and ocular ischaemic events. Repeat imaging showed stable small vessel disease. There were no microbleeds to suggest an underlying process akin to cerebral amyloid angiopathy. Fundoscopy revealed sheathing of superior retinal arterioles indicating retinal arteriopathy.

Vasculopathy in Sneddon's Syndrome
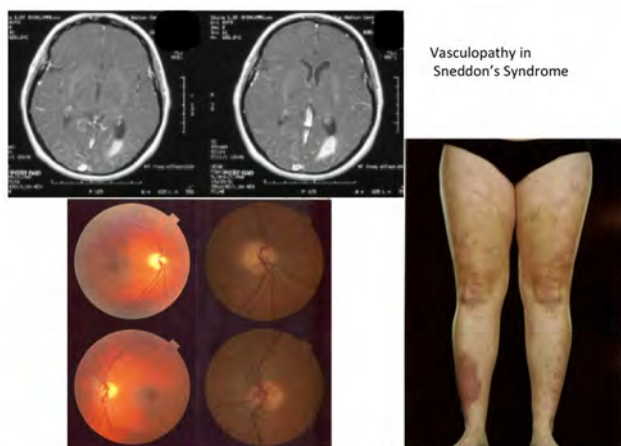
Discussion: This case highlights a therapeutic dilemma regarding antithrombotic treatment and difficulty in predicting the disease course. We propose that the fragile leash of collaterals caused the haemorrhage while the pathophysiology of ischemia may be explained by the underlying arteriopathy.

202 Interesting and challenging cases

CASE REPORT: LITHIUM INTOXICATION AS A MIMIC OF ACUTE STROKE

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Background: Lithium serves as an effective therapy for bipolar disorders but has a narrow therapeutic range. Signs of intoxication include cognitive impairment, disorientation or delirium as well as coma or death. Other neurological deficits like tremor, dizziness, myoclonus or epileptic seizures can occur. We report a patient with lithium intoxication who presented with an acute onset of focal neurological symptoms suggestive of a stroke.

Case report: A 65 year old Caucasian man presented with sudden onset of non-fluent aphasia, apraxia and mild paresis of the left arm with an NIHSS score of 4 points. He had a bipolar affective disorder, which was clinically asymptomatic on Lithium medication for years.

Results: In the emergency setting the brain computed tomography and angiography revealed no ischemia or bleeding, but a moderate stenosis in the distal part of the right internal carotid artery. Given the persistence of symptoms and supposed ischemic stroke we initiated an emergency systemic thrombolytic therapy with rt-PA 2 hours after onset of the neurological deficits. Clinical symptoms did not improve, the patient became more agitated and showed signs of delirium. The Results of comprehensive stroke investigations were negative, including no evidence of ischemia in magnetic resonance imaging. The blood lithium level was elevated to 2.53mmol/l (therapeutic range 0.5- 1.2mmol/l). The EEG showed patterns of slow waves with bifrontally accentuated beta activity which is consistent with a medically induced abnormality. After termination of Lithium medication the symptoms slowly improved.

Conclusion: Stroke mimics might be difficult to diagnose in an emergency setting and may be initially treated as a stroke. Lithium intoxication presenting with focal neurological deficits of acute onset is rarely described in literature however it should be considered in differential diagnosis of stroke.

203 Interesting and challenging cases

STROKE AS FIRST PRESENTATION OF WEGENER'S GRANULOMATOSIS IN A 72 YEAR OLD MAN

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Wegener's granulomatosis is a systemic granulomatous disease affecting small and medium sized vessels.Stroke is an uncommon neurological manifestation of Wegener's disease.

We present a case report of a 72 year old man who was referred to the stroke clinic because of right arm and leg weakness.There were no speech or visual disturbances. No history of cough,haemoptysis,epistaxis or weight loss.He felt mildly dyspnoeic on simple tasks.

He is a life long smoker,drinks minimal alcohol and has no history of asbestos exposure.

There is no history of allergy and no significant family history.

Examination revealed a red crusted rash on his axillae and over the right fibular head.He had facial rosacea and bilateral Dupytren's contractures.There was wheeze on the lower zone of the right lung on chest auscultation.Visual fields were intact with full range of eye movement and no other cranial nerve defect.Power was 4/5 in the right shoulder, elbow and hand.There were no cerebellar signs and no sensory deficit.Reflexes were normal bilaterally with down going plantars.

Investigation revealed anaemia (Hb10.7,MCV 81),elevated plasma viscosity 2.26 and normal renal function and liver function tests.Autoantibody tests showed positive cANCA (1:640) with positive PR3 and negative MPO.

CXR showed an abnormal right midzone shadow.

CT head showed patchy ischaemic changes with diffuse small vessel disease.

He had CT of the chest & abdomen which showed multiple soft tissue nodules in both lungs ranging from 5mm to 4cm,the largest within the right upper lobe.It also showed multiple mediastinal lymph nodes.

He was referred to the renal clinic and underwent a renal biopsy which confirmed a granulomatous infiltration of the kidney consistent with Wegener's disease.
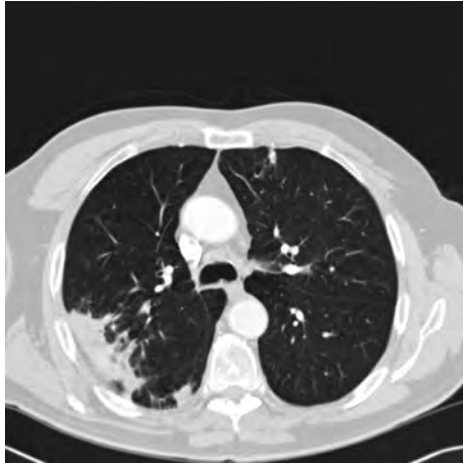
Conclusion: Vasculitis as a cause of stroke is uncommon in the elderly but it still happens and as treatment is different,stroke physicians must keep an open mind towards these unusual causes of stroke especially when there are other clues like elevated PV and CXR shadow.He was commenced on ciclophosphamide and prednisolone and later switched to azathioprine and prednisolone and his PV normalised to 1.62

204 Interesting and challenging cases

HYPERINTENSITY IN THE SUBARACHNOID SPACE ON CONTRAST-ENHANCED FLUID-ATTENUATED INVERSION-RECOVERY MAGNETIC RESONANCE IMAGING AFTER CENTRAL VENOUS CATHETER REMOVAL

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Background: In the critical care setting, there is frequent use of central venous catheterization for the administration of fluids, medications, and nutritional support. We describe the unusual complication of multiple arterial embolization after central venous catheter removal.
Case: A 61-year-old male patient was admitted because of acute renal failure. Central venous catheter was inserted through his right jugular vein to hydrate him. On the 8th hospital day, central venous catheter was removed. Five minutes after catheter removal, he developed dyspnea and left-sided hemiparesis. Because brain computed tomography was normal, he was given intravenous tissue plasminogen activator. Two hours after the onset of stroke, diffusion-weighted magnetic resonance imaging (MRI) and brain resonance angiography were normal. However, high signal was seen in the subarachnoid space over the bilateral convexities on contrast-enhanced fluid-attenuated inversion-recovery (FLAIR) MRI. Twenty hours after the onset, high signal was seen in the bilateral frontal areas on diffusion-weighted MRI. Transcranial Doppler ultrasound with agitated saline contrast was performed. With the Valsalva maneuver, 3 microembolic signals in the right middle cerebral artery (MCA) and 3 microembolic signals in the left MCA were detected after contrast injection.
Conclusion: Since clot or fibrin commonly accumulate in venous catheters, it is likely that the debris within the central venous catheter was dislodged at removal and then embolized first via the right heart to the lungs, causing dyspnea, and subsequently through a right-to-left shunt into the arterial system causing the cerebral ischemia. Loss of integrity of the blood–brain barrier (BBB) can allow a contrast agent to cross the BBB, enter the perivascular space, and then be distributed in the cerebrospinal fluid (CSF), causing hyperintensities in the CSF by contrast-enhanced FLAIR MRI.

205 Interesting and challenging cases

SUSTAINED APHASIA AND RIGHT SIDED HEMIPARESIS AFTER RECURRENT EPILEPTIC SEIZURES WITH CORTICAL LESIONS ON DIFFUSION WEIGHTED MRI, MIMICKING ACUTE LEFT HEMISPHERIC STROKE

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Background: We report a rare case of sustained aphasia and right sided hemiparesis due to recurrent seizures, associated with a distinctive hypertensive lesions on diffusion weighted MRI and clinically mimicking acute left hemispheric stroke.
Methods: An analysis of the medical history was performed, regarding cerebral imaging and clinical presentation in the course of the disease.
Results: A 67 year old female was admitted due to convulsive status epilepticus. Hepatic cirrhosis with oesophageal varices resulting from chronic alcohol abuse was reported in the medical history. After termination of recurrent epileptic seizures using anticonvulsants, she suffered from prolonged global aphasia and right sided hemiparesis. Diffusion weighted imaging (DWI) exhibited a distinctive diffusion lesion, mainly affecting the left temporal cortex and hippocampal area, but involving almost the entire left cortical hemisphere. These alterations correlated with a corresponding lowering in the ADC-mapping. Lesion pattern followed no regular vascular territory. After continuous administration of the anticonvulsant levetiracetam, she improved subsequently over weeks in the further course of the disease. At discharge, one month later, a mild hemiparesis and speech disorder was still present.
Conclusion: Epileptic seizures can cause diffusion changes on MRI. As reported in the literature, they do not respect vascular territories and show a hyperintensity in DWI with corresponding lowering in the ADC-mapping. Vasogenic and cytotoxic edema are suspected to be the primary cause of this phenomenon and a result of neuronal excitotoxicity during prolonged epileptic seizures. This is a rare case of a seizure induced, distinctive cortical MRI changes throughout the left hemisphere, presenting with classical symptoms of acute stroke.

206 Interesting and challenging cases

THROMBOLYSIS ABOVE 100 YEARS OLD, WHY NOT?

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Introduction: According to the last ESO recommendations for ischemic stroke, selected patients above 80 years old can also be treated with intravenous alteplase, although the European Medicines Agency has not yet approved its use in these very elderly stroke patients. Therefore, this off-label indication depends in each hospital of ethical committee approval and patient/family consent. Nevertheless, considering the increasing number of elderly people in European countries, more and more above 80-y-old stroke patients arrive at the hospitals in a temporal window for thrombolysis. We present an emblematic case of a patient above 100 years old.
Case Report: 101-y-old male, previously independent for daily activities, and with no history of relevant co-morbidities. Admitted with acute motor aphasia and right hemiparesis, scoring 13 in NIHSS. Brain computed tomography (CT) disclosed no acute lesions. After Discussion and consent from his family, intravenous alteplase was begun 3 hours after symptom onset. The patient had an early significant

improvement, with only residual face paresis and dysarthria (NIHSS 3). The 24-hour CT had no acute vascular lesions. The patient was discharged to home on the 4th day, with NIHSS 3, maintaining independence for daily activities.
Discussion: Age criteria for thrombolysis were arbitrarily settled in the clinical trials that lead to treatment approval. In the last years, literature has reflected the meanwhile acquired experience with this treatment, assuring the safety of thrombolysis in acute stroke after 80 years old, although age is related to a natural history of the disease with a worst prognosis. To guarantee that we do not deny to the very elderly, in advance, the hypothesis of a better functional outcome, it seems we can, with clinical sense, support treatment decision in the global predictive factors of potential risk and benefit, without specific age restriction, as was done in the presented clinical case.

207 Interesting and challenging cases

CORTICAL BLINDNESS DURING BRONCHIAL ARTERY EMBOLIZATION

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Background: Brain-embolism is a possible complication during coronary/brain/carotid angiography, but brain embolism during bronchial angiography is a rare complication. We report a case of vertebrobasilar-embolism secondary to bronchial artery VPA (polyvinyl alcohol) embolization.
Methods and Results: 25-yr woman was admitted to the hospital with hemoptysis. Thorax-CT showed a cavernous image in left superior lung probably secondary to tuberculosis, which was later confirmed. In order to control repeated hemoptysis bronchial angiography was performed. Left bronchial artery being the source of the lung lesion bleeding was detected. Artery –PVA-embolization was performed. At the end of the procedure connection between bronchial artery and left subclavian artery was detected. Contrast flow through subclavian artery to left vertebral artery was observed. Suddenly patient presented with cortical blindness. Neurologic progression occurred. Patient was transferred to ICU, finally intubation was required. MRI showed multiple small infarcts in vertebrobasilar territory secondary to PVA embolism.Due to progressive and severe neurological deterioration, anticoagulation was started with heparin to prevent thrombotic effect. Patient presented slow but good outcome.
Conclusions: Brain-embolism is a possible complication during bronchial angiography.PVA can cause stroke by embolic mechanism but progressive thrombosis or PVA brain-inflammation could explain neurologic worsening.We propose that if neurological deterioration occurs carefully anticoagulation can be a therapeutic option.

208 Interesting and challenging cases

AN INTERESTING CASE OF ANTON'S SYNDROME AND CHARLES BONNET SYNDROME

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Introduction: Visual anosognosia associated with confabulation in the setting of obvious visual loss and cortical blindness is Anton's syndrome. Patients with Anton's syndrome behave and talk as though they were sighted. Charles Bonnet syndrome (CBS) involves visual hallucinations which occur in the visually impaired who exhibit no evidence of dementia or psychiatric illness.We describe a patient with Anton's syndrome and Charles Bonnet syndrome following occipital infarct.
Case presentation: 66 years old gentleman previously fit and well was brought in after an out of hospital cardiac arrest. After a period in the ICU, he was admitted to the stroke unit as the most striking clinical feature was impairment of visual acuity with normal power and sensation.Despite an objective diminution of vision, he maintained he was able to "see" things around him. MRI brain demonstrated posterior circulation territory infarct. During his rehabilitiation he started to accept the loss of vision and confabulation diminished. However he started to experience visual hallucinations ranging from simple patterns to complicated pictures of people and animals.
Discussion: Patients with damage to the occipital lobes also have damage to their visual association cortex, which may account for their lack of awareness. The damaged visual areas are effectively disconnected from functioning areas, such as speech-language areas which, in the absence of an input, often confabulate a response. Neuropsychological mechanisms also have been postulated. Sensory deprivation has been postulated as a cause for CBS. Cortical input from memory association areas which are closely involved with the occipital lobes, are hypothesised to fill in for the visual deficit producing the hallucinogenic effect.

Conclusion: Our case is interesting as the gentleman had varying symptoms extending from visual anosognosia to visual hallucination. A suspicion of cortical blindness should be raised in patients with visual loss and occipital lobe injury.

209 Interesting and challenging cases

AGENESIS OF THE INTERNAL CAROTID ARTERY: AN IMPORTANT INCIDENTAL FINDING

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Background: Agenesis of the internal carotid artery (ICA) is a rare congenital developmental anomaly, occurring in less than 0.01% of the population and is commonly asymptomatic under normal conditions. It is often detected as an incidental finding or after a cerebrovascular event, such as subarachnoid hemorrhage after rupture of a coincidental aneurysm or cerebral infarct.
Case report: We present a case of a 53 years old woman, obese, with poorly controlled hypertension and diabetes, that previously underwent clipping of an aneurysm of the anterior comunicating artery. She presented at the emergency department with a sudden onset of dysarthria, left horizontal gaze palsy and severe right hemiparesis suggestive of left paramedian pontine stroke. She was admitted to the stroke unit where ultrasound evaluation was performed revealing a single right carotid artery. A skull base Computed Tomography (CT) scan was then performed revealing absence of the right carotid canal, confirming the congenital absence of the right ICA. Three Dimensional CT Angiography revealed a new asymptomatic saccular aneurysm at the origin of the posterior inferior cerebellar artery.
Discussion: The estimated prevalence of cerebral aneurysms in the general population is 2-4%, but the reported prevalence of aneurysms in association with absence of the ICA is 24-34%. In our patient, the time between the diagnoses of the two described aneurysms was 12 years. Few cases of recurrence of aneurysms in these patients are published. Increased hemodynamic load on the normal side along with congenital defects of the vessel wall and systemic hypertension are important factors in the development of cerebral aneurysms. Close follow-up of patients with agenesis or aplasia of ICA should be sought, even if asymptomatic, because of possible development of associated conditions such as cerebral aneurysms or abnormal collateral channels.

210 Interesting and challenging cases

BILATERAL ATHEROSCLEROTIC INTERNAL CAROTID ARTERY OCCLUSION CAUSING ACUTE BIHEMISPHERIC INFARCTIONS

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Introduction: Multiple acute brain infarctions in both cerebral hemispheres involving the anterior circulation are uncommon (affecting less 1.0%-6.0% of acute stroke patients) and usually suggest an embolic mechanism, particularly one of aortic or cardiac origin. To the best of our knowledge there has been no report of bilateral extracranial atherothrombotic internal carotid artery (ICA) occlusion causing acute bihemispheric infarctions.
Case Description: A 73-year-old man with a history of hypertension, hypercholesterolemia and smoking presented with an acute right upper arm weakness that he noticed on awakening, Admission brain CT and electrocardiogram were normal. Neurological examination disclosed a mild left hemipareris and left-side visual neglect with a NIHSS-score of 5 points. The patient underwent emergent carotid duplex evaluation showing multiple hyperechoic plaques in both common carotid arteries and acute bilateral ICA occlusion. Transcranial Doppler examination showed (i) acute bilateral middle cerebral artery (MCA) occlusion with minimal flow in right and blunted flow in left MCA and present collateral flow through reversed Ophthalmic Artery (OA) bilaterally. Acute reperfusion therapies including intravenous or intra-arterial thrombolysis as well as mechanical thrombectomy were withheld because of unknown time of stroke onset. Emergent echocardiography excluded the presence of cardiac thrombus and other source of cardiogenic embolism (including aortic arch dissection). The patient was treated with aspirin (325mg) and enoxeparin (40mg). Fourteen hours latter he became quadriplegic and lethargic (NIHSS-score: 26 points). Repeat brain CT showed bilateral cortical infarctions in both MCA territories. The patient expired the following day.

Conclusion: The current case underscores that bilateral atherosclerotic ICA occlusion may constitute an uncommon cause of acute bilateral cortical infarctions involving the anterior circulation.

211 Interesting and challenging cases

INTRACRANIAL ARTERIOVENOUS DURAL FISTULA ASSOCIATED WITH BILATERAL INTERNAL CAROTID STENOSIS

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Background: Association between extra and intracranial vascular lesions can increase difficulties in the treatment approach of each of them when they are found in the same patient. We report a case of intracranial arteriovenous dural fistula (IDAVF) in a patient with bilateral internal carotid artery stenosis.

Methods: A 70 year-old man with left hemispheric ischemic stroke. The neurosonology study revealed bilateral ICA stenosis and asymmetry between MCAs and ACoA open with right to left flow. Later a diagnostic arteriography is performed, showing several bilateral ICA stenosis, suggesting post-occlusion recanalization in left ICA. Casually an IDAVF from both middle meningeal arteries with cortical venous drainage was found.

Results: After evaluation of arteriography findings, endovascular treatment was proposed. In the same procedure, under general anesthesia, first an angioplasty and stenting of right ICA was performed and afterwards the IDAVF was closed with Onix injection into right middle meningeal artery and a mixture of Glue-Bran and Lipiodol on the left side. There was no periprocedural complications. After clinical stabilization the patient is discharged with antiplatelet therapy. One month later he remains asymptomatic.

Conclusions: IDAVF is a rare vasculopathy characterized by an abnormal arteriovenous communication. The goal of treatment is to close the point of communication for preventing intracranial bleeding and cerebral venous hypertension due to arterialization of the cortical veins. It can be successfully treated in most patiens with endovascular embolization, but sometimes surgery treatment is necessary. In the present case, the surgical aproach of fistula was not possible before a better brain blood support was guaranteed, and carotid endarterectomy would have increase blood supply to fistula. There are no guidelines about treating these pathologies in the same patients, so endovascular approach was chosen to treat both in a single procedure.

212 Interesting and challenging cases

41 YEARS OLD INTRAVENOUS DRUG USER MAN WITH BACTERIAL ENDOCARDITIS, BIVALVULAR REPLACEMENTS AND A RUPTURED CEREBRAL MYCOTIC ANEURYSM

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Background: Mycotic aneurysm is an expected complication in almost 5% of the patients treated for bacterial endocardits. Some studies suggested that treating the infective endocarditis by antibiotics early will prevent embolism and rupture of mycotic aneurysms.

Methods and Results: 41 years old man was admitted in March 2010 to Royal Gwent Hospital in Newport/South Wales following an episode of shortness of breath and fever. He is a known patient with intravenous drug abuse. On clinical examination it was confirmed that he had signs of bacterial endocarditis which was proved by an echocardiograme and a series of 6 blood cultures. He later had a bivalvular replacement as the cardiothoracic surgical team in University Hospital of Wales decided that it will be more appropriate to replace the mitral and the aortic valves in view of the severity of the cardiac pathology. The patient had a 6 weeks course of meropenem and gentamycin antibiotics treatment following the surgery and to prevent further infections. However; he developed a seizure and he was found in April 2010 paralysed on the right side of the body with signs of quadrantanopia. A contrasted CT brain has revealed a left sided large, intracerebral haematoma which was attributed to a ruptured mycotic aneurysm following an angiographic study. The patient was admitted to intensive care unit and he is currently making a good but slow progress with rehabilitation.

Conclusions: Surgical intervention in treating diseased heart valves after an infective endocarditis might enhance the rupture of a cerebral mycotic aneurysm. This case report highlights the benefits of expecting mycotic aneurysm ruptures in an infective endocarditis patient with previous history of intravenous drug use. Managing endocarditis with the appropriate antibiotics and the use of angiographical studies might be beneficial in preventing intracerebral haemorrhage resulted from a ruptured mycotic aneurysm.

213 Interesting and challenging cases

UNUSUAL PONTINE INFARCTION: WHY IS HE SO HAPPY?

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Background and Significance: Euphoria is medically recognized as a emotional state defined by a profound sense of well-being. Euphoria following a cerebral infarction is generally associated with a lesion located in the thalamus. Here we report a case of euphoria associated with an isolated pontine infarction.

Case: A 38-year-old male complaining of recurrent right hemiparesis for 1 day was admitted to our hospital. He had no history of psychiatric or neuroimmunological illnesses. His only risk factor was hypertension. He suddenly became euphoric, and at the same time he developed hemiparesis of the right limbs. No evidence of acute ischemic stroke was observed on magnetic resonance imaging (MRI) scans. Anticoagulation therapy was started immediately, but later the same day the patient developed right hemiparesis again and the weakness persisted. Re-examination of the diffusion-weighted MRI scans revealed a left pontine infarction with no other lesions in the brain.

Conclusions: or Comments: The serotonergic raphe nuclei and the locus ceruleus noradrenergic system are located in the rostral pons and caudal mesencephalon. An increase in norepinephrine or serotonin levels may induce euphoria and hyperactivity. The reticular formation is a poorly-differentiated area of the brain stem that is centered roughly in the pons. Appropriate emotional and cognitive responses to stimuli are mediated, in part, by inputs from the reticular formation to the thalamic reticular nucleus, which monitors and gates output from the thalamic intralaminar nuclei to the cerebral cortex. We speculated that the euphoria in our case may be explained by a secondary dysfunction of the cortical and thalamic connections resulting from damage to the pontine reticular formation. The present case suggests that clinicians should consider the possibility of pontine infarction when a patient presents with euphoria.

214 Interesting and challenging cases

CLINICAL AND PATHOLOGICAL MANIFESTATIONS OF A FAMILY WITH HEREDITARY ENDOTHELIOPATHY WITH RETINOPATHY AND ENCEPHALOPATHY

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Objective: To report clinical and pathological features of a family with possible hereditary endoteliopathy with retinopathy and encephalopathy.

Methods: The index case was male and was found with the symptom at 18 years old. Clincal manifestation included recurrent headache, fever, conscious disturbance and hemiplegia. Bilateral cerebral hemispheric lesions were found on MRI with low signal on T1, high signal on T2 and FLAIR, with moderate enhancement. Video EEG shows the increase of slow wave. EMG shows neurogenic damages. Similar clincal and imaging characteristics were found in the case'mother and uncle. Pathological examinations of brain, muscle and sural nerve were performed in the index case.

Results: Brain biopsy showed spongyform changes with inflammatory cell infiltration in few small vessels. Neurogenic muscular atrophy was found with biopsy of the muscle. Demyelination was found with biopsy of sural nerve. Electronmicroscope examination of the sural nerve found the thickening and delamination of the basement membrane.

Conclusion: Multiple organs injury is the characteristic of hereditary endotheliopathy and peripheral nerve may also be involved. Thickening and delamination of the basement membrane of peripheral capillaries will be helpful in diagnosis of such cases.

AN EPIDURAL CAVERNOUS HEMANGIOMA: A CASE REPORT

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Background: case description: A 30-year old male presents at the emergency department with severe lumbo-ischialgia, paresthesia and loss of strength in the right leg since one week with acute deterioration in the past night. On CT of the lumbar spine there is a soft-tissue mass extending from level L4-L5 to L5-S1. On MRI, the mass is located in the posterior epidural space and compresses the dural sac towards anterior. There is extension in both neuroforamina at the L4-L5 level. After intravenous injection of gadolinium contrast there are some focal areas of enhancement in the upper part of the mass. These features on MRI are compatible with a tumor and hemorrhage. Two days later the patient develops urinary incontinence. Surgery showed that the mass consisted of blood and nodular structures adhering to the dura mater. Histopathological diagnosis was a cavernous hemangioma.
Methods: Literature concerning epidural cavernous hemangiomas was reviewed. Through a Pubmed search eight articles were selected. We used the following search terms: epidural cavernous hemangioma, spinal cavernous hemangioma and spinal vascular malformations.
Results: Spinal epidural cavernous hemangiomas account for 5-12% of all spinal vascular lesions. Primary epidural cavernous hemangiomas (without a bony component) are very rare. Clinical presentation can be heterogeneous. CT and MRI before and after intravenous contrast are the imaging Methods of choice. A broad differential diagnosis has to be considered when a spinal epidural soft-tissue mass is visualized on imaging. Therapeutic approach of (acutely) symptomatic spinal epidural cavernous hemangiomas can be expectatio armata, radiation, embolization or surgery. When acute bleeding is present surgical decompression is the therapeutic method of choice.
Conclusion: Clinical presentation of a spinal epidural cavernous hemangioma can be heterogeneous. The diagnosis must be considered in patients presenting with acute lumbo-ischialgia. CT and MRI are helpful to differentiate from more common pathology such as a disc herniation. Therapeutic approach varies from expectatio armata to surgical resection, depending on symptomatology.

ATYPICAL FIBROMUSCULAR DYSPLASIA

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Introduction: Fibromuscular dysplasia is an uncommon disease that mainly affects carotid territory. Although clinical symptoms vary, most of the times debuts as a cerebral ischemia. Posterior territory involvement is less common.
Material and Methods: We report a 35-year with history of sporadic migraines who complains of changes in his headache characteristics.
Results: Supraaortic sonography showed a slight increase resistance wave in the left vertebral artery. The MRI showed a dissection of the extracranial left vertebral artery confirmed by CT angio, showing the presence of fibromuscular dysplasia that affects vertebral artery, basilar artery and left posterior cerebral artery. The patient had no ischemic lesions evident and he went into antiplatelet agents without ischemic episodes.
Conclusions: FMD is an uncommon disease whose clinical spectrum ranges from asymptomatic or minimally symptomatic cases, as presented, to cerebral ischemia. Antiplatelet therapy is enough to prevent arterio-arterial stroke.

CANCER, CHEMOTHERAPY AND ISCHAEMIC STROKE: TWO CASES OF ISCHAEMIC STROKE IN PATIENTS WITH PROSTATE CANCER TREATED WITH DOCETAXEL AND A REVIEW OF THE LITERATURE

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Background: There are a number of cancer specific associations with ischaemic stroke (IS) including the effects of chemotherapy (CMT). We describe two cases in which Docetaxel was implicated in the aetiology of IS and have reviewed the literature.

Methods: 2 case reports and a MEDLINE search (1980-2010) using combinations of the key words: stroke, cerebrovascular disease, cerebral infarction, chemotherapy, post-chemotherapy. Cases: 2 males (aged 67 and 74 years) with prostate cancer presented within 4 days of their 5th cycle of Docetaxel. Both had right middle cerebral artery infarction where aetiology remained unknown despite full investigation.
Results: There were 6 retrospective reviews involving 14192 patients. 48 IS and 11 TIA's (0.415%) were reported. The largest study looked at 10963 patients. 15 (0.137%) experienced 16 IS, 12 occurring within 10 days of chemotherapy and 10 after the first cycle. The commonest CMT was cisplatin and large vessel occlusion was the commonest stoke pattern. Presence of distal metastases and not CMT predicted stroke in 1 study. Only 1 IS was recorded in prospective data from 2 studies involving 288 patients (0.347%). Tamoxifen and CMT appear to increase IS risk although data from 4 studies conflicted about the comparable effects of these agents when used alone. There were 22 case reports of CMT and IS. Only 1 had received Taxane CMT. Postulated mechanisms of CMT induced stroke (7 papers) included hypomagnesaemia, vasospasm, endothelial toxicity, hypercoagulable state and hypercholesterolaemia.
Conclusion: Ischaemic stroke post-CMT is rare. Cisplatin was the commonest agent in the literature. Thromboembolism and large vessel occlusion were the commonest subtypes. The mechanism of CMT induced IS remains unknown but is probably multifactorial. CMT remains one of many factors involved in cancer induced IS. Our cases demonstrate Taxane CMT may be implicated in the aetiology but research is needed to explore this further.

LARGE VESSELS ANEURYSM AS LONG TERM COMPLICATION AFTER ATRIAL MYXOMA RESECTION

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Background: The formation of cerebral aneurysms after heart tumour removal has rarely been documented. We report the case of a patient with several brain aneurysms in vessels of different sizes, which became clinically apparent as seizures induced by ischemic - haemorrhagic lesions.
Methods and Results: A 39 years old male was admitted to our Hospital because of a sudden episode of unconsciousness with posterior aphasia and right hemiparesis. Echocardiogram showed an irregular and mobile mass in left atrium suggestive of atrial myxoma, which was operated without complications.
During its follow up, he was diagnosed of symptomatic epilepsy and developed apraxia and progressive cognitive impairment related with new small haemorrhages. Two years before, he has had cerebral haemorrhage and was discharged with the diagnosis of multiple cerebral cavernous. Nine years after the first haemorrhagic episode and the myxoma resection, a Magnetic Resonance Angiography (MRA) disclosed a new finding: the growth of the already known aneurysms and the development of new fusiform aneurysms, predominantly in large cerebral vessels.
Conclusion: Neurological complications may occur in a patient with an atrial myxoma not only at its first diagnosis, but also as a delayed complication after tumour removal. Cerebral ischemia is the most frequent complication but, even delayed and rare, myxomatous cerebral aneurysms could appear after cardiac mixoma resection.

CEREBRAL VENOUS AND INTERN CAROTID ARTERIAL THOMBOSIS AS PRESENTING MANIFESTATIONS OF A BURKITT'S LYMPHOMA

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Presenting manifestations of Burkitt's lymphoma usually are adenopathies, splenomegaly, chronic fever and general state alteration. Patients with lymphoma are at increased risk of cerebral thromboembolism,but cerebral venous thrombosis revealing a lymphoma has not been reported.
A 65 years-old man was admitted for sudden right hemiparesis. This attack was preceded by three transient events of right hemiparesis that had led to realize a first brain magnetic resonance imaging (MRI) which showed a left internal carotid thombosis. New brain MRI revealed a parietal left hematoma. Magnetic resonance venography found an obstruction of the superior sagittal sinus with an aspect of infiltration of the vascular wall, and occlusion of the left internal carotid artery. A biopsy of the sinus wall by retrograde catheterism revealed a clot with no malignant cells. A

diagnosis of cerebral hemorrage due to cerebral venous thrombosis was made and a anticoagulation therapy was started. Three months later, the patient suddenly had a right hemiplegia and consciousness disturbances. MRI showed another hematoma in the right frontal lobe and a meningeal enhancement. The venous sinus thrombosis was unchanged. A 18fluorodeoxygluse-PET-scan showed axillary adenopathies and an adenectomy revealed a Burkitt's lymphoma. Anticoagulants were stopped and chemotherapy was started. Six month later, the NIHSS was 4 and the modified Rankin score was 3.

Cerebral venous thrombosis or carotid artery occlusion have never been reported as initial manifestations of Burkitt's lymphoma. The mechanism of these thromboses is unclear. Local invasion of the vessels by tumor cells with secondary thrombosis seems possible on the basis of the MRI and the inefficiency of anticoagulation therapy.

Lymphoma should be suspected in case of arterial or venous cerebral thrombosis, or both, when no plausible cause has been found. The knowledge of this diagnosis is important in order to start the specific chemotherapy in time.

220 Interesting and challenging cases

BRACHIAL MONOPLEGIA - SINGLE SYMPTOM OF SUPERFICIAL MCA INFARCTION

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Material and Method: 6 cases of brachial monoplegia as a single symptom of a partial infarction in the superficial territory of the MCA were observed during 2006-2010.

Results: The 6 patients of the series presented in emergency for brachial monoplegia of sudden onset, with hypotonia, absent deep tendon reflexes, without sensory impairment or other neurological signs. None of the patients had evidence for ischemic lesions on CT scan. All the patients had recent ischemic lesions in the superficial territory of the MCA on MRI.The age ranged between 34-72 years, there 3 women and 3 men. 5 patients (83,8%) had different degrees of carotid artery stenosis. We found high blood pressure in 4 patients (66, 66%), hyperlipemia in 3 patients (50%), diabetes in 1 patient (16,66%).There was a complete MCA infarction with severe neurological deficit following monoplegia in 1 patient.

Discussion and Conclusion: Isolated monoparesis following cerebral infarction is rare. There was an identical clinical picture: severe motor deficit (MRS 0-1) with hypotonia and absent tendon reflexes, no other neurological signs. There was no evidence of ischemic lesion on CT, but MRI revealed recent ischemic lesions in the superficial territory of the MCA. Although multiple and various lesional types, locations and mechanisms were described in this clinical syndrome, all our patients presented partial ischemic lesions in the superficial territory of the MCA, together with significant atherosclerotic lesions of the carotid wall and an atheroembolic mechanism.

Keywords: brachial monoparesis, MCA stroke, carotid artery stenosis

221 Interesting and challenging cases

ISCHAEMIC BROWN-SÉQUARD-SYNDROME

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Background: Spinal cord infarction is a rare but often severe disorder. Because of the variety of clinical symptoms the diagnosis can be challenging, especially if the neurologic presentation do not fit in the defined vascular territories.

Methods: We present the case of a 77-year old women with acute pain in the left lower abdomen followed by mild paresis of the left leg, left-sided hypaesthesia to light touch below the T7-dermatoma and dissociated hypaesthesia of the right leg. No trauma was reported, analysis of the cerebrospinal fluid on two different occasions ruled out myelitis. Also, two MRIs of the spine were made: While the first one on the day of the entry was normal, the second one four days later revealed edema at the T7/T8-level, combined with a restricted diffusion on diffusion weighted images.

Results: Radiologic test showed a spinal cord infarction, mainly in the territoy of the posterior spinal artery.

Conclusion: Although rare, spinal cord infarction should be considered in patients with acute onset of painful Brown-Séquard-Syndrome.
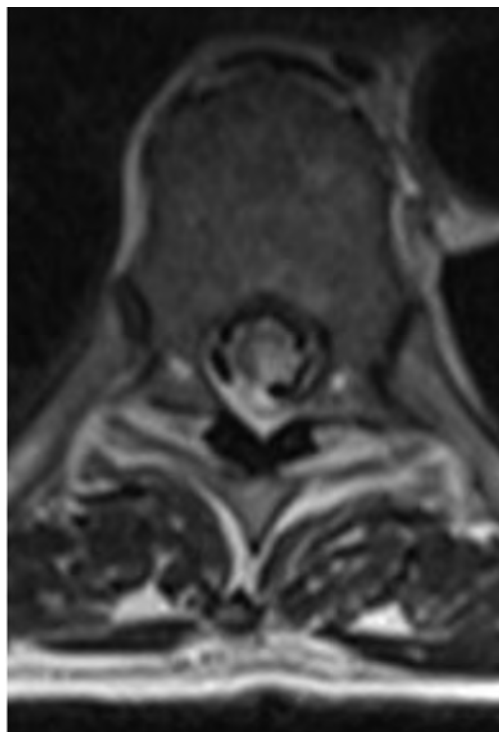
A RARE AND IMMEDIATE PRESENTATION OF HEMATOLOGICAL STROKE ETIOLOGY

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Background: Neurological complication of hematological disorders can be the initial manifestation. The most frequent hematological disorders that are complicated by hemorrhage or ischemic stroke are leukemia, aplastic anemia thrombocytopenic purpura and polycythemia. As a rule this complication signals a fatal issue.
To characterize and discuss an unusual type of cerebrovascular manifestation of polycythemia.
Method: We reviewed the clinical findings and laboratory data of 15 patients hospitalized for cerebrovascular manifestation of hematological disorders complication in our neurological service during past 5 years.
Results: Brain ischemic infarct was the common complication of leukemia (10 cases), thrombocytosis (3 cases), and polycythemia (2 cases). 13 patients had concomitant hematological symptoms.
We describe the 2 cases of male patients with right hemiparesis and aphasia du to association of 2 type of lesion: ischemic stroke and subarachnoid hemorrhage. Neurological manifestation was the initial events. Cerebral computed tomography revealed ischemic infarct and subarachnoid hemorrhage subarachnoid hemorrhage. No vascular rupture at MRI cerebral angiography.
Conclusion: Despite the multiple ethyology of stroke the identification of rare causes is not common in practice. The slightly increased incidence of thrombosis in polycythemia is attributed to high blood viscosity and reduced rate of blood flow. The cause of cerebral hemorrhage in these cases is less clear, although a number of abnormalities of platelet function and coagulation have been described. Clinical and laboratory analysis must search usually the multiple and rare causes.
Keywords: polycythemia, etiology of stroke

CEREBRAL VASCULITIS IN LYME NEUROBORRELIOSIS IS A RARE CAUSE OF STROKE

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Background: Cerebral vasculitis is an important differential diagnosis in the etiology of otherwise cryptogenic ischemic stroke, especially in the young patient. Lyme neuroborreliosis may occasionally cause cerebral vasculitis with subsequent brain infarction.
Case Report: A 38-years-old male Caucasian patient was referred to our department with a gait disorder, which had been progressive over approximately 2 months. On examination, there was a mild left-sided brachio-facial paresis and a mild proximal spastic paraparesis with bilaterally positive Babinski's sign. Brain MRI showed bilateral subcortical DWI- and T2-hyperintense lesions, compatible with acute ischemic lesions (figure). MR angiography demonstrated a severe obstruction of the left MCA and a moderate stenosis of the right MCA. Transcranial Doppler ultrasound confirmed a subtotal stenosis of the left and a moderate stenosis of the right MCA. CSF analysis revealed a pleocytosis with 467 lympho-, mono- and granulocytic cells per µL, protein was elevated to 2000 mg/L. There was intrathecal production of IgG, IgM and IgA, oligoclonal bands were positive. Blood and CSF IgG-titers and CSF IgM-titers for B. burgdorferi were markedly increased. 3 weeks of Ceftriaxone i.v. and Methylprednisolone caused clinical and CSF improvement.
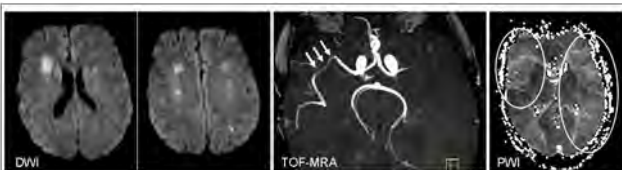
Figure: DWI images (left) show disseminated acute ischemic lesions in both MCA territories. On MRA (middle), there is a marked flow reduction with a lack of flow in the left MCA stem and a moderate narrowing of the distal right MCA (white arrows). Correspondingly, there is a delay of bolus arrival in both MCA territories on perfusion MRI (right).

Discussion: This is an unusual case of a young patient with slowly progressive neurological symptoms and MRI evidence of acute bihemispheric brain infarction caused by cerebral vasculitis associated with Lyme neuroborreliosis. Lyme neuroborreliosis should be considered a possible etiology of multilocular, subcortical stroke.

STROKE RELATED TO INTRACRANIAL STENOSIS AND AORTITIS: CRANIAL ARTERITIS / TAKAYASU DISEASE OVERLAP SYNDROME?

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Background: Giant cell arteritis (GCA) is a vasculitis of large and medium sized arteries. Its typical manifestations are temporal or cranial arteritis (CA), mainly affecting the external carotid and the ophthalmic artery, and Takayasu disease (TD) of the aortic arch and its outgoing vessels. Involvement of cerebral arteries is rare. Both entities are occasionally complicated by stroke.
Case report: A 59-year-old woman was admitted with a right-sided hemiparesis and global aphasia. Symptoms resolved after IV thrombolysis. Transcranial duplex sonography (TCDS) revealed high-grade stenoses of the left middle (MCA) and posterior cerebral arteries. Magnetic resonance imaging (MRI) showed a small infarction in the left internal capsule and confirmed the intracranial stenoses. Transesophageal echocardiography showed a circular thickening of the wall of the thoracic arch. Erythrocyte sedimentation rate (ESR) was elevated to 62 mm/h, C-reactive protein (CRP) was 25 mg/l. Cerebrospinal fluid and serologic markers of vasculitis were negative. Thoracic and abdominal MRI revealed a full-length thickening of the aortic wall and both common iliac arteries. As no feasible site for biopsy seemed accessible, we clinically diagnosed cerebral and aortic vasculitis most likely GCA. Aspirin and high dose methylprednisolone was initiated. ESR and CRP subsequently declined. On day 12, the patient developed a new infarction with a large MRI perfusion deficit in the left MCA territory. We added clopidogrel and cyclophosphamide pulse therapy and the patients symptoms improved gradually. After 6 months, we switched to methotrexate as maintenance therapy. No further ischemic events occurred. TCDS did not show any significant change.
Conclusion: In stroke related to intracranial artery stenosis GCA should be considered as a rare but important differential diagnosis. Its presentation might differ from the well defined entities of CA and TD.

INCREASED HEMORRHAGIC RISK DUE TO ASSOCIATION OF CEPHALOSPORINS AND ORAL ANTICOAGULANTS

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Background: We present the following case to highlight the use of potentially lethal drug associations without prior documentation.
Material and Method: A 56 year-old hypertensive, overweight, dyslipidemic female patient diagnosed with coronary heart disease, atrial fibrillation and left atrium thrombosis after a TIA in the left carotid territory, on statin, hormone replacement and associated antithrombotic (antiplatelet – AP and oral anticoagulant – AC) therapy, was hospitalised for acute onset of pain in the T5 dermatome rapidly followed by paraplegia after a few days of oral cefixime treatment for respiratory tract infection. Prior thoracic pain was judged to be spondylogenic.
Results: Upon admission the INR was above 10, although prior to the antibiotic treatment it was within therapeutic range. MRI of the thoracic spine revealed a cavernoma of the spinal cord with hematomyelia (Fig. 1-12) Antibiotics and APs were stopped and oral AC replaced with low molecular weight heparin (LMWH). After 7 days the cavernoma was removed. On the 3rd postoperative day LMWH was reintroduced. On the 5th postoperative day the patient developed deep vein thrombosis and fatal pulmonary embolism.
Conclusions: Associating cephalosporins with oral AC increased the INR and likely caused bleeding of the cavernoma. Unfortunately, the neurosurgical intervention was postponed to allow the effect of AP to wear off. Although with documented thrombosis of the left atrium, the patient didn't develop systemic embolism, but DVT and pulmonary embolism.
In our view, high profile surgery clinics should be equipped with devices to prevent DVT. Therapeutic protocols should be changed to allow administration of novel anticoagulants (dabigatran), with fixed doses and lesser drug interactions.

A FOOT FALLING SHARPLY

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Objective: In the neurovascular pathology, the central nature of the neurological disorder is most often evident on clinical examination. Nevertheless, some presentations are sometimes misleading. If the pseudo-ulnar palsy secondary to ischemic cerebral infarction well known, the pseudo-peroneal palsy is rare. We report a case to illustrate it.
Observations: Mr V., 84-year-old, with a history of hypertension consults in our stroke unit for a deficit of the left foot appeared suddenly 1 hour ago, after spending two hours sitting cross-legged. On examination, there is a strictly isolated deficiency of the elevator muscles of the left foot.
Discussions: The presentation (isolated deficiency of the elevator muscles of the foot) and the clinical context (cross-legged for two hours) was strongly suspected of peripheral peroneal nerve injury. However, before the brutality of the deficit, we looked for a sign of Babinski. This was positive on the left, with a reflex cutaneous plantar flexion on the right. The most likely diagnosis was therefore that of an infarct in the motor region of the foot. The MRI with diffusion sequence has confirmed the central and ischemic nature of the deficit, showing a frontal precentral hypersignal paramedian on the right side.
Conclusion: The accident mimicking peripheral neurological deficits are often diagnostic pitfalls. A thorough neurological examination is used to straighten the diagnosis, MRI confirming the centrality and ischemic disorders.

UNILATERAL MOYA-MOYA SYNDROME - ISCHEMIC PRESENTATION IN AN ADULT PATIENT

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Background and purpose: The Moya-moya syndrome is an uncommon neurovascular disease associated with different causes or even unknown etiology. This report Aims to describe a rare case of a 22-year-old woman, with atypical ischemic presentation for her age, restricted to the left cerebral hemisphere, treated with encephalo-duro-miosiangiosis.
Clinical Case: A 22-year-old woman, non caucasian, with no commorbities, ex-smoker, presenting migrainous headache for two years, developed on the last year progressive difficult to speak, to read, learn, write and even to calculate and after 18 months since the initial headache, she presented sudden right complete hemiparesis and dysarthria. She came to our service six months after the motor deficit and at the first clinical examination all the previous deficits were present in addition to right homonymous superior quadrantopsy. The Cranial Computed Tomography showed multiple cortical and subcortical ischemic infarct areas only at the left hemisphere. After that she was extensively investigated as stroke in youth people and the digital cerebral angiography showed the typical Moya-Moya pattern compatible with the transcranial Doppler findings. All the other non-invasive and laboratory exams were normal. After the diagnostic and with previous family and patient authorization, she underwent to the surgical procedure encefalo-duromiosinangiosis on the stricken hemisphere and has been accompanied in our service, with a good result in a short observation period.
Conclusion: Moya-Moya syndrome is a rare neurovascular disease which can present as ischemic (more frequent in the childhood) or hemorrhagic stroke (more common on the adult age), affecting usually both hemispheres, although it could be rarely unilateral. There still is few treatment options but the encefalo-duromiosinangiosis is a technique that can change the disease prognosis.

A MAN WITH IRREGULAR JERKING OF THE RIGHT ARM

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The case: A man presented himself with a history of transient involuntary, repetitive trembling and jerking movements of the right arm, especially after rising from sitting positions. Interictal electroencephalogram was free of epileptic discharges. In continuous video EEG monitoring one attack with irregular cloni on the right hand, but without electroencephalographic ictal activity, was registrated. An occlusion of the left internal carotid artery was detected. Imaging showed multiple borderzone infarctions. Transcranial duplex sonography detected a significantly impaired blood flow in the left MCA with a loss of autoregulation during hypercapnia. There was no evidence of cross flow via the anterior or posterior communicating arteries. Collateral blood flow was demonstrated via the ophthalmic artery and leptomeningeal pathways. A Tc-99m single photon emission computed tomography with an acetacolamide challenge showed reversible hypoperfusion in areas on the left side.
Symptoms persisted and neither endarteriectomy nor stenting of the ICA occlusion was possible, a superficial temporal artery - middle cerebral artery (STA-MCA) anastomosis was successfully performed. Afterwards focal blood flow and vasoreactivity improved and the patient remained free of symptoms.
Background: Limb shaking is an involuntary episodic abnormal movement of a limb and a symptom of carotid artery occlusive disease. It may be precipitated by postural maneuvers and can be clinically differentiated from seizures and movement disorders. Hemodynamic changes are consistent with the mechanism of perfusion insufficiency as the probable cause. EC/IC bypass surgery may be of benefit in a subgroup of patients with impaired cerebral perfusion.
Conclusion: It seems plausible that patients would benefit from improving the cerebral perfusion. A decreased frequency or complete cessation of limb shaking TIA's after EC/IC bypass or endarteriectomy is described. The presence of a simple clinical feature such as limb shaking should be used to identify patients who might benefit from a revascularization procedure to reduce the likelihood of stroke.

RECURRENT STROKE RELATED WITH GEMCITABINE-CISPLATIN CHEMOTHERAPY

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Introduction: Neoplasm is a well-established risk factor for suffering a thrombotic vascular event. However, the relationship of chemotherapic agents with these events, particularly with cerebral infarction has not been well established yet. Some publications have related to cisplatin with a slight increase in the probability of suffering a stroke, but the underlying mechanism implicated remains still unknown.
Case report: 52-year-old patient with a history of pulmonary embolism anticoagulated and large cell lung carcinoma,presente an ischemic stroke in the right middle cerebral artery territory days after the first dose of chemotherapy (cisplatin-gemcitabine). Additional studies documented a baseline hypercoagulable state. Fifteen days later, and again after administration of chemotherapic scheduled dose, undergoes a new event involving multiple ischemic areas.
Conclusions: Certain chemotherapeutic agents such as gemcitabine and cisplatin may be associated with stroke, especially in those patients who present a prothrombotic state such as the existence of alterations in the hypercoagulability

SYPHILITIC ARTERITIS ABOUT 6 CASES

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Background: Syphilis has been considered as one of the major cause of the ischeamic stroke in young patient patient.
Methode and Result: the authors report 6 cases of syphilitis arteritis from 64 cases of neurosyphilitis.in all cases, pleocytosis CSF is associated.The middle cerebral artery is the most affected.The CT sccan examination did not show any specifity.The diagnosis was based on the biological tests.
Conclusion: the authors insist systematic practice of syphilitis serology in any unknownischaemic stroke case.

ISCHAEMIC STROKE AND LEFT ATRIAL THROMBOSIS IN A SINUS RHYTHM 41 YEAR OLD MAN: A CASE REPORT

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Background: Left atrial thrombosis (LAT) is generally associated to atrial fibrillation, atrial enlargement, mitral valve stenosis and severe left ventricular

dysfunction.The prevalence, treatment and evolution of LAT in patients in sinus rhythm (SR) is unclear and the role of inherited thrombophylias in the etiology of adult ischaemic stroke remains controversial.

Methods: We describe the case, therapeutic plan and follow-up of a previous healthy 41-years-old man who was admitted in our Unit with an ischaemic stroke involving the left medium cerebral artery and a NIHSS 26.

Results: In diagnostic work-up, the patient was in SR. Transthoracic echocardiogram was normal and duplex sonography revealed an occlusion of left carotid artery (confirmed by magnetic resonance angiography). Transoesophageal echocardiography (TEE)evidenced left atrial thrombus in the absence of cardiopathy. Thrombophylic study revealed heterozygoty for PAI-1 675G>A(5G/4G)3: 5G/4G and heterozygoty for MTHFR1298A>C2:A/C genes. Patient was treated with warfarin.In a 18 months follow up, no more ischaemic events occurred and the NIHSS was 8.

Conclusion: The usual conditions associated with LAT were not present in our patient. We didn't find another reason or risk factor for thrombus formation except the genetic variants of the patient, referred above. To our knowledge, this is the first case report in the literature of a cardioembolic stroke in a pt in SR and no other risk factors detected for thrombus formation, except this genetic double heterozygothy.

232 Interesting and challenging cases

CORTICAL BLINDNESS AS A TRANSIENT ISCHEMIC ATTACK

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Background: Cortical blindness as a transient phenomenon has been described often in eclampsia, after angiography, especially of the vertebral arteries, and in patients receiving chemotherapy. However, it is rarely seen in patients with common vascular risk factors and has never been described before as a repetitive transient ischemic attacks.

Case report: Our patient, 73-year old male, with long-standing hypertension, diabetes, cardiomyopathy and coronary artery disease, had four episodes of transient cortical blindness over one-year period. Episodes occurred abruptly, lasted up to 24 hours and resolved completely. He also had one unrelated episode of transient motor dysphasia. However, although his vision significantly improved after the last episode, he was left with permanent left homonymous hemianopia. Magnetic resonance imaging showed global cerebral and cerebellar atrophy with ventricle enlargement, multiple old cortical infarctions in parietal and temporal lobes of both hemispheres and lacunar ischemia in the pons and basal ganglia bilateraly. Magnetic resonance angiography revealed marked reduction of arborization of middle and posterior cerebral arteries bilateraly. Transcranial Doppler indicated high-grade stenosis of the left posterior cerebral artery and very low mean velocities in both middle cerebral arteries. This patient's cognitive status remained normal despite numerous cortical and subcortical infarcts and chronicaly low cerebral perfusion.

Conclusion: This case confirms that although rare, classical vascular risk factors can lead to recidivant transitory ischemic atacks in the form of cortical blindness.

233 Interesting and challenging cases

SHOULD BE CAROTID ENDARTERECTOMY THE NEXT STEP IMMEDIATELY AFTER UNSUCCESSFUL INTRAVENOUS THROMBOLYSIS? CASE REPORT

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We present case report of the 64-years old acute stroke patient. At the stroke onset patient was scored NIHSS 6, CT showed media sign of the left MCA, and ultrasound finding revealed left internal carotid artery (ICA) thrombosis together with left MCA no flow confirmation. Due to temporary interventional radiologist unavailability we decided for intravenous thrombolysis (90 mg), which was given within 1.5 hour from the stroke onset. After thrombolysis ultrasound showed MCA recanalization and persisting occlusion of ICA. NIHSS improved to 4. 15 minutes later there was rapid clinical state deterioration, reflecting right side hemiplegia, forced head and eyes deviation, and global aphasia. CT together with CTA showed no acute stroke signs and persisting recanalization of the left MCA. Together with vascular surgeon we decided for urgent carotid endarterectomy, which was successfully done 3 hours after the end of thrombolysis. Second day after surgery patient experienced complication – hematoma at the operation side, and blood substitution was needed. 90 days after stroke onset patient improved to mRS 1 and NIHSS 1.

Conclusion: Carotid endarterectomy seems to be safe and successful procedure after intravenous thrombolysis in precisely selected patients, but additional clinical data are needed.

234 Interesting and challenging cases

CT PERFUSION CHANGES IN TRANSIENT ISCHEMIC ATTACK

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Background: Transient Ischemic Attack (TIA) have been rarely related to brain changes in imaging. Brain plain CT changes have been described up to 5% of patients with TIA, and in a similar percentage in MR imaging. However, to our knowledge, changes in CT perfusion maps have not been described before. We present the case of a patient with the diagnosis of TIA and CT perfusion changes.

Case Report: A 55 y/o male admitted to our hospital for coronary angioplasty and stenting presents, 4 days after the interventional procedure, neurological symptoms of 30 minutes of duration which consisted of right hemiparesis, hemianesthesia, right hemianopsy, nominative aphasia and amnesia.

Brain Computed Tomography (CT) showed no abnormalities. CT perfusion showed prolonged Mean Transit Time (MTT), low Cerebral Blood Flow (CBF), and preserved Cerebral Blood Volume (CBV). AngioCT showed no arterial stenosis or occlusion in any location, including the artery of the territory which showed CT perfusion changes.

Symptoms resolved completely after 4 hours, and brain MR 48 hours after symptoms onset showed no diffusion restriction.

Conclusions: CT perfusion may be altered in TIA when performed during symptomatic phase, even in the presence of permeable arteries evaluated with angioCT.

235 Interesting and challenging cases

BASILAR STENOSIS WITH CEREBRAL HYPOPERFUSION AND CLINICAL INSTABILITY: PROPOSAL OF A NEW INDICATION FOR ACUTE ENDOVASCULAR TREATMENT

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Background and Methods: Nowadays, acute endovascular treatment is indicated when there is a large vessel occlusion. We present two cases with critical and symptomatic basilar stenosis that were recanalized and reperfused acutely.

Results: Case 1. A 62 year-old man, ex-smoker, with history of hypertension and dylipemia, related 10-minute episodes of dizziness, dysarthria, binocular dyploia, weakness and numbness on his upper and lower left extremities. Critical stenosis of the basilar artery was observed in TCD (Vm 200 cm/sec). He was readmitted with severe dysarthria, left hemiplegia and ocular deviation towards the left side. Angio-CT imaging showed basilar critical stenosis.

Case 2. A 63 year-old man, with history of hypertension and ischaemic cardiopathy, presented a sudden episode of altered mental status followed by right hemianopia, visual agnosia, confusion and nystagmus. His NIHSS punctuation was 4 and he received i.v. rt-PA, progressing to NIHSS 17. Angio-CT imaging showed basilar critical stenosis with distal hypoperfusion.

In both cases, endovascular treatment was performed acutely, and three months later mRS and NIHSS punctuation was 0.

Conclusion: We suggest large vessel critical stenosis as a new indication of acute endovascular treatment in cases of haemodynamic ischaemia.

236 Interesting and challenging cases

FIBROMUSCULAR DYSPLASIA

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Background: Fibromuscular dysplasia is a rare vasculopathy of unknown cause that leads to degenerative changes of the intima and media of arteries of medium caliber. The involvement of the cervical vessels can be shown in 0.25 to 0.68% of angiographic studies, and the internal carotid artery the vessel most frequently involved in this situation. Clinical manifestations vary from asymptomatic to severe stroke. Several types of lesions are associated, and saccular aneurysms can be observed.

Objectives: We report 05 cases of DF in the epidemiology, pathophysiology, diagnosis and treatment.

Materials and Methods: 05 DF cases were diagnosed by digital angiography. One patient presented with spontaneous bleeding, being found in appearance compatible with DF and vertebral artery dissection intracranial lesion type. The other 04 cases were presented as supratentorial ischemic stroke. On angiography, there was a pattern in the rosary, tubular stenosis of internal carotid artery and aneurysm. Patients underwent anticoagulation and/or antiplatelet and neurosurgical treatment in the presence of an aneurysm.

Results: patients improved, with good recovery of neurological deficits and functional independence at 12 months.

Conclusion: DF a risk factor and cause of stroke, especially in young patients without significant risk factors.

237 Interesting and challenging cases

MENINGOVASCULAR NEUROSYPHILIS – A CASE REPORT

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Meningovascular neurosyphilis is an unusual cause of stroke in young adults. We report a patient with recurrent ischaemic strokes due to meningovascular neurosyphilis.

A 48-year-old patient was admitted with right-sided hemiparesis and hemihypaesthesia. Diffusion-weighted magnetic resonance imaging (MRI) demonstrated areas of restricted diffusion in the left thalamus and in the territory of the left middle cerebral artery. After developing a transient hemianopsia MRI showed another ischaemic lesion in the right occipital lobe. Except of smoking no vascular risk factors could be detected, using routine laboratory tests, thrombophilia markers and immunological blood assays. Doppler imaging, magnetic resonance angiography (MRA) of extra- and intracranial blood vessels and computed tomography angiography of the aorta, transoesophageal echocardiography and Holter EKG recordings were performed. No relevant pathology was found. After clinical improvement the patient could be discharged.

Three months later he was admitted in a confusional state with disorientation in time and place and a significant memory impairment. MRI revealed an ischaemic stroke in the territory of the right middle cerebral artery. Peripheral blood serology revealed treponema pallidum infection with a positive Venereal Disease Research Laboratory test and a positive treponema pallidum hemagglutination. Cerebrospinal fluid analysis confirmed neurosyphilis. MRA now showed vessel wall alterations in the middle cerebral artery as evidence for vasculitis. The patient received a 21-day course of intravenous penicillin G. Clinically, the patient slowly improved, but still suffered from amnestic syndrome.

Neurosyphilis is a potentially reversible cause of cerebral vasculitis and should be considered especially in younger patients with stroke. Since syphilis has become a rare disease and is not routinely tested, it remains a diagnostic challenge.

238 Interesting and challenging cases

A CASE OF QUADRIPARESIS FOLLOWING INTRAVENOUS THROMBOLYSIS OF ACUTE STROKE

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Case description: A 80 year old man was admitted with left sided weakness involving the face, arm and leg. There was no history of loss of consiousness or seizures. His past medical history included atrial fibrillation, mitral valve replacement (tissue valve), congestive cardiac failure and pulmonary fibrosis. The NIHSS score on arrival was 7 and CT head did not show any ischaemic changes or haemorrhage. He was thrombolysed with alteplase as per protocol. NIHSS score initially improved to 4 after 2 hours.

On the second day, he developed a dense weakness on the left side. A repeat CT head did not reveal any new changes. The next day, it progressed to quadriparesis with weakness on his right side involving the arm and face. A MRI scan of brain and cervical spine failed to reveal any lesion to explain the quadriparesis. He continued to deteriorate and died 2 days later from a chest infection.

A post mortem examination was done which showed an unilateral area of ischaemia in the pons which could explain the initial deterioration and bilateral multifocal ischaemic areas in the paramedian area of medulla (DEJERINE SYNDROME) involving medial lemniscus and the pyramidal tracts.

Discussion: It is possible that, despite thrombolytic therapy, thrombotic microemboli secondary to atrial fibrillation have caused the lesions, as they are both multifocal and polyphasic.

Dejerine syndrome or bilateral medial medullary syndrome is an uncommon presentation of stroke. It accounted for approximately 0.5% of all brain infarctions in a case series by Toyoda et al. [1].

To our knowledge, no similar cases have been reported in literature of Dejerine syndrome after stroke thrombolysis.

References:
1. Toyoda K, et al. Neurology 1996; 47:1141-1147.

239 Interesting and challenging cases

STROKE IN PREGNANCY: A CASE REPORT

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Introduction: A patent foramen ovale (PFO) is a remnant of embryological development due to failure of the septum primum to fuse adequately with the septum secundum. This communication between the atria can cause stroke through paradoxical embolisation.

Stroke in pregnancy is an unusual but catastrophic event; paradoxical embolism may be more frequent due to the hypercoaguable state.

Case History: A 32 year-old lady who was ten weeks pregnant was admitted to the Stroke Unit with a 1 day history of left sided weakness. She had no past medical history and no stroke risk factors. She had reduced power in her left arm and leg and a swollen left leg. A MRI of her brain showed an acute right occipital infarct and infarcts of the corpus striatum and corona radiata consistent with synchronous anterior and posterior circulation events. A Doppler ultrasound of her leg found a deep venous thrombus (DVT); she was started on low molecular weight heparin (LMWH). A bubble Echo revealed communication between the atria and a transoesophageal Echo confirmed the paradoxical passage of contrast. A cardiac MRI established that the rest of the heart was structurally normal.

Results: The investigation Results lead to the Conclusion that the cerebral infarcts were due to paradoxical emboli via a PFO from a DVT.

She was transferred to a rehabilitation bed after 11 days on the Stroke Unit. On discharge she had no neurological deficit. She remained on LMWH but was booked for percutaneous closure of the PFO before her due date.

Conclusions: This is a unique case describing a stroke during pregnancy with radiological evidence of a DVT and PFO. There is some controversy as to whether the association between PFO and stroke is clear-cut; with the finding of a coexisting DVT in this case, it can be linked to the cerebral infarcts via the PFO. There is no consensus on the treatment of patients with PFO. Percutaneous device closure of the PFO is an option for certain patients; the procedure can be performed under local anaesthetic with trivial foetal radiation.

In view of the complex nature of managing such a case, advice should be sought from stroke physicians, cardiologists and obstetricians.

240 Interesting and challenging cases

A MASQUERADER PRESENTING AS CLINICAL CHAMELEON THE MITOCHONDRIAL DISEASES DIAGNOSIS WITH THE PASSAGE OF TIME!

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In July 2010, a 47 year old lady presented with a new stroke affecting the right parietal lobe. Her relevant investigations were normal. She had also suffered right occipital infarct in November 2009 and few months later diagnosed to have grand mal seizures.

The woman's main problem was her inability to walk far since childhood and she was forced to change jobs due to this! Looking over her case notes, her first presentation to the hospital was when she was 14 years of age with dull lower abdominal pain when appendicectomy was done but appendix was found to be normal. Her general practitioner referred her to the hospital thrice for exertional shortness of breath and cramps in calves on walking at 26, 30 and 39 years of age. Relevant clinical tests were normal but ABG showed low pCO2. She was diagnosed to have hyperventilation syndrome and reassured. She was picked up to have hypothyroidism. At 36 years of age, she was found to have bilateral pale discs without any pathological cupping. At 38 years of age she developed sensorineural hearing loss and needed hearing aid. In 2006, she was found to have hypertension, chronic kidney disease stage3 and mixed hyperlipidaemia. Her renal ultrasound was normal, renal biopsy showed only mild interstitial fibrosis. She is due for cataract surgery in late January 2011. She presented to us with stroke in July 2010 when we found that her serum lactate was very high at 9 without any explanation for this.

A clinical suspicion of mitochondrial disease was confirmed with muscle biopsy showing ragged red cell fibres. Genetic tests for MELAS 3243 and for POLG mutation were negative.

General awareness of this condition is important for stroke physicians and allied speciality as some cases may be missed. The incidence of this condition may be higher than reported. Secondly, it is always important to link the past medical history carefully as rare conditions may be picked up.

241 Interesting and challenging cases

VENTRICULITIS CAUSED BY INFECTION WITH STREPTOCOCCUS MILLERI GROUP (SMG) INFECTION

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Background: Cerebral Ventriculitis is a potentially life-threatening and neurologically disabling condition, If not diagnosed and treated in time.There are few causative factors including trauma,an immunocompromised host, and few organisms like Staphylococcus species, gram-positive cocci consistent with skin flora, Streptococcus milleri, Streptococcus pneumonia and gram-negative rods. It is manifested clinically by high-grade fever and clinical signs of meningitis, including nuchal rigidity, photophobia, decreased mental status, seizures, or moribund appearance. Ventriculitis can be diagnosed by microbiological tests on the CSF. Computed tomographic (CT) imaging and magnetic resonance (MR) imaging are investigations of choice which show ventricular debris as the most characteristic finding, and it is characterized by irregular level. Hydrocephalus and ependymal enhancement are less frequent signs: The Streptococcus milleri group (SMG) belongs to the group of viridans streptococci and known for their marked tendency to cause abscesses and occasionally ventriculitis. The distinct species are related with infection at different sites. In a considerable part of reported cases though no definite origin of bacteraemia can be identified.

Method: We present a case who has a Background history of myocardial Infarction, arthritis, atrial Fibrillation, recently treated pneumonia. He initially presented with nonspecific symptoms followed by acute deterioration as manifested by sudden drop in GCS associated with Seizures; decorticate posture and planters up going. Urgent CT Brain was done and findings were consistent with ventriculitis (Figure 1). Urgent Neurosurgical referral was made. External Ventricular drain was done and draining frank pus grew Streptococcus milleri. CSF and blood culture from admission also grew Streptococcus milleri. He was treated extensively with prolonged course of Benzyl Penicillin and intrathecal Vancomycin. He had prolonged rehabilitation for 4 months followed by near full recovery.

Cerebrovascular Diseases

Acute stroke: new treatment concepts

290 Acute stroke: new treatment concepts

IMPACT OF APOPTOSIS REPRESSOR WITH CASPASE RECRUITMENT DOMAIN (ARC) PROTEIN DELIVERY ON STROKE OUTCOME

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The protein Apoptosis Repressor with a CARD Domain (ARC) has been shown to protect against oxidative stress-induced apoptosis by interfering with both, the death receptor dependent and the mitotic signaling pathway. In this work we probed the hypothesis if ARC is neuroprotective in experimental stroke in vitro and in vivo.

In primary neuronal cultures the ARC protein levels were significantly reduced after oxygen glucose deprivation (OGD). Furthermore, a) downregulation of the ARC protein by RNA-interference resulted in higher susceptibility to OGD and b) the Introduction of recombinant TAT-ARC protein revealed a dose-dependent, neuroprotective effect.

Immunohistochemical analysis of mouse brains after focal cerebral ischemia displayed marked loss of ARC positive neurons at early time points after damage. Therefore we used TAT-mediated delivery to compare the neuroprotective effect of the native ARC protein with that of the non-degradable TAT-ARC K3R, 149D and the non-functional CARD domain mutant TAT-ARC L31F, G69R.

In our in vivo model, 8 week old C57/BL6 mice were subjected to 60 min. middle cerebral artery occlusion (MCAO) while the TAT-proteins were stereotactically applied into the contralateral side ventricle. The infarct sizes measured by 7 Tesla small animal scanner magnetic resonance tomography after 24 and 72 hours using T2-weighted sequences showed a marked reduction in lesion size for the native and K3R,149D-mutant.

Consistent Results were obtained with a behavioral analysis (rotarod and pole test) 1 day before and 72 h after reperfusion time). Interestingly, immunoblot analysis of TAT-ARC treated brains after MCAO exhibited a strong reduction of JNK-3 in comparison to TAT-beta-Gal treated brains, indicating that ARC interferes upstream of JNK-3 with the apoptotic pathway.

In summary, TAT-mediated delivery of the ARC-protein improves the outcome after hypoxic damage in vitro and in vivo and thus is a promising candidate for molecular therapy in stroke.

291 Acute stroke: new treatment concepts

DOUBLE-BLIND, PLACEBO-CONTROLLED, CLINICAL STUDY TO INVESTIGATE THE SAFETY AND EFFICACY OF NEUROAID ON MOTOR RECOVERY AFTER ISCHEMIC STROKE

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Background and Objective: Stroke is the leading cause of severe neurological disability. To date, no effective treatment has been found for reducing stroke-induced disability. NeuroAid as a Traditional Chinese Medicine has been developed to aid post-stoke recovery. Our study aim was to investigate the safety and efficacy of NeuroAid on motor recovery after ischemic stroke.
Methods: In a double-blind, placebo-controlled clinical trial study on 150 patients with a recent (less than 3 month) ischemic stroke, patients were given either NeuroAid (100 patients) or placebo (50 patients), 4 capsules 3 times a day, as an add-on to standard medication of post stroke for 3 months. The patients have visited at the beginning and every 10 days in the first months and every two weeks in the second and third month. The efficacy endpoint was improvement of impairment of the affects upper and lower limbs as assessed on the Fugl-Meyer Assessment (FMA).
Results: Baseline characteristics for gender, age and elapsed time from stroke onset and risk factors were not significantly different between two groups (p>0.05). There were no difference in FMA score at baseline; 53.69±23.01 in the NeuroAid and 54.96±24.27 in the control group, p=0.755. FMA scores increases significantly in NeuroAid comparing to controls in 4th week (77.13±19.22 vs. 63.50±24.21; p<0.001), 8th week (82.51±14.27 vs. 72.06±21.41; p=0.001) and 12th week (86.22±12.34 vs. 82.78±14.93;p<0.001) after medication. Repeated measured analysis showed statistically difference in FMA during 12 months between two groups (p<0.001). Patients showed a good tolerability to treatment and adverse events were mild and transient.
Conclusion: NeuroAid showed better motor recovery than placebo and was safe on top of standard ischemic stroke medication. It was more effective in motor recovery in subjects with severe and moderate than mild patients. However, still more studies are needed to evaluate safety and efficacy of Neuroaid.

292 Acute stroke: new treatment concepts

ENDOVASCULAR TREATMENT OF STROKE WITH UNKNOWN TIME OF ONSET: SINGLE CENTER PRELIMINARY RESULTS

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Background: Currently, treatment options for patients with wake up strokes or strokes with unknown time of onset (UTO) remain limited. With the advance of neuroimaging and endovascular treatment (EVT), selected patients might have a chance for a therapeutic option. We sought to compare clinical outcome after EVT in patients with known time of onset (KTO) and in those with UTO.
Methods: We prospectively registered patients who underwent endovascular treatment (EVT) during 2010. Recanalization (TICI 2b-3), complications and outcome were recorded. SICH was defined as a worsening of 4 points in the NIHSS score within 36 hours in any bleeding. Favorable outcome was defined as a modified Rankin score <3 at 3 months.
Results: A total of 73 patients were studied, 24 with UTO and 49 with KTO. Age was 61.8±11 vs 67±12 respectively, p=0.007 and baseline NIHSS was 17 [13,22] and 18 [16,20]. For UTO/KTO, site of occlusion was M1-MCA in 9/15, M2-MCA in 3/6, TICA in 6/9, proximal ICA 0/2, tandem 2/11, vertebrobasilar 4/5, ACP 0/1. Median time from last seen normal to groin puncture was 655 [605,825] vs 309 [253,358] minutes, p<0.001 and to recanalization was 701 [585,875] vs 362[289,407], p<0.001. Recanalization was seen in 58.3% vs 66.7%, p=0.5. SICH occurred in 4.2% and 10.4% (p=0.3), Discharge mRS <3 was 37.5% and 31.9% (p=0.3) and 7th day mortality 4.2% and 4.3%, (p=0.9). Favorable outcome was achieved in 60% vs 37%, p=0.1 of patients who had completed the 3 month follow-up.
Conclusions: In our series, endovascular treatment of AIS patients with unknown time of onset and selected with multimodal imaging, seems to have comparable recanalization rates and favorable outcome than in patients with known time of onset. Hemorrhagic complications and mortality were similar in both cohorts. Larger series are needed to support this hypothesis, which is based on physiopathology rather than time-based selection for EVT.

293 Acute stroke: new treatment concepts

IMPACT OF TELEMEDICINE ON ACUTE MANAGEMENT OF STROKE PATIENTS UNDERGOING ENDOVASCULAR PROCEDURES

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Telemedicine (TM) improves stroke care in remote areas. We aimed to assess the benefits of TM to select patients for endovascular treatments.

Methods: In our Stroke Centre urgent intra-arterial procedures for acute stroke patients may be primarily admitted or referred from other hospitals with or without TM. TM allow early treatment decision based on remote patient evaluation and CT assessment which according to our protocol is not repeated if time from CT to groin is <90 minutes. Moreover TM allows obtaining informed consent for endovascular procedures before the transfer. We studied outcome measures according to patients origin: primary admission, TM linked Hospital (TMH:2 centers) or Hospitals without TM (nonTMH:7 centers). Clinical improvement was considered if a decrease in NIHSS≥4 points was achieved, good functional outcome if modified Rankin scale at 3 months was<2.

Results: During 2 years, 122 patients received endovascular treatment: primary admissions: 74 (63.1%), TMH: 25 (20.5%), nonTM: 20 (16.4%). There were no differences in baseline characteristics including age (71/ 71.6/ 66.5 p=0.25), baseline NIHSS (18.5/ 19/ 18 p=0.57) and previous administration of iv.tPA (56.5/ 56.5/ 57.9 p=0.95). Patients transferred from TMH had similar clinical improvement (50 Vs 52.8; p=0.51) and good functional outcome (31.6% Vs 36; p=0.722) as primarily admitted patients. Conversely patients from nonTMH presented lesser degree improvement (27.8%) and less good outcome (5.6%;) than TMH patients (p=0.019/ p=0.046) and primary admissions (p=0.05/p=0.013). Patients transferred from TMH had non-significant shorter time from symptom onset-to door (207 Vs 238 minutes; p=0.48) but significantly shorter door-to-groin time (47 Vs 69 minutes; p=0.047). The rate of recanalization (TIMI 2-3) was similar in all groups (75%/66.6%/68.4%; p=0.682). After adjusting for distance to Stroke Center, being transferred from a nonTMH independently predicted a poor functional outcome (OR:0.1; 95%CI: 0.01-0.82; p=0.032).

Conclusion: TM assessment to select patients for endovascular procedures improves efficiency in stroke management and may benefit early and long-term outcome in patients receiving IA procedures

294 Acute stroke: new treatment concepts

POOR RESPONSE TO THROMBOLYSIS IN ACUTE STROKE IS PREDICTED BY OLD AGE AND SEVERE NEUROLOGICAL IMPAIRMENT

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Background: Patients recover upon successful thrombolysis but remain severely impaired in lacking reperfusion. This is reflected by small infarct lesions after successful recanalization and large infarct lesions involving the paraventricular white matter in lacking recanalization. We sought to investigate the clinical effect of systemic thrombolysis in acute stroke.

Methods: In this prospective mono-center study 252 patients were subjected to thrombolysis with 20 mg recombinant tissue plasminogen activator (rtPA) followed by an infusion of body weight adjusted tirofiban between January 2005 and December 2007. Neurological impairment was assessed with the modified Rankin Scale (mRS) and the Barthel Index (BI). After discharge the patients were pursued for up to 36 months when a telephone assessment was performed using mRS and BI.

Results: 192 patients (70±13 years, 50 percent males) had complete data until follow-up. 81% of the patients had a middle cerebral artery territory infarct. The median impairment at onset was 4 (mRS) and 30 (BI). During the stay on the Stroke Unit 13 patients deceased due to malignant infarction, 7 patients (3%) due to fatal cerebral hemorrhage. At discharge 29% of the patients had a mRS of 0 or 1. These patients were younger than the more severely affected patients. 18 percent of patients deceased within 100 days which was predicted by older age (76 + 10 years, p<0.05), more severe affection (mRS 5, p<0.0001), and the patients more frequently had atrial fibrillation (p<0.03) than the surviving patients. The surviving patients improved further (p<0.0001) leaving 59% with a mRS of 0 and 1 at follow-up.

Conclusions: Combined thrombolysis with low dose rt-PA and tirofiban accords with thrombolysis with body-weight adjusted rt-PA. The factors predicting early death after thrombolysis were old age and severe neurological impairment. More than half of the surviving patients improved continuously to no or a minimal neurological impairment.

295 Acute stroke: new treatment concepts

PRESTROKE USE OF BETA-BLOCKERS DOES NOT AFFECT ISCHEMIC STROKE SEVERITY AND OUTCOME

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Background: Beta-blockers attenuate sympathetic activity, which has shown to be a negative prognostic factor in the acute phase of stroke. Two studies investigating the effects of pre-ischemic stroke use of beta-blockers on stroke severity produced conflicting Results. We examined the effect of pre-stroke use of beta-blockers on ischemic stroke severity and 3 months functional outcome.

Methods: The relation between pre-stroke use of beta-blockers and both stroke severity and functional outcome was investigated in 1375 acute ischemic stroke patients who had been included in 2 placebo-controlled trials with lubeluzole (LUB-INT-5 and LUB-INT-9). Stroke severity was assessed by either the National Institute of Health Stroke Scale (NIHSS) or the European Stroke Scale (ESS). A modified Rankin scale (mRS) score of > 3 at 3 months was used as measure for poor functional outcome.

Results: 266 patients were on beta-blockers prior to stroke onset, and 105 of them continued treatment. Pretreatment with beta-blockers was not associated with lower baseline stroke severity (OR = 1.14; 95% CI = 0.87-1.49). There was no difference in stroke severity between non-users and those on either a selective beta-blocker (OR = 1.12; 95% CI = 0.81-1.53) or a non selective beta-blocker (OR =1.18; 95% CI = 0.76-1.83). The likelihood of a poor outcome at 3 months was neither reduced by prestroke use of beta-blocker (OR = 0.96; 95% CI = 0.74-1.27) nor when beta-blocker use was further continued after stroke onset (OR = 0.85; 95% CI = 0.57-1.27).

Conclusion: Prestroke use of beta-blockers does not appear to influence stroke severity and functional outcome at 3 months.

296 Acute stroke: new treatment concepts

TO TEACH TO TREAT – TO TREAT TO TEACH A TELEMEDICAL STROKE PROJECT OVER 12,000KM

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Stroke unit treatment is effective in reducing mortality and disability after stroke, but it's not available in many rural particular areas.

For acute stroke care in nonspecialized hospitals, telemedicine is used to make neurological expertise available; to overcome distances and also offers a long-time benefit for patients.

This process consist of the set-up specialized local stroke wards, continuous medical education and telemedical consultation.

A telemedical network with Krankenhaus Nordwest, Frankfurt am Main Germany and Jerudong Park Medical Center, Brunei Darussalam is established. German medical stuff support JPMC in stroke unit treatment with a project of excellence "to teach to treat – to treat to teach".

This includes acute support 24/7, exchange programs, daily conferences over 12,00km, daily lectures and built up of laboratories, as well as rehabilitation.

Only after 3 months of set-up phase, since 07.2010, hemicraniectomies, hypothermia and thrombolysis has been performed the 1st ones in Borneo and out-standing in south East Asia.

The only difference between Brunei and Germany is, that the patients are waiting too long to come to JPMC. In this short project period one can say, how successful it is, now they have a stroke unit locally and Bruneian hospitals do not send patients out of Brunei.

297 Acute stroke: new treatment concepts

SINGLE CENTER EXPERIENCE WITH OVER 40 PATIENTS WITH THE TREVO™ SYSTEM - RECANALIZATION AND 90 DAY OUTCOMES

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Background: Clinical outcome in acute ischemic stroke has been shown to be strongly linked to revascularization and lysis of thrombus is often not successful in proximal or large vessel occlusions. We report the early experience with a novel stentriever device (Trevo) that was designed to address these issues.

Method: Adoption of a revised patient selection protocol supporting the use of Stentriever technology like the Trevo device has been implemented at Hospital Clinic de Barcelona. Trevo was utilized solely in a retrospective series of 41 patients. The Trevo device was delivered through a Microcatheter (m/c) and unsheathed by pulling back on the m/c, leaving the device directly in the thrombus. This allowed the device to incorporate into the thrombus, followed by retrieval of the thrombus into the guide catheter. Analysis was performed on Trevo patients where no other adjuvant device or pharmacology employed to demonstrate the potential of such a system in improving recanalization success and patient clinical outcomes.

Results: Final Results are being tabulated for the final evaluation phase. The mean age was 69 years and baseline NIHSS = 18. Time-to-treatment varied widely and will be reported in the final analysis. The occlusion location was distributed in the ICA, M1, M2 and basilar segments. The device reached the target occlusion in all cases. Partial revascularization was achieved in most cases upon immediate deployment. Final recanalization success TICI 2b/3 was achieved in 89% of cases and TICI 2a or greater was achieved in 97% of patients. There was no device related complications. In our experiences with other mechanical devices and IA rt-PA, Results are trending to be more positive than any other IA procedure.

Conclusions: The Trevo system quickly restores flow and can be employed over a variety of different vessel occlusions in both the anterior and posterior circulations, and suggest that it may reduce procedural times, increase acute recanalization rates, improve discharge NIHSS and 90 day mRS of these patients. It may be an interesting technology to include in patient selection protocols for large vessel, proximal occlusions.

298 Acute stroke: new treatment concepts

NOVEL ANALYSIS METHODOLOGY INDICATES EXTENDED WINDOW LOW-DOSE IV ABCIXIMAB IMPROVES OUTCOME

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Background: We previously reported promising Results compared to historical rt-PA controls and IA case series using low dose IV abciximab (ABX) and a short course of heparin with an extended time window in patients ineligible for rt-PA. We selected a 30% lower dose of ABX because our platelet inhibition data indicated we achieved inhibition within ranges proposed as effective in the cardiac literature. We developed a novel case control matching methodology (pPAIRS©; Mandava and Kent, Stroke 2010) which we employed here to compare our case series to subjects in the NINDS control arm. To select comparable controls, we used the 2 hour post-randomization time point in the NINDS placebo subjects for matching criteria.

Methods: 44 patients with suspected large vessel occlusion and ineligible for IV rt-PA presenting within 6 hrs for anterior and 12 hrs for posterior circulation were treated with ABX (0.2 mg/kg max 16 mg bolus and 0.05ug/kg/min 12 hour infusion) along with 36 hours IV heparin. Hemorrhage rate, mortality and 90 day mRS were obtained. To compare outcomes, pPAIRS© was used to find the nearest neighbors in 3d space for NIHSS, age and glucose, selecting from the control arm of the NINDS non-lacunar patients database. Further matching by territory and gender was assessed.

Results: Matching was excellent: Median NIHSS of ABX compared to controls was 17.5 vs 17.0 (p=0.98). Mean age was 66.6 vs 66.4 (p=0.88). Mean glucose was 149 vs 147 (p=0.93). 57% of ABX patients achieved an mRS 0-2 vs 34% in the matched NINDS controls (p=.02, McNemars). Mortality was 25% in both groups. Symptomatic and asymptomatic hemorrhages were similar (ABX: 2% and 9% vs control: 0%; p>0.1). Benefit was comparable in anterior and posterior circulations and in both genders.

Conclusion: Our Results indicate that IV abciximab with a short course of heparin appears safe and comparison with matched historical controls suggests that outcomes may be improved. A randomized trial is warranted.

299 Acute stroke: new treatment concepts

BODY TEMPERATURE, INFLAMMATORY MARKERS AND BRAIN TEMPERATURE AFTER ISCHAEMIC STROKE

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Objective: Brain temperature rises after stroke: the cause is uncertain. We investigated the relationship of brain temperature after stroke with body temperature and circulating markers of inflammation.

Methods: We recruited patients with acute ischaemic stroke and measured brain temperature at hospital admission and at 5 days after stroke onset, with multi-voxel magnetic resonance spectroscopic imaging across the acute ischaemic stroke lesion and normal brain determined by diffusion weighted imaging (DWI). We measured body temperature with digital aural thermometers four-hourly for up to five days. We drew blood daily for up to 5 days after stroke, and measured interleukin-6, C-reactive protein and fibrinogen.

Results: Amongst 44 patients, at admission the average temperature in DWI abnormal brain was 38.40C (95% CI: 38.2 to 38.6), in normal brain was 37.70C (95% CI 37.6 to 37.7) and body temperature was 36.40C (IQR 36 to 36.70C). Higher (mean) levels of interleukin-6, C-reactive protein and fibrinogen were

associated with higher temperatures in DWI normal brain tissue at both scan times and with higher mean body temperature. There was no strong evidence that mean marker levels or mean body temperature were more strongly correlated with temperature in abnormal brain than temperature in normal brain.

Interpretation: Systemic inflammation after stroke is a potential cause of a rise in brain temperature. The relationship between body temperature and regional brain temperature after stroke is complex, and may be different at different times after stroke.

300 Acute stroke: new treatment concepts

RETRIEVABLE STENTS REDUCE TIME TO RECANALIZATION AND USE OF THROMBOLYTICS IN ACUTE ENDOVASCULAR ISCHEMIC STROKE TREATMENT

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Background: Retrievable stents are a new treatment option for endovascular revascularization in acute ischemic stroke patients. Retrievable stents offer the fast and high recanalization rate of stents and the final thrombus removal of mechanical thrombectomy devices. This study assessed the impact of retrievable stents on the multi-modal approach for endovascular stroke treatment.

Methods: All acute ischemic stroke patients treated by endovascular revascularization therapy during a 6 months period were included. Multi-modal endovascular therapy included thrombaspiration, thrombus disruption, thrombolysis, balloon angioplasty (PTA), and stent placement in 23 patients (Group A). A retrievable stent was used (Group A) in addition to multi-modal therapy in 17 patients (Group B). Baseline characteristics, occlusion sites, urokinase dose, recanalization rate, and time to recanalization were compared between the groups.

Results: Fourty patients were included. Median NIHSS scores were lower in Group A compared to Group B on admission (12.5 vs. 19.0; p = 0.018) but were not significantly different at day 1 (10 vs. 14; p = 0.6). Recanalization rate was higher when a retrievable stent was used in addition to multi-modal therapy (94% in Group B vs. 78% in Group A; p = 0.17), and time to recanalization was significantly reduced (median time to recanalization 52.5 min [Group B] vs. 90 min [Group A]; p = 0.001). Less intra-arterial thrombolysis was used in patients of Group B compared to Group A (53% vs. 87%, respectively; p = 0.017) and median urokinase dose was lower in Group B (250.000 IE vs. 700.000 IE [Group B]; p = 0.006).

Conclusion: Retrievable stents further increase recanalization rate of multi-modal endovascular revasczularization therapy for acute ischemic stroke. More important they significantly reduce time to recanalization and the additional use of thrombolytics.

301 Acute stroke: new treatment concepts

OUTCOMES OF MECHANICAL ENDOVASCULAR THERAPY FOR ACUTE ISCHEMIC STROKE: A CLINICAL REGISTRY STUDY AND SYSTEMATIC REVIEW

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Background and purpose: Recanalization is a powerful predictor of stroke outcome in patients with arterial occlusion. Intravenous (IV) recombinant tissue plasminogen activator (rt-PA) is limited by its recanalization rate, which may be improved with mechanical endovascular therapy (MET). However, the benefit and safety of MET remain to be determined. The aim of this study was to give reliable estimates of efficacy and safety outcomes of MET.

Methods: We analyzed data from our prospective clinical registry and conducted a systematic review of all previous studies using MET published between January 1966 and November 2009.

Results: From April 2007 to November 2009, 47 patients with acute stroke were treated with MET at Bichat hospital. The literature search identified 31 previous studies involving a total of 1066 subjects. In the meta-analysis, including our registry data, the overall recanalization rate was 79% (95% CI, 73-84). Meta-analysis of clinical outcomes showed a pooled estimate of 40% (95% CI, 34-46; 27 studies) for favorable outcome, 28% (95% CI, 23-33; 28 studies) for mortality, and 8% (95% CI, 6-10; 27 studies) for symptomatic intracranial hemorrhage.

The likelihood of a favorable outcome increased with systematic use of chemical thrombolysis (odds ratio, 1.99; 95% CI, 1.23-3.22) and with proportion of patients with isolated middle cerebral artery occlusion (odds ratio per 10% increase, 1.14; 95% CI, 1.04-1.25).

Conclusions: MET is associated with acceptable safety and efficacy in stroke patients, and may be a therapeutic option in those presenting with isolated middle cerebral artery occlusion.

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302 Acute stroke: new treatment concepts

THE MECHANISTIC STUDY OF NETRIN-1 PROTECTIVE EFFECTS AGAINST ISCHEMIC STROKE

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Background: Stroke and many other neuronal diseases have created a huge burden for our society. In our preliminary study, we identified netrin-1's protective effects in ischemic stroke animal model. We further showed that the anti-apoptotic ability of netrin-1 was very likely mediated through the dependent receptor pathway, which is rarely investigated in apoptotic neuronal diseases. In the current study we pursuit the molecular mechanism underline the protective effect of netrin-1.

Methods: We utilize PC12 and SHS-Y5Y cell lines for our mechanistic studies. Cells were placed in hypoxia condition to mimic stroke condition. Real-time PCR and RT-PCR were used to detect changes in mRNA level. Changes in protein expression and phosphorylation level were measured by Western blotting. MTT assay and cell counts were used to determine the effects of hypoxia and treatments to cell survival. RNA interference was used to suppress the expression of possible signaling mediators to determine their roles in conducting the signal.

Results: We determine the optimum hypoxia condition in PC12 and SHS-Y5Y cells with HIF-1 expression level and detect the expression of netrin-1 and its receptors, DCC and UNC5H2 under the same condition. We also detect the expression of p53 under the same condition and compare our Results with those in the animal model. We then test whether netrin-1 exerts the same protective effects in cells as in the animal model. By using RNAi, we determine the role and DAP-kinase and p19ARF in netrin-1's anti-apoptotic signal pathway.

Conclusion: We established cellular model to study netrin-1 protective effects against ischemic stroke in vitro. With the Results of this study, we show the potential of the ligands of dependent receptors such as netrin-1 to serve as a novel treatment option in acute stroke.

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303 Acute stroke: new treatment concepts

90 DAY FUNCTIONAL OUTCOME WITH CEREBRAL PERFUSION AUGMENTATION STRATIFIED BY AGE

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Background: The "Partial Aortic Occlusion for Cerebral Perfusion Augmentation: Safety and Efficacy of NeuroFlo in Acute Ischemic Stroke (SENTIS) Trial" prospectively randomized 515 patients to test the safety and efficacy of a novel catheter (NeuroFloTM) in subjects with cortical strokes presenting within 14 hours from onset of symptoms. We present the effect of age on the 90 day mRS 0-2 outcome.

Methods: The primary efficacy endpoint on a modified intent-to-treat population was a global disability endpoint indexing disability, neurologic deficit, and activities of daily living at 90 days. Secondary endpoints included mortality, intracranial hemorrhage, mRS 0-2 outcome and mRS shift analysis. We report the 90 day mRS of 0-2 in patients in ages less than 70 and over 70 years of age.

Results: The primary efficacy endpoint on the entire enrolled population did not reach statistical significance (OR 1.17; CI 0.81–1.67; p=0.41). However, we noted that advancing age had a positive effect on the 90 day mRS 0-2 outcome in this cohort with patients over age 70 (OR 1.98; CI 1.02–4.03; p=0.04) showing better Results than those under age 70 (OR 1.04; CI 0.53–1.49; p=0.89). The positive effect was further amplified in patients over the age of 80 (OR 4.03; CI 1.5–12; p=0.01).

Conclusion: Our study shows that cerebral blood flow augmentation with NeuroFlo shows improving benefits with advancing age. This was evident in subjects over the age of 70 years (50% of the study population). The mechanisms for better outcome with advancing age are not clear but may be related to age based differences in baseline collateral status and/or hemodynamic support.

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304 Acute stroke: new treatment concepts

COMPARISON OF INTERVENTIONAL ACUTE AND 90 DAY OUTCOMES IN ACUTE ISCHEMIC STROKE (AIS) – TREVO™, MERCI® AND INTRA-ARTERIAL RT-PA – A RETROSPECTIVE SINGLE CENTER EXPERIENCE FROM HOSPITAL CLINIC DE BARCELONA

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Background: Thrombolysis in AIS is often less successful in recanalization in larger vessel occlusions. IA options provide more direct interaction with larger thrombus burden, and may result in recanalization and good clinical outcomes for patients. Each of these modalities has been studies in trials and registries, and rarely compared to assess recanalization and patient outcomes.

Methods: Retrospective analysis of 76 patients where IA lytic, Merci & Trevo where employed at the Hospital Clinic de Barcelona. This was a comparable patient subset based on age, sex and NIHSSS. No limitations were placed on the selection of patients or use of adjuvant IV rt-PA. Each device was utilized per the instructions for use.

Results: Analysis is on-going for mRS, Hemorrhage and other parameters early Results are ending as follows: Median age is 69 and median NIHSS is 18. The occlusions were located in the ICA (27%), MCA (61%), and Vertebrobasilar (12%). Revascularization was assessed with the TICI scale.

Parameter	Trevo	Merci	IA rt-PA
TICI 2a+	97.4%	88.2%	50%
mRS	Ongoing	Ongoing	Ongoing
Tx time (mins)	69	85	129
Symp Hem	Ongoing	Ongoing	Ongoing

Late-breaking Results, including updated demographics, procedural and 90d outcomes will be reported at the time of presentation.

Conclusions: Highest revascularization rates were achieved with the Trevo system and also contributed to shorter procedural times. There were no events or hemorrhage attributed to the Trevo device in our reported series. Mechanical revascularization and in particular, Trevo demonstrates promising Results for clinical outcomes with Results trending towards better mRS for the Trevo group providing faster recanalization, increased recanalization and better clinical outcomes.

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305 Acute stroke: new treatment concepts

FAST AND EFFICIENT RECANALISATION IN ACUTE STROKE WITH A SELF EXPANDING RETRIEVABLE STENT SYSTEM

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Background: Mechanical recanalisation is a relatively new and promising option in acute stroke treatment. A fast and efficient restore of blood flow is the main factor for a better clinical outcome.

Methods: Patients with an acute ischemic stroke due to proximal vessel occlusion in the anterior or posterior circulation were treated with a self expanding and retrievable Stentsystem (Solitaire AB/FR) and partially with additional mechanical devices and iv-bridging lysis.

Results: 71 Patients presented with a proximal vessel occlusion (M1:28, M2,5, ICA: 2, ICA+MCA:10, Carotid-bifurcation:13, BA/VA: 13). All were treated with the Solitaire AB/FR Device, 7 with additional mechanical Devices (Catch/Snare/Bonnet) and 23 Patients had a pretreatment with iv-bridging lysis. 91% of the vessels were fully recanalized with this treatment (TIMI 0->3). In average mechanical thrombectomy took 35 min from angio start to full recanalisation.

Conclusions: Mechanical Thrombectomy with the Solitaire Stent Results in higher rates of recanalisation compared to standard iv-lysis with rtPa. Additionally restore of the blood flow is achieved in a short period of time. In our experience patients can strongly benefit from this treatment.

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306 Acute stroke: new treatment concepts

IMPACT OF PRESENTING NIHSS ON 90 DAY OUTCOME AFTER TREATMENT WITH COLLATERAL BLOOD FLOW AUGMENTATION FOR ISCHEMIC STROKE

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Background: A novel catheter treatment (NeuroFloTM) that increases cerebral blood flow via partial occlusion of the descending aorta was recently tested in ischemic stroke out to 14 hours. This analysis investigated if mRS 0-2 outcome was affected by presenting NIHSS score with the hypothesis that moderate stroke would be more favorable than mild (high control response rate) and severe (low treatment response rate).

Methods: SENTIS was a randomized trial of the safety and efficacy of NeuroFlo treatment in improving neurological outcome versus standard medical management in acute stroke. The primary efficacy endpoint was a global disability endpoint indexing disability, neurologic deficit, and activities of daily living at 90 days with a secondary endpoint of 90 day mRS 0-2. SENTIS enrolled 515 patients with NIHSS ranging from 5 to 18. We report the outcomes in patients with mild (NIHSS: 5-7), moderate (NIHSS: 8-14) and more severe (NIHSS: 15-18) deficits.

Results: While the overall study did not reach statistical significance in the primary or secondary outcome variables, there was a clear difference in 90 day mRS 0-2 outcomes in relationship to the presenting NIHSS. Patients with moderate stroke had the best outcome (NIHSS: 8-14; odds ratio 1.8; p=0.05) compared to patients with mild (NIHSS: 5-7; odds ratio 1.2; p=0.69) or severe (NIHSS 15-18; odds ratio 0.6; p=0.45) strokes.

Conclusion: Similar to Results from other trials, this intervention demonstrates greater treatment effect in moderate strokes, informing not only the potential clinical utility of this intervention but also the design of future trials for ischemic stroke.

307 Acute stroke: new treatment concepts

REMODELLING OF ACUTELY SYMPTOMATIC UNSTABLE CAROTID ATHEROSCLEROTIC PLAQUES WITH MEDICAL THERAPY: A SINGLE CENTER EXPERIENCE

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Introduction: No defined treatment guidelines exist for symptomatic carotid plaques with pedunculated intraluminal thrombi (pILT). We studied the safety profile and efficacy of triple antithrombotic therapy (ASA, clopidogrel and IV heparin) in such patients.

Methods: A retrospective review of clinical and imaging features of a cohort of patients with strokes/TIAs resulting from carotid plaques with pILT who underwent repeat CT Angiography (CTA). All patients received triple therapy within 24 hours of presentation. Two readers blinded to clinical data read baseline and follow-up CTA. Adverse events and imaging change in plaque characteristics were the outcome measures.

Results: 17 patients (male 12/17, mean age 65±11 yrs) were identified and studied. Clinical presentation was anterior circulation strokes 12/17 and hemispheric TIAs 5/17. Initial CTA was performed mean 1.2 + 0.7 days from symptom onset. Repeat CTA was performed mean 15.3+13.1 days after treatment initiation. Follow up CTAs showed complete resolution of the pedunculated component of the ILTs in all subjects. The mean % stenosis decreased from 62.5% + 18.8% at baseline to 44.1% +24.0% at follow-up. Mean plaque diameter decreased from 0.48±0.11 cm to 0.39±0.15 cm, mean plaque length decreased from 2.12±0.72 cm to 1.73±0.87 cm. During therapy one patient had minor GI bleeding. None had TIAs or strokes. Over a follow-up of 3 months, 1 patient had a hemispheric TIA. Subsequently 11/17 underwent carotid revascularization and 6/17 continued on dual antiplatelets because stenosis was not deemed severe enough for revascularization.

Conclusion: In this small series of acutely symptomatic carotid atherosclerotic plaques with pILT, triple therapy appeared to be safe. Triple therapy completely resolved the pedunculated component of ILT and also reduced the degree of stenosis, and plaque diameter. Prospective larger studies are needed to further validate these Results.

308 Acute stroke: new treatment concepts

DOES GENDER INFLUENCE THE EVOLUTION OF PATIENTS TREATED WITH INTRAARTERIAL PROCEDURES?

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Background: We aimed to evaluate whether gender differences influence recanalization,early and long-term outcome and mortality in acute stroke patients treated with intraarterial (IA) reperfusion procedures.

Methods: Consecutive stroke patients treated with IA procedures between September 2006 and August 2010 were analyzed. Baseline clinical characteristics,different endovascular approaches and response to endovascular procedures (recanalization,clinical evolution, hemorrhagic transformation, mortality and functional outcome) were evaluated according to gender.

Results: We included 121 patients; mean age 70.4. 57 (47.1%) were women (W). W were older (p=0.002), had more atrial fibrillation (p=0.014) and previous treatment with coumadin (35.7% vs 15.6%; p=0.01). No gender differences were observed in baseline NIHSS (W 19 vs men (M) 20; p=0.946), symptoms to groin-time (W 217.5min vs M 232.8, p=0.512) or door to groin-time (W 85.3min vs M 75.7, p=0,251). The occluded vessels and clot locations were similar in both groups. Rate of pre-treatment with ivtPA was lower in W (47.3% vs 67.64%, p=0.047). During IA procedure 10.2% W vs 10% M were treated with tPA alone and 18.4% vs 34% with isolated mechanical procedures (p=0.199). 71.7% W required more than one IA technique to achieve recanalization comparing to 56% M (p=n.s).

Recanalization after IA procedures was similar between W and M (72.7% vs 71.7%, p=0.899) and occurred at same time (mean symptoms to recanalization-time: W 329.9 min vs M 338.1, p=0.778). No differences were found in clinical improvement at discharge (W 47.1% vs M 49.1%, p=0.830), hemorrhagic transformation (34.6% vs 30.4%, p=0.637) or in-hospital mortality (32.1% vs 35% p=0.745). At 3 months, 31.9% of patients achieved good outcome in both genders (p=1).

Conclusions: Despite older age and higher prevalence of atrial fibrillation, W had similar response to endovascular reperfusion therapies than M.
W received more frequently primary IA therapy because of higher rate of previous anticoagulant therapy.

309 Acute stroke: new treatment concepts

THE EFFECT OF NEUROAID™ (MLC601) ON CEREBRAL BLOOD FLOW VELOCITY IN SUBJECTS' POST BRAIN INFARCT IN THE MIDDLE CEREBRAL ARTERY TERRITORY

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Background: Stroke is the third common cause of mortality and the most common cause of morbidity in adults.
MLC601 (NeuroAiD™) is a treatment indicated for post stroke recovery. An increase of impaired cerebral blood flow, a marker of the micro-circulation, may be an important parameter for recovery processes. The aim of this study was to investigate the effect of MLC601 on cerebral blood flow velocity as an indirect evidence of cerebral blood flow increase in post stroke subjects.

Methods: This is a double-blinded, placebo controlled, randomized study of 80 subjects included within a week of stroke onset. All subjects were given either MLC601 or placebo, 4 capsules, 3 times a day for 3 months. Cerebral blood flow velocity within the middle cerebral artery, with blood flow velocity measured by transcranial Doppler (TCD), Barthel index score and modified Rankin scale was assessed at baseline and at 3 months.

Results: The mean change in cerebral blood flow velocity in the MLC601 treatment group (15.9) was significantly increased (p=0.009) compared to the placebo group (9.6). Subjects in the treatment group also showed a significant difference in the mean rank of modified rankin scale (p<0.001) and mean change of the Barthel Index: 36 versus 29 in the placebo group (p<0.001).

Conclusion: This is the first study suggesting that treatment with MLC601 may increase cerebral blood flow in stroke subjects. This may be mediated by an effect on stimulating microcirculation, an important process contributing to neuroplasticity in the central nervous system. This effect on cerebral blood flow may be associated with improvement in measures of functional recovery.

310 Acute stroke: new treatment concepts

EFFECT OF EARLY CILOSTAZOL IN THE ACUTE PHASE OF NON-CARDIOEMBOLIC STROKE

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Background & Purpose: A neurological deterioration against the antithrombotic treatment was occasionally observed in the acute phase of ischemic stroke (progressive stroke). We investigated the effect of early cilostazol for progressive stroke.

Subjects & Methods: For the present study, 239 first-ever stroke patients who were admitted to our stroke center within 72 hours after the onset and were diagnosed as having non-cardioembolic stroke with NIHSS score of 7 or less were prospectively included. For the acute treatment during the first 7 days, all patients were divided into 2 groups: 114 patients were treated only with intravenous ozagrel sodium (Group O), and the other 125 patients were treated with intravenous ozagrel sodium plus oral cilostazol of 200mg/day (Group-C). After the acute antithrombotic treatment of 7 days, all patients were treated with aspirin, cilostazol, or clopidogrel. We observed a neurological deterioration with or without stroke recurrence or any death during the first 21 days and the outcome at 3 months after admission. Modified Rankin Scale of 0 or 1 was defined as a good outcome.

Results: There was no significant difference in the baseline characteristics and NIHSS score on admission between the Group-C and the Group-O patients. A NIHSS score worsening of ≥1-point or any death in the Group-C was observed as frequently as those in the Group-A (20% vs 24%). However, a good outcome at 3 months after admission was observed more frequently in the Group-C than the Group-A patients (68% vs 55%, p=0.0428). On multivariate analysis, early cilostazol (OR, 3.38; 95% CI, 1.58-7.26) was positively, and NIHSS score on admission (OR, 0.58; 95% CI, 0.48-0.71), NIHSS score worsening of ≥1-point (OR, 0.08; 95% CI, 0.03-0.21), and age (OR, 0.92; 95% CI, 0.88-0.95) were negatively associated with a good outcome. In the Group-C, 9 (36%) of the 25 patients with a neurological deterioration also showed a good outcome. On the other hand, only 4 (15%) of the 27 patients showed a good outcome in the Group-O.

Conclusions: In non-cardioembolic stroke, early oral cilostazol in the acute phase might be associated with a good outcome against the progressive stroke.

311 Acute stroke: new treatment concepts

IMPACT OF G-CSF ON DENDRITIC CELLS IN EXPERIMENTAL STROKE

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Introduction: Stroke leads to extensive inflammatory processes, which are assumed to secondarily worsen neurological outcome. Characterized by their ability to induce a T cell specific immune response, dendritic cells are important regulators of the immune system. To investigate their role in poststroke inflammation we examined the impact of G-CSF, which has been shown to suppress DC recruitment after myocardial infarct, in an experimental stroke model.

Methods: Stroke was introduced in 70 male Wistar rats by occlusion of the middle cerebral artery, followed by reperfusion after 1 hour (tMCAO). G-CSF was applied once 30 minutes after induced tMCAO or daily for the next seven days. Cerebral migration of DCs (Ox62+), T lymphocytes (CD3+) and macrophages/microglia (CD68+) was investigated using immuno-histochemical staining. Cerebral transcription levels of TLR2 and TLR4, which are involved in DC activation, and the cytokines IFN-g and IL-10 were examined by quantitative real-time PCR.

Results: In both modes of treatment, G-CSF led to a reduction of the infarct size and an improved neurological outcome. The acute application of G-CSF caused a significant decrease in cerebral DCs, T lymphocytes and macrophages/microglia. Both the acute and daily treatment with G-CSF inhibited the expression of TLR2 and TLR4, which shows a decreased activation of DCs. Apart from that, daily G-CSF application was associated with an increase in IL-10 and a reduction of IFN-g in the infarcted brain hemisphere, indicating a shift from Th1/Th2 ratio towards an enhanced formation of Th2 cells.

Conclusion: Anti-inflammatory effects of G-CSF seem to be based on both suppressed TLR mediated DC stimulation and an inhibited DC migration into the infarcted brain. Suppressed DC-mediated inflammation as well as the lowering of Th1/Th2 ratio might contribute to the reduction of the infarct size and thus may provide a potential therapeutical approach for neuroprotection after experimental stroke.

312 Acute stroke: new treatment concepts

EFFECT OF ALLOPURINOL IN ISCHEMIC STROKE PROGNOSIS

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Background: Oxidative stress is a major contributor to brain damage in patients with ischaemic stroke and the production of free radicals with xanthine oxidase (XO) has been suggested to play an important role in tissue injury following ischemic stroke. This study evaluated the effect of allopurinol as a potent drug against XO activity, in ischemic stroke patients with high level serum of uric acid.

Methods & Materials: In this interventional study, we performed a randomized, double-blind, controlled study to investigate the effect of a 3-month course of allopurinol (200mg/d) vs. placebo on patient functional outcome in new diagnosed non hemorrhagic ischemic stroke patients on admission. They have increased serum level of uric acid and did not receive allopurinol before. All cases randomized in two 30-patinet groups; the "intervention" group who received allopurinol (200 mg/d) for three months, and the placebo group. All patients were on antiplatelet and regular physiotherapy. Patients' outcome was evaluated by modified Rankin Scale (MRS) on admission and after 3 months.

Results: Baseline serum uric acid was 9±3.2 mg/dl and 8.4±1.1 mg/dl in the allopurinol and placebo groups, respectively. There were no serious adverse events related to treatment. The mean baseline MRS was 3.2±0.8 in the intervention group and 3.4±0.8 in the control group. The MRS after 3 month was 2.4±1.8 in the intervention group and 3.2±1.6 in the control group. The mean MRS decreased significantly in the intervention group (p=0.007) with borderline nonsignificant change in the controls (p=0.064). The change of MRS was greater in the intervention group comparing with that in the controls in a borderline nonsignificant trend (p=0.075). The mortality rate was 10% in the intervention group vs. 20% in the controls (p=0.236).

Conclusion: According to this study, oral allopurinol may protect the patients with ischemic stroke and lead to better prognosis in 3 month follow-up.

313 Acute stroke: new treatment concepts

SELECTING STROKE PATIENTS WITH UNKNOWN TIME OF SYMPTOM ONSET FOR THROMBOLYSIS BY NEGATIVE FLUID-ATTENUATED INVERSION RECOVERY IMAGING

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Background: Up to a quarter of patients with acute ischemic stroke are presenting as stroke with unknown onset (SUO), most of them with so called wake-up stroke (WUS). For the reason of unknown time window they are generally excluded from thrombolysis (IVTPA). However, there are data from an analysis of MRI in acute stroke with known time showing that negative fluid attenuated inversion recovery (FLAIR) sequences may serve as a "tissue clock" to identify stroke patients who are highly likely to be within the 3-hour time window. (Thomalla et al. Annal Neurol 2009).

Methods: Patients with AIS without known time of symptom onset and who were eligible for MRI examination were offered IV TPA as compassionate treatment, when they met following criteria: exclusion of hemorrhage, Infarction if the anterior circulation, positive mismatch on MRI (≥20%) and negative FLAIR imaging in the area of the AIS as shown by diffusion-weighted sequences. A comparison was made to patients who received IVTPA with known time window.

Results: From a total of 49 patients 39 were eligible for MRI (37 with WUS), 19 of those were excluded from IVTPA (FLAIR +,9; DWI > MCA territory 1/3,7; no mismatch, 3). Twenty patients received IVTPA. There was no difference on NIHSS median/range: IVTPA/no IVTPA/control: 9.0/31 vs. 6.5/31 vs. 7.0/30 at baseline; 4.5/33 vs. 3.5/30 vs. 3.0/36 at day 4; p=n.s. Parenchymal hematoma (PH) type occurred in 1 patient of both, the IVTPA and no IVTPA group. One PH type 2 with deterioration of ≥ 4 on the NIHSS occurred in the control group. After 3 months (not done for controls, mRS median/range was 2/6vs. 4/6; 3 out of 20 IVTPA patients but 5 out of 15 no IVTPA patients (4 were lost to follow-up) had died, p=n.s.

Conclusion: Selection of patients with SUO for IVTPA using MRI including FLAIR-weighted sequence as a tissue clock is feasible and appears to be safe. Further clinical studies are required to prove this new treatment concept.

315 Acute stroke: new treatment concepts

HEMODYNAMIC EFFECTS OF EXTERNAL COUNTERPULSATION ON CEREBRAL CIRCULATION IS A DIFFERENT MEASURE OF IMPAIRED CEREBRAL AUTOREGULATION FROM VASOMOTOR REACTIVITY

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Background: External counterpulation (ECP) is a novel method to augment cerebral blood flow during diastole, which may benefit acute ischemic stroke patients. We aimed to explore the correlation between the augmented hemodynamic effect of ECP and cerebral vasomotor reactivity.

Methods: We recruited 32 recent ischemic stroke patients with large artery occlusive disease and 20 healthy elderly controls. All underwent ECP treatment and breathholding test combined with transcranial Doppler monitoring on bilateral

middle cerebral arteries (MCA). We designated the ipsilateral or contralateral MCA based on the side of the recent infarct, while we used the average of both sides in the controls. Cerebral augmentation index (CAI) was calculated based on the formula (mean velocity during ECP -baseline mean velocity)/baseline mean velocity*100%. Vasomotor reactivity was assessed by using the breathholding index (BHI).

Results: The MCA mean flow velocities in stroke group significantly increased after ECP (CAI ipsilateral 9.856±9.057, contralateral 9.235±7.624) but not in the controls, (CAI -0.469±2.892, p<0.001). BHIs were smaller in the stroke group (ipsilateral 0.723±0.437, contralateral 0.864±0.470) than that of the controls (1.405±0.455, p =0.011). CAI did not correlate with BHI in the ipsilateral or contralateral side of stroke group as well as in controls. BHI was significantly lower on the ipsilateral side than the contralateral side, p= 0.049, but CAI showed not difference.

Conclusion: Dynamic augmentation effects as measured by CAI were different from the well established vasomotor reactivity. CAI is a measure of how well the brain accommodates blood flow augmentation, independent of vasomotor reactivity.

316 Acute stroke: new treatment concepts

ATTRIBUTING FACTORS ASSOCIATED WITH HEMODYNAMIC INSTABILITY AFTER CAROTID ARTERY ANGIOPLASTY AND STENT

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Background: Hemodynamic instability (HI) after carotid artery stent (CAS) is a common phenomenon and is attributed to the stretching of the carotid sinus baroreceptor. Hemodynamic depression (HD) including reflex hypotension and bradycardia is more common and could show adverse outcomes after CAS. But, in practice, reflex hypertension is also common and could be strongly related with hyperperfusion syndrome. The purposes of this study were to assess the incidence of the type of HI and evaluate the associated factors.

Methods: A total of 66 patients (median age, 65 years) with carotid artery stenosis who were treated with CAS between March 2008 and May 2010 were included. Demographic factors, anatomic characteristics of carotid plaque and vital signs at baseline were collected. Reflex hypotension was defined as any decrease in systolic blood pressure (BP) of more than 40% or any systolic BP lower than 90mmHg during and after CAS. Reflex hypertension was defined as any increase in systolic BP more than 20mmHg. Univariate and multivariate analysis were performed to evaluate factors influencing HI.

Results: The incidence of reflex hypotension, bradycardia, and both was 32%, 16%, and 13%, respectively. In addition, 7 patients (13%) showed reflex hypertension. Multiple regression analysis showed the pre-CAS status of contralateral side were significantly associated with HI. Moreover, the stenosis proximity to the bifurcation and direction of plaque were the significant contributing factors of HD. Two patients showed hemorrhagic transformation after CAS, and hyperperfusion syndrome was strongly related with reflex hypertension.

Discussion: HI occurs with the significant percentage. Considering the possible relationship of HI with adverse events, it is essential to find exact predicting factors and prohibit the HI. Based on our Results, the characteristics of anatomical factors might be the most valuable points for the accurate prediction.

317 Acute stroke: new treatment concepts

DEVELOPMENT OF NEW PARP-1 INHIBITOR AND ITS ROLE IN ISCHEMIC STROKE; INFARCT VOLUME DECREASING EFFECT AND NEUROPROTECTIVE MECHANISMS

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Background: Poly (ADP-ribose) polymerase (PARP) is a nuclear enzyme in eukaryotic cells which is involved in the regulation of many cellular functions. But, the overactivation of PARP has recently been emphasized as one of the pathogenic mechanisms of stroke and neurodegenerative disorders.

We designed and synthesized candidate molecular compounds showing PARP-1 inhibition, and evaluated the neuroprotective effects on ischemic stroke including infarct volume with various injection times and dosages.

Methods: We synthesized candidate compounds that contain non-aromatic amides as potential PARP-1 inhibitors with docking study and evaluated the structure-activity relationship and biolological activities. After sacrifice, the brains were isolated and sliced in the coronal plane at 2-mm intervals. The coronal slices were incubated in PBS containing 2% 2,3,5-TTC at room temperature for 1 hour, and

then fixed in 10% phosphate-buffered formalin. The infarct area was determined by image analyzer. The Various dosage and therapeutic time window were evaluated to assess the efficacy of candidate compounds.

Results: After analyzing data of solubility, rat Pk study, BBB permeability, mouse & beagle single- or repeated-dose toxicity, genetic toxicity tests, we selected JI-1236, -1260 as 2nd preclinical candidates. Pharmacokinetic, toxicological and efficacy data lead us to select JI-1260 as final preclincal candidate. When treating with various dose of JI-1260 in ischemic animal models, 63% reduction of infarct volume was observed in treatment of 20 mg/kg. In the experiments of JI-1260 therapeutic windows, the maximun effect was detected at 2 hours. JI-1260 has been proven the safety from analyzing toxicity test.

Discussion: Our Results suggest that PARP-1 inhibitor could be a useful therapeutic candidate for ischemic stroke. Further evaluation of this class of derivatives is ongoing.

318 Acute stroke: new treatment concepts

TREATING LARGE ARTERY STROKES USING THE SOLITAIRE STENT RETRIEVAL. ANGIOGRAPHIC AND CLINICAL EXPERIENCE

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Objectives: Ischemic stroke may be treated intraarterially using a clot-retrieval (CR) device. Stent-retrival devices are emerging as an alternative that may offer efficient revascularization in a timely manner. We aim to describe our initial experience with a self expanding and fully retrievable stent (Solitaire AB; ev 3 Inc, Plymouth, MN) in the treatment of acute ischemic stroke.

Methods: We retrospectively studied all patients with ischemic stroke within 6 hours and underwent CR using the Solitaire stent between July 2009 and May 2010. Efficacy of revascularization was assessed using the pre and post treatment TIMI score. Clinical evaluation included pre treatment NIHSS and follow up mRS.

Findings: Eleven patients were treated in the study period. Median age was 68 (range 28-85). All patients had complete large artery occlusion in the anterior circulation (TIMI 0). Seven patients had M1 occlusion and 4 had M2 occlusion. Median symptom to procedure time was 3.17 hours (range 2.45-6.0). Median admission NIHSS was 20 (range 12-26). Successful device deployment was achieved in all patients. Two patients received IV tPA as a bridging therapy before the endovascular procedure. All patients received intra-arterial tPA during the procedure (max dose 15mg). The median number of device passes was 3 (range 1-6). Successful revascularization defined as TIMI score 2-3 was achieved in 10 of 11 (90.9%) while full recanalization (TIMI 3) was achieved in 8/11 cases (73%). Distal embolization accured in 3/11 (27%). No device related complications were encountered. One patient developed symptomatic fatal hemorrhagic transformation. Two in hospital deaths occurred. Patient were re-evaluated at a median of 6 months after stroke. 3/11 (27.3%) had a good outcome (mRS 0-2) and 8/11 (72.7%) had a poor outcome.

Conclusions: Our experience with the Solitaire stent shows it to be effective as a revascuariztion device. The success rate and complications are comparable with current devices. The clinical Results are encouraging. Further prospective evaluation of stent-retrieval devices is warranted.

319 Acute stroke: new treatment concepts

CHANGE OF PARADIGM? - CARDIAC OUTPUT INSTEAD OF MEAN ARTERIAL PRESSURE ENHANCES CEREBRAL PERFUSION IN LARGE ISCHEMIC STROKE

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Background: In acute ischemic stroke penumbral perfusion is mainly maintained by cortical or subcortical insufficient collateral flow. To date to optimize penumbral perfusion mean arterial pressure (MAP) is enhanced either by i.v. fluids or vasopressor use. Conversely especially in patients with pre-existing left ventricular insufficiency enhancement of MAP may lead to reduced cardiac index (CI). We hypothesized that cerebral perfusion is dependent on CI rather than MAP.

Methods: In patients with large hemispheric stroke cerebral perfusion was assessed by transcranial duplexsonography (TCCD) as well as transcranial perfusion sonography (TPS) according to previously decribed Methods. Mean flow velocities (mFV) of the middle cerebral artery (MCA) as well as time to peak values (TTP) within the affected and non-affected hemisphere were assessed. Via PiCCO-monitoring the following hemodynamic parameters were documented: MAP, CI, systemic vascular resistence index (SVRI) and heart rate (HR). After

optimizing of CI patients received sonographic follow-up. MFV as well as TTP were correlated with MAP and CI and values before and after CI enhancement were compared.

Results: 10 consecutive patients with large MCA stroke were included into the study. MAP was kept above 70mmHg in all patients and ranged from 73 to 110mmHg. CI ranged between 2,1 and 5,9. TTP of the non-affected as well as the affected hemisphere correlated highly significantly with CI with an inverse correlation (non affected side: r= -0.894, p<0.01; affected side: r=-0,802, p < 0.01). Also by enhancing CI there was a significant increase of TTP and mFV. Conversly correlation of TTP and mFV with MAD was not significant.

Conclusion: Maintaining penumbral perfusion is essential especially in large hemispheric stroke and is based on MAP so far. We were able to show, that increase of CI enhances cerebral perfusion and correlation of CI with cerebral perfusion parameters is significant whilst correlation with MAP is not. Thus to optimize cerebral perfusion and penumbral flow optimization of CI should be the targeted hemodynamic value. Clinical studies are now needed to underline this change of concept.

320 Acute stroke: new treatment concepts

INHIBITORS OF OXIDATIVE PHOSPHORILATION IN ACUTE STROKE: PRELIMINARY DATA IN RATS

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Background: The induction of a hypometabolic state soon after acute ischemic stroke may contribute to brain protection against ischemia. Inhibitors of oxidative phosphorilation can induce hypometabolic states. We studied the effect of hydrogen sulphide, an inhibitor of oxidative phosphorilation, in a rat model for acute ischemic stroke by permanent middle cerebral artery occlusion (MCAO).

Methods: Adult Sprague-Dawley rats were distributed to a control group (permanent MCAO alone) and a treatment group (permanent MCAO + inhalation of 40 ppM hydrogen sulphide). We analyzed functional deficit by an adapted evaluation score (Rogers scale) and lesion volume by magnetic resonance imaging (MRI) at 24 hours and 14 days after MCAO. Rats were sacrificed on day 14 and cell death was assessed by TUNEL analysis.

Results: Preliminary data showed a benefit in functional deficit in the treatment arm. There was also a decrease in infarct size both at 24 hours (9.76% versus 16.80%) and at 14 days (8.50% versus 17.22%). TUNEL analysis showed a decrease in the expression of TUNEL positive cells in the peri-infarct border zone (18±7.07 versus 58±12.73).

Conclusion: Hydrogen sulphide inhalation after acute ischemic stroke was associated with an improvement in functional recovery and a decrease in infarct volume and cell death in rats. Preliminary data presented in this study has to be confirmed by future investigation.

321 Acute stroke: new treatment concepts

EFFECTS OF DIPYRIDAMOLE ON THROMBOLYSIS AND RECANALISATION IN A MOUSE MODEL OF THROMBOEMBOLIC STROKE

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Background: Dipyridamole (DPM) is known as a drug for secondary stroke prevention. Other beneficial effects beyond platelet inhibition include anti-inflammatory and anti-oxidative properties that could act neuroprotective. The aim of the present study was to examine if DPM accelerates clot resolution in acute stroke in a mouse model of thromboembolic stroke. This was done by cerebral blood flow measurements. Further analysis included stroke size measurements by magnetic resonance imaging (MRI).

Methods: Thromboembolic stroke was induced by murine thrombin injection into the MCA of C57 black/6J mice. 20 min later 96 μg/kg DPM (Boehringer Ingelheim) (n = 4) or NaCl (0.9%) (n = 5) respectively was given intravenously for 20 min. To induce thrombolysis all mice were treated with 10 mg/kg rt-PA (Actilyse®, Boehringer Ingelheim) for 40 min, 40 min after stroke induction. All mice further got 120 mg/kg DPM or placebo by gavage ten times every 12 hours resulting in a therapeutic plasma level of 1.5 μg/ml blood. The efficiency of DPM to support rt-PA mediated thrombolysis and its effect on infarct volume were measured by laser Doppler flowmetry and 9.4 T MRI on day 1, 8 and 15 after clot formation.

Results: Thrombin injection resulted in stable clot formation followed by cortical brain injury. Laser Doppler flowmetry analysis of 3 mice showed recanalisation

after DPM + rt-PA treatment beginning 5 min after starting of DPM injection. In contrast placebo + rt-PA treated mice (n = 4) showed no recanalisation up to 2h. MRI observed from 6 mice on day 1, 8 and 15 showed smaller infarct sizes of 3.41±3,97 mm³ in DPM + rt-PA treated (n = 2) compared to 28.25±21,6 mm³ in placebo + rt-PA treated mice.

Conclusion: In a thrombin mouse model for thromboembolic stroke and reperfusion first Results indicate that DPM could have a supporting role in clot resolution after thromboembolic stroke, resulting in smaller infarct sizes measured by 9.4 T MRI.

322 Acute stroke: new treatment concepts

A NOVEL THERAPEUTIC APPROACH FOR ACUTE ISCHEMIC STROKE IN DIABETIC PATIENTS

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Background: Several studies have demonstrated the link between diabetes (DM) and stroke as well as increased oxidative stress. Guidelines stress the need to normalize glycemic levels with insulin in the acute phase of stroke. But would this be enough, or are other therapeutic resources available for diabetic patients with stroke?

Material and Method: 104 consecutive patients with lacunar (L) and non-lacunar (NL) ischemic strokes (TOAST criteria) hospitalised between 2003 - 2006 were scored on the National Institute of Health Stroke Scale (NIHSS) on admission and had the Barthel Index (BI) evaluated at discharge. DM was diagnosed and classified according to the ADA criteria. Serum malondialdehyde (MDA) was measured on admission and on days 3 and 7 from stroke onset to assess the course of oxidative stress.

Results: We recorded 32 L and 72 NL strokes. DM proved an important risk factor for L: 86% of DM patients developed lacunae, and DM was recorded in 37.5% of L strokes, as compared to 2.8% in NL. DM was second in frequency only to hypertension, present as risk factor in 93.8% of L patients.

DM significantly increased stroke severity in both groups: NIHSS on admission was 3.6 times higher for L and 2.9 times higher for NL respectively (p<0.05). DM also impaired recovery after stroke; at discharge DM patients had significantly lower BI than non-diabetics, the difference being 16.2 for L (p<0.05) and 38.9 for NL (p<0.02). Oxidative stress was increased in DM. We found higher MDA levels in DM patients at stroke onset as well as on days 3 and 7, while the characteristic course of oxidative stress for the 2 subtypes was maintained.

Conclusions: DM increases stroke severity and worsens outcome in both L and NL stroke. The increased oxidative stress (higher MDA levels) suggests a possible beneficial effect of antioxidants associated to insulin, in order to prevent extension of brain lesions. The functional Results will depend on the presence of salvageable tissue.

323 Acute stroke: new treatment concepts

CT PERFUSION GUIDED HYPERTENSIVE THERAPY FOR ACUTE STROKE

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Background: Hypertensive for acute stroke has been reported in the past with good Results. Although the patient selection criteria is not clear. We describe a case of acute stroke that presented to the hospital outside the window period and received blood pressure augmentation therapy.

Methods: Case report.

Results/Case report: 29 year old african american women presented to the ED with acute onset of headache followed by left sided weakness that started 8 hours prior to hospital presentation. Patient had a past medical history of migraine headaches. On arrival her NIHSS was 10. A CT of the head did not show any abnormalities. CT angiogram showed filling defect in the right M1 with some flow distal to the clot. CT perfusion was performed that demonstrated no loss of blood volume but increased mean transit time and reduced blood flow to the entire MCA territory. Patient was not a candidate for IV or IA tPA due to presentation after 8 hours. She was admitted to NICU and hypertensive therapy was initiated using IV Phenylepherine. Her base line mean arterial pressure (MAP) was 100 mmHg. The goal was kept at 140mmHg. Clinically patient's NIHSS improved to 1. A repeat CT perfusion performed at this blood pressure next day demonstrated significant improvement of blood flow. A repeat CT angiogram showed some improvement in the blood flow through the occluded M1 segment. Patient remained in NICU for 3 days with gradual decline in MAP goal to wean off phenylepherine. No complication related to phenylepherine occured. Her NIHSS remained 1 on discharge.

Conclusion: Management of acute stroke patients presenting outside the tPA window period is still controversial. We utilized the perfusion study to treat the patient with blood pressure augmentation. Our case report demonstrate that blood pressure augmentation in acute stroke can improve clinical outcome. Perfusion studies can be utilized for patient selection.

ANALYSIS OF THE EXPECTATION FOR STEM CELL THERAPY IN PATIENTS WITH STROKE

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Background: It is hoped that stem cells will provide an inexhaustible source of neurons and glia for therapies aimed at cell replacement or neuroprotection in neurological disorders including stroke. The present study evaluated the expectation for stem cell therapy in patients with stroke through the questionnaire survey.
Method: From June 2010 to January 2011, a total of 133 patients who suffered stroke at least 3 months (90days) before the survey were enrolled. Participants were asked questions about their demographics, co-morbidity, education level, onset and outcome of stroke and expectations for stem cell therapy as follows: prevention of re-attack of stroke, improvement of physical function, improvement of emotional problem and improvement of memory function. Patients were also asked about being willing to have stem cell therapy in spite of unknown side effects and reasonable price. Univariate and multivariate analysis were performed to evaluate factors influencing stem cell therapy expectation.
Results: Fifty-six patients (42%) were willing to have stem cell therapy in spite of unknown side effects. Among them, 53 (94.6%) expected physical function improvement and 53 (94.6%) expected prevention of re-attack of stroke. The majority patient (36%) disclosed $1000 to $5000 was reasonable price of stem cell therapy. Expectation of stem cell therapy were associated with following factors: high NIH stroke scale score, high modified Ranking score, knowledge of stem cell therapy and short stroke onset. Multivariate analysis indicated that high NIH stroke scale score (OR 1.760, 95% CI 1.103-2.801) was the only independently associated factor.
Conclusion: Expectation of stem cell therapy in chronic stroke patients were high especially severely disabled patients. In addition, most of patient expected physical function improvement or prevention of stroke re-attack. In future stem cell trial, clinicians may consider the patients' expectation for stem cell therapy.

NEUROPROTECTION EFFECTIVENESS DEPENDS ON THE SIZE AND LOCATION OF THE ISCHEMIC STROKE FOCUS

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Background: Neuroprotection effect and its dependence on focus dimension and location have been studied in ischemic stroke (IS). Effect of two versions of neuroprotective therapy: with neurotransmitter, and antioxidant effects were compared.
Methods: A pilot study of the neuroprotective therapy dependence on the location and size of ischemic stroke. 62 patients with IS were included: cortical IS – 15 patients, white matter, and subcortex IS - 16 patients, a posterior IS - 14 patients and with ischemic zone more than 1/3 hemisphere 17 patients. Baselines Barthel Index (BI) was similar in subgroups. All patients received adequate therapy in a stroke unit. Patients were randomized to receive one of two options for neuroprotective therapies: 1 – choline alfoscerat (1000 mg daily) or 2 - alpha-lipoic acid (600 mg daily) and magnesium sulfate (25% - 10ml daily). All preparations were administered to 48 hours of stroke onset for 10 days. The Results were evaluated by BI.
Results: There was no significant difference in BI in treatment groups with cortical foci on the 28th day of treatment (1 – 90.0 + 4.2, 2 – 87.0+4.5). In large focuses (1 - 55,1±3,2, 2 - 74,0±5,4), in those in subcortex and white matter foci (1 - 59,9±3,4,2 -80,2±5,6), in posterior strokes (1 -76,8±1,2, 2 -96,1±1,3) the medications of the second therapy option were more effective (p<0.05).
Conclusion: Different location and dimension of stroke determine difference in perfusion and metabolic requirements of damaged tissue, different cell composition, appeared in the zone of ischemic injury (white and gray matter, subcortical nuclei, brainstem structures, big zone with massive cell destruction). Pharmacological agents with neurotransmitter functions can be effective in strokes with high percentage of comparatively safe neurons in the focus zone. This is seen in comparatively small cortex strokes. In large IS, subcortical, white matter and stem strokes antioxidants can be more effective.

SAFETY AND EFFICACY OF INTRAVASCULAR SONOTHROMBOLYSIS USING EKOS SYSTEM - A PILOT STUDY

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Background: Sonothrombolysis is a new therapeutic procedure for arterial recanalization. The aim of study was to confirm the safety and efficacy of intravascular sonothrombolysis using EKOS system with 3F mikrocatheter EkoSonic and 2.05 – 2.35 MHz ultrasound frequencies in acute stroke patients.
Methods: All patients 1) admitted to the stroke unit since August 2009 to November 2010, 2) with stroke symptoms onset within 8 hours, 3) signed informed consent, and 4) acute middle cerebral artery (MCA) or basilar artery (BA) occlusion persisted after IVT administration or with IVT contraindication were enrolled to the study. Treatment using EKOS system started within 8 hours after stroke onset. Neurological status using NIHSS at admission, before EKOS treatment, 24 hours and 7 days after stroke onset, recanalization of the occluded artery at the end of EKOS treatment, symptomatic intracerebral bleeding (SICH) on control CT after 24 hours, and disability 3 months after stroke onset using the modified Rankin Scale (mRS) were evaluated.
Results: Nine patients were included in the pilot study (6 males, 3 females, mean age 65±10.4 years) with NIHSS 10-33 (median 19.0) at admission. Five patients had MCA occlusion, 4 patients had BA occlusion. Complete recanalization at the end of EKOS treatment was achieved in 2 (55%) patients. Median NIHSS at the end of EKOS treatment/24 hours/7 days after stroke onset were 17.0/12.0/6.0, resp. No SICH was detected on control CT. Four patients were independent at 3 months (mRS≤3); median mRS 4.
Conclusion: EKOS system seems to be a new treatment option for acute stroke patients.

EXTERNAL CAROTID ARTERY STENTING AS ALTERNATIVE REVASCULARIZATION MODALITIES IN STROKE PATIENTS WITH SYMPTOMATIC IPSILATERAL INTERNAL CAROTID ARTERY OCCLUSION: SINGLE CENTER EXPERIENCE

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Background: The external carotid artery (ECA) anastomoses in many distal territories supplied by the internal carotid artery (ICA) and is an important source of collateral circulation to the brain. Stenosis of the ECA in ipsilateral ICA occlusion can produce ischemic sequelae.
Objective: To examine the effectiveness of ECA stenting in treating symptomatic ipsilateral ICA occlusion.
Methods: We retrospectively reviewed patient databases in our center to identify all individuals who underwent ECA stenting after 2002. For all discovered cases, we used a common submission form to harvest relevant demographic information, clinical data, procedural details, and follow-up Results for further analysis.
Results: 17 patients (median age, 66 years; range, 45-82 years) were identified for our cohort. Vessel disease involvement included severe ECA stenosis ≥ 60% in 15 patients and ipsilateral ICA occlusion in all patients. Presenting symptoms included signs of transient ischemic attack, stroke, and amaurosis fugax. ECA stenting was associated with preservation of neurological status in 11 patients and resolution of symptoms in 6 patients at a median follow-up time of 22 months (range, 4-81 months; mean, 29 months). Symptomatic in-stent restenosis did not occur within any patient during the follow-up course.
Conclusion: ECA stenting in symptomatic ipsilateral ICA disease found to be a potentially effective strategy to preserve neurological function and to relieve ischemic symptoms in clinical scenario of symptomatic ipsilateral ICA occlusion. Further investigation with larger studies and longer follow-up periods is warranted to elucidate the true indications of this management strategy.

EFFICACY AND SAFETY OF LOW DOSE INTRAVENOUS RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR (RT-PA) THERAPY FOR ACUTE ISCHEMIC STROKE

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Background: Low dose intravenous (IV) rt-PA therapy for acute ischemic stroke is being explored in many Asian countries. The purpose of this study was to assess the efficacy and safety of low dose IV rt-PA therapy.

Methods: This study was carried out at the stroke unit of Christian Medical College, Ludhiana, India, between 2008-2010. Selection of the patients receiving low dose (0.6mg/kg) and standard dose (0.9mg/kg) of IV rt-PA was at the discretion of the treating neurologist. Demographic information, stroke severity (NIHSS score), onset to door time, door to needle time, rates of asymptomatic and symptomatic hemorrhages and mortality rates for the low and high dose groups were documented. Outcome was assessed at ≥3 month follow-up using modified Rankin Scale (mRS >2: poor outcome).

Results: Of the total 715 acute stroke patients included, 32 (4.5%) patients were thrombolysed with IV rt-PA. Twenty seven (84.4%) of 32 patients received low dose and five (14.6%) patients received standard dose. The two groups did not differ in stroke severity (median NIHSS score at admission; low dose: 14.0±5.0 vs. standard dose: 11.0±4.5, p=0.78), mean onset to door time [low dose: 63.9±35.7 minutes (min) vs. standard dose: 39.0±30.5 min, p=0.15], mean door to needle time (low dose: 92.1±35.3 min vs. standard dose: 100.4±23.9 min, p=0.62), asymptomatic hemorrhage [low dose: 2/27 (7.41%) vs. standard dose: 1/5 (20.0%), p=0.41] and the symptomatic hemorrhage [low dose: 1/27 (3.7%) vs. standard dose: 1/5 (20.0%), p=0.29]. Similarly, the outcome [poor outcome; low dose: 12/27 (44.5%) vs. standard dose: 1/5 (20.0%), p=0.35] and the mortality rates [low dose: 7/27 (25.9%) vs. standard dose: 1/5 (20.0%), p=1.00] did not differ among the 2 groups.

Conclusion: The efficacy and safety of low dose IV rt-PA therapy is comparable to that of standard dose therapy. However, our Results need to be confirmed in a large randomized controlled trial.

Clinical Trials

329 Clinical trials

PRACTICAL APPROACHES TO IMPROVE FEASIBILITY OF PATIENT RECRUITMENT TO HYPERACUTE STROKE TRIALS USING IMAGING

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Background: Acute clinical trials increasingly require complex imaging on a Background of rt-PA as standard, restricting recruitment to select patients and centres. We tested the feasibility of pragmatic use of complex imaging in a prospective multicentre observational study.
Methods: We recruited patients with ischemic stroke in 3 stroke centres. Adult patients suitable for CT or MR within 6 hours of stroke onset, with no contraindication to iv. contrast, underwent CT, CT perfusion and CT angiography or MR, MR perfusion and MR angiography, <6hrs, at 72hrs and 1 month after stroke. We recorded baseline clinical details; baseline OCSP and NIHSS; NIHSS at 3, 7 and 30 days; mRS at 1 and 3 months. We used imaging equipment (including research MR at all sites) and local protocols. Image data were processed centrally, qualitatively and quantitatively by in house and commercial software.
Results: Of 360 patients screened from 21/04/2008 to 31/03/2010, we recruited 83 eligible patients (23%), median age 70.8 (max 89), 60% male. Main reasons for non inclusion were: mild stroke/too late 121 (34%), outside 9am-5pm 59 (16%), intolerant of imaging 12 (3%), refused consent 17 (5%), recruited to a competing study 52 (14%). Of the 83 recruited, 65% were hypertensive, 27% in AF, 34% had IHD. Median baseline NIHSS was 7 range 1:30, 75% were TACS or PACS. 46% received rt-PA (+2 randomised in IST3 to control). At baseline, 78% had CT and 24% had MR; 72 had 72hr imaging (79% by MR) and 48 had 30 day imaging (92% by MR). Main reasons for not obtaining follow-up imaging were death (10) or too unwell (20). No problems occurred in processing CT and MR data from the same patients.
Conclusion: Assessment with CT at baseline increases acute stroke study recruitment by up to 4-fold versus using only MR; most patients tolerate MR at 72hrs or more. High recruitment rates can be achieved in spite of complex imaging assessments and thrombolysis, through pragmatic approaches to imaging.

330 Clinical trials

VIRTUAL REALITY-ENRICHED GAIT TRAINING TO IMPROVE MOTIVATION AND REHABILITATION OUTCOME IN SUBACUTE STROKE PATIENTS

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Background: Robotic gait devices allow an early and intensive rehabilitation in stroke patients. A reason for the controversial Discussion about their effectiveness might be patient's lack of motivation and active participation. Virtual reality (VR) is a promising tool to increase patient's engagement in therapy, what is considered to be crucial for therapeutic success.
The EU funded project MIMICS (www.mimics.ethz.ch) is taking this approach, enhancing the robotic driven-gait orthosis Lokomat by adding immersive multi-modal virtual environments. The objective of this study was to prove the efficacy of VR-approaches on intrinsic motivation and walking related outcomes in subacute stroke patients.

Methods: Subjects participating in this randomized controlled clinical trial underwent a 4-week gait training (3 sessions/wk) using the Lokomat with or without VR. Motivation was measured using the Intrinsic Motivation Inventory (IMI). The Functional Ambulation Classification (FAC) and the 10m walk test were used as walking related outcome measures at baseline, end of study and a 2-week follow-up.
Results: Preliminary data analysis includes 10 stroke patients. High IMI subscales were found in both groups with better values for the VR group, however not significant. The patients using VR improved from FAC<1 to FAC 0-2 (Median=1; IQR=1.50) at the end of intervention. At the follow-up they reached FAC scores between 1 and 4 (Median=2; IQR=2.25) and differed significantly from the patients performing conventional Lokomat (p=0.025). Moreover a significant group effect (p=0.010) was found regarding the walking speed over 10 meters, with non-significant differences at baseline.
Conclusion: Our preliminary Results show higher motivation and considerably augmented improvements of gait function in patients performing VR-enriched gait therapy. As this is an ongoing study we suggest that these findings can be statistically confirmed by the final analysis with 10 additional patients.

331 Clinical trials

ASYMPTOMATIC CAROTID STENOSIS TRIAL-2 (ACST-2) OPERATORS ARE MORE EXPERIENCED AND NOW EMPLOY A WIDER RANGE OF NEWER STENTING DEVICES – UPDATE ON THE ONGOING STENTING VERSUS SURGERY TRIAL

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Introduction: Worldwide, 70% of carotid stenting procedures are performed on asymptomatic patients. Recently CREST reported comparable Results for carotid endarterectomy (CEA) vs stenting (CAS) in asymptomatic patients. Large registries with carefully and independently monitored Results in several thousand asymptomatic patients, have also reported that peri-procedural Results for both procedures were comparable and acceptably safe. No long-term trial has yet compared procedures and devices in current use.
Methods: The ACST-2 is a large randomised trial comparing CEA vs CAS in asymptomatic patients. Primary objectives of the trial are: 1) to compare peri-procedural risks (MI, stroke and death within 30 days). 2) to evaluate long-term (up to 5 or more years) prevention of stroke, particularly disabling or fatal stroke in the two treatment groups. To join the trial operators must submit a track record for independent review.
Results: By July 2010, 219 operators had joined ACST-2 (100 centres in 27 countries). There were 156 CEA operators with a combined experience of 53,456 procedures, range 25-1700 and 121 CAS operators with a combined experience of 18,141 procedures, range 25-800. This combined CEA and CAS experience included 71,604 procedures. A wide range of devices (Wallstent being the most popular, 22%) and techniques (including reverse flow device useage) are now in use in the trial. Only CE marked devices are employed.
Conclusion: For asymptomatic patients with significant carotid artery stenosis, stenting may now be as effective as surgery. It is unethical to conduct a trial that is too small, with little experience as it will either fail to answer the question or may be published with inappropriate Conclusions. To provide reliable evidence ACST-2 needs at least 5000 randomised patients. The publication of the first CREST Results suggests that stenting may be a real alternative to surgery in asymptomatic patients when intervention is considered necessary.

334 Clinical trials

SYNTHESIS EXPANSION: AN ONGOING RANDOMIZED CONTROLLED TRIAL ON FAST TRACK INTRA-ARTERIAL THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE. DATA ON THE FIRST 200 PATIENTS

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Background: Reperfusion in ischemic stroke can be pursued by either systemic intravenous thrombolysis (IVT) or intra-arterial thrombolysis (IAT). However, IVT with Alteplase within 4.5 h of symptom onset in selected patients, remains the only medication of proved efficacy. No randomized controlled trials (RCT) have been published so far to compare the two modalities. To explore this, after a pilot phase on 54 patients, we started the SYNTHESIS Expansion trial. Here we present the baseline characteristics of the first 200 randomized patients considered for the interim analysis.

Methods: Non-profit, ongoing, multicenter RCT, open-label, with blinded follow-up aiming to determine whether endovascular treatment (i.e. IAT with alteplase alone, associated to, or substituted by mechanical mechanical clot disruption and/or retrieval), compared with IVT with Alteplase, increases the proportion of independent survivors at 3 months. Eligibility applies to patients with symptomatic, ischemic stroke, seen within 4.5 h of onset, being able to initiate iv Alteplase immediately and IAT as soon as possible and, in any case, not later than 6 h of stroke onset. Enrolment will be completed with 350 patients.

Results: 21 centers are participating and the first 200 patients (97 allocated IAT and 103 IVT) were randomized between February 2008 and September 2010. Mean age was 65.2 years (SD±11.8), 113 were men, the median NIHSS was 14 (range 2-25), in 17 patients the stroke was in the posterior circulation and in 19, out of 97 allocated IAT, a device was used. The median time from stroke onset to start to treatment was 3h and 44 minutes for IAT (range: 1:30 to 5:45) and 2h and 45 minutes for IVT (range: 0:55 to 4:15).

Conclusion: The main difference between the current study and previous RCTs on IAT is the quicker time to IAT. It is to establish whether the rapidity of IAT is compensated by a major efficacy.

335 Clinical Trials

SELECTION CRITERIA DESIGN DETERMINES EFFICACY OF CLINICAL TRIAL CONDUCTION – EXPERIENCES FROM THE BETA-BLOCKER IN ACUTE ISCHEMIC STROKE (BIAS) TRIAL

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Background: Many acute interventional stroke trials suffer from unstable and low recruitment rates. We initiated a study on beta-blockers in acute ischemic stroke. Selection criteria had to be modified from initial design due to the ethics committee verdict – participation of patients not able to give informed consent was not allowed. We started recruitment, but encountered a low rate of patients meeting selection criteria being able to consent. We hypothesized that redefinition of over-restrictive criteria would improve currently slow recruitment without undermining reasonable selection.

Methods: We implemented a tool to identify the quantity of patients meeting the most important selection criteria. We ranked criteria according to their impact on recruitment and redefined the most challenging ones as far as possible without affecting the initially desired study population. We then performed an analysis of a second period to review efficacy of the amendment.

Results: During a period of 10 weeks a total of 671 individuals were screened for in- and exclusion criteria. Three patients could be included, leading to a rate of 0.4 per 100. After hereby identifying the most challenging ones, we agreed on 3 criteria that were modifiable without introducing selection bias. Upper age limit of 85 years was removed, maximum delay of index event to treatment was extended from 12 to 18 hours and definition of the event does not further require DWI proof of infarction. During the second period of screening 4 out of 220 patients screened were included in a time span of one month. This rate of 1.8 per 100 signifies an augmentation by a factor of 4.

Conclusion: Definition of selection criteria is crucial for stable recruitment. If initially defined selection profiles seem to be over-exclusive, an intensified screening may provide the means to redefine criteria and thereby improve recruitment.

Cerebrovascular Diseases

Experimental studies

383 Experimental studies

DICKKOPF-1 SERUM LEVELS ARE INCREASED AFTER STROKE AND REFLECT THE ISCHEMIA-INDUCED TISSUE LEVELS

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Background: Dickkopf-1 (Dkk-1) is a secreted glycoprotein that acts as an extracellular inhibitor of the Wnt canonical pathway. A growing body of evidence shows that inhibition of the canonical Wnt pathway contributes to the process of neuronal damage, in models of acute and chronic neurodegenerative disorders. Recently, we have shown that Dkk-1 is early induced in cortical neurons of mice subjected to permanent middle cerebral artery (MCA) occlusion, as well as in corticostriatal neurons of rats undergoing transient focal ischemia induced by infusion of endothelin-1. The Dkk-1-mediated inhibition of the Wnt pathway likely synergizes with the classical proapoptotic program triggered by p53 and lowers the threshold for neuronal death. The altered Wnt signaling would increase degradation of beta-catenin with consequent deprivation of a trophic support to the neurons. A corollary to this hypothetic scenario is that the expression of Dkk-1 occurs in peri-necrotic areas, where apoptotic mechanisms would underly acute neurodegenerative processes. Aim of this study was to test whether brain levels of Dkk-1 are reflected by changes in serum levels.

Methods: The study was carried out in mice and rats undergoing focal cerebral ischemia. We measured serum and brain Dkk-1 levels following the ischemic insult by ELISA. We extended the study to patients with ischemic stroke and samples were collected at different times after the onset of symptoms (1, 2, 5, 8 and 11 days).

Results: There was a significant increase in serum levels of Dkk-1 in mice at 6 hours and in rats at 24 hours post-ischemia. Dkk-1 tissue expression, in the mice with permanent MCA occlusion, was increased at 6 hours, and the infarct volume (measured by histology at 24 hours) positively correlated with the serum levels. We found a transient increase of Dkk-1 serum levels in patients with acute stroke at 5 days after the onset of symptoms (170±70 pg/ml in patients and 92±40 pg/ml in control subjects).

Conclusions: These data may suggest the potential use of Dkk-1 serum levels as a peripheral biomarker of peri-necrotic damage.

384 Experimental studies

NEUROPROTECTIVE AND NEUROREGENERATIVE EFFECTS OF THE PEPTIDE HORMONE GHRELIN AFTER CEREBRAL ISCHEMIA

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Introduction: The peptide hormone Ghrelin is known as the ligand of the growth hormone secretagogue receptor and affects pituitary hormone secretion, gastrointestinal function and the cardiovascular and immune system. Recently it has been shown that Ghrelin also influences key mechanisms of the CNS. Ghrelin crosses the blood-brain barrier and binds to hippocampal neurons thereby promoting dendritic spine synapse formation and proliferation of progenitor cells. These finings led to the assumption that Ghrelin might exert neuroprotective and neuroregenerative effects in the brain.

We assessed the hypothesis that a pharmacological stimulation with Ghrelin influences cellular mechanisms of post-ischemic neuroprotection and neuroregeneration and improves functional and structural recovery.

Methods: In order to investigate immediate neuroprotective effects, Ghrelin (80μg/kg) was administered 1 hour after middle cerebral artery occlusion (MCAO). Brains were removed 24h after ischemia and the effect of Ghrelin treatment on infarct volumes was analyzed.

In order to examine neuroregenerative effects, Ghrelin (50 μg/kg) was administered on 5 consecutive days starting 24 hours after photothrombotic ischemia. Functional recovery was assessed by the adhesive tape removal test and the cylinder test performed weekly for 4 weeks. Brains were removed 4 weeks after ischemia. Post-ischemic neurogenesis was quantified using antibodies against Bromodeoxyuridine and Doublecortin.

Results: Treatment with Ghrelin improved functional recovery following photothrombotic stroke. In close apposition to the enhanced sensorimotor recovery, the pharmacological stimulation with Ghrelin significantly increased the generation of newborn hippocampal neurons. In addition, the treatment with Ghrelin reduced infarct volumes after MCAO.

Conclusion: In the present study, we demonstrated that Ghrelin may promote the structural and functional recovery following ischemia. The recently discovered neurotrophic properties and the effects on functional and structural recovery demonstrated in this study underscore the potential of Ghrelin as a promising agent for the treatment of ischemic stroke.

385 Experimental studies

EXPRESSION OF THE ENDOCANNABINOID RECEPTORS IN HUMAN STROKE

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Background: The endocannabinoid system (ECs) is up-regulated in several neurological diseases.

Our aim was to evaluate the cerebral expression of endocannabinoid receptors 1 and 2 (CB1, CB2) in the autoptic tissue from twelve patients died between two days and one week after a first acute cerebral infarction in middle cerebral artery territory.

Methods: The cerebral tissue was collected for each subject within 24 hrs after death. Ischemic region and contralateral normal appearing area were identified in each subject. After usual tissue preprocessing (deparaffinization, PBS washing and blocking serum addition), 2-μm-thick cerebral sections were incubated with the specific primary CB antibodies (Cayman Chemical Company). Thereafter all cerebral sections were hematoxylin treated. For each section total cell number and total CB-positive cells were counted and, for each area in every subject, the CB-positive cell count ratio was calculated. Differences in CB expression among different regions were evaluated using Student's t-test.

Results: In normal tissue, CB1-positive neurons were the large majority, whereas a few non-neuronal cells expressed CB1. In the ischemic area, there was a significant increase of CB1-positive non-neuronal cells (p=0.01 as compared to normal tissue values).

In normal appearing areas CB2 receptors were expressed in some neurons and in most of non-neuronal cells. No differences in CB2 staining were found between ischemic and normal areas.

Conclusions: In line with previous animal studies, we found an increase of CB1 expression in ischemic regions, due to non-neuronal cells staining, reflecting the inflammatory reaction induced by stroke. Whether such response mediates neuroprotective actions or excitotoxicity-related detrimental effects is still unclear. Moreover several normal appearing cortical CB2-positive neurons were discovered, suggesting a functional role for CB2 receptor in normal neurons.

386 Experimental studies

LOCAL ACTIVATION OF SKELETAL MUSCLE APOPTOSIS IN THE PARETIC LEG AFTER STROKE DEPENDS ON DIRECT DENERVATION IN A MCAO MOUSE MODEL

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Background: Weight loss is a common observation after stroke and nutritional status contributes to post-stroke recovery and rehabilitation progress. Weight loss due to impaired feeding and disuse atrophy are clinically recognised. However, mechanisms of catabolic stimulation in skeletal muscle in relation to the degree of brain damage and muscle denervation has not been investigated in detail.

Methods: We investigated skeletal muscle apoptotic activation in a model of acute focal cerebral ischaemia produced by temporal occlusion of the mouse middle cerebral artery (MCAO). Caspase 3 (C3) and caspase 6 (C6) activity of the gastrocnemius muscle were assessed 3 and 7 days after MCAO-induced stroke in both, the paretic and non-paretic leg. Global body composition (fat and lean tissue by NMR) and gastrocnemium muscle were assessed in relation to infarct size.

Results: Activity of caspase 3 and caspase 6 were up-regulated after stroke compared to sham in the paretic and non-paretic leg at day 3 (C3 +548% and +454%; C6 +145% and +134%, respectively; all p<0.001) and still increased at day 7 (C3 +194% and +248%, p<0.05). This was accompanied by progressing wasting of the gastrocnemius muscle until day 7 (paretic leg –20%, non-paretic leg -19%, both p<0.01) and global lean tissue loss (day 3 –17%, day 7 –12%, p<0.05 vs. baseline). Infarct volume directly related to C3 and C6 activity only in the paretic leg (C3 r=0.72, C6 r=0.78, p<0.01) but not in the non-paretic leg (p>0.5).

Conclusion: Increased apoptosis accounts for skeletal muscle wasting after stroke. While global muscle degradation may result from systemic signals, denervation may trigger local signals towards increased apoptosis in the paretic leg that are not seen in the non-paretic leg.

387 Experimental studies

TARGETING ISCHEMIC DEPOLARIZATION DURING RECURRENT ISCHEMIA AFTER ACUTE STROKE

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Background: Secondary cerebral injury in acute stroke may be exacerbated by recurrent ischemia. We examined the ability of ischemic cortex to support anoxic depolarization (AD) and whether carbetapentane (CP) or dibucaine (DB) attenuates AD as with non-stroke slices.

Methods: Focal cerebral ischemia was induced in male C57/BL6 mice (20-25g) by intraluminal occlusion of the MCA for 30min (n=24 mice). Harvested brain slices 350μm thick (n=97 slices) were then incubated in artificial CSF (aCSF) at 34C for up to 4 hours. By observing changes in regional light transmittance (delta LT) in the ipsi- and contralateral hemispheres upon oxygen-glucose deprivation (OGD), we were able to observe ischemic depolarization directly [Cerebral Cortex 17,787]. AD latency was measured as the time at which an elevated LT wavefront was imaged after OGD onset. Peak delta LT indicated maximal tissue swelling, while the ensuing nadir indicated maximal dendritic beading (neuronal damage) post-AD. Both values were measured in the ipsi- and contralateral hemispheres with/without exposure to 30 μM CP, 3 μM DB and 10 μM DB.

Results: OGD induced ischemic depolarization at similar time points in the ipsi- and contralateral hemisphere [ipsilateral vs contralateral: AD latency 341±70 sec (n=29) vs 311±63 (n=29), p = 0.098]. However peak LT was greater in the contralateral hemisphere [ipsi- vs contralateral: 22±0.11% (n=26) vs 30±0.10% (n=26), p=0.0085]. Nadir values were not significantly different. CP and DB delayed AD onset ipsilaterally [30μM CP vs control: 416±89 sec (n=13) vs 341±70 (n=29), p= 0.014]; 10μM DB vs control: 439±124 sec (n=12) vs 341±70 sec (n=29), p=0.022)]. DB but not CP attenuated tissue swelling during AD.

Conclusions: Following acute stroke, peri-infarct tissue remains susceptible to ischemic depolarization. CP and DB increases the resistance of peri-infarct tissue to recurrent ischemia and may attenuate the damage caused by recurrent ischemic depolarization.

388 Experimental studies

CIRCULATING ENDOTHELIAL PROGENITOR CELLS COUNT IN ACUTE ISCHEMIC STROKE PATIENTS PRE-TREATED WITH STATINS

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Objectives: Ischemic stroke patients pre-treated with statins (PS) show a better outcome than no treated patients (non-PS). Circulating Endothelial Progenitor Cells (EPCs) have been associated with the prognosis of patients with ischemic stroke. In fact, previous studies suggested a correlation between the increase of endothelial progenitor cell (EPC) count and the functional outcome after ischemic stroke.

Therefore, we tested the hypothesis that in patients with ischemic stroke, the pre-treatment with statins is associated with an increase of circulating EPCs.

Methods: Consecutive stroke patients within the first 48 hours from symptoms onset were prospectively included in the study. We evaluated the pre-treatment with statins. Blood samples were collected at baseline, day 7 and day 90 after stroke onset.

EPC were measured by flow cytometry within 30 minutes after blood collection. We considered that a cell was an EPC when it was labeled for the following 3 markers: CD34, AC133 and KDR. EPC counts were adjusted for the lympho-monocytic population in each sample. Statistics: Chi-square, U-Mann-Whitney, t-Student.

Results: We studied 131 patients, whose mean age was 71.7±12 years, and 62.6% of them were men. Pre-treatment with statins was recorded in 32.1% of patients.

Compared with non-PS patients, the PS group suffered more frequently from ischemic heart disease (p<0.0001) and hypercholesterolemia (p<0.0001).

CPEs count in PS vs non-PS patients was superior at baseline (Mean 0.006±0.01 vs 0.002±0.006%, p=0.015) and at day 7 (Mean 0.012±0.014 vs 0.006±0.014%, p=0.029). The 3 months count was equivalent (Mean 0.001±0.003 vs 0.0078±0.03%, p=0.49).

Therefore, there was a statistically significant increase in the CPEs count at baseline and at day 7 in the PS group.

Conclusions: In Conclusion, the pre-treatment with statins is associated with an increased EPC count in patients with acute and subacute ischemic stroke. The increase of EPC suggests a novel beneficial effect of statin therapy in patients with stroke.

389 Experimental studies

CHARACTERIZATION OF THE CYTOKINE PRODUCTION OF T CELLS AND ANTIGEN-PRESENTING CELLS IN THE POSTISCHEMIC INFLAMMATORY RESPONSE FOLLOWING STROKE

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Background: Inflammatory mechanisms play a key role in the pathophysiology of postischemic tissue damage following stroke. The different immune cell subpopulations are integrated in a complex cytokine network, which is composed of pro- and antiinflammatory cytokines. The goal of our study is to elucidate immunological mechanisms underlying the activation of the immune system in the ischemic brain.

Methods: Intracellular cytokine production was analyzed by FACS analysis in immune cell subpopulations following temporary occlusion of the middle cerebral artery (MCAO) in mice and subsequent purification of immune cells out of the brain.

Results: At day 1, the cytokine production in T cells is dominated by Interferon gamma (INFg) and TNF alpha in CD4 and CD8 positive T cells. On day 3, gamma delta T cells (gd T cells) emerge in the ischemic hemisphere, which are major producers of IL17A. Regarding antigen-presenting cells (APCs), macrophages and microglial cells are the major producers of TNF alpha. Next, we utilized lymphocyte deficient Rag1 mice to analyze the interplay between T cells and APCs. According with published data Rag 1 mice exhibited smaller infarct volumes 3 days post stroke. Additionally, the deficiency in lymphocytes resulted in substantial decrease in TNF production in macrophages whereas the microglia-derived TNF production was unaffected.

Conclusion: Initially, the cytokine milieu in the ischemic hemisphere is dominated by INFg and TNF alpha produced by CD4 and CD8 T cells. Then atypical T cells producing IL17A invade. In parallel macrophages and microglial cells produce large amounts of TNF. T cells seem to play a central role already in the orchestration of the initial immune response, since the activation of pro-inflammatory macrophages is decreased in Rag 1 mice. The further characterization of the immunological mechanisms will provide valuable insights into the role of different immune cell population and cytokine pathways in stroke.

NEW APPROACH FOR THE QUANTIFICATION OF BLOOD BRAIN BARRIER INJURY DURING ISCHEMIA-REPERFUSION IN RAT TMCAO MODEL

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Background: Blood brain barrier (BBB) opening during ischemia allows plasma continuants to enter the brain and possibly damage cells. Traditionally the extravasations of plasma contents in cerebral lesions have been visualized by the systemic administration of Evans Blue (EB) stain. The tight correlation between the ischemia duration, the size of the ischemic territory and barrier opening have been described before. The following method suggests a new technique for the assessment of barrier disruption, based on the measurement the EB stained albumin content of the CSF.

Methods: Severe vascular disruption and ischemic injury was induced in adult CD rats by transient occlusion of the middle cerebral artery for 1, 6, 12 hours, followed by 60 minutes of reperfusion (n=5/group). Evans Blue (2% 0,5ml/100g) was administered through the tail vein 5 minutes prior to the removal of the occluding filament. CSF samples were collected from the cisterna magna at the end of the reperfusion period. After perfusion fixation transverse sections were prepared 6mm posterior from the frontal pole of the brain. Images of EB-stained sections were captured using a digital scanner, and analyzed with an image analysis software. The albumin content of the CSF was measured in 50ul samples, using an ordinary fluorescence microplate reader (FLUOstar OPTIMA) with 540nm excitation wavelength and emission detection set to 680nm. Emission values were correlated with the planimetric data obtained from the sections using multiple regression analysis.

Results: With increasing ischemia duration, greater quantities of EB stained albumin invaded and marked the ischemic region in a characteristic pattern. Similarly, the fluoro-emission values of the liquor samples increased gradually, and showed significant correlation ($p<0.05$) with the territory of the Evans Blue stained area of the brain sections, allowing a simple and accurate estimation of the blood brain barrier permeability.

PROTECTIVE EFFECT OF ERYTHROPOIETIN IN EARLY AND DELAYED POSTISCHEMIC PERIOD IN RAT MODEL OF FOCAL CEREBRAL ISCHEMIA

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Aim: To investigate protective effect of erythropoietin (EPO) administration 3 and 12 hours after focal cerebral ischemia.

Methods: The experiments were performed in male Wistar rats weighting 200-250 g. Transient focal cerebral ischemia was induced by 30-min left middle cerebral artery (MCA) endovascular occlusion with subsequent reperfusion for 48 hours. Presence of ischemia was verified using ultrasound Doppler of the MCA cortical branch. The same approach was used to exclude the animals with subarachnoid hemorrhage. EPO was administered intraperitoneally at a dose of 5000 IU/kg. Experimental protocol included 3 groups of animals: 1. Controls (n=8) – 30 min of ischemia and 48 h reperfusion; 2. EPO3 (n=5) – EPO administration 3 hours after ischemia; 3. EPO12 (n=6) – EPO administration 12 hours after ischemia. At 48 hours after ischemia, neurological deficit (Garcia score) and severity of brain edema according to asymmetry of cerebral hemispheres were evaluated. Infarct size was determined with triphenyltetrazolium chloride (0,1%) staining.

Results: EPO administration 3 and 12 hours after focal cerebral ischemia decreased infarct size by more than 60% as compared to controls (p=0,003 and p=0,002, respectively). Initially, all rats had no evidence of neurological deficit and Garcia score was 18. Severity of neurological deficit after EPO administration 3 and 12 hours after focal cerebral ischemia was significantly lesser than in controls (p=0,006 and p=0,003, respectively). The extent of brain edema was significantly reduced after EPO administration at both 3 and 12 hours after ischemia (p=0,014 and p=0,013, respectively).

Conclusions: EPO administration at a dose of 5000 IU/kg 3 and 12 hours after cerebral ischemia resulted in robust neuroprotective effect in the rat model. The protective effect of EPO was manifested by reduction in infarct size, neurological deficit, and severity of brain edema.

IRON OVERLOAD INCREASES BRAIN DAMAGE INDUCED BY EXPERIMENTAL ISCHEMIA

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Background: Clinical (Dávalos et al. 2000) and experimental studies (Castellanos et al. 2002) showed that higher levels of iron were associated to a worse outcome after stroke. In addition, it has been demonstrated that treatment with iron chelating agents after stroke might reduce ischemic injury (Patt et al. 1990, Millerot-Serrurot et al. 2008). However, other authors did not observe this deleterious effect of iron in experimental ischemia (Millerot et al. 2005). The objective of this study was to evaluate the contribution of iron overload to ischemic damage using different models.

Methods: Mice were fed for 8 weeks with a standard diet or with a diet supplemented with 2.5% carbonyl iron to simulate iron overload. Mice were submitted to permanent ischemia by using two models (in situ thromboembolic and distal ligature models) and to transient focal ischemia (ligature model). In situ thromboembolic model was carried out as previously described (Orset et al. 2007) injecting thrombin in the middle cerebral artery (MCA). In the ligature model, the ipsilateral common carotid and the MCA were tied permanently (permanent model), or for 1 or 3 hours (transient model) (n=7). 24 hours after surgery the infarct volume was measured by TTC staining.

Results: Animals submitted to permanent ischemia had the same infarct volume, either in the in situ thromboembolic model (17.5±3.8% vs 16.5±4.1%) or in the ligature model (14.9±5.6% vs 13.4±3.8%), with or without iron overload respectively. However, in mice submitted to transient ischemia, early (1 hour; 9.8±5.8% vs 3.4±1.9% in control group) but not late reperfusion (3 hours; 12.6±4.4 vs 13.5±2.9 in control group) increased ischemic damaged in the iron overload group.

Conclusions: Iron worsens ischemic damaged induced by early reperfusion in the transient model. These Results strongly suggest that iron plays an important role in penumbra evolution to infarct and subsequent worsening in the outcome after stroke.

AN ANIMAL MODEL OF STROKE IN EFFECTIVELY ANTICOAGULATED MICE – HEMORRHAGIC TRANSFORMATION, EFFECTS OF THROMBOLYSIS AND THERAPEUTIC POTENTIAL OF PCC

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Background: Oral anticoagulant treatment (OAT) is the standard of primary and secondary stroke prevention in patients with atrial fibrillation (AF), whose number is rising according to demographic trends. Although it importantly reduces the risk of stroke in patients with AF, approximately 30% of patients with cardioembolic strokes are on OAT at the time of their stroke. The Aims of this study were to evaluate the influence of effective OAT on the risk of spontaneous hemorrhagic transformation (HT) after stroke and to determine the effect of prior OAT on the risk of rt-PA-associated HT.

Methods: To achieve effective OAT, warfarin (1 mg/kg/24 h) was administered orally. Where indicated, mice received i.v. human rt-PA (10 mg/kg) or human PCC (100 IU/kg) after 3 h right middle cerebral artery occlusion (MCAO). Ischemic lesion size (TTC staining) and blood distribution were observed macroscopically. HT blood volume was assessed with a photometric hemoglobin assay.

Results: HT blood volume after 3 h MCAO was 0.3±0.4 μl in controls vs. 4.2±1.7 μl at an INR of 2 (p<0.05) and 5.2±2.7μl at an INR of 3 (p<0.001). Treatment with rt-PA after 3 h MCAO led to a comparable degree of HT (4.0±0.5 μl, p < 0.001 vs. control) which was greatly potentiated by prior OAT. When PCC were given just before the administration of rt-PA, this effect could be reversed completely (15.0±3.8 μl in OAT mice who received rt-PA vs. 3.8±0.7 μl in mice whose coagulation was restored with PCC, p<0.001).

Conclusion: Effective OAT led to significant HAT both at an INR of 2 and an INR of 3 which was comparable to the degree of HAT in OAT-naïve animals who received rt-PA. Rt-PA treatment in mice under effective OAT caused large hematomas, but interestingly, this could be reversed by prior administration of PCC. While prior warfarin treatment had a more than additive effect on the HAT risk after rt-PA administration, PCC had a therapeutic effect in our animal model.

NEUROPROTECTION BY FREEZING ISCHEMIC PENUMBRA EVOLUTION WITH A PSD95 INHIBITOR

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NA-1 is a promising neuroprotectant that uncouples post-synaptic density protein PSD-95 from neurotoxic signaling pathways following stroke and has been shown to reduce stroke volume and improve neurological outcome in multiple models of cerebral ischemia. Here we test the hypothesis that NA-1 delays the progressive growth of the ischemic core and preserves the ischemic penumbra following permanent middle cerebral artery occlusion (pMCAO) in rats.

Rats undergoing pMCAO induced by the filament model were blindly randomized to receive NA-1 (7.5mg/kg, n=8) or placebo (saline, n=8) over 5min starting at 1h post-MCAO. Perfusion and diffusion weighted MRI (PWI and DWI) were obtained with a 4.7T Bruker system from 30 to 180min post-MCAO to determine cerebral blood flow (CBF) and apparent diffusion coefficient (ADC) maps. The maps were used for volumetric and region of interest (ROI) analysis. At 24h animals were neurologically scored (0 to 5) and brains stained with TTC to ascertain infarct volumes corrected for edema.

Final infarct volume was significantly decreased by 30.3% in the NA-1-treated animals compared to controls. Relative to controls, NA-1 significantly attenuated DWI lesion growth and preserved the DWI/PWI-mismatch (ischemic penumbra) (Figure 1). There was a significant improvement in 24h neurological scores in the NA-1 group compared to controls, 1.8±0.5 and 2.8±1.0 respectively (p=0.02, Mann-Whitney). The ROI analysis showed no significant difference of CBF between treatment groups, or between time points within a treatment group in the ischemic core or penumbra.
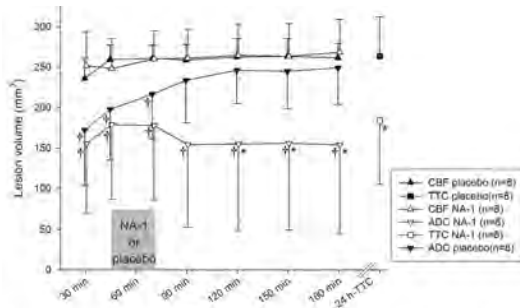
Figure 1 Temporal evolution of DWI and PWI derived ischemic lesion volumes and 24h TTC derived final infarct volume. *p<0.05 between placebo and NA-1 treated animals. †p<0.05 between CBF and ADC derived ischemic lesion volumes

NA-1 significantly preserved the ischemic penumbra, by slowing the progression of DWI lesion volume. NA-1 reduced 24h infarct volume and improved neurological scores as compared to controls. These effects occurred without any change in CBF and support a direct neuroprotective effect of NA-1. These data support further research to determine whether NA-1 has clinical utility in ischemic stroke.

NOVEL LONGITUDINAL DEFINITIONS OF ASPIRIN AND CLOPIDOGREL 'NON-RESPONSIVENESS' ON THE PFA-100: RESULTS FROM THE TRINITY ANTIPLATELET RESPONSIVENESS (TRAP) STUDY

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Background: Ex vivo antiplatelet non-responsiveness is usually defined on the basis of "cross-sectional, case-control" data. "Longitudinal definitions" of non-responsiveness derived from individuals studied before and after starting antiplatelet therapy may be more informative.

Methods: Platelet function inhibition was assessed with PFA-100 Collagen-Epinephrine (C-EPI) and Collagen-ADP (C-ADP) cartridges, and platelet activation (CD62P, CD63, and leucocyte-platelet complex formation) was quantified with unstimulated whole-blood flow cytometry in a pilot, longitudinal study in ischaemic cerebrovascular disease (CVD) patients. Patients were assessed at baseline (≤4 weeks of TIA or ischaemic stroke), and at 14 days (14d) and >90 days (90d) after changing treatment from (i) no medication to aspirin monotherapy (N=26), or (ii) aspirin to

clopidogrel monotherapy (N=22). "Ex vivo" antiplatelet non-responsiveness' was defined as failure to prolong relevant PFA-100 closure times compared with the patient's baseline reading by more than twice the coefficient of variation of the assay.

Results: (i) C-EPI closure times increased at 14d and 90d after commencing aspirin (P≤0.002; Fig. 1a); 24% at 14d and 18% at 90d were "aspirin non-responsive". Platelet activation status was unaffected by aspirin (P≥0.09). (ii) C-ADP closure times increased at 14d (P=0.001; Fig. 1b), but not at 90d (P=0.09) after changing from aspirin to clopidogrel; 41% at 14d and 35% at 90d were "clopidogrel non-responsive". % neutrophil-platelet complexes decreased at 14d (P=0.02), but this reduction was not maintained 90d after changing to clopidogrel (P=0.3).

Figure 1a

Collagen-Epinephrine closure time in response to commencement of aspirin
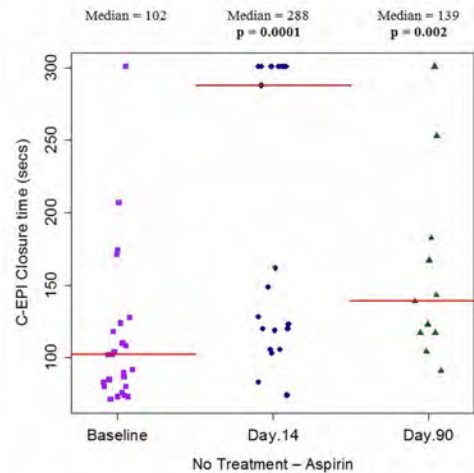
Each point represents a single patient; red lines represent medians; p values compare median values on aspirin at 14d and 90 d with the median value at baseline on no medication (Wilcoxon signed rank test).

Figure 1b

Collagen ADP closure times in response to changing from aspirin to clopidogrel
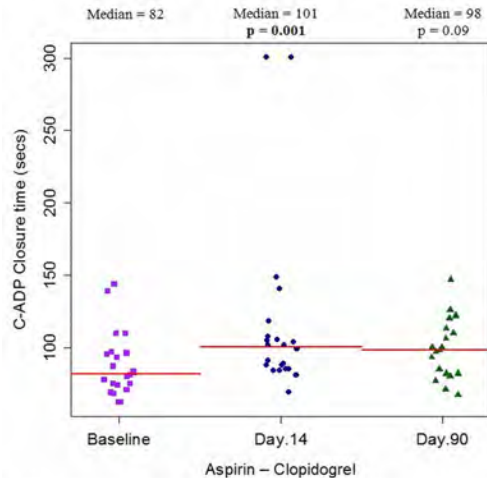
Each point represents a single patient; red lines represent medians; p values compare median values on clopidogrel at 14d and 90d with the median value at baseline on aspirin (Wilcoxon signed rank test).

Conclusions: The PFA-100 C-EPI cartridge could be used to monitor "aspirin responsiveness" longitudinally in ischaemic CVD. The C-ADP cartridge does not reliably detect the antiplatelet effects of clopidogrel, and unstimulated whole blood flow cytometry is not sensitive at detecting changes in platelet activation in response to aspirin or clopidogrel.

BETA-NGF SERUM LEVELS INCREASE AFTER INTRA-ARTERIAL INJECTION OF AUTOLOGOUS BONE-MARROW MONONUCLEAR CELLS (BM-MNC) IN ACUTE ISCHEMIC STROKE PATIENTS. A CONTROLLED CLINICAL TRIAL

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Background: BM-MNC intra-arterial transplantation has proven beneficial effects in experimental models of ischemic stroke. BM-MNCs synthesize a broad spectrum of growth factors and cytokines. Granulocyte-macrophage colony-stimulating factor (GM-CSF) and beta nerve growth factor (bNGF) have neuroprotective properties in animal models of cerebral ischemia. We investigate the changes of serum levels of GM-CSF and BNGF after autologous transplantation of BM-MNC in acute ischemic stroke patients. Registered at ClinicalTrials.gov as: NCT00761982.

Methods: Eight cases (BM-MNC-treated) and nine controls (BM-MNC-non-treated), all with MCA ischemic strokes, were included. Autologous BM-MNC was intra-arterially injected between 5 and 9 days after stroke in cases. Blood samples were drawn before and 4, 8 and 90 days after transplantation. GM-CSF and BNGF levels were determined by enzyme-linked immunosorbent assay (ELISA).

Results: After transplantation GM-CSF levels did not change significantly between patients treated with BM-MNC and controls. There were no differences in BNGF baseline levels in both groups (11.4±2.9 ng/mL in cases vs 12.9±2.7 ng/mL in controls, p=0.71). However, a significant decrease of BNGF appeared during the first week in controls that was not present in BM-MNC-treated patients: BNGF levels after 4 days (10.3±3.1 vs 8.5±2.9, p=0.68), 8 days (12.8±2.7 vs 3.9±2.5, p=0.029) and 90 days (16.5±5.4 vs 14.2±5.1, p=0.76).

Conclusion: Higher plasma BNGF level is found in ischemic stroke patients after eight days of injection of BM-MNC compared to controls, probably related to secretory function of BM-MNC in ischemic environment. Further research is necessary for elucidating the role of BNGF in autologous transplantation of BM-MNC in human ischemic stroke.

ENDOGENOUS NEUROGENESIS IS ENHANCED AFTER CEREBRAL ISCHEMIA IN EPHRIN-B3 DEFICIENT MICE BUT FAILS TO IMPROVE FUNCTIONAL RECOVERY

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Background: Stroke stimulates neurogenesis and subventricular zone-(SVZ)-derived neural precursor cells (NPCs) proliferate and migrate towards the lesion site without contributing to functional outcome. Although ephrin proteins have been shown to negatively regulate neurogenesis under physiological conditions, their role in brain to ischemia is largely unknown. We therefore studied post-stroke neurogenesis, brain injury and functional outcome for up to 4 weeks in ephrin-B3 deficient (–/–) and wild type (+/+) mice.

Methods: Mice were subjected to middle cerebral artery occlusion. Infarct injury, neurogenesis and motor coordination were analyzed for up to 4 weeks after stroke. For in vitro studies, SVZ-derived NPCs were prepared from 6-8 week old ephrin-B3–/– and ephrin-B3+/+ mice and exposed to oxygen-glucose-deprivation (OGD), thereafter.

Results: Cultivated NPCs from ephrin-B3–/– mice showed enhanced cell proliferation under non-ischemic conditions, but showed no difference in cell injury rates after OGD as compared to controls. In vivo, enhanced cell proliferation and neuronal differentiation was noticed around the lesion site of ephrin-B3–/– mice as compared to ephrin-B3+/+ mice. However, prominent post-ischemic neurogenesis in ephrin-B3–/– mice was accompanied by increased ischemic injury and motor coordination deficits in these animals that persisted up to 4 weeks after stroke. Ischemic injury in ephrin-B3–/– mice was associated with enhanced acute caspase-3 activation as assessed by cleavage of Ac-DEVD-AMC in brain lysates. Whereas inhibition of caspase-3 had no effect on brain injury in ephrin-B3+/+ animals, infarct size in ephrin-B3–/– mice was strongly reduced suggesting that caspase-3 might play a role in the injury-aggravating effects of ephrin-B3–/–.

Conclusion: Endogenous neurogenesis in ephrin-B3–/– mice is enhanced after stroke, but fails to contribute to functional recovery due to high caspase-3-mediated aggravation of ischemic injury in these animals.

ACUTE EFFECTS OF INTRAVASCULAR STATINS IN FOCAL CEREBRAL ISCHEMIA ARE DEPENDENT ON BLOOD BRAIN BARRIER PERMEABILITY

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Background: The acute effects of intravascular statins on transient focal ischemia were assessed in the isolated guinea pig brain. This new stroke model allows the functional preservation of vascular and neuronal compartments and the blood-brain barrier (BBB). A major advantage of this experimental model is to be focused on the early phases of cerebral ischemia using a multi-modal efficacy analysis.
In a first set of experiments, nanomolar doses of simvastatin lactone (lipophilic) and simvastatin acid (hydrophilic) were administered 60 minutes before the onset of ischemia. In a second set of experiments, nanomolar doses of pravastatin (hydrophilic) was administered 60 minutes before or immediately after the onset of ischemia.

Methods: Middle cerebral artery was transiently tied for 30 min, followed by 90 min of reperfusion. Brain activity in multiple cortical areas and cerebrovascular tone were continuously recorded. MAP-2 immunohistochemistry was used to assess ischemic injury. Cortical samples were assayed for Akt activation, Erk activation and total antioxidant capacity.

Results: Brains pre-treated with simvastatin lactone or post-treated with pravastatin showed i) preservation of MAP-2 immunoreactivity, ii) activation of ERK signaling in the ischemic hemisphere and iii) increase in whole-brain antioxidant capacity. Moreover, brains pre-treated with simvastatin lactone showed reduced ischemic depolarizations. Pre-treatment with simvastatin acid or pravastatin was ineffective. Vascular resistance recordings and Akt signaling were unchanged by any statin treatment.

Conclusions: Our findings suggest that intravascular statins require entering brain tissue, either by their BBB-crossing properties or by BBB-disruption caused by reperfusion injury, in order to provide rapid protection from early ischemic injury.

NEUROPROTECTIVE EFFECT OF BAICALEIN IN EXPERIMENTAL ISCHEMIA-REPERFUSION BRAIN INJURY

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Background & Purpose: Ischemia-reperfusion (I-R) injury is a major complication that occurs during ischemic stroke. Phosphorylation of the signal transducer and activator of transcription (STAT-1) has recently been reported to promote apoptotic cell death in neurons following I-R injury. Baicalein, a flavonoid originally isolated from the roots of Scutellaria baicalensis Georgi, has neuroprotective effects. This study examined whether pretreatment with baicalein could protect neurons against I/R-induced brain injury and evaluated the effect of baicalein on STAT-1 phosphorylation.

Methods: Baicalein was administered to rats for 10 days before induction of middle cerebral artery occlusion (MCAO). MCAO with reperfusion was induced in rats. Then, infarct volume, the level of neuron specific enolase, and STAT-1 phosphorylation were assessed. Malondialdehyde content was assessed using thiobarbituric acid reactive substance (TBARS).

Results: Infarction volume decreased in rats pretreated with baicalein, as compared to the vehicle-treated group (baicalein 10 mg/kg, 30 mg/kg vs. vehicle, 17.45±2.4%, 9.04±1.94% vs. 25.93±1.25% p<0.01). The release of neuron-specific enolase (2.34±0.89 ng/mL, 1.12±0.51 ng/mL vs. 6.39±1.14 ng/mL; p<0.01) and the production of TBARS (1.62±0.32 ng/mL, 1.07±0.32 ng/mL vs. 2.38±0.23 ng/mL; p<0.05) decreased significantly following baicalein treatment. Baicalein also reduced STAT-1 phosphorylation (0.0251 and 0.0238 vs. 0.0376), which was enhanced in brains subjected to I-R.

Conclusions: These Results suggest that pretreatment with baicalein protects neurons from cerebral I-R injury and that the inhibitory effect of baicalein on STAT-1 phosphorylation might contribute, at least in part, to brain neuroprotection.

EMG PATTERNS OF MUSCLE ACTIVATION OF NOVEL REHABILITATION PROGRAMME IN HEALTHY INDIVIDUALS

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Introduction: A novel ontogenetic based stroke rehabilitation programme is based on a sequence of muscle trigger exercises, activating muscles from core to proximal and distal ones. Steps of the programme are a sequence of exercises in starting positions, from supine to standing. A programme exercise protocol and its EMG patterns of muscle activation have been studied in acute stroke patients.
Methods: The study included 10 acute stroke patients with hemiplegia of varying degrees and 10 healthy adult volunteers. The study protocol included neurological and physiotherapy clinical examination and biomechanical assessment of programme exercises, by Qualysis motion capture system 8 of OQUS-500 cameras and surface EMG by ME 6000. Six muscles were monitored on both sides: sternocleidomastoideus, trapezius, biceps, triceps brachii, rectus femoris, adductor magnus. The exercises are performed and monitored in 7 test positions, consequently from lying to standing on the knees.
Results: Patterns of muscle activation varied significantly in patients and in healthy controls.
Patterns of muscle activation demonstrated marked difference if done in different starting positions, which could be an influence of gravity force vector.

1. Head turn in supine showed bilateral high activity of sternocleidomastoideus and trapezius. When done in standing, there was unilateral activity of these muscles.
2. Unilateral arm rising in supine showed activity of triceps brachii, rectus femoris and adductor magnus on the side of the movement. When done in standing, there was also activation of trapezius and biceps of the same side, concurrent with the muscles, active in supine.

Conclusion: There were different patterns of muscle activation in test movements, when done in different test positions. This might relate to a gravity vector change. As there were various patterns of muscle activation registered. Patterns of muscle activation in exercises and test movement desire further research.

EMG PATTERNS OF MOVEMENT OF NOVEL REHABILITATION PROGRAMME IN ACUTE STROKE

M.A. Bulatova, V.I. Skvortsova, G.E. Ivanova, D.V. Skvortsov, E.A. Kovrazhkina, A.Y. Suvorov
Russian Govornment Medical University, Moscow, Russian Federation

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Methods: A novel ontogenetic based rehabilitation programme was investigated for its efficacy in acute stroke patients. The study included 10 acute stroke patients with hemiplegia of varying degrees and 10 healthy adult volunteers. The study protocol included neurological and physiotherapy clinical examination and biomechanical assessment of programme exercises by Qualysis motion capture system 8 of OQUS-500 cameras and surface EMG by ME 6000. Six muscles were monitored on both sides: sternocleidomastoideus, trapezius, biceps, triceps brachii, rectus femoris, adductor magnus. The exercises are performed and monitored in 7 test positions, consequently from lying to standing on the knees.
Results: Three patterns of EMG activity were distinguished: the first one resembles one of a healthy person but would present lower EMG activity on the side of the lesion. The second is higher and prolonged activity of some muscles on the side of lesion when compared with like of non-paretic side in some of the exercises. It correlated with muscle tone increase (Modifies Ashford Scale 2 or higher). The third is activation of normally silent muscles of non-paretic side in test movements. This was registered in patients with Barthel index 85 or lower.
Discussion: Three pattern of muscle activation could give some keys for understanding, prevention and treatment of spasticity and movement impairment in acute stroke patients.

CCR2-DEPENDENT MONOCYTE RECRUITMENT IS A CRITICAL PREREQUISITE FOR BRAIN REPAIR AFTER EXPERIMENTAL ISCHEMIC STROKE

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Background: Brain ischemia triggers local inflammation that mediates secondary infarct growth but also repair processes in subacute stages after stroke. We addressed the role of hematogenous monocyte/macrophage (MO/MP) recruitment in stroke lesion development.
Methods: We used knock-out, bone marrow chimeric, and monocyte-deplted mice to study the role of circulating MO/MP in the photothrombosis and transient middle cerebral artery occlusion models of focal cerebral ischemia.
Results: Early MO/MP recruitment after ischemia was characterized by an immature CCR2+Ly6chiCX3CR1lo monocyte phenotype that was gradually replaced by CCR2-Ly6cloCX3CR1hi MO/MP. This was paralleled by a shift from pro-inflammatory towards repair-associated gene expression. Selective depletion of circulating MO/MP reduced lesion infiltration by MO/MP only if administered within 2 days of ischemia. MO/MP-depleted and bone marrow chimeric mice lacking peripheral CCR2+ MO/MP developed secondary hemorrhagic conversion of the infarctions. This was associated with decreased expression of transforming growth factor (TGF)-beta1 and the TGF-beta-activating protease thrombospondin-1, and reduced deposition of collagen-4 in the microvascular matrix of the lesions.
Conclusions: Our data demonstrate that early monocyte infiltration is a critical prerequisite for brain repair after ischemic stroke. Interference with CCR2-dependent monocyte recruitment increases the risk of hemorrhagic infarct conversion.

TRACKING IRON LABELLED STEM CELLS IN STROKE: A SYSTEMATIC REVIEW

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Background: Labelling stem cells with iron and tracking their movement with non-invasive magnetic resonance imaging (MRI) may help improve our understanding of their underlying mechanism of action. This review was aimed to establish the most favourable labelling technique in the context of experimental stroke models for potential application to human clinical trials.
Methods: Two independent authors systematically searched Medline and Embase up to June 2010 for studies examining experimental stroke with iron-labelled stem cells. Data was collected on label technique, administration regimen (cell type, time post ictus, dose, route), stroke type (transient, permanent, photothrombotic) and outcome (evidence of migration, transdifferentiaition, function, lesion volume). Study quality was assessed using an 8-point scale.
Results: 17 publications containing 25 experimental paradigms were identified. Mesenchymal stem cells (MSC) (n=11) and Neural Progenitor Cells (n=8) were used most commonly and the majority were labelled with ferumoxide (n=16); the use of a transfection agent (e.g. protamine sulphate), a compound that enhances cellular iron uptake, was inconsistent. Iron labelled MSCs did not appear to transdifferentiate into neurons or glia. Study quality was low - none used blinded outcome assessments and only one study utilised randomisation for animal selection, potentially introducing significant bias.
Conclusion: Drugs already licensed for humans, such as ferumoxide and protamine sulphate could be translated for use in clinical trials. Further research is needed using higher quality experimental models that mimic human stroke. The incorporation of iron into the cell to provide sufficient MRI contrast needs to be balanced with cell viability and function.

THE EFFECT OF BEE VENOM ACUPUNCTURE ON PHOTOCHEMICAL THROMBOTIC INFARCTION ANIMAL MODEL

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Background and Aims: Acupuncture has been used for stroke recovery in East Asia for centuries. Bee venom (BV) has been proved to be therapeutically beneficial for inflammatory or painful conditions such as arthritis. The purpose of this study is evaluation of the effects of bee venom acupuncture (BVA) on the photochemical thrombotic ischemic cortical injury.

Methods: Sprague-Dawley rats were assigned to nine groups and cortical photothrombosis was induced in the sensorimotor cortex. Three acupuncture points (Dazhui-GV14, Quchi-LI11 and Zusanli-S36) were chosen and treated with BV (0.08ug/kg) on POD1, POD3 and POD5. The effect of BVA stimulaton on the size of the brain infarct after ischemia was examined by TTC staining. The effects of BVA on neurogenesis, angiogenesis, apoptosis and catecholaminergic activation were analyzed by immunohistochemical study. The pathophysiologic mechanisms of BVA on stroke were evaluated by p-SAPK/JNK and p-Akt.

Results: SA and BVA decreased the infarction volume after ischemia and this effect showed more prominent in BVA than SA. BVA increased the NeuN and RECA-1 but decreased cerebral apoptosis in ischemia group. There were increases of c-Fos and DBH expression in Locus Cerulean (LC) after acupuncture (SA, BVA). The TH expression also increased in Locus Cerulean (LC) and Substantia nigra, compact part, dorsal tier (SNCD) after acupuncture (SA, BVA). These effects were more prominent in BVA than SA. The activations of JNK1/2 and Akt were increased by BVA.

Conclusion: We found that BVA promote neurogenesis, angiogenesis and anti-apoptosis after ischemic injury, possibly through activation of brainstem catecholaminergic neurons, JNK1/2 and Akt pathways. Our Results suggest that BVA may be used for the effective ways to treatment of cerebral ischemia.

406 Experimental studies

IMPROVED FUNCTIONAL RECOVERY AFTER STROKE THROUGH ENHANCEMENT OF THE ENDOGENOUS NEUROGENESIS IN AGED RATS

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Background: In adult rats the endogenous neurogenesis is maintained in the subventricular zone and the dentate gyrus of the hippocampus and could be used to improve post-stroke outcome. Here we asked if stimulations of endogenous neurogenesis before or after stroke in aged rats, which are known to be more severly affected by stroke than young rats, may improve recuperation after stroke.

Methods: Stroke was induced by middle cerebral artery occlusion (MCAO) in aged rats and neurogenesis was stimulated at different time points using neurogenesis enhancer, pentylentetrazole or EC stimulation. After MCAO, rats were behaviorally tested for 7 weeks and. global gene expression and immunhistochemical analyses of the periinfacted region was done.

Results: Our Results indicate that stimulation of neurogenesis at 4 wks before stroke does not improve post-stroke outcome. In contrast, stimulation of post-stroke neurogenesis is beneficial for behavioral recovery of aged rats. Global gene expression analysis has shown many new feature of gene expression associated with aging and led to identification of over 400 new genes involved in stroke pathophysiology. Immunohistochemistry has revealed many new features related to the neurovascular unit in the aged post-stroke animals.

Conclusion: Stimulation of post-stroke neurogenesis is beneficial for behavioral recovery of aged rats.

407 Experimental studies

CIRCULATING RETICULATED PLATELETS INFLUENCE THE EX VIVO RESPONSE TO ASPIRIN, BUT NOT DIPYRIDAMOLE OR CLOPIDOGREL, IN THE EARLY PHASE AFTER TIA OR ISCHAEMIC STROKE – INITIAL RESULTS FROM THE TRINITY ANTIPLATELET RESPONSIVENESS (TRAP) STUDY

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Background: Reticulated platelets are young platelets containing a residual amount of megakaryocyte-derived mRNA. The relationship between circulating reticulated platelets and "antiplatelet non-responsiveness/resistance" in ischaemic cerebrovascular disease (CVD) is unknown.

Methods: We performed a longitudinal, case-crossover study in patients ≤ 4 weeks of TIA or ischaemic stroke onset who changed from (i) no medication to aspirin

(n=18), (ii) aspirin to aspirin & dipyridamole MR combination therapy (n=47); or (iii) aspirin to clopidogrel monotherapy (n=23). Patients were studied at baseline and ≥ 14 days (14d) after altering therapy, and also ≥ 90d after changing treatment where possible. Whole blood flow cytometry was used to assess the % reticulated platelets (%RP), and inhibition of platelet function was assessed with the PFA-100. "Ex vivo" antiplatelet non-responsiveness' was defined as failure to prolong relevant PFA-100 closure times compared with the patient's baseline reading by more than twice the coefficient of variation of the assay.

Results: Median %RP was unaffected by commencing aspirin (P≥0.1); aspirin non-responders had higher %RP than responders at 14d (28.9% vs. 16.3%, P=0.01) but not at 90d (P=0.5), although only 8 patients in this subgroup had 90d follow up. Adding dipyridamole MR to aspirin did not reduce %RP (P≥0.3), and was similar in dipyridamole non-responders and responders (P≥0.5). Changing from aspirin to clopidogrel did not influence %RP at 14d (P=0.5), but increased the %RP at 90d vs. baseline (21.2% vs. 12.6%, P=0.0006); %RP was similar in clopidogrel non-responders and responders (P≥0.2).

Discussion: Circulating reticulated platelet levels contribute to ex vivo aspirin non-responsiveness, but not dipyridamole or clopidogrel non-responsiveness on the PFA-100 early after TIA or stroke onset. Changing from aspirin to clopidogrel increased the %RP at 90d, indicating that aspirin may stabilise reticulated platelet formation or release.

408 Experimental studies

MLC 901 (NEUROAID10), A TRADITIONAL CHINESE MEDICINE PROTECTS THE BRAIN AGAINST GLOBAL ISCHEMIA IN RATS

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Background: Global ischemia leads to neuronal damage in the vulnerable hippocampal CA1 field and to deficits in motor and cognitive functions. Today mild hypothermia remains the only therapy for human patients. The need for new therapeutic strategies is imperative. NeuroAid (MLC601 and MLC901), a Traditional Chinese Medicine (TCM) which is used in China to facilitate recovery of patients after stroke has been described in a model of focal ischemia as a protective drug with neurogenerative and neuroproliferative properties. The aim of this work was to investigate the therapeutic efficacy of MLC901 on brain injury and motor deficits induced by ischemia.

Methods: Ischemia was induced by4-vessel occlusion for 20 min. MLC901 (Moleac) was administered by 1 i.p. injection at the concentration of 74, 7.4, 0.74 or 0.074 mg/ml 30 min, 1, 2 or 3 hours after ischemia followed by one injection/day after reperfusion. Motor and cognitive performances were tested by the grip test and the Morris water maze (MWM),. The neuronal damage was assessed.

Results: Ischemia resulted in degeneration of CA1 neurons. MLC901 (0.074mg/ml) prevented necrosis and apoptosis of neurons up to 3 hours after ischemia. MLC901 led to a decrease in Bax expression and MDA levels induced by the ischemia. We demonstrated the critical role of Akt pathway in the MLC901-mediated neuroprotection against CA1 brain injury. MLC901 enhanced the neurogenesis and stimulated BDNF expression. MLC901 induced an improvement of the strength force. In the MWM, when compared to ischemic rats, MLC901 reduced the escape latency and swim distance and increased the time spent in the plateform quadrant.

Conclusion: This work demonstrates that MLC901 can offer a potent protection against global ischemia-induced brain injury with resulting preservation of learning and memory abilities. MLC901 can represent a novel therapeutic strategy after cardiac arrest or coronary surgery with a time-window of protection clinically interesting.

409 Experimental studies

RELATION OF MMP ACTIVATION AND OXIDATIVE CONDITIONS IN BLOOD PLASMA AT ACUTE ISCHEMIC STROKE

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Background: Among the markers, relating to the pathological processes in acute ischemic stroke (IS), are matrix metalloproteinases (MMPs), the oxidant/antioxidant balance, and one of the acute phase proteins - C-reactive protein (CRP).

We examined the relationship between blood MMPs, glutathione level, and CRP within the first 24 hours of acute ischemic stroke onset.

Methods: We studied 30 IS patients and 21 community-based healthy controls. Non-fasting venous blood was obtained within 24 h after stroke onset and at baseline for controls. We estimated the plasma levels of MMP-9 and MMP-12 using zymography, ELISA, and Western blotting Methods, measured plasma concentration of total reduced (tGSH) and oxidized (GSSG) forms of glutathione using the BIOXYTECH GSH/GSSG kit (OXIS, USA), and monitored the plasma concentration of CRP by ELISA. Group of healthy controls consisted of volunteers with normal CRP values. Group of patients was characterized by moderately elevated CRP values.

Results: IS patients exhibited reliably higher plasma concentration of MMP-9 compared with healthy controls (P=0.04). The full-blown correlation between MMP-9 activation and the increased plasma MMP-9 concentration was observed in case of IS patients. The same activity of MMP-12 characterized healthy volunteers and IS patients. GSHt concentration did not differ in controls and IS patients (P=0.275), but GSSG content in plasma increased highly significantly (P=0.001) at acute ischemic stroke.

Conclusions: GSSG transport is active, and the marked increase of its concentration in plasma could be the result of export from neural tissue and blood cells into plasma, defending cells against oxidative stress. The oxidative conditions may activate MMP-9, besides, MMP-12 has the ability to activate other MMPs. The equal quantity of MMP-12 in normal and IS plasma, and the disrupted GSSG/GSH balance point that MMP-9 activation is the result of developed oxidative conditions rather then the MMP-12 action.

410 Experimental studies

A COMPARISON OF TWO STROKE DEVICES: THE NEW ACANDIS APERIO CLOT REMOVAL DEVICE AND THE EV3 SOLITAIRE AB

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In this study, the safety and efficacy of the new Acandis Aperio device was tested against the EV3 Solitaire AB device.

Experimental thrombi were prepared using a rotating tube clot generating system developed by Acandis. To enhance visibility, the thrombi were loaded with Barium Sulfate. Thrombi were injected in lengths of 10mm and the target vessel occlusion was verified by the TICI score. A microcatheter was placed distal to the thrombus. The devices were placed with the proximal third within the thrombus and retrieved under continuous aspiration in ist unleashed state with the microcatheter into the guiding sheath. The procedure was repeated, if the control angiogram showed a TICI score under two.

23 procedures (Acandis device) and 18 procedures (EV3 device) were performed and the TICI scores afterwards were compared as well as the number of attempts to reach recanalization and the rate of device-related complications. In addition, the efficacy, accuracy, visibility of the insertion of the delivery system, the device deployment and the overall clot removal procedure were compared. Vasospasm, vascular perforation, intramural arterial dissection, or embolization of a previously uninvolved territory, were defined as device related complications. Both devices demonstrated a high recanalization rate of 100% in the target vessel and excellent device performance with no device related complications. No significant differences in the above criteria were found between the two devices.

411 Experimental studies

REMOTE ISCHAEMIC PRECONDITIONING USING A TOURNIQUET RESULTS IN A VARIABLE DEGREE OF NEURONAL INJURY FOLLOWING GLOBAL CEREBRAL ISCHAEMIA

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Background: Remote ischaemic preconditioning (RP) has been shown to protect the brain from ischaemic injury in animal models and represents a potential protective strategy for acute stroke. These models have used clamping of the femoral artery to invoke RP. In order to be translated into clinical practice RP must be shown to protect the brain using limb ischaemia induced by external compression.

Methods: An 8-minute 4-vessel occlusion model of global cerebral ischaemia (GI) was used in male Wistar rats. Tourniquets were applied to both lower limbs to induce RP immediately prior to GI. The duration of RP (3*10 minutes ischaemia/reperfusion) has previously been shown to be effective in protecting the brain from ischaemic injury using femoral artery clamps. Temperature was regulated

for 24 hours following GI and histological analysis of the CA1 region of the hippocampus was measured at 7 days by a blinded assessor.

Results: Mean CA1 neuronal densities (cells per mm ± SE): sham RP+sham GI, 171±14 (n=5); sham RP+GI, 26±9 (n=4); RP+GI, 82±31 (n=5). GI resulted in significant neuronal damage to the CA1 region compared to sham GI, but there was no significant protection following RP+GI compared to GI alone (P=0.16). The variance ratio showed a significant difference in variances between RP+GI and GI groups (P<0.05). A variable degree of limb neuropraxia occurred in the rats following RP.

Conclusion: External application of a tourniquet produces highly variable degrees of neuroprotection in this model. This limits the potential for investigating the RP signal. The reason for the variability is not clear. The neuropraxia observed following RP may point to why the variability was seen, as an intact neuronal supply is required for RP. Further experiments using deliberate nerve damage or a non-neuropathic RP stimulus are required to understand the reasons why this model of RP does not provide consistent neuroprotection.

412 Experimental studies

DEGREE OF BLOOD FLOW RESTORATION AFTER TRANSIENT OCCLUSION OF THE MIDDLE CEREBRAL ARTERY ASSOCIATE WITH 24-HOUR MORTALITY AND INFARCT VOLUME IN RATS

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Background: The purpose of this work was to evaluate relationship between the degree of blood flow restoration, mortality rate and infarct volume in rats with transient occlusion of the middle cerebral artery (MCAO).

Methods: 3-month-old 30 male Wistar rats were subjected to 60 minutes MCAO by an intraluminal monofilament. Before, during and after occlusion rats were examined at 7 Tesla MR tomograph: 3D TOF MRA, Diffusion-weighted images (DWI) and T2-weighted images (T2-WI). Infarct volume was processed using "ImageJ"; software (NIH, USA) and was calculated on T2-WI and DWI by a semi-automatic method.

Results: MRI including MRA did not reveal any pathological changes in the brains of intact animals. At the end of monofilament occlusion MRA did not reveal any blood flow in MCAO. At the first 15 minutes after removal of monofilament MRA revealed three types of blood flow restoration: full restoration (19 animals), low reflow (6) and no reflow (5). 24-hour survival rate was maximal in animals with full restoration of blood flow (94,7%), this rate was 83,3% in low reflow group and significantly low in no reflow group (20%; p=0,029 in compare with full restoration group). There were combination of cortical and subcortical ischemic lesions in all animals with no and low, and in 13 from 19 rats with full blood flow restoration, but another 6 (20%) rats from last group had only subcortical lesions including basal ganglia and hippocamp. At the 24-th hour after MCAO volumes of the brain infarct at DWI in groups of animals with full and low blood flow restoration were not differ but in group with no reflow the volume of infarct was at 1,6 and 1,4 more than in another two groups.

Conclusion: There was different degree of blood flow restoration after transient MCAO in rats. Phenomena of no reflow was associated with more high 24-hour mortality and bigger infarct volume.

413 Experimental studies

ENHANCED POST-STROKE PLASTICITY AND RECOVERY INDUCED BY NEURAL STEM CELL TRANSPLANTATION

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Stem cell transplantation promises new hope for the treatment of ischemic stroke. Strong evidence support that delayed transplantation of neural precursor cells (NPC) in mice after stroke reduces neurodegenerative processes by suppressing reactive inflammation and glial responses. However, the question whether transplanted cells enhance endogenous repair mechanism after cerebral ischemia, remains still open. In this study we aimed at analyzing, both functionally and morphologically, whether delayed (72 hours after ischemia) systemic NPC transplantation can enhance plasticity processes.

Functional deficit and functional recovery were studied by modified neurological severity score (mNSS) and grip strenght test. Plastic reorganization was characterized by sterological-based analysis of dextran amine labeled controlateral pyramidal tract sprouting, axonal transport and degeneration as well as assessment of motor spinal circuits. Interestingly enough, NPC were found to persist in the perischemic

area up to 60 days after transplantation and to induce a persistent functional amelioration of clinical disability. Moreover the lesioned corticospinal tract of transplanted mice showed less neurodegeneration than that of controls. Finally NPC enhanced the axonal sprouting from the contralesional pyramidal tract into the red and facial nuclei, as well as at cervical spinal enlargement. Here we found that neural stem cell transplantation may aid recovery from ischemic stroke through enhancement of neuronal cortical plasticity.

414 Experimental studies

MIDDLE CEREBRAL ARTERY OCCLUSION: COMPARISON OF SEVERAL RAT MODELS OF FOCAL CEREBRAL ISCHEMIA

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Background: The present study was aimed at investigation and comparison of several rat models of focal cerebral ischemia induced by middle cerebral artery (MCA) ligation.
Methods: Five models of focal cerebral ischemia in the adult male Wistar rats were tested: 1. Isolated left MCA ligation; 2. 40-min left MCA occlusion; 3. Permanent ligation of both left common carotid artery (CCA) and left MCA; 4. Permanent bilateral common carotid artery (BCCA) and left MCA ligation; 5. Permanent left MCA ligation and 40-min BCCA occlusion with reperfusion. Cerebral blood flow and anatomical area at risk (comprises ischemic penumbra and ischemic core) were determined in the following groups: 1, 2, 3. Blood flow in the MCA vascular bed was measured with use of Doppler ultrasound. Evans blue was used for delineation of anatomic area at risk. Histochemical determination of infarct size with triphenyltetrazolium chloride staining, evaluation of neurological deficit (Garcia score) and extent of brain swelling (asymmetry of cerebral hemisphere) were performed 48 hours after ischemia in all groups.
Results: The evidence for ischemic cerebral injury was obtained in all groups. Ischemia models in groups 1 and 2 produced small infarct size and anatomical area at risk. These protocols were not associated with neurological deficit or brain swelling. Ischemia model in group 3 resulted in significant variability in infarct size, anatomical area at risk and brain swelling with no neurological deficit. Ischemia models in groups 4 and 5 demonstrated the best characteristics: reproducible data on infarct size, anatomical area at risk, extent of brain swelling and neurological deficit. Ischemia model in group 4 was associated with infectious complications; in contrast, ischemia in group 5 didn't produce infection.
Conclusions: Permanent left MCA ligation with 40-min bilateral CCA occlusion can be recommended for preclinical research as the most reproducible and reliable model of focal cerebral ischemia.

415 Experimental studies

SAFETY EVALUATION OF LOW-FREQUENCY TRANSCRANIAL SONOTHROMBOLYSIS USING ACUTE ISCHEMIC STROKE RAT WITH HYPERTENSION

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Background and purpose: Low-frequency transcranial ultrasound (LFTUS) was demonstrated by many experimental studies to be more efficient for enhancement of thrombolysis. However some studies also showed that it might be dangerous to intracranial tissues. We have already reported that LFTUS with appropriate parameters could be both effective and safe in a thromboembolic middle cerebral artery occlusion (MCAO) stroke model of rats without hypertension history. This study further tested its safety with a permanent MCAO model of spontaneously hypertensive rats (SHR).
Methods: Right MCAO was introduced in male SHR with intraluminal nylon suture. Rats exhibiting left hemiparesis were randomly assigned to 1 of 4 groups: (1) NS (n=8): intravenous administration of normal saline (NS) as placebo 3 hours after MCAO; (2) NS+LFTUS (n=10): NS administration and simultaneously LFTUS application for 1 hour (480.4 kHz, continuous wave, at an intensity of 0.3 W/cm^{2}); (3) tPA (n=11): intravenous administration of alteplase (tissue plasminogen activator, tPA) instead of NS; or (4) tPA+LFTUS (n=11): tPA administration and application of LFTUS. Twenty-four hours after treatment, neurological change was evaluated and brains were removed and examined histologically.
Results: There was no significant difference (p>0.25) in neurological and body weight changes, infarct and edema ratio and hemorrhagic transformation among the 4 groups.

Conclusions: Our findings suggest that sonothrombolytic treatment with LFTUS with appropriate parameters might be a safe method of treatment for ischemic stroke patients even with a history of hypertension.

416 Experimental studies

NEW INSIGHTS ON THE ROLE OF TEMPERATURE AND GLUTAMATE IN STROKE PROGRESSION: A MR SPECTROSCOPY STUDY

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Background: The existence of a relationship between poor outcome in ischemic stroke patients and the presence of elevated body temperature and high glutamate levels on admission has been already reported. So far, a clear relationship between both factors, from a mechanistic point of view, has not been established. Here we present an in vivo study of the relationship between the increment of body temperature, cerebral temperature and glutamate levels in an animal model of stroke.
Methods: 56 rats (Male, Sprague Dawley, 280-320g) were subjected to transient (90 min) occlusion of the middle cerebral artery (MCAO) under 3 temperature conditions: hypo- (33°C), normo- (37°C) and hyperthermia (39°C), and an additional group of animals at 33°C was treated with glutamate. Cerebral temperature and brain glutamate, lactate and N-acetyl aspartate (NAA) levels were analyzed by means of MRI spectroscopy, in both ischemic and healthy brain regions, for a period of 4 h from the induction of stroke (including occlusion and reperfusion periods). Serum glutamate levels were determined by HPLC, form blood samples withdrawn during the 4 h period. Infarct volumes were measured during the occlusion (t=80 min, DWI) and at day 7 (T2 MRI). MR studies were conducted on a 9.4 T system (Bruker Biospec).
Results: animals subjected to hypothermia showed increased serum and brain glutamate levels, and an increased infarct volume at day 7 (p>0.0001), while animals subjected to hypo or normothermia showed more moderated increases of serum and brain glutamate levels, and presented a reduction of infarct volume at 7 day (p>0.0001). The injection of exogenous glutamate reduces the beneficial effects of hyperthermia.
Conclusion: There is a direct relationship between temperature of the brain and brain and serurm levels of glutamate, indicating a plausible cause-consequence relationship of both effects.

417 Experimental studies

COMPARISON OF DIFFERENT SONOTHROMBOLYTIC TECHNIQUES TO IMPROVE SMALL ARTERY REPERFUSION AFTER REVERSAL OF MCA OCCLUSION

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Background: Clinical and animal studies prove significant treatment effects of microbubble enhanced sonothrombolysis of MCA occlusion. After successful recanalisation of MCA occlusion, relevant perfusion deficits may persist within the MCA territory. In this animal study, we evaluated the effect of different sonothrombolytic techniques for treatment of the no-reflow phenomenon within the MCA territory.
Methods: Wistar rats were subjected to filament occlusion of the right middle cerebral artery (MCA). Reperfusion was established after 90 minutes. Animals were then randomised to no treatment, treatment with rt-PA or treatment with transcranial ultrasound with or without rt-PA and with or without microbubbles. Blinded outcome evaluation consisted of quantitative 3D micro-CT angiography and quantification of vascular volume in nano-CT angiography (900nm[3] voxel size).
Results: Nano-CT revealed severely compromised microcirculation in untreated animals after MCA reperfusion. Rt-PA partially improved hemispheric perfusion. Impairment was completely reversed in animals receiving rt-PA and contrast enhanced ultrasound (CEUS). This combination was more effective than treatment with either CEUS without rt-PA or rt-PA and ultrasound and ultrasound alone.
Conclusions: This animal study shows that sonothrombolysis, especially in combination with microbubbles, displays beneficial effects on the level of the cerebral microvasculature. The Results give evidence of sonothrombolytic efficacy beyond large artery recanalisation.

Vascular biology

418 Vascular biology

ANGIOGENIC PROPERTIES OF MONOMERIC C-REACTIVE PROTEIN AND NOTCH-3 RECEPTOR DEPEND ON GAMMA-SECRETASE ACTIVITY WITH A COMMON SIGNALING PATHWAY THROUGH PI3K/AKT

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Background: We previously demonstrated the pro-angiogenic activities of the monomeric C-reactive protein (mCRP) and synergy with the arterial/venous cell differentiator Notch-3/Fc in cultured endothelial cells (EC). The molecular mechanisms associated with mCRP/Notch-3 receptor signalling (co-expressed in plaque microvessels) have not been investigated.

Methods: EC and smooth muscle cell (SMC) proliferation, migration, in 2D and 3D cultures were used to study the effects of mCRP and Notch-3 after treatment with inhibitors of both mCRP and Notch-3 activation. The signaling pathways were investigated by Western blotting and phospho-site protein screening performed by Kinexus.

Results: mCRP and Notch-3/Fc increased EC and SMC proliferation, migration and differentiation in collagen gel and Matrigel, with a synergistic effect induced by mCRP/Notch-3/Fc together. A Kinexus screen showed that the main phospho-protein expression induced by mCRP in EC was the phospho-Insulin Receptor Substrate-1 a substrate of gamma-secretase dependent IGF1 receptor. Treatment with the inhibitors showed that DAPT totally blocked Notch-3/Fc or mCRP/Notch-3/Fc-induced angiogenesis. A complete inhibition of mCRP-induced endothelial tube formation was only observed with DAPT. Treatment with LY294002 did not change mCRP or Notch-3/Fc-induced endothelial tube formation however; LY294002 +/- DAPT fully inhibited the pro-angiogenic effects of mCRP, Notch-3/Fc and mCRP/Notch-3/Fc on EC or SMC in all other assays. Both inhibitors and their combination LY294002/DAPT fully inhibited mCRP-induced phospho-Akt expression whereas Notch-3/Fc induced phospho-Akt expression was only inhibited by DAPT.

Conclusions: We showed the requirement of gamma-secretase and PI-3 kinase in mediating mCRP pro-angiogenic activity, common key proteins required in Notch-3 function. Notch-3 may confer stability to rapidly growing blood vessels in unstable atherosclerotic plaques.

419 Vascular biology

INCREASED ARTERIAL STIFFNESS IN CRYPTOGENIC STROKE WITHOUT A LARGE PFO THAN WITH A LARGE PFO

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Introduction: Aortic stiffness is an important marker of cardiovascular health, and an independent predictor of cardiovascular mortality. Younger patients with unexplained stroke may have unrecognised vascular disease. While there is some evidence of endothelial dysfunction in those with cryptogenic stroke (CS) without patent foramen ovale (PFO) when compared with those with PFO, arterial stiffness has not been reported in this cohort.

We investigated if young patients with cryptogenic stroke and no PFO (or small PFO) have evidence of arterial stiffness when compared with young patients with cryptogenic stroke and PFO, and with healthy controls.

Methods: Patients of ≤55 years with CS and complete work up (including bubble-echo) were invited to participate. Healthy controls were recruited from a database by invitation.

We performed seated and lying assessment of arterial stiffness parameters, using the SphygmoCor system. Our pre-specified primary outcome measure was the difference in aortic stiffness (assessed by carotid-femoral pulse-wave velocity (cfPWV)) between those with and without a large PFO.

Results: 31 cases (20 with large PFO) and 33 controls were studied. Those with CS and a large PFO were older than those with CS without large PFO, and than controls (49 vs 38 vs 37 years).

cfPWV was lower in the large PFO group than the not-large PFO group (6.4 vs 7.3 m/s; p=.022). There was no difference in mean PWV between cases and controls (6.7 vs 6.7 m/s). Considering the 3 groups (controls, CS with a large PFO, CS without a large PFO) there was a trend to a difference in mean cfPWV (F=2.402; p=.099). However, in a linear regression model with age and sex, grouping was not an significant predictor of cfPWV.

Conclusion: In CS, those without a large PFO have increased arterial stiffness compared with those with a large PFO. However this was not independent of age in this small study. Vascular disease should be considered in those with unexplained stroke without a large PFO.

420 Vascular biology

QUANTITATIVE ELECTRICAL CORRELATES OF CEREBRAL VASODILATORY RESERVE IN SYMPTOMATIC CAROTID OR MIDDLE CEREBRAL ARTERY STENO-OCCLUSIVE DISEASE

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Background: Intracranial stenosis is associated with high-risk of stroke recurrence. In severe stenosis, perfusion is maintained by cerebral autoregulation (CA). CA may be impaired due to inadequate cerebral vasodilatory reserve (CVR). However, the Methods of assessing CVR with transcranial Doppler (TCD) and acetazolamide-challenged HMPAO-SPECT may not be reliable in some patients. While TCD fails in patients with insufficient temporal acoustic windows, SPECT imaging may not be reliable in patients with bilateral severe steno-occlusive disease. Quantitative electroencephalography (QEEG) monitors electrical brain activity with excellent spatial and temporal resolution. We aimed to assess the utility of QEEG in assessing CVR in patients with severe stenosis of carotid (ICA) or middle cerebral arteries (MCA).

Methodology: Symptomatic patients with severe steno-occlusive disease of ICA or MCA were evaluated for CVR with TCD monitoring during voluntary breath-holding. Breath holding index (BHI) of <0.69 was considered to represent impaired CVR. Continuous EEG was performed simultaneously with TCD and quantitative analysis was performed. Patients with impaired CVR were further evaluated with acetazolamide-challenged HMPAO-SPECT.

Results: 21 patients (16 males, mean age 67yrs) with severe intracranial steno-occlusive disease and impaired CVR on TCD were included. 3 patients suffered from bilateral severe disease. 7/21 patients, with BHI<0.3, were found to have significantly impaired perfusion and CVR on SPECT imaging. All 7 patients showed significant abnormalities on QEEG. Of the 3 patients with bilateral severe stenosis, 2 had BHI<0.3 in bilateral MCAs but, only 1 demonstrated abnormality on SPECT. QEEG demonstrated abnormal Results in both the patients.

Conclusion: Impaired CVR influence cerebral electrical activity and the dynamic changes can be observed reliably with QEEG. Our preliminary pilot data supports this hypothesis. QEEG might help in evaluating CVR even in patients with insufficient temporal acoustic windows or bilateral severe steno-occlusive disease and help in identifying a target group of patients for possible revascularization.

421 Vascular biology

THE RELATIONSHIP BETWEEN CX3CR1 POLYMORPHISMS AND CAROTID ARTERY STENOSIS

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Objective: To study the association of V249I and T280M polymorphisms of Fractalkine receptor CX3CR1 with carotid artery stenosis.

Methods: We studied 318 patients with carotid artery stenosis and compared with 292 subjects without carotid artery stenosis that diagnosised by color duplex ultrasound criteria. V249I and T280M polymorphic genotype of CX3CR1 were determined by polymerase chain reaction- restriction fragment length polymorphism (PCR-RFLP) and sequencing analysis.

Results: The genotypes of MM and TM were associated with reduced risk of carotid artery stenosis (OR=0.646, 95% CI: 0.451-0.928; P=0.017).No differences were observed in the II, VI, or VV genotype (OR=1.012, 95% CI: 0.731-1.403; P=0.940). The genotypes of II and VI in patients with stable plaques were more frequent than in vulnerable plaques (95% CI: 0.387-0.962; P=0.033). Multiple Logistic regression analysis revealed that the genotypes of MM and TM were an independent risk factor for carotid artery stenosis (OR=1.847, 95% CI: 1.091-3.127; P=0.022).

Conclusion: The genotypes of MM and TM are an independent risk factor for carotid artery stenosis,and the genotypes of II and VI are associated with the stability of carotid artery plaques.

Keywords: CX3CR1; carotid aretry stenosis; atherosclerosis; polymorphisms.

422 Vascular biology

GENE EXPRESSION ANALYSIS OF MATRIX METALLOPROTEINASES AND THEIR INHIBITORS IN AN IN-VITRO STROKE MODEL – BENEFICIAL EFFECTS OF STATIN THERAPY

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Background: Matrix metalloproteinases (MMPs) as zinc-binding proteolytic enzymes are key players in blood-brain barrier (BBB) breakdown during ischemic stroke. Their effect is antagonized by the tissue inhibitor of metalloproteinases (TIMPs). Statins have shown to dampen the MMP metabolism in various cell types in-vitro. In this study, we investigated the MMP and TIMP gene expression during the time-course of oxygen glucose deprivation (OGD) and the effect of statin exposure.

Methods: Cultured human brain microvascular endothelial cells were subjected to OGD (6, 12, 18 and 24 hrs). Expression of MMP-2, MMP-9, TIMP-1 and TIMP-2 were measured by real time quantitative PCR. In a second step, cells were pretreated with simvastatin 5 μM for 24 hours and subjected to 12 hrs of OGD. Each experiment was repeated 5 times.

Results: OGD induced a clear increase in MMP-2 expression (p <0.001), reaching a plateau after 12 hrs. MMP-9 expression was constantly detectable at only very low levels (ca. 200 fold lower than MMP-2). TIMP-1 expression declined over time, reaching significance after 24 hrs (p =0.001), while TIMP-2 expression remained stable over 24 hrs of OGD. Treatment with simvastatin significantly reduced the expression of MMP-2 (p <0.001) and altered the expression of TIMP-1 and TIMP-2 (both p <0.001).

Discussion: Our Results suggest that human brain endothelial cells are a source of MMP-2, but not MMP-9 during cerebral ischemia. Gene expression of TIMP-1 declined over time, whereas TIMP-2 expression remained stable. Pretreatment with simvastatin effectively dampened MMP-2 gene expression and enhanced the expression of TIMP-1 and TIMP-2. Thus pretreatment with simvastatin might have protective effects on BBB breakdown in ischemic stroke.

423 Vascular biology

SERUM FERRITIN IS NOT AN ACUTE PHASE PROTEIN AFTER EXPERIMENTAL STROKE

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Background: Some clinical studies pointed out that high levels of iron measured as serum ferritin, were associated to a worse outcome after stroke (Dávalos et al. 2000) and even to a higher risk of hemorrhagic transformation after t-PA treatment (Millán et al. 2007). However, it is not known whether ischemic damage might increase ferritin levels as an acute phase protein or rather if iron overload shown as high serum ferritin affects stroke outcome (Millerot et al. 2005). The objective of this work is to study the effect of stroke on serum ferritin.

Methods: Mice were fed for 8 weeks with a standard diet or with a diet supplemented with 2.5% carbonyl iron to simulate iron overload. Mice were submitted to focal permanent ischemia by the in situ thromboembolic model; or to transient focal ischemia by ligature model. An additional sham group was made as a control. In situ thromboembolic model was carried out as previously described (Orset et al. 2007) injecting thrombin in the middle cerebral artery (MCA) (n=5). In the ligature model the ipsilateral common carotid and the MCA were tied for 1 or 3 hours (transient model) (n=7-6). 100 μl of blood was collected through the tail before, 3 and 24 hours after the ischemia. Finally, serum ferritin was measured.

Results: Treatment with iron diet produced a significant increase on the basal levels of serum ferritin in all the groups studied (100±30% in control group, 380±119% in iron overload group; basal level in control group was 170±59 ng/ml). However, serum ferritin did not change after permanent or transient ischemia in any group (control groups: 137±48% and 97±23% at 3 and 24 hours respectively after ischemia; and iron overload groups: 394±115% and 372±129% at 3 and 24 hours respectively after ischemia).

Conclusions: Serum ferritin levels do not change after cerebral ischemia. Ferritin is a good indicator of iron levels but it is not an acute phase reactive protein after experimental ischemia.

424 Vascular biology

HYPERCHOLESTEROLEMIA IMPAIRS BLOOD-BRAIN BARRIER INTEGRITY IN THE ISCHEMIC BRAIN

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Stroke occurs mainly in aged patient, and correlates with serum cholesterol levels. Blood-brain barrier plays a pivotal role in brain homeostasis, and the role of hypercholesterolemia in blood-brain barrier dysfunction upon ischemic stroke is not clear. To elucidate the effect of hypercholesterolemia on blood-brain damage upon stroke, we used mice fed with normal chow, normal diet, or high fat chow, western diet, subjected to 30 min middle cerebral artery (MCA) occlusion. Using protein expression, interaction studies and enzymatic activity assays, we show that hypercholesterolemia increases blood-brain barrier permeability, translated by increased brain swelling and IgG extravasation, without effect on neuronal injury. Moreover, we showed that hypercholesterolemia contributes in worsening blood-brain barrier dysfunction upon stroke by enhancing lipid peroxidation, assessed by malondialdehyde (MDA) concentration, and increasing oxidized low-density lipoprotein (oxLDL) production. At the molecular level, we show that hypercholesterolemia contributes in increasing calpain-1/2 protease activity caused mainly by excessive downregulation of its endogenous inhibitor calpastatin, enhancing MMP-2/9 protease activity, and inducing RhoA overactivation, through the guanine exchange factor (GEF), leukemia-associated Rho GEF (LARG). This exacerbated edema observed in hypercholesterolemia is accompanied by tight junction protein, occludin, downregulation. We report here, a clinical relevant observation, where hypercholesterolemia, a major stroke risk factor, contributes in worsening the blood-brain barrier dysfunction upon stroke, by modulating endothelial intracellular mechanisms.

425 Vascular biology

TIME COURSE OF THE SERUM INFLAMMATORY BIOMARKERS FOLLOWING AN ACUTE CEREBRAL ISCHEMIA

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Background: There are limited data regarding natural time course of the serum level of inflammatory biomarkers after an acute ischemic stroke.

Objective: To investigate the extent and natural course of serum inflammatory cytokines level and it's relationship to stroke outcome.

Methods: Patients with acute ischemic stroke within 6 hours were included in this study. Demographic data, initial stroke severity and blood samples at arrival (<6 hrs), 6, 12, and 24 hrs and at 3 and 7 days after symptoms onset were prospectively collected. All patients were treated in acute stroke unit according to standard acute stroke treatment protocol. Serum biomarkers levels including MCP-1, MMP-9, TIMP-1, IL-6, IL-8 and CRP were measured using commercially available immunoassays. Patients were divided into 3 groups as mild moderate and severe stroke according to the initial NIHSS score of < 4, 5-14 and > 15 respectively. Time course and level of each inflammatory biomarker were determined in each group.

Results: In all, 63 patients were enrolled in which 28.1, 34.4 and 37.5% were mild, moderate and severe stroke. The mean age (+SD) was 66.63+12.49 years. Men comprised of 53.1%. Analysis of plasma samples is pending.

Conclusion: Our Results may open an opportunity for an approach using anti-inflammatory agents in patients with an acute ischemic stroke.

Small vessel stroke and white matter disease

452 Small vessel stroke and white matter disease

POPULATION-BASED STUDY OF LEUKOARAIOSIS IN PATIENTS WITH TIA OR STROKE IN RELATION TO AETIOLOGICAL SUBTYPE, VASCULAR RISK FACTORS, BLOOD BIOMARKERS AND PROGNOSIS

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Background: Leukoaraiosis is strongly associated with age and hypertension, but there is conflicting evidence as to whether it is causally associated with ischaemic stroke. We assessed clinical and laboratory associations and prognostic significance of leukoaraiosis in a prospective population-based study.
Methods: Two independent observers evaluated the presence and severity of leukoaraiosis on CT brain imaging in the first 1000 consecutive patients with TIA or stroke in the Oxford Vascular Study (OXVASC). Leukoaraiosis was related to aetiological subtype of the TIA or stroke (TOAST), vascular risk factors, a panel of inflammatory, thrombotic or neuronal blood biomarkers and risk of recurrent stroke.
Results: Inter-observer agreement on presence of leukoaraiosis was good (kappa=0.66, 95%CI 0.61-0.71, p<0.0001). On univariate analysis of vascular risk factors, leukoaraiosis was associated with age, hypertension, smoking, PVD and diabetes, but only age (OR/10yrs=2.69, 2.28-3.13, p<0.0001) and hypertension (OR=1.54, 1.12-2.12, p=0.008) were associated on multivariate analysis. Associations with biomarkers were only weak after adjustment for age and sex, most notably for vWF, PZ1, DDimer, Fibrinogen (haemostatic), TNF (inflammatory), FABP and NSE (neuronal damage). However, leukoaraiosis was strongly associated with lacunar TIA or stroke (age and sex-adjusted OR=1.96, 1.30-2.96, p=0.001) and only predicted recurrent stroke in this subgroup (HR=3.28, 1.41-7.63, p=0.006; HR adjusted for age and sex = 2.65, 1.08-6.45, p=0.03).
Conclusions: Leukoaraiosis is strongly associated with age and hypertension, but not with other measured risk factors or biomarkers. However, the independent association of leukoaraiosis with both incident lacunar ischaemic events and risk of recurrence suggests that they must have other environmental or genetic aetiological risk factors in common beyond their shared association with age and hypertension.

453 Small vessel stroke and white matter disease

THE ASSOCIATION BETWEEN RETINAL VASCULAR FRACTAL DIMENSIONS AND CEREBRAL WHITE MATTER LESIONS IN HEALTHY OLDER PEOPLE

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Background: Cerebral white matter lesions (WML) on magnetic resonance imaging (MRI) are common in the elderly and associated with significant morbidity and mortality. Their cause is unknown. Retinal vascular abnormalities are putative markers of cerebral small vessel disease. Retinal vascular fractal dimensions are associated with lacunar stroke. We hypothesised that retinal vascular fractal dimension (a measure of branching complexity) would be decreased in subjects with WML.
Methods: We recruited from the Lothian Birth Cohort 1936, a cohort of generally healthy subjects from Edinburgh, UK born in 1936 and followed up between 2007 and 2010 for this data collection. We collected demographic data, took digital retinal photographs of both eyes, and performed MRI brain scans (T2, FLAIR, GRE, T1 sequences). We used semi-automated techniques to calculate mono (Dbox) and multifractal (D0) dimensions for the retinal vessels of the left eye (arteries and venules combined) and assessed deep and periventricular WML with the Fazekas score.

Results: Of 524 subjects with retinal and imaging data, mean age 72.49 years (SD 0.71 years), 49% had hypertension and 10% diabetes. Fractal dimensions were normally distributed. The mean monofractal dimension was 1.42 (SD 0.024) and multifractal dimension 1.68 (SD 0.026). With linear regression, increasing age was associated with decreased monofractal Dbox (standardised beta co-efficient -0.0036, p<0.001) but Dbox was not associated with either deep (beta co-efficient -0.0021, p=0.21) or periventricular (beta co-efficient 0.00013, p=0.94) white matter scores. Multifractal dimensions were not significantly associated with WML scores or age.
Conclusion: In this large study, we found no significant association between retinal fractal dimension and cerebral white matter lesions confirming earlier Results in patients with stroke. We also confirm previous associations between decreased monofractal dimensions and increasing age.

454 Small vessel stroke and white matter disease

SYSTEMIC INFLAMMATORY MARKERS IN SMALL VESSEL DISEASE AND ATHEROTHROMBOTIC STROKES

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Background: Despite the high prevalence of lacunar infarcts much is yet unknown about its physiopathology. The importance of an immunological process in atherothrombotic stroke has been well established, nonetheless, its role in lacunar infarcts is still not well established.
Methods: Retrospective revision of the clinical files of all patients admitted in a tertiary stroke centre with the diagnosis of ischemic stroke from January 2009 to December 2010. Clinical and demographic variables were recorded. The etiology of the vascular events was defined according to the modified TOAST criteria. Patients with atherothrombotic and likely atherothrombotic strokes were analysed together. For patients with the diagnosis of small vessel disease (SVD) or atherothrombotic strokes the values of ultrasensitive C Reactive Protein (us-CRP, normal cutoff point for local laboratory: 0.5mg/dL) and leukocyte count on admission were evaluated. All patients with a Background of chronic inflammatory disease, malignancy, active infection or hospitalized at the time of onset were excluded from the analysis.
Results: We identified 356 patients with SVD or atherothrombotic infarcts. Fifty-three had exclusion criteria. From the remaining 303 patients, 116 (38.3%) had SVD and 187 (61.7%) atherothrombotic infarcts. Mean age was 70.13 years (SD: 12.32) and 181 (59.7%) were male. No statistically significant differences in us-CRP (1.6 mg/dL, SD: 3.84 for SVD vs. 1.1, SD: 2.05 for atherothrombotic; p=0.13) nor leukocyte count (8.5×1000 cells/μL, SD: 2.92 for SVD vs. 8.73, SD:2.77 for atherothrombotic; p=0.56) were found.
Conclusion: Our Results show that the systemic markers of inflammation are equally raised in atherothrombotic and SVD strokes. These findings support the concept of an immune mechanism underlying lacunar infarcts. However these facts do not allow a Conclusion on the exact mechanisms of this activation, presumably different than in atherothrombotic strokes.

455 Small vessel stroke and white matter disease

GENE EXPRESSION PROFILING IN THE CORTEX OF SPONTANEOUSLY HYPERTENSIVE RATS SHOWS ABNORMAL METABOLISMS AND REDUCED HYPOXIC/OXIDATIVE STRESS TOLERANCE CAPACITIES

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Objectives: Cerebral small vessel disease (SVD) is an important cause of stroke, cognitive decline and vascular dementia (VaD). The molecular mechanisms involved in the development and progression of SVD are not yet completely understood.

As hypertension is one of the major risk factors for developing the disease, Spontaneously Hypertensive Rats (SHR) are considered a good experimental model for the study of neuropathological changes appearing in the brain, as they share several similarities with essential hypertension in human. We previously described cellular differences in the brain of this rat strain leading to signs of neuronal hypoxia in the brain of older animals [1].

Methods: To identify genes and pathways involved in the development of small vessel disease, we performed comparison of gene expression in the cortex of 2 and 9-month-old SHR with age-matched normotensive Wistar Kyoto (WKY) rats using oligonucleotide-based microarray technology. Quantitative qPCR was used to confirm the differences in expression for selected genes.

Results: This analysis revealed significant downregulations in the expression of genes involved in the energy and lipid metabolisms, in mitochondrial function, in oxidative stress, and in hypoxia preconditioning in 2 as well as 9-month old SHR. Moreover, genes involved in endothelial proliferation were overexpressed in both SHR groups, confirming our histological observations.

Conclusions: These Results indicate that the brains of SHR suffer form mitochondrial dysfunction, energy failure and increased oxidative stress. This genetic analysis gives new insights about pathways accounting for the development of deep ischemic infarcts observed in small vessel disease which will ultimately lead to the establishment of preventive therapeutic options for patients at risk.

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456 Small vessel stroke and white matter disease

EVALUATION OF SILENT CEREBRAL LESIONS IN PATIENTS WITH FIRST ISCHEMIC STROKE ATTACK

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Background: Silent cerebral lesions, which were detected by imaging Methods, were defined as silent cerebral infarction (SCI) and lökoariosis (LA). In this study, we aimed to evaluate the frequency silent cerebral lesions, identify the risk factors of silent cerebral lesions and their impact on the prognosis of stroke in patients with first-ever ischemic stroke.

Methods: A total of 114 (58 male/56 female) patients with first-ever ischemic stroke that underwent brain MRI were enrolled in this study.Clinical, laboratory and MRI Results were recorded in all patients. Clinical features, laboratory Results were compared in the patients with and without SCI. Patients with SCI were divided into single and multiple and their lesion distribution, clinical, laboratory characteristics and risk factors were evaluated. Patients' clinical and laboratory Results were compared with LA severity, which were evaluated by Fazekas, and their risk factors were evaluated.

Results: The mean age was 65,99 years in all patients. SCI was detected in 90 patients and the most common localization was periventricular white matter (PVWM) (%33). High BMI, hypertension, and hyperlipidemia (HL) were associated with SCI (p=0,023, p=0,012, p=0,019), while there was no association with LA (p>0,05). Multiple-SCI group with cholesterol (p=0,011) and LDL (p=0,009) levels were higher than the group with single-SCI. Lower ejection fraction was associated with SCI and the severity of LA (p=0,029, p=0,036). Hemoglobin and hematocrit values were low in adv-PWMH. The presence of SCI had no effect on stroke recurrence, mortality and prognosis. Multiple logistic regression analysis showed that HL and the presence of adv-PWMH were an independent risk factor for SCI.

Conclusion: The prevalence of SCI and LA are higher in stroke patients. Increased LA severity is related to poor stroke prognosis and disability. Both the presence of SCI and LA are related to age and presence of lower ejection fraction.While the hemoglobin and hematocrit levels are related to only presence of LA, SCI are related to presence of HT, HL and high BMI. It is considered that different factors may be play role in development of SCI and LA.

457 Small vessel stroke and white matter disease

INCREASED BRACHIAL-ANKLE PULSE WAVE VELOCITY IS INDEPENDENTLY ASSOCIATED WITH SILENT BRAIN INFARCTION

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Background: Silent brain infarction (SBI) and white matter hyperintesities (WMHs) are risk factors for stroke. We previously reported the independent association of WMHs and arteriosclerosis. However, the association between SBI and arteriosclerosis is not yet clear. The aim of this study was to identify the arteriosclerotic characteristics associated with SBI.

Methods: We cross-sectionally included 240 consecutive patients with no history of stroke. We measured brachial-ankle pulse wave velocity (baPWV), ankle brachial pressure index, intima-media thickness of the common carotid artery, and performed magnetic resonance imaging (MRI) of the brain. SBI was defined as a focal lesion of at least 3 mm in diameter on MRI scans. WMHs were defined as periventricular hyperintensity (Fazekas grade >2) and/or separate deep white matter hyperintense signals (Fazekas grade >1). We determined the prevalence of SBI, WMHs, hypertension, hypercholesterolemia, diabetes mellitus, ischemic heart disease, and smoking. We compared two groups of patients defined by the presence or absence of SBI, using multiple logistic regression analyses.

Results: A total of 42 patients (18%) had SBI. In multivariate analysis, WMHs (OR 3.57, 95% CI 1.70–7.67) and baPWV (by 1 m/s, OR 1.11, 95% CI 1.02–1.22) were independently associated with SBI. The baPWV cutoff value for detection of SBI was 17.49 m/s with 69% sensitivity and 60% specificity (area under the receiver operating characteristic curve = 0.67±0.04, 95% CI 0.58-0.76).

Conclusions: Increased baPWV is associated with SBI. Management of increased baPWV may help to prevent SBI and stroke.

458 Small vessel stroke and white matter disease

THE EFFECT OF INFARCTS ON THE ASSESSMENT OF BRAIN ATROPHY IN LONGITUDINAL STUDIES

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Background: Infarcts and haemorrhages cause brain tissue loss and replacement by CSF. Brain atrophy is commonly measured as brain volume change in cross-sectional and longitudinal studies. We investigated the effect that failing to account for focal tissue loss due to stroke might have on the measurement of brain atrophy.

Methods: We used data from 46 patients (mean age 72 years) with lacunar or mild cortical ischemic stroke[1] who had MR scans at presentation and 2.5 years later. CSF volumes were measured as a proxy for brain volume using multispectral image fusion of T2-, T2*-, T1- weighted and FLAIR images (MCMxxxVI)[2]. Infarcts (33 in 46 patients) were masked using manually-edited, optimized thresholding on FLAIR. We compared CSF volumes with/without infarcts.

Results: The mean total CSF volume at baseline excluding infarcts was 272.7ml and it increased by 23.8% at 2.5 years. Including tissue loss due to infarct gave a mean baseline CSF volume of 272.4ml and a mean increase of 22.8% at 2.5yrs, i.e. only 1% less than previously calculated. However, this masked considerable individual variation: 24 patients had no tissue loss due to infarct; 7 had lacunes at baseline of mean volume 0.3ml that increased by 0.07ml at 2.5yrs; 20 patients had tissue loss due to stroke of up to 21.2ml at 2.5yrs representing up to 6.1% of the change in total CSF volume.

Conclusion: Progressive brain atrophy of as little as a few percent per year has been associated with dementia, therefore studies of brain atrophy in normal ageing, dementia or stroke need to avoid inflating the apparent brain atrophy rate by removing the tissue loss due to infarct from the brain volume measurement.
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459 Small vessel stroke and white matter disease

COMPARATIVE STUDY OF THE COGNITIVE PROFILE OF PATIENTS WITH RIGH VERSUS LEFT LACUNAR THALAMIC INFARCT

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Background: Lacunes or cerebral infarction of lacunar type are an ischemic infarction of less than 20 mm of diameter and located in the territory of cerebral penetrating arteriole. We are interested in the study of lacunar thalamic infarct because this subcortical structure are modulated and facilitate communication between all areas of the cerebral cortex.

Methods: 22 patients who presented lacunar thalamic infarct were admitted consecutively in the Department of Neurology of Parc Tauli of Sabadell and Hospital Sagrat Cor of Barcelona. The patients were classified into two groups according the presence of right or left thalamic infarct (LLTI) demonstrated by MRI. All the patients underwent a comprehensive neuropsychological test.

Results: The patients with right lacunar thalamic infarct (RLTI) (43,5%) and LLTI (52,2%) presented hypertension in the 65,2% and diabetes mellitus in the 21,7%. The most usual clinical diagnosis was pure sensory syndrome in the 60,9%. There were no statistical significant differences between groups in gender, education and general cognitive assessment (MMSE LLTI 27,33±2,18 vs RLTI 28,7±1,82). There were significant differences in the age of LLTI group's patients (77,75±10,84 vs 67,9±8,08;p=0,028). The group with LLTI infarct showed a poorer performance in the long delay verbal memory (6,66± 3,74 vs 9,90±2,60;p=0.032).

Conclusion: The LLTI group showed a poorer neuropsychological performance, especially in the long delay verbal memory. The memory dysfunction associated with lacunar thalamic lesions appears to be correlated with disruptions of mamillo-thalamic tract.This tract connects the anterior thalamic nuclear group with the mamillary body, which in turns is linked with hippocampus and entorhinal cortex and this neural system is involved in learning and memory performance. Our findings support the hypothesis that lateralization of cognitive processing of visual and verbal material exists at the thalamic as well as at the cortical level.

460 Small vessel stroke and white matter disease

AN INCOMPLETE CIRCLE OF WILLIS INCREASES RISK OF WHITE MATTER DISEASE

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Microangiopathy causes white matter disease (WMD), partly through hypoperfusion. We hypothesise that an incomplete circle of Willis with consequent risk of hypoperfusion also contributes to white matter disease. 90 patients over 50 years old were randomly selected from a radiology database. All had MRI and time of flight MR Angiography between July 2008 and July 2009. Circle of Willis (CoW) abnormalities were independently rated by two readers, as normal, complete or incomplete. Where no vessel abnormality was detected, patients were rated normal. Where vessel hypoplasia but not aplasia was noted patients were rated complete. Where vessel aplasia was noted patients were rated incomplete. White matter lesions were independently scored by two separate readers, blinded to MRA findings. The Fazekas WMD score was used. Kappa inter-rater reliability between both WMD investigators was 0.57. 56% of patient MRIs analysed were male. The individual prevalence of each circle of Willis variants in our sample was similar to that reported by Riggs and Rupp. A 37% increase in white matter lesions was observed in patients who possess an incomplete circle of Willis (n=21) compared with age and gender matched patients who possess a complete circle of Willis (n=69) (WMD score 6.52 Vs 4.11 p=0.03). Mean age was 65 yrs in both groups. WMD scores were equal in patients who possessed a normal circle of Willis (n=33) and those who possessed a complete circle of Willis (n=31), (4.11 V 4.13). Patients with unilateral CoW variants did not demonstrate an increased WMD score on the side of the variant. This result indicates that people with impaired cerebral anastomosis are at greater risk of developing white matter lesions and suggests a hypoperfusion mechanism may be contributary.

461 Small vessel stroke and white matter disease

CADASIL-LIKE PHENOTYPES AND NOTCH3 GENE ALTERATIONS: MISSENSE SEQUENCE VARIANTS OR CYSTEINE-SPARING MUTATIONS?

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Background: CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is the most common heritable cause of small vessel disease. It is caused by highly stereotyped mutations of NOTCH3 gene leading to an odd number of cysteine residues. In spite of this, several patients/families with a CADASIL-like phenotype without NOTCH3 gene mutations have been reported, some of them harbouring alterations presumed to correspond to sequence variants.

Methods: We report a Portuguese family with a CADASIL-like phenotype associated with a NOTCH3 alteration.

Results: The proband is a 58-year-old hypertensive male with history of recurrent lacunar stroke since age 54Y. Since his 50s he reported episodes of sensorineural hearing loss, vertigo, and nausea. He subsequently developed pseudobulbar palsy

and subcortical vascular dementia. Two of his sisters (age 66 and 62 respectively) had depressive symptoms, and suffered minor strokes in their 60s. All had history of migraine without aura. Brain MRIs of the proband and both sisters revealed extensive leukoencephalopathy not involving the temporal poles. Their father had suffered minor strokes since age 45Y and dementia at the age of 60. Their grandmother had suffered from migraine with aura and died from suicide in the 4th decade. NOTCH3 screening revealed a missense sequence variant (p.S978R) in exon 18, not previously reported, in the proband and both sisters. No other alteration was identified in exons 2-23. Two other sisters and one brother were asymptomatic, had no relevant white matter lesions, and proved negative for this NOTCH3 alteration. Skin biopsy in the proband was normal.

Conclusion: We report a family with a CADASIL-like phenotype associated with a NOTCH3 alteration of unknown significance. Further studies are needed in order to determine if this is a sequence variant or a cysteine-sparing mutation.

462 Small vessel stroke and white matter disease

WHITE MATTER HYPERINTENSITIES AND ENDOTHELIAL FUNCTION

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Background: White matter hyperintensities (WMHs) are frequently observed in normal subjects, but a large proportion is in patients with deterioration in the functional domains of the brain. This lesion has been associated with Alzheimer disease, subcortical vascular dementia, and genetic disorders. Nevertheless, the mechanism of WMHs is unclear. The purpose of this study is to identify whether WMHs is related to endothelial function.

Methods: We prospectively recruited 55 health concerned participants who were older than 65 years in a university hospital. All participants underwent diagnostic studies with routine blood tests and cardiologic workups. We excluded patients without MRI acquisition and no flow-mediated dilatation (FMD) test. Patient evaluation included demographics, medical history, and stroke risk factors. Endothelium-dependent FMD was analyzed by inflating a blood pressure cuff on the forearm and measurement was performed by using cross-sectional imaging with M-mode in the right brachial artery for 90 seconds. The volume of WMHs was evaluated using ezDICOM software on T2-weighted MRI. According to FMD values, patients were divided into stratified triplets: Group 1 (n=18, FMD 1.7-5.9%), Group 2 (n=18, FMD 6.1-7.9%), and Group 3 (n=19, 8.2-15.7). Demographics, stroke risk factors, and radiological factors (number of lacune, number of microbleeds, and volume of WMHs) were compared. We analyzed a correlation coefficient between the volume of WMHs and FMD value.

Results: Mean age was 73.5±5.1years (ranged 66 to 87 years). There was a significant difference of WMLs volume among group 1, group 2, and group 3 (36.8±30.2 vs. 24.9±20.5 vs. 14.8±21.5; p=0.003). There were no significant differences of demographics, risk factors, and other radiological factors. The Pearson correlation analysis showed a significant correlation between the volume of leukoaraiosis and FMD value (r=-0.404, p=0.002).

Conclusions: Our study suggests that endothelial dysfunction can be an important determinant associated with cerebral WMHs.

463 Small vessel stroke and white matter disease

VITAMIN B12 DEFICIENCY IN FIRST-EVER LACUNAR STROKE PATIENTS IS ASSOCIATED WITH POST-STROKE FATIGUE AND DEPRESSION

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Background and purpose: Vitamin B12 deficiency is often seen in lacunar stroke patients. Symptoms of fatigue and depression are frequently reported post-stroke, but relationships of vitamin B12 deficiency with fatigue and depression have never been studied in lacunar stroke patients.

Methods: In 40 first-ever lacunar stroke patients, all of whom had brain MRI, vitamin B12 levels were determined and self-report questionnaires for fatigue and depression were completed. Vitamin B12 deficiency was defined as a concentration <150 pmol/L.

Results: First-ever lacunar stroke patients with vitamin B12 deficiency reported significantly more fatigue (90.7 versus 59.4; p=.001) and depressive symptoms (6.62 versus 3.89; p<.05) than those without. In regression analyses, vitamin B12 deficiency was a significant predictor for fatigue and depressive symptoms independent of age and the presence of periventricular white matter lesions.

Conclusions: Vitamin B12 deficiency is associated with increased levels of fatigue and depression in first-ever lacunar stroke patients. Future research is suggested to

investigate other patient populations and the effects of vitamin B12 suppletion in lacunar stroke patients on fatigue and depression.

CARDIOVASCULAR RISK FACTORS AND DISEASES AS PREDICTORS FOR COGNITIVE DISTURBANCES IN CHRONIC KIDNEY DISEASE

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Cognitive and memory deficits are common findings in patients with chronic kidney disease (CKD). Previous studies have shown that verbal memory and cognitive flexibility are the most often affected domains. There is strong evidence for association between CKD with cardiovascular risk factors and diseases, which increase susceptibility for microinfarcts, lacunar infarcts and white matter changes. The precise link between these risk factors and cognition remains vague.

56 patients with stage 3-4 CKD (66±12 yrs.) were prospectively compared with a group of 21 patients with end-stage renal disease (ESRD) on dialysis (CKD 5; 60±15 yrs.) and a control group of 52 patients without CKD (59±11 yrs.). All participants were assessed with a neuropsychological test battery comprising tests for memory, information processing, cognitive flexibility and visuospatial abilities. Clinical and laboratory data were acquired.

Both groups of patients with CKD and ESRD performed significantly worse in comparison to the control group most of the cognitive measurements. Furthermore, patients with ESRD showed a significantly worse performance in scores for global cognition and in measurements for visuospatial abilities compared to patients with CKD 3-4 and healthy participants. The most important predictors for cognitive performance in the group of patients with CKD 3-4 were fibrinogen, parathyreoid hormone and intima-media thickness, indicating a role of inflammation in the pathogenesis of cognitive deficits. In patients with ESRD, on the other hand, cognitive deficits were predicted by HbA1c and body mass index, suggesting metabolic influences on cognitive disturbances.

Impaired kidney function is associated with deficits in specific cognitive domains with impairments becoming worse in the ESRD. Both the cognitive profile and the predictors of cognitive deficits differ between CKD 3-4 and ESRD, pointing towards different aetiologies of cognitive deficits in both conditions.

IMPAIRED KIDNEY FUNCTION IS RELATED TO SILENT MARKERS OF CEREBRAL SMALL VESSEL DISEASE IN PATIENTS WITH FIRST EVER LACUNAR STROKE

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Background: In population based studies impaired kidney function (KF) is associated with silent markers of cerebral small vessel disease (SVD) on brain MRI. We studied whether impaired KF relates to silent markers of cerebral SVD on MRI in first ever lacunar stroke patients.

Methods: We measured glomerular filtration rate using the Cockcroft-Gault equation in 114 first ever lacunar stroke patients. Impaired KF was defined as low glomerular infiltration rate <60 ml/min/1.73 m². Brain MRI scans of these patients were assessed for presence of silent lacunar infarcts and for periventricular and deep white matter lesions (WML) graded according to the Fazekas classification. The relationship between KF and markers of cerebral SVD was assessed by chi-square testing.

Results: We found impaired KF in 37 (32.5%) of 114 first ever lacunar stroke patients. Patients with impaired KF were significantly older (74.2 vs. 61.5 years old, p = 0.000) and used diuretic drugs more frequent (18.2% vs. 2.8%, p = 0.012). Hypertension was not significantly more frequent in patients with impaired KF (42.9% vs. 56.0%, p = 0.119). Extensive periventricular WML were seen in 20 (54.1%) patients with impaired KF compared to 15 (19.5%) patients with normal KF (OR 1.8; 95% CI 1.2 - 2.5). Extensive deep WML were also more frequent in patients with impaired KF (19 (51.4%)) compared to patients with normal KF (19 (24.7%), OR 1.5; 95% CI 1.1 - 2.2). Silent lacunar infarcts were seen in 31 patients (81.1%) with impaired KF compared to 43 patients (55.8%) with normal KF (OR 2.3; 95% CI 1.1 - 4.8).

Conclusion: In patients with first ever lacunar stroke impaired KF is associated with extensive WML and silent lacunar infarcts on MRI. We will perform additional analyses to test whether this association is independent of age and antihypertensive

drugs. Our study, like previous studies suggests a link between cerebral SVD and vascular disease of the kidney.

VOLUMETRY OF LESIONS IN MICROVASCULAR CEREBRAL DISEASE. A MRI BASED STUDY

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Background: A volumetry of lesions in microvascular cerebral disease is desirable for individual disease follow up, therapy control, correlation to clinical data and a possible surrogate marker for cognitive impairment in vascular dementia. Recent studies adressed brain tissue segmentation in MRI being basic for description and segmentation of cerebral white matter diseases.

Methods: This paper presents preliminary data of an automated segmentation and volumetry algorithm in cerebral small vessel disease. High resolution T1-weighted and fluid attenuated inversion recovery (FLAIR) scans in 1.5 Tesla MRI were used. First step of image analysis was unified segmentation of gray matter, white matter and cerebrospinal fluid by SPM8 in T1-weighted MRI data. In the second step the gray matter segmentation was used to find white matter lesions in the FLAIR scan with different thresholds. At least a MATLAB algorithm was implemented to determine the volume of the detected white matter lesions. The reproductibility of all steps were tested. The obtained volumes were compared with the Results of visual inspection of FLAIR scans by blinded specialists. The algorithm was applied to MRI scans of three patients (3 males, age between 60 and 80 years) with different degrees of microvascular cerebral disease.

Results: In two of three patients with marked disease there was a good correlation of automatically assessed lesion volume and visual analysis. In the third patient with less and diffuse white matter signal increase the algorithm seems to underestimate the lesion volume, obviously due to a threshold value problem.

Discussion: First Results of this study are promising. The threshold value problem has to be solved by more applications. Moreover the possible advantage of higher magnetic fields (3 Tesla) has to be tested.

ENHANCED PLASMA VISCOSITY IN UNSELECTED STROKE-UNIT PATIENTS - A LABORATORY HINT OF THE PRESENCE OF SMALL VESSEL DISEASE

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Introduction: Enhanced plasma viscosity (PV) in stroke patients is well known. In order to determine enhanced plasma viscosity in different stroke subtype, plasma viscosity was measured within the first 24 hours in 163 unselected patients (m = 79, f = 84, age 71±15) admitted to the stroke unit of the department of neurology.

Methods: According to clinical data, CCT or MRI embolic, macro vascular, small vessel disease, other possible reasons of stroke were classified. Under clinical aspects Stroke, TIA, or Stroke-"MIMIK's" (i.e. epilepsy, intracerebral bleeding, vertigo…) were separated. Supposed reasons of Stroke – i.e. Stroke classification – are under clinical conditions not of clear cut evidence. Therefore patients with AA and MRT sings of SAE were classified under both items. Statistical analysis was based on absence of a possible stroke reason vs. presence or possible presence of stroke reason. I.e. compared were values from patients with no signs of SAE vs. those with signs of SAE. In addition heart failure, diabetes, nicotine abuse and hypertension were sub classified. PV was measured by a Capillary Tube Plasma Viscometer.

Results: Stroke MIMIKS (n=33, PV = 1,22±0,06 cp) showed a significant different PV (p<0,001) compared to stroke (n=94, PV = 1,30±0.1 cp) or TIA patients (n=36, PV = 1,28±0,09). In the further analysis MIMIK's were excluded.

No PV difference according to the presence of risk factors (diabetes (n= 41), hypertension (n= 97), cardiac insuffiency (n= 27) or nicotine abuse (n= 23)) could be detected. Presence of large vessel disease (n = 43) PV = 1,30±0.1 cp or not (PV=1,28±0.09 cp) was indifferent; possible presence of embolic stroke (n= 54) PV= 1,28±0,1 cp or not (PV= 1,29±0.09 cp) showed no relevance. Only the presence of small vessel disease n= 83 PV= 1,31±0,1 cp) or not (PV= 1,26±0,09 cp) resulted in a significant difference of PV (P=0.012).

Conclusion: Further studies with more patients are needed to test the hypothesis that enhanced PV might be an independent risk factor of stroke caused by small vessel disease – or only a surrogate marker of small vessel disease.

468 Small vessel stroke and white matter disease

VEGF RECEPTOR IN VASCULAR SMOOTH MUSCLE MYOCYTES OF SMALL PENETRATING ARTERIES IN AGED HUMAN BRAIN

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Background: VEGF receptor 2 (VEGFR2) is a major mediator of vascular remodeling, and is at the center of several vascular pathologies, including atherosclerosis, and blood brain barrier dysfunction. VEGFR2 function is well known in endothelial cells and also in neurons. We recently observed VEGFR2 in vascular smooth muscle cells (VSMC) of small arteries in human brain. Here we aim to test the hypotheses that VEGFR2 in VSMC of small penetrating arteries is associated with: i) age, ii) vessel sclerosis.

Methods: Paraffin sections of human caudate/putamen from aged cases with neuropathologically-diagnosed small vessel disease (n=15, mean (SD) age: 80 (11) y), aged control cases with minimal brain pathology (n=11, age: 83 (7) y), and young controls (n=5, age range 11-40 y), were labeled immunohistochemically for VEGFR2. Donated brain tissue was primarily from the OPTIMA cohort. In small arterial vessels (10-200 micron outer diameter, data from 281 vessels) VEGFR2 abundance in the VSMC layer was graded by three independent, blinded observers using a 4 point scale, and sclerotic index (S.I.) was estimated.

Results: In aged cases, VEGFR2 was routinely observed in VSMC. Abundance of VEGFR2 was greater in aged cases than in young controls (p<0.05) but did not differ significantly between SVD cases and aged controls. Median S.I. for SVD brains was 0.46 (IQR: 035-0.60), significantly greater than that of aged controls (0.39, IQR 0.30-0.48) and young controls (0.39, IQR 0.30-0.50). At the level of individual vessels, VEGFR2 abundance was associated with S.I. (p<0.01).

Conclusion: VEGFR2 expression in VSMC of penetrating arteries was positively associated with age, and with vessel thickening. This suggests a possible role for VEGFR2 in vascular smooth muscle cells of aged brain.

469 Small vessel stroke and white matter disease

BLOOD TRACE ELEMENTS CONTENT CHANGES IN PATIENTS WITH LACUNAR STROKE AFTER INFLUENCE OF INTRAVENOUS LASER IRRADIATION OF BLOOD

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Background and purpose: This study was conducted in order to evaluate the effect of intravenous laser irradiation of blood (ILIB) on the blood trace elements concentration in acute phase of lacunar infarcts (LI) in combination with chronicle cerebral ischaemia (CCI) resulting from cerebral small vessel disease (CSVD).

Material and Methods: We assessed the blood trace elements concentration (Ca, Mg, Fe, Cu, Zn, Li and Al) by the method of atomic-emission spectroscopy in 17 patients of the main group (middle age 65±11,3 year) and 14 patients of the control group (middle age 60,3±15,8 year) with LI at 1-3 days of stroke and after course of treatment (10-12 days). Patients of the main group in addition to the basic therapy (aspirin and magnesium) received ILIB by the semi-conductor laser at wave length 0,67μm, and radiation power at the end of the light guide – 2,0-3,0 mW with application time 20 minutes, 7-8 procedures per course.

Results: In all patients was significantly increased blood concentrations of Ca - by 84% (p<0,01), Cu - by 100% (p<0,001) and Al –by 75% (p<0,05) with simultaneously Li level decrease by 90% (p<0,05) in comparison with the data of healthy donors. Course application of ILIB led to the normalization of Cu and Al blood concentration and to the increase of Fe level by 105% (p<0,05) in patients of the main group. The reduced concentration of Li level was noted in patients of both groups before and after treatment.

Conclusion: This study suggests that Li blood level decrease may be a marker of hypoxic brain tissue damage in acute phase of LI in combination with CCI resulting from CSVD. Intravenous laser irradiation of blood lead to trace elements redistribution in different body compartment together with antystressor mechanisms mobilization.

470 Small vessel stroke and white matter disease

ULTRA-EARLY THROMBOLYSIS IN CAPSULAR WARNING SYNDROME

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Background: We present two cases of pontine warning syndrome treated with "classic" antithrombotic therapy and one capsular warning syndrome treated with t-PA in the first 15 minutes from the onset of the ongoing episode.

Methods: First two patients presented daily for 2-3 days at least 4-5 episodes of motor deficit of limbs and dysarthria, without any response to loading dose of aspirin, clopidogrel, or both and finally due to lack of response, iv heparin, associated with high dose of atorvastatin and avoidance of reducing blood pressure below 180mmHg. Despite all those measures both developed pontine paramedian infarction (MRI confirmed) with hemiplegia. The third patient was a 52 year-old man, hypertensive and smoker with three episodes of left motors deficits of left limbs at home, with duration estimated between 5 and 30 minutes and admitted during the last episode of deficit with a normal cerebral CT scan at 120 minutes from the onset of first TIA. Blood pressure value was 210/105mmHg, reduced to 170-180mmHg with 20mg of iv Urapidil. Just before deciding a thrombolytic therapy the last deficit completely subsided but reoccurred after 10 minutes. Bearing in mind the evolution of the first two patients and similar bad prognosis in literature (more than 40% of patients developed hemiplegia with "classic" antithrombotic therapy) we decided to start iv thrombolysis 15 minutes after onset of the last attack.

Results: In spite of thrombolytic therapy the last motor deficit persisted proving not to be a new TIA and 24 hours later MRI confirm definite ischemia in internal capsule region. Angio MRI and ultrasound didn't showed any large vessel lesions. Anyway the improvement of motor deficit occurred much faster than expected for this location.

Conclusion: Capsular and pontine paramedian warning TIA's remain a severe prognosis condition with unclear mechanisms of lesions, part of them resistant to all type of antithrombotic and early thrombolytic therapy.

471 Small vessel stroke and white matter disease

AUTOPSY CONFIRMS CADASIL IN A NOVEL MUTATION OF THE GENE NOTCH3

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Background: CADASIL is a hereditary mid adulthood onset vascular dementia, with diffuse white matter lesions and subcortical infarcts, due to mutations of Notch3, a gene in chromosome 19p13 that codifies a transmembrane receptor. Most mutations described are on exons 3 and 4. We report a case with autopsy data in a CADASIL patient with a new Notch3 mutation.

Case Report: Mood and emotional disturbances and cognition decline were first noted in a previous healthy female at age 46. At age 47, she had already little spontaneous speech and showed a pseudobulbar affect. There was a global cognitive decline involving multiple domains, suggestive of predominantly subcortical dementia. There were no focal neurological signs. Known family history was irrelevant. Screening for prothrombotic states, Lyme, syphilis and HIV infection were negative. Cervical and transcranial ultrasound duplex and cardiac study were normal. Electroencephalography showed a diffuse theta-delta slowing. Brain MRI disclosed multiple subcortical lacunar infarctions and diffuse white matter T2 hyperintensities, including anterior temporal pole and external capsule. Molecular genetic analysis of the gene Notch3 detected a mutation W1028C on exon 19. During 6 years the patient progressively worsened the cognitive impairment. At age 51, already mute and bedridden, she started seizures, and died at age 52. Brain necropsy showed arterial walls infiltrated by basophilic material in white matter, subarachnoid space, basal ganglia and rarely in cortex; there were multiple lacunar infarcts and axonal loss in white matter. Nevertheless, 3 skin samples did not reveal any typical changes of the disease.

Discussion: Mutation W1028C has not been previously reported in CADASIL. However, the clinical, imaging and pathological evidence for the diagnosis, together with the lack of other aetiologies, confirms its pathogenic role.

Intracerebral/subarachnoid haemorrhage and venous diseases

525 Intracerebral/subarachnoid haemorrhage and venous diseases

DIFFERENT SPATIAL TRAJECTORIES OF HEMATOMA ENLARGEMENT DEPENDING ON HEMATOMA LOCATION ARE RELATED TO EARLY NEUROLOGIC DETERIORATION AFTER ACUTE INTRACEREBRAL HEMORRHAGE

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Background: Hematoma growth (HG) has been shown to be an independent determinant of death and disability after intracerebral hemorrhage (ICH). However, depending on ICH location, a predominant spatial growth direction may affect functionally critical or clinically eloquent structures leading to early neurological deterioration (END). We aimed to investigate the spatial HG behaviour and the impact of the main HG trajectory on clinical course in patients with acute ICH.
Methods: We prospectively studied patients with acute supratentorial ICH. Patients underwent baseline (<6h) and 24h CT scans, as well as a CTA (<6h) for the blinded detection of spot sign (SS). ICHs were classified as lobar, basal ganglia (BG), thalamic, or multiple locations. Longitudinal (L), transversal (T), and altitudinal (A) ICH diameters were calculated at baseline and 24h CTs, and HG trajectory was calculated from each diameter. We defined HG as ICH enlargement >33% or >6mL at 24h, and END as increase ≥4 points in the NIHSS score or death at 24h.
Results: A total of 124 consecutive patients were included. By ICH location, 28.2% were lobar, 38.7% were located in BG, 18.5% in the thalamus, and 14.5% in multiple locations. Median baseline ICH volume was 15 [7.8–38.1] mL. At 24h HG occurred in 34% of patients and 24.2% experienced END. CTA SS was present in 19.8% of patients, and its distribution predicted the main trajectory of HG in 81.3% of them. L trajectory of HG was significantly related to END in lobar (0.93 [0.5–1.5] vs. 0.1 [0–0.55] mm, p=0.002), and in BG (1.55 [1.3–1.8] vs. 0.17 [0–0.4] mm, p=0.015) ICH, while T trajectory was associated with END in BG (0.8 [0–0.8] vs. 0 [0–0.2] mm, p=0.01) and in thalamic (0.5 [0–1.3] vs. 0 [0–0.1] mm, p=0.002) ICH.
Conclusions: In patients with acute ICH, the distribution of CTA SS heralds the main direction of HG. The spatial behaviour of HG is related to END: L trajectory of HG in lobar and BG ICH, as well as T trajectory in BG and thalamic ICH.

526 Intracerebral/subarachnoid haemorrhage and venous diseases

D-DIMER LEVELS IN FINNISH PATIENTS WITH CEREBRAL VENOUS THROMBOSIS

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Background: Cerebral venous thrombosis (CVT) is a rare type of stroke with a wide spectrum of presentations and causes making accurate diagnosis challenging. D-dimer levels almost always increase in CVT patients, but their sensitivity may not be high enough to serve as a screening test.
Methods: We included all consecutive patients with an angiographically proven CVT, treated in our hospital from 1987 to 2010 with D-dimer levels measured before initiation of anticoagulant treatment. D-dimer was defined as negative if <0.5mg/L. A level >2.0mg/L represented high D-dimer. Symptom duration fell into acute (≤1day), subacute (2-14 days) and chronic (>14 days).
Results: In total of 73 patients D-dimer was measured before initiation of anticoagulant treatment, with a mean level of 1.96mg/L (range 0.05-13.0mg/L). 56 patients (76.7%) were women. In 9 (12%) patients, D-dimer was negative, and of these, 7 presented with subacute and 2 with chronic mode of symptom development. Of the patients with negative D-dimer three patients had no obvious risk factors of CVT.
High D-dimer levels were associated with impaired cognition (disorientation or impaired consciousness), thrombosis in multiple sinuses, and higher risk of death (chi-sqr P=0.04 for all).

	D-dimer <0.5	D-dimer 0.5-2.0	D-dimer >2.0
n (% of total)	9 (12%)	37 (52%)	25 (35%)
Female	5 (56%)	30 (81%)	19 (27%)
Age, mean (range)	39 (25-61)	39 (18-65)	38 (18-78)
No risk factors	3 (30%)	4 (11%)	1 (4%)
NIHSS* at admission, mean (range)	3 (0-27)	1 (0-15)	4 (0-23)
Impaired cognition or conciousness	0	0	3 (12%)
Focal symptoms	6 (67%)	21 (57%)	17 (68%)
Headache only	2 (22%)	13 (35%)	4 (16%)
Number of thrombosed sinuses,mean (range)	2 (1-4)	2 (1-5)	3 (1-5)
isolated s. transversus thrombosis	3 (30%)	4 (11%)	2 (8%)
isolated s.sagittalis superior thrombosis	0	7 (19%)	2 (8%)
no parenchymal lesions	6 (67%)	24 (65%)	14 (56%)
mRS* at 6 months, mean (range)	0.8 (0-2)	0.7 (0-3)	1.3 (0-6)
NIHSS at 6 months,mean (range)	0 (0-0)	0 (0-2)	0 (0-6)
Dead at 6 months	0	0	2 (8%)

*NIHSS: National Institute of Health Stroke Scale; mRS: Modified Rankin Scale.

Conclusions: Blood D-dimer level is not a reliable test to rule out venous sinus thrombosis.
However, in clinical practice high D-dimer levels might be useful in detecting patients with more severe disease and potentially worse prognosis.

527 Intracerebral/subarachnoid haemorrhage and venous diseases

INCIDENCE OF HYPONATREMIA IN PATIENTS WITH INTRACEREBRAL HEMORRHAGE WITH INTRAVENTRICULAR AFFECTION

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Background: In subarachnoid hemorrhage (SAH) estimates of incidence of hyponatremia varies between 15 and 60%. Cerebral salt wasting syndrome and syndrome of inappropriate ADH secretion are frequent causes. No data about the

incidence of hyponatremia in intraventricular hemorrhage (IVH) exist. In this study we wanted to assess the incidence of hyponatremia in IVH.

Methods: Patients suffering from IVH treated on our neurological intensive care unit in the period from 2006 to 2008 were included. Patients with primary SAH were excluded. Sodium levels were measured daily in routine lab. Lowest sodium levels were analysed and categorized in normal, mild hyponatremia between 135 and 130mmol/l, moderate between 130 and 120mmol/l and severe below 120mmol/l. Sodium levels were correlated with clinical and outcome data.

Results: 129 patients with IVH were treated in this period. 3-months-mortality was 52%. 40 patients with comfort care treatment were excluded and therefore 89 patients remained for analysis. No patient suffered from severe hyponatremia. Only three patients (3.4%) developed moderate and 47 (52.8%) patients mild hyponatremia. In 39 patients sodium levels were normal. No significant difference in clinical and outcome data could be detected.

Conclusion: We first report on the incidence of hyponatremia in IVH. Cumulative incidence is about 56%, moderate hyponatremia occurred in about 3%. Cumulative incidence of hyponatremmia is about the same with 59% as in SAH whereas moderate to severe hyponatremia is more frequent in SAH with about 15%. In SAH the risk of developing hyponatremia is significantly increased with large amounts of subarachnoid blood, enlargement of the third ventricle or presence of suprasellar or intraventricular blood. Additional risk factors include exacerbation of brain edema. No significant difference in these factors could be detected in this cohort. In Conclusion, hyponatremia is a common but not life-threatening complication in IVH.

528 Intracerebral/subarachnoid haemorrhage and venous diseases

CONTRAST EXTRAVASATION ON CT ANGIOGRAPHY PREDICTS CLINICAL OUTCOME IN PRIMARY INTRACEREBRAL HEMORRHAGE: A PROSPECTIVE STUDY WITH 139 CASES

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Background: Recently several retrospective studies showed that contrast extravasation on CT angiography (CTA) performed in acute stage is associated with poor outcome and mortality in primary intracerebral hemorrhage (ICH). Our prospective study aimed to examine the predictive value of contrast extravasation on multi-detector CTA (MDCTA) for clinical outcome.

Methods: In 139 consecutive patients (95 male; age: 56±12 years) with primary ICH admitted within 6 hours of symptom onset noncontrast CT (NCCT) and MDCTA on admission were performed, as well as follow-up NCCT at 24-hours. MDCTA images were reviewed by a neurologist and neuroradiologist independently to identify the presence of contrast extravasation. ICH and intraventricular hemorrhage (IVH) volumes at baseline and 24-hour follow-up were evaluated by computer-assisted volumetric analysis. Clinical outcome was assessed by modified Rankin Scale (mRS) at discharge and 90 days.

Results: The mean time from symptom onset to MDCTA evaluation was 3.3 hours (SD 1.5 hours). Median hematoma volume on baseline NCCT was 14.6 ml (range 0.5 to 130.0 ml), and median IVH volume was 3.9 ml (range 0 to 56.4 ml). Contrast extravasation and hematoma expansion was seen in 30 (21.6%) and 32 (23.2%) patients respectively. The presence of contrast extravasation was significantly associated with increased hematoma expansion, in-hospital mortality and poor outcome on discharge, mortality and poor clinical outcome at 3-month follow-up (P<0.05). In multivariate analysis, contrast extravasation was the most powerful independent predictor (OR=10.4, 95% CI 3.15-34.33, P<0.0001) for 90-day poor clinical outcome, followed by the presence of IVH (OR 3.19, 95% CI 1.42-7.17, P=0.005) and initial hematoma volume (OR 1.04, 95% CI 1.01-1.08, P=0.012).

Conclusion: The presence of contrast extravasation on MDCTA in the hyperacute ICH patients independently and strongly predicts poor clinical outcome.

529 Intracerebral/subarachnoid haemorrhage and venous diseases

SECONDARY INFARCTION IN SINGLE OR IN MULTIPLE VASCULAR TERRITORIES: TWO DIFFERENT ENTITIES FOLLOWING SUBARACHNOID HAEMORRHAGE?

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Background: The pathogenesis of secondary infarctions (SI) after aneurysmal subarachnoid haemorrhage (SAH) is poorly understood. To assess whether SI in single (SSI) or in multiple (MSI) vascular territories represent different disease entities, we compared clinical profiles of patients with these patterns of SI.

Methods: CT-and MRI-examinations of 448 patients were reviewed for new infarctions within 28 days after SAH, and categorized into SSI or MSI. Only patients with adequate follow-up imaging to exclude any new (clinically undetected) infarctions were included. Procedure-related infarctions were excluded. Odds ratios (OR's) with corresponding 95% confidence intervals (CI) were calculated for patients with SSI or MSI versus patients without SI to analyze differences in demographic characteristics, vascular risk factors, disease-related characteristics and treatment modalities.

Results: Thirty-six patients had SSI, 53 MSI and 180 no SI. In patients with MSI compared with patients with SSI OR's were >1.5 times higher for multiple vascular risk factors (MSI: 5.4 (2.3→13) versus SSI: 1.2 (0.5→2.8)), poor clinical condition on admission (MSI: 4.6 (2.4→8.9) versus SSI: 2.4 (1.1→5.2)), initial loss of consciousness (MSI: 2.6 (1.3→5.3) versus SSI: 1.1 (0.5→2.3)) and large amounts of intraventricular blood (MSI: 2.9 (1.4→5.8) versus SSI: 1.5 (0.7→3.2)). In multivariate analysis OR's remained higher in MSI for presence of multiple vascular risk factors (MSI: 1.9 (1.2→2.9) versus SSI: 1.1 (0.8→1.7)) and initial loss of consciousness (MSI: 3.0 (1.0→8.9) versus SSI: 1.6 (0.6→4.0)).

Conclusions: MSI was related to the same characteristics as SSI but to a larger extent. Our findings suggest that SSI and MSI after SAH are not distinct disease entities, but consequences of an increasing severity both of the initial SAH and of pre-existing atherosclerosis, and therefore different degrees of the same pathophysiological process.

530 Intracerebral/subarachnoid haemorrhage and venous diseases

INCREASED EXPRESSION OF TOLL-LIKE RECEPTORS 2 AND 4 IS ASSOCIATED WITH POOR OUTCOME IN INTRACEREBRAL HEMORRHAGE

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Background: Inflammatory response in the early acute phase of intracerebral hemorrhage (ICH) is associated with subsequent enlargement of the hematoma and poor outcome. Since inflammatory response could be a consequence of the Toll-like receptors (TLR) activation, our aim was to study the influence of TLR2 and 4 expression in the outcome of ICH.

Methods: 141 patients with primary ICH (male, 46.8%; mean age, 75.9±12.3 y) within 24 hours of symptoms onset (mean time 6.6±5.2 h) were consecutively included in the study. The main outcome variable was poor functional outcome at 3 months (modified Rankin scale ≥3), considering initial ICH volume and residual cavity volume measured by CT as secondary variables. Mean expression of TLR2 and 4 on monocytes and neutrophils were analyzed on admission by flow cytometry. ROC analysis was used to select the best predictive value for TLR2 and 4 expression due to a lack of linearity.

Results: Patients with poor outcome (n=84) showed increased expression of TLR2 and 4 in both monocytes and neutrophils at admission (all p<0.0001). However, only expression levels of TLR2 >5000 (OR, 49.7; CI95%, 15.0 - 164.5) and TLR4 >4400 AFU (Arbitrary Fluorescent Units) (OR, 100.5; CI95%, 21.8 - 464.0) in monocytes were independently associated with poor functional outcome after adjustment for age, previous antiplatelets, us-CRP, platelets, INR, ICH topography, ventricular extension, ICH volume and NIHSS at admission. On the other hand, no association was found between TLR2 and 4 expression and initial ICH volume. Nevertheless, TLR2 and 4 expression at admission in both monocytes (β=0.002 and β=0.002, respectively) and neutrophils (β=0.018 and β=0.008, respectively) were independently associated with residual cavity (all p<0.0001) after adjustment for alcohol consumption, us-CRP, INR and initial ICH volume.

Conclusion: Increased expression of TLR2 and 4 is associated with poor functional outcome and greater residual cavity in ICH patients.

531 Intracerebral/subarachnoid haemorrhage and venous diseases

THE EFFECT OF INTERLEUKIN-1 RECEPTOR ANTAGONIST (IL-1RA) ON INFLAMMATORY BIOMARKERS IN SUBARACHNOID HAEMORRHAGE (SAH)

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Introduction: Delayed cerebral ischaemia (DCI) is a common response to SAH, but adequate strategies for its prevention and treatment are absent. Interleukin-1 is a key orchestrator of inflammation contributing to the ischaemic process. There is encouraging efficacy and safety data for IL-1Ra in patients with stroke as well as efficacy data in experimental models. Intravenous (IV) IL-1Ra penetrates the blood-brain barrier in SAH patients, achieving CSF concentrations that are neuroprotective in rats. We tested the hypothesis that IV IL-1Ra reduces central and peripheral inflammatory markers in SAH patients, when compared to placebo, as measured by the area under the curve for intereukin-6 (IL-6) and C-reactive protein (CRP).

Methods: We completed a small, phase two randomised, controlled, double-blind trial across two UK neurosurgical centres (Salford and Cambridge). Eligibiliy criteria included adults suffering an aneurysmal SAH and placement of an external ventricular drain within 72 h of ictus. Patients were randomised to either IL-1Ra (Kineret®) or placebo. A 500 mg bolus of IL-1Ra was infused over 1 min, followed by a 10 mg/kg/h infusion over 24 h, and serial samples of blood and CSF were taken at set time-points over the subsequent 7 days. Adverse events reporting was as per MHRA and sponsor guidelines.

Results: 254 patients were screened between June 2009 and April 2010. 56 patients were potentially eligible and 18 were recruited. 13 received the investigational medicinal product (six active, seven placebo). Twelve infusions were completed. There were 20 adverse and serious adverse events occurring in nine patients. None was attributable to the study infusion. There was a significant decrease in plasma (p=0.041) and CSF (p=0.0183) IL-6 concentrations at 24h. There was a non-significant decrease in plasma CRP concentration at 72 h.

Discussion: This study suggests that IV IL-1Ra is biologically active after SAH. The plasma CRP concentration may not have dropped significantly due to the small sample size. These findings, in conjunction with recent preclinical data have now informed a phase 2 trial of subcutaneous IL-1Ra in SAH patients.

532 Intracerebral/subarachnoid haemorrhage and venous diseases

HISTOPATHOLOGICAL EFFECTS OF DIFFERENT THERAPY STRATEGIES IN EXPERIMENTAL SINUS THROMBOSIS

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Background: The optimal treatment for cerebral venous thrombosis is still under debate. The histological consequences of different treatments have not been systematically studied and may be of value in this debate.

Methods: Thrombosis of the superior sagittal sinus was induced in rats by topical application of ferric chloride. Animals were treated six hours after operation with subcutaneous injection of 450 IU/kg enoxaparin twice daily (n=10), with 10 mg recombinant tissue plasminogen activator (rtPA)/kg (n=12), and with 6 mg abciximab/kg (n=10). Eleven animals were treated with saline (controls) and 4 animals were sham operated without thrombosis induction. Animals were sacificed on day 7. Coronal brain slices were stained with hematoxylin-eosin (HE), and against glial fibrillary acidic protein (GFAP), and factor VIII. Histology was quantified in parasagittal and temporal regions of interest.

Results: Compared to controls, counts of pyknotic neurons on HE stain were significantly lower in the enoxaparin group. Counts for GFAP expressing astrocytes were highest in the enoxaparin (p<0.001) and rt-PA (p<0.05) treated groups. Angiogenesis definded as factor VIII expressing vessels was significantly (p<0.01) higher in the enoxaparin and significantly lower (p<0.01) in the rt-PA group compared to controls.

Conclusions: Overall based on histology and compared with the natural course in controls, enoxaparin seems to exert a more beneficial therpetic effect than rt-PA or abciximab.

533 Intracerebral/subarachnoid haemorrhage and venous diseases

ANTICOAGULATION REVERSAL AND OUTCOME IN PATIENTS WITH INTRACEREBRAL HAEMORRHAGE ASSOCIATED WITH ORAL ANTICOAGULANTS: A MULTICENTRE STUDY

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Background: Oral anticoagulation related intracerebral haemorrehgae (OAT-ICH) has been associated with a high mortality, however there are no universally accepted guidelines about the optimal treatment for reversal of anticoagulation.

Objective: Our aim was to investigate the management of short-term therapy in the reversal of anticoagulation in patients with OAT-ICH in our area and its relationship with clinical outcome.

Methods: We reviewed the records of all consecutive patients with OAT-ICH admitted to 6 universitary hospitals between 2004 and 2008. Demographic variables, vascular risk factors, INR values at admission, radiological variables on the cranial CT at admission, the treatments used to reverse the anticoagulation and intrahospital mortality were recorded.

Results: 101 patients were studied, with a mean age of 76 years and a mean hematoma volume of 41 cc. 25.7% of patients did not receive any treatment for anticoagulation reversal. 32.7% received prothrombin complex concentrate (PCC) and vitamin K; 22.6% were treated with vitamin K; 8% received PCC; 8% fresh frozen plasma (FFP) and vitamin K; 1% FFP and 2% FFP+PCC+vitamin K. Mortality was significantly lower in those patients treated with PCC and vitamin K (p=0.02).

Conclusion: Our study suggests that anticoagulation reversal with PCC and vitamin K Results in a significant reduction in mortality of patients with OAT-ICH.

534 Intracerebral/subarachnoid haemorrhage and venous diseases

HIGH PRO-BNP LEVELS AT ADMISSION ARE ASSOCIATED WITH POOR LONG-TERM FUNCTIONAL OUTCOME IN PATIENTS WITH INTRACEREBRAL HEMORRHAGE

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Background: Brain natriuretic peptide (BNP) is a molecular marker of brain damage. Our objective is to demonstrate whether pro-BNP levels determine the long-term functional outcome in patients with intracerebral hemorrhage (ICH).

Methods: We prospectively studied 134 consecutive patients with first episode of ICH <24 hours from onset. A blood sample was obtained at admission for the determination of pro-BNP levels. Brain CT was performed at admission to assess the ICH volume. Functional outcome was evaluated at 3 and 6 months and 1 year, by modified Rankin scale (mRS) categorized in a poor (mRS> 3) and good (mRS ≤ 2) outcome.

Results: 79 patients (59.5%) showed poor outcome at 3 months, 66 patients (49.3%) at 6 months and 65 patients (48.5%) at 1 year. Patients with poor outcome showed higher levels of pro-BNP (3480±8736 vs. 504±799 pg/mL, p = 0.013). Using ROC curves we found that the best cut-off point to predict the poor outcome for pro-BNP was 450 pg/mL (sensitivity: 75.6%, specificity: 70%, area under the curve: 0.770). In the logistic regression model levels of pro-BNP ≥450 pg/mL were independently associated with poor outcome at 3 months (OR: 4.718, 95% CI: 1.113 to 20.001), 6 months (OR: 7.215, 95% CI: 1.03 -50.518) and 1 year (OR: 9.389, 95% CI: 1.274 to 69.178).

Conclusions: High levels of pro-BNP on admission predict a worse functional outcome at 3 months, 6 months and 1 year in patients with ICH.

ENDOVASCULAR TREATMENT OF ISOLATED DISSECTING ANEURYSM OF THE POSTERIOR INFERIOR CEREBELLAR ARTERY

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Purpose: Isolated dissecting aneurysm of the posterior inferior cerebellar artery (PICA) are rare but has a high risk of re-bleeding. Recently, endovascular treatment has been proposed as an alternative to surgery, but still they present a therapeutic challenge. We report Results of various endovascular treatments in patients with isolated PICA dissecting aneurysms.
Material and Methods: Twelve patients (mean age: 43 years, range: 15-58, M:F=5:7) with isolated PICA dissecting aneurysms were treated by novel endovascular techniques (graft stent insertion in three, coiling of aneurysmal sac in seven, and occlusion of parent artery by coil in two) in our institution between March 2005 and May 2010. Clinical presentations were acute subarachnoid hemorrhage in eight patients, ischemia in two, severe headache in one and incidentally founded in one. Preprocedural occlusion test performed in five patients. We carefully examed presence of contrast filling of the PICA by collaterals during parent artery occlusion.
Results: On immediate follow-up angiograms, dissecting aneurysms were successfully occluded in all patients. PICA flow was well preserved in ten of twelve patients by collaterals and sluggish PICA flow in remaining two with parent artery occlusion. One patient developed ipsilateral PICA territory infarction two days after parent artery occlusion using coils but fully recovered at discharge. There was no procedure-related neurologic complication in the other patients. Angiographic follow-up (mean: 17.1month, range: 4-45months) was available in all patients. Follow-up angiograms showed total occlusion of aneurysms with well preserved PICA flow by collaterals in all patients. There was no newly developed neurologic event or re-bleeding (Modified Rankin scales: zero) in all patients during clinical follow-up periods (mean: 40.3month, range: 6-60months).
Conclusion: Various endovascular techniques could be effective and safe treatment modality of the isolated PICA dissecting aneurysm.

PROGNOSIS AND TREATMENT OF INTRACRANIAL DURAL ARTERIOVENOUS FISTULAE: A SYSTEMATIC REVIEW

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Background: Dural arteriovenous fistulae (dAVF) are a rare cause of intracranial haemorrhage (ICH), which may be recurrent. We systematically reviewed the published literature for factors associated with dAVF ICH and estimates of the effects of treatment.
Methods: We searched Ovid Medline (from 1966), Embase (from 1980) and the Cochrane Library on June 17th 2008. We sought studies of >20 adults with dAVF, using objective clinical outcomes to assess associations with mode of presentation, untreated prognosis or the effects of treatment.
Results: In 15 studies of retrospective associations between dAVF vascular anatomy and prior mode of presentation (1,437 participants), retrograde leptomeningeal venous drainage was retrospectively associated with ICH at initial presentation (odds ratio [OR] 24, 95% CI 14 to 41, heterogeneity [I2] 9%). In seven studies of untreated clinical course, one study identified venous varix and another identified retrograde leptomeningeal venous drainage as statistically significant predictors of future ICH. In 31 studies of treatment outcome, the principal risks after treatment were death (1.5% [95%CI 0.9 to 2.2]), non-fatal ICH (0.9% [95%CI 0.5 to 1.5]), and non-fatal cerebral infarction (1.6% [95%CI 0.9 to 2.6]); composite outcome 3.9% (95%CI 2.5 to 5.7). The risk of the composite outcome was 2.0% (95%CI 0.7 to 3.9) in 11 studies of endovascular embolisation alone (678 participants), but 5.4% (95%CI 3.5 to 7.6) in 20 studies (649 participants) of multimodality treatment (embolisation ± surgery ± radiosurgery).
Conclusion: Retrograde leptomeningeal venous drainage is strongly associated with ICH at dAVF presentation, but predictors of subsequent ICH are less well defined. Treatment complication rates were lower after embolisation alone than multimodality treatment in non-randomised studies. Long-term outcome is uncertain, as is the management strategy for dAVF without retrograde leptomeningeal venous drainage.

ON-ADMISSION ANEMIA IS AN INDEPENDENT PREDICTOR OF LARGER HEMORRHAGE VOLUMES IN SPONTANEOUS ICH

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Background: There are only two studies so far that have investigated anemia status in patients with acute intracerebral hemorrhage. On-admisson-anemia (OAA) has been associated independently with larger parenchymal hemorrhage volumes and lower hemoglobin levels during hospital stay were an independent predictor for poor functional outcome. This is the first study investigating OAA in spontaneous ICH.
Methods: This retrospective analysis included 174 consecutive patients (OAA: n=56; without OAA: n=118) with spontaneous supratentorial hemorrhage. Clinical data including the pre-admission status, neuroradiological findings, initial presentation, in-hospital measures and outcome were evaluated through institutional databases, patient's medical charts and by mailed questionnaires. Logistic regression analyses were calculated for parameters associated with OAA and testing for a true positive association between OAA and larger ICH volumes was undertaken.
Results: Patients with OAA had a poorer initial neurological status, larger ICH volumes, greater IVH extent, more midline shifting, an increased mortality and poorer functional outcome in univariate analyses. The receiver operating characteristics curve revealed, that OAA has an accurate and true positive association with larger hemorrhage volumes for all spontaneous ICH patients in our study (AUC > 0.7; p=0.001; (CI 95%): 0.57-0.75). In the multivariate analyses OAA was an independent predictor of larger ICH volumes. Further, OAA did not reveal an independent effect on functional outcome at 3 months or 1 year, but did show a trend for an increased mortality.
Conclusion: In patients with spontaneous supratentorial ICH OAA had a true positive association and was an independent predictor of larger ICH volumes. The question for future studies remains whether OAA beyond ist association with larger ICH volumes has independent effects that influence mortality, which might open up new therapeutic avenues.

PROPHYLACTIC ANTISEIZURE DRUGS FOR INTRACEREBRAL HEMORRHAGE

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Background: Patients with intracerebral hemorrhage (ICH) are at increased risk for both early seizures and later epilepsy. There is a common, but unproven, practice of prescribing a prophylactic antiseizure drug (PAD) to prevent seizures, but the safety and efficacy of this practice is unclear. Our objective was to evaluate whether patients presenting with ICH benefit from PAD prescription.
Methods: All patients with acute, nontraumatic ICH admitted to our institution in the calendar years 2004 and 2007 were included. We retrospectively reviewed the records for baseline characteristics, hospital course, PAD use, early seizures, length of stay, discharge disposition, and death.
Results: We found 157 patients meeting our criteria, of whom 29% were prescribed a PAD, and 8% had early seizures. Of patients prescribed a PAD, 11% had an early seizure, versus 6% who were not prescribed a PAD. Death or hospice discharge was less common in patients prescribed a PAD, while length of stay was longer, however neither of these differences were significant after adjustment for multiple comparisons.
Conclusions: We confirm previous reports that patients with ICH are at an increased risk for early seizures, but PAD use in our series was not significantly associated with changes in the risk of early seizures, long-term epilepsy, disability, or death.

HYPOPITUITARISM AFTER SUBARACHNOID HEMORRHAGE(SAH), A REVIEW

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Background: Fatigue, decrease in level of activity and quality of life are common in the long term after subarachnoid haemorrhage (SAH). They resemble the symptoms frequently found in patients with endocrine dysfunction. Pituitary dysfunction may be the result of SAH or its complications and long term complaints after SAH may partially be explained by endocrine dysfunction.

We reviewed the literature to clarify the rate, pattern and severity of endocrine abnormalities after SAH.

Methods: In a MEDLINE search for studies published between 1995 and 2011, we used the term subarachnoid hemorrhage in combination with pituitary, hypopituitarism, growth hormone deficiency, hypogonadism, hypocortisolism, hypothyroidism and diabetes insipidus. We selected all studies reporting endocrine function at least 3 month after SAH and regarded prevalence, pathogenesis, risk factors, clinical course and outcome.

Results: We identified 9 articles describing pituitary function in the long term after SAH. The prevalence of endocrine dysfunction varied from 4 to 55%. In addition, the pituitary axes that were affected differed strongly between the studies. However, the quality of data is low. Large cohorts clearly describing consecutive patients are missing and most studies included selective patients. Finally, Methods of laboratory measurements differed strongly and were frequently inadequate.

Conclusion: In spite of increasing number of publications the last years, data is insufficient to clarify the role of hypopituitarism in patients after SAH. Currently we are conducting a prospective cohort study to determine the prevalence of hypopituitarism in 120 subjects surviving SAH, using a routine standardized hormonal screening protocol. In addition we will identify prognostic neurological determinants for the development of hypopituitarism following SAH.

540 Intracerebral/subarachnoid haemorrhage and venous diseases

INDEPENDENT EFFECTS OF ON-ADMISSION ANEMIA IN MINOR-VOLUME INTRACEREBRAL HEMORRHAGE

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Background: There is only one study so far that has investigated on-admisson-anemia (OAA) in patients with acute ICH. OAA was an independent predictor of larger parenchymal hemorrhage volumes and a potential independent effect of OAA on 30 day mortality has been discussed. In this study we tried to evaluate, whether OAA exerts independent effects influencing mortality beyond its association with larger hemorrhage volumes in spontaneous ICH.

Methods: This retrospective analysis included 174 consecutive patients with spontaneous supratentorial ICH. Clinical data including the pre-admission-status, neuroradiological, initial status, in-hospital measures and outcome were evaluated through institutional databases, patient's medical charts and by mailed questionnaires. To potentially exclude dominant volume effects a sub-analysis for minor-volume ICH (volume ≤30cm^3) patients (n=103) was calculated. Logistic regression analyses for parameters associated with OAA in minor-volume ICH were undertaken.

Results: Minor-volume ICH patients with OAA revealed no statistically significant differences for pre-admission, neuroradiological initial presentation and in hospital measures, but did show a significantly increased mortality and poorer functional outcome in univariate analyses. The locally weighted scatterplot smoothing showed a less dominant volume effect influencing functional outcome in OAA patients of the minor-volume cohort. In the multivariate sub-analysis OAA was independently associated with an increased short-term mortality. Further independent predictors of an increased short-term mortality were the ICH-Score and age of the patients.

Conclusion: In spontaneous ICH OAA has independent effects influencing short-term mortality, especially in those patients whom might have the best chance of survival and decent recovery. Further prospective studies are urgently needed to elucidate these mechanisms of short-term detoriation to possibly implement new therapeutic approaches.

541 Intracerebral/subarachnoid haemorrhage and venous diseases

CONVEXITY VENOUS SUBARACHNOID HEMORRHAGE FOLLOWING MULTIPLE THROMBOSIS OF CEREBRAL VENOUS SINUSES DUE TO LEIDEN MUTATION OF FACTOR V

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Background: Cerebral venous sinus thrombosis (CVST) may represent itself through a wide spectrum of clinical manifestations and can be difficult to diagnose. However, venous subarachnoid hemorrhage (SAH) on cerebral hemisphere convexity as initial presentation of CVST has been rarely reported. If so, it usually follows thrombosis of superior sagittal sinus. Herein we present a 59-year old male with a history of deep venous thrombosis of his left lower extremity who developed an occipital headache followed by jerks of his left upper extremity and transitory lost of consciousness.

Methods: The patient was examined clinically, followed by head CT, MR, MRA and laboratory tests.

Results: Complete left homonymous hemianopsy and mild left hemiparesis was found clinically and venous subarachnoidal hemorrhage (SAH) was observed by CT over convexity of the right hemisphere. Multiple thromboses of cerebral venous sinuses ad left jugular vein as well as brain oedema were confirmed by brain MR and MRA (thrombosis of left jugular vein, left sigmoid sinus, both transverse sinuses and superior sagittal sinus).

Emergency laboratory revealed elevated D-dimer (2568µg/l) and further diagnostic work-up revealed resistance to activated C-protein due to Leiden mutation of factor V present in heterozygote form. Common prothrombotic states were excluded. The patient improved after treatment with low-molecular heparin and was discharged from the hospital with oral anticoagulant warfarin.

Conclusions: According to our knowledge this is the first report of CVST followed by convexity venous SAH due to Leiden mutation of factor V in heterozygote form. The treatment with low molecular heparin and warfarin was successful in our case.

542 Intracerebral/subarachnoid haemorrhage and venous diseases

THE IMPACT OF G-CSF IN ICH

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Background: The hematopoietic granulocyte-colony stimulating factor (G-CSF) is a growth factor promoting differentiation and proliferation of primarily myeloic cell lines. However, emerging evidence grows that G-CSF induces neuroprotective effects in ischemic stroke. Little is known about the impact of G-CSF after intracerebral hemorrhage (ICH). This study investigates the role of G-CSF after ICH regarding functional outcome and histology.

Methods: 58 male wistar rats with an age-range of 10 to 11 weeks (292–383 g) were stereotactically operated to induce a 70 ml right striatal intracerebral hemorrhage from autologous blood. Intracerebral application of G-CSF (60 µg/kg) was induced during surgery (n=17). Intraperitoneal administration of G-CSF (60 µg/kgKG) and BRDU (50 mg/kgKG, all rodents) was performed daily after surgery for five days (n=15). Mortality due to anaesthesia was 6,9% (4 von 58), due to surgical procedures or postoperative suffering was 0%. Rodents were examined (weight, signs of pains) and scored with the neurological deficit score (NDS) before and daily after interventions. After 7 days of survival rodents were euthanatized and fixed in 4% PFA. Sections were cut in 40 µm coronar slices and afterwards stained with a BRDU/DAB for cell counting- and volumetric procedures.

Results: The NDS shows more severe impairment in the ICB/G-CSF-groups (intracerebral, intraperitoneal) versus the surgery-only group in the first 5 days. Improvement is seen shortly before euthanasia. Weight development remains below controls. Histological and volumetric procedures are still outstanding.

Conclusions: The administration of G-CSF after experimental ICH currently does not promote neuroprotective effects in the acute phase. Further Results may elucidate the role of G-CSF in ICH.

543 Intracerebral/subarachnoid haemorrhage and venous diseases

CEREBRAL ANGIOBEHCET SYNDROME:CLINICAL AND NEURORADIOLOGICAL STUDY OF 24 CASES

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Background: Cerebral angiobehcet syndrome is one of neurobehcet subgroups frequently encountered in Morocco. we report 24 cases of cerebral angiobehcet.

Method and Result: Retrospective study of 24 cases of cerebral angiobecet extracted between 65 cases of neurobehcet.The analyse of result show that sudden onset of focal neurological deficit affecting men more than women and usually preceded by cardinals symptoms of behcet disease, the neurological deficit is subcortical and/or brainstem distribution in the majority of cases.MRI is more

effective than CT scan to detecting area of infarct and veins thrombosis.The main aspect was the constant involvement of cerebral deep veins.The authors insist to favorable follow up under anticoagulant and steroids.

Conclusion: The angiobehcet cerebral in our country is dominated by venous didease, particulary the cerebral deep veins.

544 Intracerebral/subarachnoid haemorrhage and venous diseases

CAN ANTICOAGULATED-PATIENTS BENEFIT FROM LONG-TERM ANTICOAGULATION AFTER INTRACEREBRAL HEMORRHAGE?

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Background: ICH is the most feared complication of warfarin anticoagulation. The worsening effect of anticoagulation has been demonstrated and the failure to rapidly normalize coagulation further increases haematoma expansion. Much controversy exists over whether patients with previous bleeding are at increased risk to receive anticoagulation therapy. Besides long-term efficacy of stroke prevention is not well-known.

Methods: We reviewed 3025 medical charts, laboratory data, and radiological findings of consecutive patients with stroke at Bellvitge University Hospital between 2003 and 2009. A total of 388 (13%) patients had presented spontaneous haemorrhage, We identified 49 patients with spontaneous anticoagulation-related haemorrhages of the central nervous.

Results: The international normalized ratio (INR) was 2.5±0.7. Upon admission to the hospital only two patients with prosthetic valves had a supratherapeutic INR (3.7 and 4.0) that most likely contributed to her injuries. Treatment options for warfarin reversal include vitamin K 25% (4 patients with INR<2), fresh frozen plasma (10%), prothrombin complex concentrates (65%). Mortality at 24 hours after haemorrhage was 10%, thirty percent in first week and 40% during follow-up. Hematoma enlargement after at first 24 hours after hemorrhagic symptoms and therapy was 25% of patients treated with anticoagulants.

Long-term anticoagulation for the prevention of ischemic strokes after hemorrhage stroke was reintroduced in 40% after 7±4 days (patients with prosthetic valve or high-risk atrial fibrillation).

No one had a symptomatic haemorrhage and only two patients (5%) had new thromboembolic events as transient ischemic attacks during follow-up.

Conclusion: Recurrent bleeding and future thrombo-embolic event rates in patients who require anticoagulation following ICH is insignificant.

Notwithstanding hypertension and anticoagulants must be carefully and rigorously monitored (INR) in these group of high-risk patients.

545 Intracerebral/subarachnoid haemorrhage and venous diseases

CEREBRAL VENOUS THROMBOSIS: THE ROLE OF DISMETABOLIC CONDITIONS

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Introduction: Lipids, in particular elevated triglyceride levels, through effects on blood viscosity and coagulation cascade, may contribute to the development of deep venous thrombosis. This association has been investigated in a few studies, with conflicting results.

There might be two major possible mechanisms of action: 1) dismetabolic conditions, such as diabetes, dislipidemia, and in particular hypertriglyceridemia, may alter blood viscosity. 2) Triglyceride levels have an inverse correlation with activated protein C and seems to increase factor VIIc, factor VIII, factor IX, and fibrinogen levels.

The role of lipids in the development of cerebral venous thrombosis (CVT) has been poorly studied.

The aim of the present study was to investigate the association between acute blood lipids and fasting plasma glucose in patients with CVT.

Methods: Out of 16 patients (10 F; 6 M; mean age = 43.9±16.1) admitted to our ward for acute CVT we recorded plasma fasting glucose, cholesterol and triglycerides during the acute phase (T0) and after 6-month follow-up (T1). The metabolic parameters observed in the acute phase were then compared with those of 16 acute stroke patients (controls).

Results: In CVT patients we observed higher concentrations of fasting plasma triglycerides between T0 and T1 (p<0.01) as well as in comparison to controls (p=0.011). No difference was observed for fasting plasma glucose and cholesterol.

Conclusion: Our findings suggest that elevated triglyceride levels may be important in the development of CVT. Total cholesterol and fasting glucose levels do not appear to play a role. Additional studies should be performed to confirm these findings. The recruitment of patients in this study is still ongoing.

Vascular imaging

546 Vascular imaging

TOF-MRA IS RELIABLE TO EVALUATE THE MIDDLE CEREBRAL ARTERY OBSTRUCTION DEGREE IN ACUTE STROKE: AN INTER- AND INTRA-OBSERVER MULTICENTER STUDY

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Introduction: Artery recanalisation is one of the best predictors of good outcome after acute ischemic stroke. Recanalisation could be used as a surrogate marker for outcome when it can be assessed and graded reliably. The purpose of this study was to analyse the inter- and intra-observer reliability of the middle cerebral artery (MCA) obstruction degree on time of flight magnetic resonance angiography (TOF-MRA).
Methods: 91 patients with first ever stroke in the MCA territory were prospectively included in a multicenter study. They underwent MRI with TOF-MRA within 12 hours after symptoms onset. Two blinded observers quantified the MCA obstruction degree on the TOF-MRA according to the adapted Thrombolysis In Myocardial Infarction (TIMI) grading system as complete (3), partial (2), minimal (1) or no (0) obstruction. To limit recall bias, evaluations by the same investigator were performed 15 days apart. Dichotomized (TIMI 0-1 versus 2-3) and ordinal TIMI analyses were performed. Inter- and intra-observer reliability was categorized from poor to excellent depending on kappa values.
Results: The median delay between symptom onset and MRI was 6 hours. Analysis of TOF-MRA was impossible in 2.5% for M1 segment and 7% for M2 segment due to technical limitations. The inter- and intra-observer reliability was good to excellent for the dichotomized TIMI grades (kappa ranging from 0,69 to 0,93) as well as for the ordinal TIMI grades (kappa ranging from 0,72 to 0,96).
Conclusion: The substantial reproducibility of the dichotomized and the ordinal TIMI grading system makes the MRA TOF sequence a reliable tool to evaluate MCA obstruction degree in the clinical practice as well as in clinical research.

547 Vascular imaging

RELATIVE BLOOD FLOW CHANGES MEASURED USING CALIBRATED DOPPLER SPECTRAL POWER AT VARYING HEMATOCRIT LEVELS: AN IN-VITRO STUDY

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Background: An important limitation of transcranial Doppler (TCD) instrumentation is the inability to measure blood flow volume or vessel size. In theory, the power of the Doppler signal is proportional to volume of blood passing through the ultrasound sample volume. Utilizing information from both the power signal and the full spectrum of Doppler frequencies, indices of changes in vessel size and blood flow can be derived. In this study we have carried out a zero-calibration of the flow index values in an attempt to reduce inaccuracies due to inhomogeneous insonation and artefacts. The aim of this in vitro study was to examine the ability of these indices to measure relative changes in flow and vessel size at varying hematocrit values.
Methods: The study was carried out using a closed-loop system. Silicone tubes of 2, 3, and 4 mm diameters were insonated at an angle of 45oC using 2 MHZ probes. Flow was: 320, 240, 150 or 320 ml/min. and hematocrit values were 10, 20, 29 and 42%. Flow indexes (FI) were calculated using specially designed software and cross-section area indexes were calculated by dividing the flow indexes with the maximum velocities.

Results: The flow index (FI) for each tube diameter with a constant hematocrit showed a strong linear correlation with the actual flow rate (r =1 - 0.95). The area index (AI) remained relatively constant at different flow rates and the percentage AI showed a strong correlation with tube diameters (r =1 - 0.96). The AI values varied significantly however, when hematocrit values were increased from 10 to 42%.
Conclusions: This in vitro study has shown that relative changes in blood flow and cross-section indexes may be measured using TCD. However, it is important to take into account changes in hematocrit values when assessing relative flow changes using frequency-weighted power of the Doppler signal.

548 Vascular imaging

DETECTION OF CAROTID ATHEROSCLEROSIS USING A NEW MULTI-PURPOSE PROBE

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Background: Multi-purpose probes may be used in a variety of medical settings. The aim of this study was to compare a newly developed multi-purpose probe to a "state of the art" carotid probe.
Methods: 83 patients, 20 healthy volunteers examined by two physicians alternately using a standard probe (GEVivid 7-M12-12 MHz) or the multi-purposeprobe (GE G9L-9MHz).10 of 20 healthy volunteers were examined twice analyzing within-sonographers reproducibility and 29 other volunteers were examined twice with the G9L probe or the M12 L probe analyzing within-sonographers reproducibility and between – sonographers reproducibility. The physicians were blinded for eachother's Results. Measurements included right and left sides Carotid IMT (CCA, bifurcation, ICA), plaque and stenosis detection and visibility of the vertebral arteries.
Results: A good correlation for IMT measurements using the two probes was found. Left CCA (ICC=0.909) Left bifurcation (ICC= 0.683), left ICA (ICC= 0.751), right CCA (ICC= 0.843), right bifurcation (ICC= 0.783), right ICA (ICC= 0.593). Carotid plaque detection was almost similar for the two probes (kappa= 0.939). All 206 vertebral arteries were correctly detected with the standard probe and 198 (96%) using the multi-purpose probe.The Interobserver and Intraobserver agreements showed no systematic errors.
Conclusion: This new multi-purpose probe can be used to examine atherosclerosis in the carotid arteries eventhough some weaknesses still exist when compared to a "state of the art" carotid probe.

549 Vascular imaging

FLAIR VASCULAR HYPERINTENSITIES IN SYMPTOMATIC ICA AND MCA OCCLUSION- COMMON EPIPHENOMENON OR INDICATOR OF FUNCTIONAL COLLATERAL FLOW? A 3T-MRI OBSERVATIONAL STUDY

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Background: Hyperintense vessel signs (FVH) can be observed on FLAIR-MRI sequences in patients with acute ischemic stroke. It is assumed that FVH represents leptomeningeal collateral blood flow. Aim of this study was to describe the impact of presence and number of FVH on initial infarction morphology and final stroke volume in patients with symptomatic ICA or MCA occlusion.
Methods: The 1000+ MRI imaging database was reviewed for patients with symptomatic stenosis or occlusion of ICA and/or MCA. Vessel occlusions were identified in MRA-TOF and graded with the TIMI score. DWI, FLAIR and PI lesion volume were analyzed. Presence and number of FVH was evaluated in MCA-ASPECT areas. Follow up after 48 hours and 5-7 days was included if available.
Results: 83 patients with ICA or MCA occlusion/stenosis were included in data analysis. FVH were detectable in 74 (89%) of 83 patients (age 74 years; male 53%;

median NIHSS 6). Of those, 44 patients received a complete imaging follow up protocol. Stenosis/Occlusion was located in ICA in 6, ICA and M1 in 10, M1 in 8, M2 in 14 and M3 in 6 patients. Median number of observed FVH was 5 (2-7). Dichotomization in FVH ≤ 4 (group 1) and FVH > 4 (group 2) on admission showed significantly initial larger perfusion deficit in group 2 (77,01 vs. 206,72 cmm; p=0.001), infarction volume (4.84 vs. 21.63 cmm; p=0.084) and corresponding mismatch (42.11 vs. 143.21cmm; p=0.002). Final infarction volume (29.63 vs. 55.21cmm) and NIHSS at discharge (3.5 vs. 6) showed the same trend. Ratio of initial PI deficit and final infarction volume adjusted for initial DWI lesion was higher in group 2 (1.69 vs. 4.26).

Discussion: FVHs are common in symptomatic vessel occlusion and quantity correlates with initial DWI- lesion volume and PI deficit. Regarding the potentially salvable tissue represented by the initial mismatch, proportional infarction evolution was smaller in patients with >4 FVH implicating a functional role of FVH for the tissue at risk.

550 Vascular imaging

QUANTITATIVE ASSESSMENT OF CHANGES IN COMPONENTS WITHIN CAROTID PLAQUES DURING CILOSTAZOL ADMINISTRATION BY USING NON-GATED MAGNETIC RESONANCE PLAQUE IMAGING

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Background: Cilostazol, an antiplatelet agent, is reported to involute carotid plaques, but its effects on intraplaque components are not known. Hence, we quantitatively analyzed the changes within the carotid plaques during cilostazol administration by using non-gated magnetic resonance (MR) plaque imaging.

Methods: We prospectively examined 12 consecutive patients with carotid stenosis (age, 56–78 years). 1.5-T MR plaque imaging and 3D ultrasonography (US) were performed at the baseline as well as at 3 and 6 months after initiating cilostazol therapy (200 mg/d). We obtained radial-scan non-gated axial T1-weighted images with a repetition time/echo time of 500/12 ms. The contrast ratio (CR) of the carotid plaque against the adjacent muscle was measured, and the areas of the intraplaque components, i.e., of fibrous tissue, lipid, and hemorrhage, were calculated using a plaque analysis software package and cutoff values obtained from our previous histopathological correlation study (CR: fibrous tissue, <1.2; lipid, 1.2–1.6; hemorrhage, >1.6). We also measured the volume and gray scale median (GSM) of the plaques by using 3D-US data.

Results: The 3D-US data revealed that the plaque volume decreased (baseline, 0.52±0.41 cm³; 3 months, 0.46±0.36 cm³; 6 months, 0.44±0.39 cm³) and The GSM slightly increased (38.8±25.0; 40.3±26.4; 45.5±25.4) after cilostazol administration. MR plaque imaging revealed that the CR of the plaque tended to decrease after cilostazol administration (1.20±0.18; 1.15±0.13; 1.13±0.09). In addition, the area of the fibrous component tended to increase (58.8±19.8%; 65.0±18.6%; 66.5±19.1%), while that of lipid and hemorrhagic components tended to decrease (lipid: 31.4±14.1%; 28.6±11.7%; 27.6±13.6%; hemorrhage: 9.8±17.5%; 6.4±10.3%; 6.0±6.8%) after cilostazol administration.

Conclusion: Non-gated MR plaque imaging can quantitatively evaluate changes that occur within carotid plaques during therapy.

551 Vascular imaging

INTRACRANIAL VESSEL WALL IMAGING WITH MPIR-TSE AT 7.0 TESLA IN ISCHEMIC STROKE AND TIA PATIENTS

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Background: Little is known about the contribution of intracranial atheroma to ischemic stroke. With conventional angiography Methods intracranial atheroma only become visible when giving rise to luminal narrowing, occurring late due to remodeling of affected arteries (1). We have used 3D Magnetization Prepared Inversion Recovery Turbo Spin Echo (3D MPIR-TSE) (2) to image intracranial vessel wall of patients with increased chance of having intracranial atherosclerosis.

Methods: This study was approved by the IRB of the UMC Utrecht. 19 patients presenting with TIA (n=10) or ischemic stroke (n=9) were imaged after obtaining informed consent. Imaging was performed at 7 Tesla MRI. All patients were scanned with previously described MPIR-TSE sequence (2) (Table). For possible depiction of plaque, gadolinium-containing contrast agent was administered. For confirmation of observed vessels seen on MPIR-TSE images, a TOF-MRA (fast field echo sequence) was added (Table 1).

Table 1

Scan parameter	MPIR-TSE	TOF-MRA
FOV (mm)	220 × 180 × 13	180 × 180 × 110
Acquired resolution (mm)	0.8 × 0.8 × 0.8	0.4 × 0.5 × 0.6
Orientation	transverse	transverse
TR/TE/TI (ms)	6050/23/1770	22/2.5/–
TSE-factor	60	–
NSA	2	1
Magn. prep. mixing time (ms)	250	–
SENSE factor	–	2.5 RL
Duration (min:sec)	12:38	9:40

Results: In 3 patients MPIR-TSE exams lacked quality for vessel wall assessment due to motion artifacts. In the 16 remaining patients, atherosclerotic lesions in intracranial arteries were identified in 4 of 10 TIA patients (40%) and 4 of 6 stroke patients (67%), totaling 25 lesions. Only 3 of 25 lesions resulted in luminal stenosis (Figure 1). 7 of 25 lesions showed enhancement after contrast administration (Figure 1, C). In 6 patients an intracranial lesion was present in an artery of the flow territory in which the ischemic event had occurred.
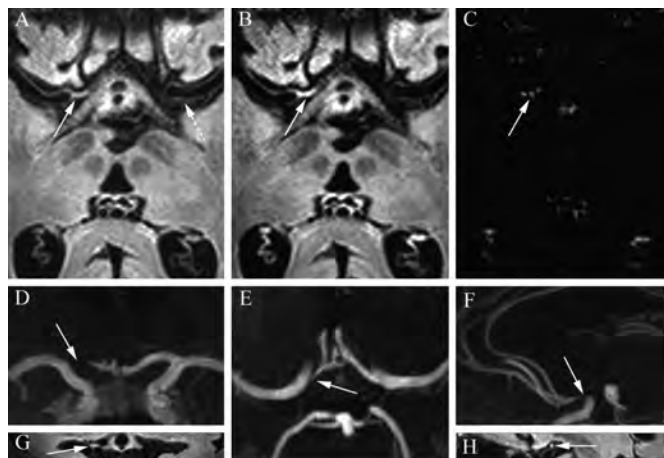
Figure 1. 76-year-old female, TIA left MCA territory. A-B, Transverse MPIR-TSE image, normal MCA vessel wall (dashed arrow) and collapsed A1 segment (arrow), before and after contrast administration. Enhancement of collapsed proximal ACA was visible on subtracted image (C). D-F, Coronal, transverse and sagittal TOF-MRA images show corresponding absence of flow with no patent lumen in proximal part of the ACA (arrow). G-H, coronal and sagittal MPIR-TSE reconstructions.

Conclusion: Intracranial vessel wall and its pathology can be depicted with MPIR-TSE imaging on 7 Tesla MRI in ischemic stroke and TIA patients. This allows studying the role of intracranial atherosclerosis in stroke and TIA in more detail.

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552 Vascular imaging

CAROTID ATHEROSCLEROSIS IS ASSOCIATED WITH LOWER COGNITIVE TEST RESULTS IN A STROKE-FREE MIDDLE-AGED POPULATION. THE TROMSØ STUDY

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Background: Carotid artery atherosclerosis is a major risk factor for stroke and subsequent cognitive impairment. Prospective studies indicate that also subclinical carotid atherosclerosis is associated with a higher risk of cognitive decline and dementia in elderly persons. The relationship between degrees of carotid atherosclerosis and cognitive function in a middle-aged general population is less known.
Methods: In a prospective study we followed a stroke-free middle-aged population of 4371 participants (mean age 59 yrs) who at baseline underwent carotid ultrasound examination and assessment of cardiovascular risk factors and 7 years later tests of cognitive function. Associations between intima-media thickness (IMT), number of plaques and total plaque area and cognitive test scores on verbal memory, digit-symbol coding and tapping tests were assessed in linear regression models.
Results: Presence of plaque and number of plaques were associated with lower test scores on the verbal memory test and on the digit-symbol coding test in the multivariable regression model adjusted for sex, age, education, depression and cardiovascular risk factors. Total plaque area was associated with lower cognitive scores on the verbal memory test, whereas IMT was associated with lower scores on the digit-symbol coding test. No significant association was seen between carotid atherosclerosis and the tapping test scores.
Conclusions: In this middle-aged general population we found that subclinical carotid atherosclerosis measured as IMT, number of plaques and total plaque area were independent risk factors for lower cognitive test scores after 7 years of follow-up.

553 Vascular imaging

INTERNAL JUGULAR VENOUS DRAINAGE IN PATIENTS WITH MULTIPLE SCLEROSIS. DO THEY NEED VENOUS ANGIOPLASTY

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Background: The idea that chronic cerebrospinal venous insufficiency (CCSVI) may cause multiple sclerosis (MS) has been proposed. Our goal was to determine if hemodynamically significant stenosis of IJVs of MS patients could be demonstrated.
Methods: 62 patients with RR-MS (mean age 36 y; 18 male, 44 female) were examined by duplex ultrasound in 2 centers. Morphologic and hemodynamic parameters were measured in the proximal (near to skull base), middle and distal parts (just above the subclavian vein junction) of IJVs both sides.
Results: Mean cross-sectional area in the proximal part of IJV was 0,39 and 0,33 cm^2 (right and left side respectively), the medial part 0,5 and 0,48 cm^2, the distal part 1,12 and 0,82 cm^2, the latter values differed significantly (p<0,001). Time averaged mean velocities (TAMV) in the proximal part were 16,6 and 16,3; the middle part 16,3 and 16,2; the distal part 13,5 and 15,9 cm/s. Volume flows (VFs) in the proximal part were 352 and 305; the middle part 429 and 380; the distal part 815 and 591 ml/min, the latter values differed significantly (p=0,01). Only in 1 patient was the maximal VF as low as 116 ml/min, all other patients had substantially higher values. Reflux was observed in the distal part near the venous valves (136 and 116 ms) and in few cases in the middle part (98 and 115 ms) of IJV but not in the proximal part. We have not found correlation between Tr and VF. The IJVs were scanned in color and power mode from the most proximal part to the distal part just below the junction of subclavian vein: no hemodynamically significant stenosis has been found.
Conclusion: We have not found any hemodynamically significant stenosis. Although about 50% lumen reduction was detected in two patients secondary to venous valve intrusion, the VF was > 300 ml/min both cases proving sufficient venous outflow despite the moderate morphological stenosis. No correlation was found between Tr and VF suggesting that reflux is not an indicator of venous insufficiency but the consequence of venous valve movement. Based on these Results catheter-dilatation does not seem to be a rational approach in the treatment of MS.

554 Vascular imaging

3-TESLA HIGH-SPATIAL-RESOLUTION CONTRAST-ENHANCED MR ANGIOGRAPHY WITH PARALLEL IMAGING IN CEREBRAL VENOUS AND SINUS THROMBOSIS

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Background: Contrast-enhanced (CE) 3D MR venography (MRV) and CE 3D magnetization-prepared rapid acquisition of gradient echo (MP-RAGE) sequences are increasingly used Methods for evaluation of the intracranial venous system. Our aim was to compare CE MRV, 2D time-of-flight (TOF) MRV, and MP-RAGE sequences at 3T for the visualization of cerebral venous thrombosis.
Methods: Patients with suspected or known cerebral venous thrombosis were examined prospectively by TOF MRV, CE MRV and MP-RAGE sequences. In 11 consecutive patients (11 women; mean age, 42.5 years; age range, 25-70 years) with venous thrombosis, scores according to overall image quality, presence or absence (score P), and differentiation (score D) of venous thrombosis were evaluated.
Results: In all measurements, overall image quality ranged between good to excellent. In 20 of 52 venous structures (38.5%), score P was the same at TOF MRV, CE MRV, and MP-RAGE sequences. Venous thrombosis was definitely or almost definitely present or absent with TOF MRV in 20 of 52 (38.5%), with CE MRV in 97 of 99 (97.9%), and with MP-RAGE sequences in 86 of 99 (86.9%) venous structures. In all venous structures with uncertain diagnosis on TOF MRV, thrombosis was definitely or almost definitely present or absent with CE MRV and MP-RAGE sequences. Differentiation of thrombosis was better at CE MRV (score D 3.33) than at MP-RAGE sequences (score D 2.78) followed by TOF MRV (score D 1.32).
Conclusion: CE MRV was superior to TOF MRV and MP-RAGE sequences in visualizing cerebral venous thrombosis.

555 Vascular imaging

FABRY DISEASE: ASYMPTOMATIC CNS IMAGING AND FUNCTIONAL CHANGES IN A PATIENT COHORT

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Background and Objective: Cerebrovascular disease (CVD) is a major complication of Fabry disease (FD) that may progress asymptomatically at its early stages. We used ultrasound scanning of the common carotid arteries (CCA), functional transcranial Doppler (fTCD), brain magnetic resonance imaging (MRI) and angiography (MRA) to screen for structural and hemodynamic central nervous system (CNS) abnormalities in 12 adult FD patients with no clinical evidence of CVD.
Methods: All subjects underwent a comprehensive baseline neurological examination. CCA intima-media thickness (IMT) was measured on ultrasound scanning. Resting blood flow velocities and the hemodynamic response to visual stimulation were assessed by fTCD of the posterior cerebral arteries (PCA). Brain ischemic lesions were identified on MRI, which also allowed estimations of white matter (WM) and gray matter (GM) volumes. The morphology of the major brain vessels and the diameter of the basilar arteries (BA) were evaluated by MRA.
Results: The study cohort included five males (27.4±11.5 years) and seven females (41.7±10.6 years). As compared to healthy controls or normal reference ranges, FD patients had significantly increased mean CCA-IMT (0.77±0.23 mm) and BA diameters (3.66±0.72 mm), lower peak systolic (48.68±10.00 cm/s) and end diastolic PCA resting blood flows, and higher GM/WM volume ratios. Small WM lesions were identified in all patients aged >45 years. Eight patients (three males) showed abnormally elongated and/or tortuous brain arteries. Results of fTCD suggested disturbed neurovascular coupling in the visual cortex.
Conclusions: FD patients may have asymptomatic CNS abnormalities, including fTCD evidence of early cortical vascular dysfunction.

556 Vascular imaging

DETERMINANTS OF CAROTID PLAQUE BEHAVIOR: JUXTALUMINAL VERSUS GLOBAL ECHOGENICITY

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Background: It has been demonstrated that the symptomatic carotid plaques are hypoechoic on ultrasound, whereas the asymptomatic ones are hyperechoic. The aim of this study was to determine whether the juxtaluminal plaque echogenicity might prove to be a better discriminator of the symptomatic and asymptomatic status, as compared to the global plaque echogenicity.

Methods: The analysis involved imaging by duplex of 407 plaques of more than 50% stenosis (312 patients,189 symptomatic and 218 asymptomatic plaques) in a longitudinal fashion, capturing, digitisation and normalisation in a computer in a standard way. The global plaque Grey Scale Median (GSMglobal) was evaluated to distinguish dark (low GSM) from bright (high GSM) plaques. Subsequently, juxtaluminal half plaque area GSM (GSMjuxtaluminal) was evaluated semi-quantitatively in the same computer software. Stenosis was evaluated on duplex.

Results: Symptomatic plaques were associated with median GSMglobal of 8 whereas the asymptomatic ones of 31 (p=0.0001). The corresponding values for the median GSMjuxtaluminal were: 4 for symptomatic plaques and 33 for asymptomatic ones (p=0.0001). ROC curves demonstrated a very marginal superiority of GSMjuxtaluminal over GSMglobal in separating the symptomatic from the asymptomatic plaques (difference between areas: 0.03, p=0.029). Median stenosis for the symptomatic plaques was 80% and for the asymptomatic ones 70% (p=0.0001).

Conclusion: Our Results suggested that the juxtaluminal plaque echogenicity might have a very marginal superiority over the global plaque echogenicity in separating symptomatic and asymptomatic plaques. This position might be clarified in natural history studies of asymptomatic individuals with carotid plaques, having as an end point the development of stroke.

557 Vascular imaging

INTRA AND INTER-OBSERVER RELIABILITY OF A TEMPLATE METHOD TO DETECT INTRACRANIAL OCCLUSIVE DISEASE

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Background: Large artery intracranial occlusive disease (LAICOD) causes 8-10% of strokes in North America and 30-50% in Asia. LAICOID can be detected with high accurancy by CT angiography (CTA), however there is not a validated method. We developed and tested the inter- and intraobserver reliability of a new easy and quick method to detect LAICOID with CTA.

Methods: Post-contrast axial 3 mm-reconstruction CTA images were retrieved from Utrecht Stroke Unit Database. We assessed Intracranial Carotid Artery (ICA) (occlusion or normal) and Middle Cerebral Artery (MCA): M1 (occlusion, stenosis or normal) and M2 (occlusion or normal). Stenosis is defined as any focal vascular narrowing. Occlusion is defined as any stop of contrast in the vessels. Some CTA images of occlusion and stenosis were used as a template during the training and rating of the observers. Observer A assessed 99 CTA scans twice. Observer B rated scans from 1 to 60. Observer C rated scans from 30 to 90. We compared the rating obtained and used K statistic to assess agreement.

Results: We found an almost perfect intra-observer agreement in detection of ICA occlusion (K=1) and in evaluation of M1 (K=0,91: IC 0,83-0,98) and M2 (K=0,92: IC 0,82-1). Inter-observer agreement was almost perfect for detection of ICA occlusion (K=1) and substantial for M1: A vs B (K=0,81: IC 0,67-0,95); A vs C (K=0,72: IC 0,56-0,89); B vs C (K=0,80: IC 0,59-1) and for M2: A vs B (K= 0,79: IC 0,6-0,96); A vs C (K= 0,71: IC 0,5-0,91); B vs C (K= 0,66: IC 0,3-1).

Conclusion: Intra and inter-observer reliability was satisfactory especially for the evaluation of intracranial occlusion of ICA and intracranial occlusion and stenosis of M1. Post-contrast axial 3 mm-reconstruction CTA images can be used as an easy and quick method for the detection of occlusion or stenosis of intracranial ICA and MCA. The method could be used in routine clinical practice and retrospective study.

558 Vascular imaging

PREDICTIVE VALUE OF FLAIR AND DWI FOR THE IDENTIFICATION OF ACUTE ISCHEMIC STROKE PATIENTS WITHIN 4.5 HOURS OF SYMPTOM ONSET – PRELIMINARY RESULTS OF THE PRE-FLAIR STUDY

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Background: A mismatch between acute ischemic lesions detected by diffusion weighted imaging (DWI) and negative fluid-attenuated inversion recovery (FLAIR) was suggested to be indicative of an early stage of stroke in previous single-centre studies. We aimed to identify predictors of lesion visibility on FLAIR in a large prospective multi-centre study.

Methods: Patients with acute stroke and well-defined symptom onset were studied by stroke MRI including DWI and FLAIR. The visibility of acute ischemic lesions on DWI and of corresponding lesions on FLAIR was judged in consensus by two observers. Univariate and multivariate analysis was performed to identify predictors of lesion visibility on FLAIR.

Results: 643 data sets were collected from 10 centers or data bases. 100 data sets (15.6%) had to be excluded from analysis due to bad MRI quality or the presence of multiple infarctions of acute to subacute age precluding attribution of acute symptoms to one distinct lesion. Within the remaining 543 data sets an acute ischemic lesion was visible on DWI in n=516 (95.0%) and on FLAIR in n=271 (49.9%). Patients with visible corresponding FLAIR lesions were compared to patients with negative FLAIR. FLAIR positive patients were younger (63 vs. 70 years, p<0.001), time to MRI was longer (267 vs. 143 min, p<0.001), DWI lesion volume was larger (9.5 vs. 5.7 ml, p=0.001), and severe leukoaraiosis was less frequent (24% vs. 36%, p=0.003). Multivariate analysis identified a longer time from symptom onset to MRI, a larger DWI lesion volume and the absence of severe leukoaraiosis as independent predictors of visibility of acute ischemic lesions on FLAIR.

Conclusion: Time from symptom onset and lesion volume appear to be the main factors influencing the visibility of acute ischemic lesions on FLAIR. Leukoaraiosis has to be taken into account as a potential confounding factor.

559 Vascular imaging

STANDARD CLINICAL BOLUS TRACKING PERFUSION WEIGHTED MRI DATA CAN BE USED TO GENERATE MAPS OF THE MAJOR CEREBRAL VASCULAR TERRITORIES

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Background: The nature and endurance of the collateral blood supply in acute stroke is speculated to play a key role in tissue survival, yet research in this area is limited by the lack of appropriate imaging modalities to characterize and quantify collateral flow. We present the first Results of a novel post-processing technique that can label and quantify the extent of the major vascular territories including the predominant source of collateral supply into the hypo-perfused region using standard clinical bolus tracking perfusion MRI.

Methods: We selected data from two acute stroke patients (sub 6 h) both with M1 occlusions affecting more than half of the MCA territory and no motion artefact in the perfusion acquisition. We applied an algorithm that uses subtle changes in bolus shape across voxels to infer the pathway of flow from the proximal vessels towards the periphery. Labels were assigned to each of the 6 feeding vessels and the vascular territory maps were generated. Each voxel is colored by its dominant source of flow.

Results: See fig. Patient 1 had a complete M1 occlusion with no residual flow visible on MRA. The vascular territory maps indicate the right MCA territory supplied mainly by PCA leptomeningeal collaterals caudally and ACA collaterals rostrally. Patient 2 had acute and 24h imaging. The vascular territory maps show an acute pattern much like patient 1, but returning to an almost completely symmetric distribution between hemispheres at 24h.

| Patient 1 | Patient 2 |
| Right M1 Occlusion | Right M1 Occlusion / Post-Recanalization |

Left MCA — blue
Right MCA — green
Left ACA — red
Right ACA — pink
Left PCA — magenta
Right PCA — cyan

*Non-colored areas indicate insufficient tracer concentration for computation
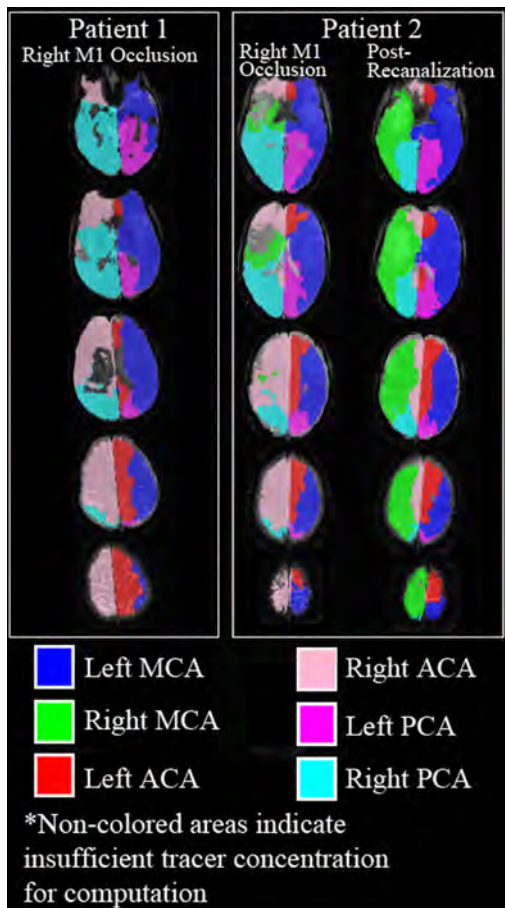
Conclusion: The presented post-processing method offers information on vascular supply territories that complements conventional perfusion maps. We speculate that integration of collateral supply information may enhance the utility of perfusion and diffusion weighted imaging and ultimately lead to more accurate selection of treatment responders. This new post-processing method has the potential to characterise and quantify collateral circulation with no need for additional hardware or longer acquisition times.

561 Vascular imaging

CEREBRAL LUXURY PERFUSION IN EARLY POST-STROKE PERIOD DESPITE PERSISTENT ARTERIAL OCCLUSION

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Background: Cerebral autoregulation (CA) maintains uniform blood flow. In acute ischemic stroke (AIS), CA is usually impaired and, owing to impaired vasomotor response, rapid recanalization of an occluded artery might result in abnormally increased regional blood flow- "Luxury perfusion" (LP). We describe LP and its hemodynamic consequences in a patient with persistent arterial occlusion.
Methods: We present the clinical course and salient radiological findings in AIS due to carotid dissection.
Result: A 49-years old man presented with 1-day history of multiple transient episodes of right-sided weakness. The episodes were precipitated by exertion and each lasted 5-10 minutes. Brain MRI revealed multiple acute infarcts in left middle cerebral artery (MCA) territory. Catheter angiography suggested left internal carotid artery (ICA) dissection. Considerable neurological fluctuations occured during first few days, related to change in blood-pressure and body position. CT perfusion imaging demonstrated prolonged Mean transit-time in left MCA territory with elevated cerebral blood-volume and blood-flow, representing LP (despite occluded ICA). Perfusion and vasodilatory reserve evaluated by HMPAO-SPECT confirmed LP in the left hemisphere (55% counts versus 45% on right on baseline scan. Interestingly, vasodilatory challenge with acetazolamide induced paradoxical

reduction in perfusion in left hemisphere (counts 47% versus 53% on right). Intracranial steal phenomenon (reversed Robin Hood syndrome) was observed during vasomotor reactivity (VMR) assessments with transcranial Doppler. Anti-thrombotics, statins and "head-down" position with liberal intravenous fluids for 2-week resulted in good clinical recovery. No intracranial steal phenomenon was noted on TCD-VMR evaluations at 3 months. He has remained symptom-free during 11 months of follow up.
Conclusion: Luxury perfusion can occur in patients with persistent arterial occlusion & appears protective. However, it may not withstand vasodilatory challenges & contribute towards neurological fluctuations during early phase of AIS. Early recognition & appropriate measures can prevent further tissue injury.

562 Vascular imaging

PROPOSED ANGIOGRAPHIC CRITERIA FOR MEASUREMENT OF VERTEBRAL ARTERY ORIGIN STENOSIS, THE VERTEBRAL ORIGIN TREATMENT WITH ENDOVASCULAR THERAPY (VOTE) METHOD

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Introduction: No standard measurement criteria for vertebral artery origin (VAO) stenosis have been established. We hypothesized that inter-rater agreement of VAO stenosis measurement could be improved with exclusion of the tortuous V1 segment in measuring normal artery diameter.
Methods: A retrospective database of patients with VAO stenosis was accessed and a consecutive series of ten patients was identified. Magnified cervical angiograms were reviewed independently by three experienced angiographers on a digital imaging system and stenosis was measured using a digital caliper. The equation for measurement of VAO stenosis was $[1 - (Dstenosis/Dnormal)] \times 100$, where D stenosis was the diameter of the most stenotic portion of the lesion. The first method allowed unrestricted use of the V1 segment for measurement of Dnormal. In the second method, Dnormal was the diameter of the first, straight, disease-free portion of the V2 segment with exclusion of any region of post-stenotic dilatation. Average interobserver agreement for stenosis variance of 10% and 5%, intraclass correlation coefficient (ICC), and kappa were calculated for each of the two measurement Methods.
Results: Ten consecutive patients with VAO stenosis were reviewed. No tandem lesions were present. Mean stenosis was 71.9% (SD 10.7) with the first method and 66.9% (SD 10.6) with the second method. Average interobserver agreements were 80% with the first method and 87% with the proposed method. ICC showed higher inter-rater agreement if the tortuous proximal V1 segment was excluded in measurement of the normal diameter (ICC = 0.7750), when compared to the unrestricted use of the V1 segment for measurement of normal diameter (ICC = 0.7256). Kappa statistics were the best between the 3 raters with 10% variance with the exclusion of the tortuous V1 segment at 0.73 (overall agreement 87%).
Conclusions: Exclusion of the tortuous V1 portion in measurement of the normal diameter shows improved inter-rater agreement and allows a simple method for measurement of high-grade VAO stenosis. If validated in larger series, these criteria can be a consistent method of measurement in future studies.

563 Vascular imaging

MODIFICATION OF ALBERTA STROKE PROGRAM EARLY COMPUTERIZED TOMOGRAPHY SCORE (ASPECTS) IN STROKE PATIENTS

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Background: Since early signs of major MCA territory infarction in CT is considered as an exclusion criteria in thrombolysis therapy, physicians must be able to reliably identify scans with this finding. However, estimation of ischemic tissue extent is hampered by modest interobserver agreement among experts.
Methods: The modified ASPECTS system was designed by a stroke neurologist. The modified ASPECTS is calculated from two standard axial cuts, one at the level of the thalamus and basal ganglia, and one just rustral to the ganglionic structures. For modified ASPECTS, the territory of MCA is alloted 8 points. The modified ASPECTS is assessed by systematically scoring each of 7 regions (M1-M7) on the CT scan. The evaluated cortical regions M1 to M6 is the same as ASPECTS system. The M7 region includes subcortical structures (internal capsule, lentiform nucleus, external capsule, insular ribbon) and insular cortex. The caudate head is not included in modified ASPECTS because it has dual blood supply from the MCA and anterior cerebral artery. One point is deduced for partial or total involvement by ischemic tissue in any of the M1 through M6 designated regions and two points is deduced

in partial or total M7 region involvement. A score of 8 implies no evidence of new early signs of ischemia in the MCA territory. A progressively lower score indicates more extensive ischemic changes. Modified ASPECT score is dichodomized at <6 or ≥6. Patients with modified ASPECTS <6 have high probability of hemorrhagic transformation of brain infarct following tPA therapy.

Conclusion: Modified ASPECTS is a semiquantitaive, localization weighted estimation of ischemic tissue volume within the MCA territory. We modified ASPECTS to increase the interobserver agreement for estimation of ischemic brain area among experts.

564 Vascular imaging

PULSATILITY INDEX OF CEREBRAL ARTERIES ARE ASSOCIATED WITH INTRACRANIAL CAROTID ARTERY CALCIFICATION

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Background: Pulsatility index (PI) has been postulated to represent vascular resistance distal to an examined artery. The aim of this study was to evaluate the association between cerebral artery calcification and PIs of the cerebral arteries in patients with ischemic stroke.

Methods: We identified 259 consecutive patients with ischemic stroke. Calcification of intracranial carotid arteries were graded and PIs of middle cerebral arteries (MCA) were measured. Patients with proximal internal carotid artery stenosis were excluded.

Results: Univariate analysis revealed that PIs of MCA were significantly correlated with carotid artery calcification (r=0.276, p<0.001) and age (r=0.444, p<0.001). Multiple linear regression analysis indicated that carotid artery calcification was independently associated with PIs of MCA (β=0.028, p<0.01), even adjusted for the potential confounders.

Conclusion: Severity of carotid artery calcification was directly associated with elevation of PI. This findings suggest that PIs may represent arterial stiffening caused by arterial calcification.

565 Vascular imaging

ASSOCIATION OF ANTIEPILEPTIC DRUG THERAPY WITH INCREASED COMMON CAROTID ARTERY INTIMA-MEDIA THICKNESS: A MULTI-CENTER PILOT STUDY

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Background & Purpose: Recent studies have indicated that antiepileptic drug therapy (AED) or epilepsy itself may contribute to acceleration of atherosclerosis in adult epileptic patients. We cross-sectionally evaluated the potential association of AED with asymptomatic atherosclerosis in a pilot multi-center study.

Subjects & Methods: Common Carotid Artery Intima-Media Thickness Thickness (CCA-IMT) was evaluated by means of high-resolution B-mode carotid ultrasound examination in consecutive patients with epilepsy (under AED for at least 3 months) and normal individuals. Demographic characteristics, vascular risk factors and biochemical indices of metabolic profile (blood lipids, fasting blood-sugar homocysteine, folic acid, high-sensitivity C-Reactive-Protein) were documented in all cases.

Results: A total of 35 patients with epilepsy (mean age 36±17years, 53% men) and 35 controls (mean age 35±16years, 48% men) were evaluated. The two groups did not differ (p>0.1) in terms of demographic characteristics, vascular risk factors and biochemical indices. Patients with epilepsy tended to have higher CCA-IMT values (0.64±0.16mm) compared to controls (0.58±0.18mm;p=0.189). Duration of AED tended to positively correlate to CCA intima-media thickening (r=0.229;p=0.186). For the given effect size (0.06mm higher CCA-IMT in epileptic patients) a sample of 260 individuals (130 controls and 130 patients) would be needed to detect a statistically significant difference between the two groups with an alpha value of 0.05 and a power of 81%.

Conclusions: Our preliminary findings indicate that AED may contribute to accelerated atherosclerosis in adult epileptics independent of demographic

characteristic, vascular risk factors and metabolic indices. A sample of 130 patients and 130 controls will be needed to formally test this hypothesis.

567 Vascular imaging

AORTIC ARCH PLAQUE (AAP): A MULTIMODAL IMAGING STUDY

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Background: Atherosclerotic aortic arch plaques (AAP) have been linked to an increased risk of thromboembolic events as a cause of acute ischemic stroke of undetermined etiology. Objectives: The aim of the study is to compare 2 imaging modalities in identifying the AAP in stroke patients with undetermined etiology.

Methods: We performed transesophageal echocardiography (TEE) and multislice computerized tomography (MSCT) of the aortic arch on 30 patients with acute ischemic stroke of undetermined cause from a total series of 150 non-selected patients with acute ischemic stroke studied prospectively by clinical evaluation, laboratory investigations, cranial computed tomography; color coded duplex ultrasonography of the carotid arteries and transcranial Doppler (TCD).

Results: Using transesophageal echocardiography eight patients (29.6%) had atherosclerotic aortic arch plaques, while using Multislice computerized tomography atherosclerotic aortic arch plaques were detected in twelve patients (40%). Atherosclerotic aortic arch plaques were significantly related to older age, male gender, hypertension, ischemic heart disease and low-grade atherosclerotic carotid lesions. Multislice computerized tomography of the aortic arch was more sensitive than transesophageal echocardiography in detecting the site, size and characters of atherosclerotic aortic arch plaques.

Conclusion: Atherosclerotic aortic arch plaques are a frequent finding in patients with acute ischemic stroke of undetermined cause supporting the hypothesis that aortic plaques have embolic potential. In addition, multislice computerized tomography is more sensitive than transesophageal echocardiography in detecting atherosclerotic aortic arch plaques with better characterization of these plaques especially relevant one.

568 Vascular imaging

DETECTION OF INTRACRANIAL ATHEROSCLEROSIS IN GREECE: A PROSPECTIVE TRANSCRANIAL DOPPLER STUDY

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Background & Purpose: Intracranial atherosclerosis (IA) is a potential source of acute cerebral ischemia (ACI) that carries a high risk of recurrent stroke. A recent survey has documented that less than one-third of ACI patients in Europe are admitted in hospitals with all imaging techniques available to detect IA and reported substantial differences between countries (with Greek hospitals having the lowest rate of available neuroimaging modalities for IA detection). To the best of our knowledge, there are no data available regarding the prevalence of IA in Greece. We conducted a prospective Transcranial Doppler sonography (TCD) study to document the prevalence of IA in ACI patients.

Subjects & Methods: Consecutive patients with acute ischemic stroke (AIS) or transient ischemic attack (TIA) were prospectively evaluated with TCD/TCCD over an 18-month period. Demographic characteristics and stroke risk factors were documented. The previously validated criteria of SONIA trial were used for detection of >50% intracranial stenosis with TCD. MRA/DSA was performed to confirm the diagnosis in cases with abnormal TCD findings. Patients with suboptimal temporal windows were excluded.

Results: A total of 156 consecutive patients with ACI (67% men, mean age 58±14years, 60% AIS) were evaluated. IA (detected by TCD and confirmed by angiography) was documented in 15 patients (9.6%, 95%CI:5.5%-15.4%). The location of intracranial stenoses was as follows: M1/M2 MCA (47%), ACA (7%), PCA (13%), TICA (13%) and VA (20%). The only difference between ACI patients with and without IA (in terms of demographics and stroke risk factors) was the higher prevalence of hypertension in IA patients (87% vs. 55%;p=0.025).

Conclusions: Our pilot study indicates that for every 10 patients admitted with AIS/TIA, one has IA as the underlying cause of ACI. These preliminary findings support further collaborative initiatives among Greek stroke physicians to increase the yield of IA detection in patients with ACI.

569 Vascular imaging

SAFETY OF USING CAROTID DOPPLER AS THE SOLE INVESTIGATION TO DETERMINE THE DEGREE OF CAROTID ARTERY STENOSIS REQUIRING CAROTID ENDARTERECTOMY

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Background: Combined data from the ECST, NACSET and the VA trials showed benefit in Carotid Endarterectomy in patients with 50% to 69% stenosis of internal carotid artery in recent ipsilateral embolic stroke and greater benefit in those with 70% or more without near occlusion. Carotid Endarterectomy has a low but recognisable complication rate including mortality of around 1-2% in the first few days. Therefore accurate estimation of the stenosis is of paramount importance to avoid unnecessary surgery. Carotid Doppler (CD) is widely used as a diagnostic as well as a screening tool to identify carotid stenosis.

Method: We retrospectively analysed scans from 36 patients (72 vessels) who had CD and CT angiography of carotid arteries in the same admission for any variations in results. The variation were analysed on the basis of whether the difference would have led to a different clinical decision or not.

Results: There were 49 vessels of less than 50% stenosis, 11 between 50-70%, 7 over 70% and 5 complete occlusions on CT angiogram findings. There were a total of 15 (20.83%) over estimations of carotid stenosis which would have led to an unnecessary surgery and 3 (4.17%) under estimation of completely occluded vessels which again would have resulted in the same. 14 of the 15 over estimations (93.33%) were for 50-70% stenosis and the other over 70% when all were less than 50%.

Conclusion: Though CD is cost effective and less invasive it can be less accurate and very much user dependent. Recent Cochrane review showed that CD for 70-99% stenosis showed a sensitivity of 0.89, (95% CI 0.85 to 0.92); specificity 0.84, (95% CI 0.77 to 0.89) but data for 50-69% stenoses were too sparse to be reliable. Our observation adds evidence to the fact that CD is less reliable especially in the 50-70% stenosis group and should be clarified with a more accurate investigation if surgery is to be contemplated.

570 Vascular imaging

ROLE OF TRANSCRANIAL DOPPLER IN CRYPTOGENIC STROKE. WHERE DOES IT FIT?

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Introduction: Early studies suggest that 40% of patients with acute ischemic stroke have no obvious cause i.e. cryptogenic stroke. Transcranial Doppler (TCD) has been an useful tool to detect right to left shunt (RLS) indicating paradoxical embolism as a possible causative factor for stroke.

Method: A retrospective audit of all patients undergoing TCD at Northampton General Hospital between 2008 and 2010. Basic Demographics, clinical diagnosis, other vascular risk factors, TCD positives and subsequent Trans Oesophageal Echo (TOE) positives, referral to device closure and subsequent complications were noted.

Results: 86 patients underwent TCD (46 females) with a mean age of 44.6 years. Majority were referred from Stroke department (85%) though patients with other diagnoses were referred from cardiology and neurology departments. 40% had a clinical diagnosis of Stroke /TIA with no vascular risk factors, 47% with vascular risk factors and 13% with clinical diagnosis of migraine among those referred for TCD. TCD was positive for RLS in 53% of total patients and 85% of them were subsequently found to be positive in TOE. All TOE positives were referred for RLS closure and nearly one third of total patients who underwent TCD had a device closure for patent foramen ovale. Palpitations and headache (10%) were the common side effects reported post procedure which subsided within 4-6 months post device closure.

Conclusion: From our experience, TCD remains a valuable, non invasive and sensitive screening tool to diagnose RLS prior to more invasive TOE which may not be tolerated in many patients.Nearly one third with cryptogenic stroke were referred for device closure for patent foramen ovale, though reliable evidence from four major ongoing randomised controlled trials are awaited.

571 Vascular imaging

PREDICTION OF CAROTID PLAQUE CHARACTERISTICS BY USING NON-GATED MAGNETIC RESONANCE PLAQUE IMAGING: CORRELATION WITH THE HISTOLOGICAL FINDINGS OF CAROTID ENDARTERECTOMY SPECIMENS

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Background: Electrocardiograph (ECG)-gating method is usually used in carotid plaque imaging; however, it can deteriorate intraplaque contrast because of inappropriate and varied repetition time (TR). Hence, in this study, we attempted to determine whether non-gated magnetic resonance (MR) plaque imaging with appropriately fixed TRs can accurately evaluate intraplaque characteristics by correlating with the histological findings of the specimens excised by carotid endarterectomy (CEA).

Methods: We prospectively examined 40 consecutive patients with symptomatic carotid stenosis who underwent CEA (age, 59–82 years) by using a 1.5-T scanner. Axial T1-weighted images (T1WI) with a TR of 500 ms, and proton density- and T2-weighted images (PDWI and T2WI) with a TR of 3000 ms were obtained using a self-navigated radial scan as the motion correction technique instead of ECG-gating. Signal intensity of the carotid plaque and adjacent muscle were measured, and the contrast ratio (CR) of the former to the latter was correlated with the histological findings of the CEA specimens.

Results: On T1WI, the CRs of the carotid plaques in which the main components were histologically confirmed to be fibrous tissue, lipid, and hemorrhage were 0.54–1.17, 1.10–1.53, and 1.40–2.29, respectively; the CR differed significantly among the 3 components ($p < 0.001$). When the cutoff value was set at >1.15, sensitivity and specificity for discriminating lipid and hemorrhage from the fibrous tissue were 97% and 89%, respectively. In contrast, CRs on PDWI showed remarkable overlaps between the groups (fibrous, 0.84–1.52; lipid, 0.86–1.82; and hemorrhage, 0.96–2.30). On T2WI, CRs of the plaque with lipid were significantly higher than those with hemorrhage (fibrous, 1.51–3.79; lipid, 2.34–5.10; and hemorrhage, 1.47–3.62) ($p = 0.01$).

Conclusion: Non-gated MR plaque imaging, particularly T1WI, can readily predict the intraplaque characteristics of the carotid artery with high sensitivity and specificity.

572 Vascular imaging

PERFUSION CT AS A PREDICTOR OF CLINICAL IMPROVEMENT AFTER INTRAVENOUS THROMBOLYSIS

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Background: Clinical improvement after intravenous thrombolysis has been related to several factors, including age, time after symptoms onset, gender, location and size of the occluded vessel.

Presence of early signs of infarction in plain CT and a poor mismatch measured by MR imaging have also been related with a bad clinical prognosis after thrombolysis. However, CT perfusion has not been established before as a useful clinical predictor after thrombolytic therapy.

Patients and Methods: Between April 2009 and June 2010, all stroke patients in which Perfusion CT was performed in the acute phase were prospectively included in this study.

In each patient, clinical improvement was meassured by NIHSS at admission and discharge, and admission perfusion CT data (including MTT, CBF and CBV) was obtained.

Two main groups were established: intravenously thrombolysed and non thrombolysed. In both main groups, perfusion CT mismatch Results were divided in 5 categories, according to the percentage of mismatch: 0%, 50%, 75%, 100%. In each category, clinical improvement (NIHSS difference mean) in the treated group was compared to a control non-thrombolysed group of similar perfusion mismatch using T student statistical analysis.

Results: In the period of the study, 47 perfusion CTs were performed in acute stroke patients admitted to our hospital. 18 were treated with intravenous thrombolytic therapy (rTPA 0.9mg/kg), while 29 were not.

Difference means of NIHSS (NIHSS at admission-Discharge NIHSS) in the treated group was 8.1 and in the non treated 2.9. T Student for this data was significant with $p<0.05$.

In a subgroup analysis, NIHSS improvement was greater in the thrombolysed 100% mismatch category (T Student with $p<0.05$).

Conclusion: In our series, clinical improvement is superior in treated patients compared to controls. This improvement is related to brain perfusion CT mismatch, being superior in the 100% CT Perfusion mismatch group. CT perfusion mismatch should be evaluated in bigger "n" studies as a predictor of clinical response after intravenous thrombolytic treatment in acute stroke.

573 Vascular imaging

VASCULAR OCCLUSION AS IMAGING BIOMARKER IN SELECTING ACUTE ISCHAEMIC STROKE PATIENTS FOR TREATMENT WITH DESMOTEPLASE

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Background: Desmoteplase is a novel, highly fibrin-specific and non-neurotoxic thrombolytic agent. Evidence of safety and efficacy was obtained in two phase II trials (DIAS and DEDAS). The DIAS-2 phase III trial did not replicate the positive phase II efficacy findings. Post-hoc analyses were performed with the aim to predict treatment responders based upon CT and MR angiography.
Methods: The predictive value of infarct volume and TIMI grade at baseline with respect to drug response measured by clinical outcome at day 90 was investigated using DIAS-2 data. Patients were grouped according to vessel status (TIMI grade) for logistic regression of clinical response, applying the data from DIAS-2 as well as the pooled data from DIAS, DEDAS and DIAS-2.
Results: In DIAS-2, a substantial number of perfusion-selected patients (126/179, 70%) presented with a normal flow or low-grade stenosis (TIMI 2-3) at screening. Detailed Results concerning clinical response in patients grouped by vessel status at baseline will be presented at first time at the ESC.
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574 Vascular imaging

CEREBRAL VASCULITIS: OPTIMIZING VESSEL WALL MRI IMAGING AT 3-TESLA

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Purpose: Conventional MRI findings suggestive of cerebral vasculitis are rather non-specific. These range from vessel irregularities to cerebral parenchymal changes. A more optimized approach would include systematic imaging of the arterial vessel wall, which would allow for standardized follow-up studies to monitor disease progress and response to treatment.
Methods: The MRI sequences are optimized for higher magnetic field scanners, e.g. 3-Tesla MRI, however they can be performed at 1.5-Tesla. In addition to the standard MRI and the MR-angiographic series, the following sequences were performed; isotropic ultrathin heavy-T2-weighted sequence, time-of-flight MR-angiography before and after intravenous gadolinium administration as well as double inversion, dark blood, fat suppressed T2 and gadolinium enhanced T1-weighted images. Co-registration of the sequences provided even more accurate understanding of the pathological process.
Results: Two cases were followed-up by the aforementioned technique. In a documented case of cerebral vasculitis the follow-up revealed progressive stenosis, with obvious wall thickening and enhancement involving the distal segment of the left internal carotid artery as well as the A1- and M1- segments of the ipsilateral anterior and middle cerebral arteries respectively. The images were of good quality and could be reproduced over several follow-up studies.
Conclusion: An optimized MRI technique for vessel wall imaging can allow for standardized follow-up examinations for cerebral vasculitis, thus guiding further diagnostic work-ups and therapeutic decisions.

575 Vascular imaging

PRESENCE OF ASYMMETRY OF INTERNAL CEREBRAL VEINS ON THE FOLLOW UP CT ANGIOGRAPHY IS ASSOCIATED WITH POOR OUTCOME IN ANTERIOR CIRCULATION ISCHEMIC STROKE PATIENTS TREATED WITH INTRAVENOUS THROMBOLYSIS

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Background: Significant numbers of acute ischemic stroke (AIS) patients recover with timely intravenous tissue plasminogen activator (IV-TPA). However, rates & extent of recovery remain variable. Early identification of reliable predictors of functional outcomes is important for planning rehabilitation strategies. We hypothesized that cerebral hypoperfusion due to acute internal carotid or middle cerebral artery occlusions would impair venous drainage. 2 internal cerebral veins (ICV) drain the deep parts of hemispheres and consistently seen on CT angiography (CTA. They are parallel, run very close to each other & minor asymmetric filling can be easily diagnosed. Thus, ICV asymmetry on post-TPA CTA may persist on the follow-up CTA in patients who do not achieve recanalisation with TPA. We aimed at evaluating whether the presence of ICV asymmetry on follow-up CTA can predict the final outcome.
Methods: Consecutive AIS patients treated with IV-TPA from Jan2007 to March2010 were included. Posterior circulation strokes were excluded. ICV asymmetry was assessed in both pre-TPA and follow up CTA. Data were analyzed for the early predictors of function outcome.
Results: Of the total of 1918 AIS patients admitted to our center, 189 (9.9%) eligible cases were treated with IV-TPA; mean age 64±13 years; 102 (59%) males & median NIHSS 16 points. Hypertension was the commonest vascular risk factor in 144 (76%) and 63 (33%) patients suffered from atrial fibrillation (AF). Overall, 96 (51%) patients achieved good functional outcome (mRS 0-1 at 3 months). ICV asymmetry could be assessed only in 107 (57%) and 74 (39%) patients on their pre-TPA and follow up CTA films, respectively. Increasing age (RR1.02;95%CI 0.97-1.01,p=0.02), AF (RR 1.38;95%CI1.04-1.83, p=0.03), pre-TPA NIHSS (RR per 1-point increase 1.09;95%CI 1.04-1.16, p=0.01) score and ICV asymmetry on follow up CTA (RR 3.75;95%CI 2.33-6.06,p<0.0001) were associated with poor outcome at 3 months.
Conclusion: Presence of the asymmetry of internal cerebral veins on the follow up CT angiography in acute ischemic stroke patients treated with IV-TPA can be used as an early predictor of poor functional outcome.

576 Vascular imaging

ANGIOGRAPHIC EVIDENCE OF CEREBRAL PHYSIOLOGIC SHUNTING DUE TO 'LUXURY PERFUSION' IN AN ISCHEMIC BED

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Background: Oxygen extraction decreases in ischemic brain tissue. This causes luxury perfusion phenomenon. Relatively increased blood flow undergoes physiologic shunting. We demonstrate angiographic evidence of this phenomenon.
Case report: 59 year old man suffered subarachnoid hemorrhage due to a ruptured anterior communicating aneurysm. During the course of his care he suffered ischemic injury to the areas of his left hemisphere. Catheter based cerebral angiography was performed to assess for vasospasm. Angiographic images showed early appearance of a cortical vein which overlayed the ischemic gyrus. This was consistent with arteriovenous shunting. This finding was not seen on initial angiogram performed for endovascular coiling of the cerebral aneurysm. We present angiographic evidence of this infrequently reported phenomenon and discuss pathophysiology of luxury perfusion.
Conclusion: Luxury perfusion which can be present in an ischemic tissue causes macrophysiologic shunting of arterial blood. This arteriovenous shunting can be evident on catheter based cerebral angiography.

577 Vascular imaging

DETERMINANTS OF INTRACRANIAL STENOSIS IN AN UNSELECTED POPULATION OF NEUROLOGICAL PATIENTS IN NORTHERN ISRAEL

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Background: There are currently no data on intracranial stenoses in population of northern Israel.
Patients and Methods: Data on demographic and risk factors alongside with TCD data for 1150 consecutive unselected patients hospitalized in the department of Neurology since 2004 were included in the study. The intracranial stenosis was defined as any case when mean cerebral blood flow velocity in any of MCAs was greater than 90 cm/sec. On the whole, there were 133 non vascular patients, 247 patients with TIA and 780 stroke patients.
Results: There were eighty nine patients with and 1071 patients without intracranial stenosis. The patients with intracranial stenosis were older (67.3±12.5 years vs 65.7±12.5 years, ns) and had significantly more frequent vascular risk factors

(hypertension, hyperlipidemia and diabetes), as well as vascular disease (ischemic heart disease). We did not find any ethnic (Arab versus Jewish patients) differences between groups. These findings did not change after adjustment by age and sex.

Conclusions: Our findings emphasize that vascular risk factors (hypertension, diabetes, hyperlipidemia) rather than ethnic disparities are important determinants of intracranial stenosis in population of unselected neurological patients in northern Israel.

578 Vascular imaging

COLLATERAL PATHWAYS IN PATIENTS WITH SYMPTOMATIC CAROTID ARTERY STENOSIS AND SPONTANEOUS CAROTID ARTERY DISSECTION

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Background: Collateral pathways can protect perfusion in the event of severe stenosis or occlusion of an internal carotid artery (ICA). Primary collateral vessels (PCV) are those that can respond quickly to low perfusion pressure with simple reversal of flow. Due to the temporal differences in the installation of low perfusion pressure between patients with symptomatic carotid artery stenosis (SCAS) and those with spontaneous carotid artery dissection (SCAD), the size and patency of PCV may be a critical risk factor for cerebral infarction in p'atients with severe stenosis or occlusion of an ICA.

Materials & Methods: MR angiography was performed in 21 patients with SCAS and 22 patients with SCAD. We evaluated the presence and diameter of the anterior communicating artery (AcA) the A1 segments of the anterior cerebral arteries, the posterior communicating arteries (PcA) and the P1 segments of the posterior cerebral arteries. Pathways were assumed to be present if the diameter of arterial segments was>1mm; Comparison between patients was performed using the χ^2 test.

Results: A balanced configuration was present in 19% of patients with SCAS vs 18.2% in SCAD. There were no more invisible A1 segments (4 vs. 5, p<0.01). The AcA was invisible in 2 patients with SCAS versus 1 patient with SCAD. The most common alteration in PCV was PcA absence (46.6% in SCAS patients vs 52.4% in SCAD patients, p>0.05). Finally P1 absence was present in 1 patient with SCAS and in 1 patient with SCAD. When an alteration in PCVs was present we observed more infarcts and more extension when compared with balanced configuration (p=0.04).

Conclusion: Compromised PCV are equally distributed between patients with SCAS and SCAD. The availability of PCV affects the likelihood of ischemic infarction in the patients studied. The information acquired through MR angiography about PCV patency may provide data with clinical relevance for early management, especially where an endovascular approach is available.

579 Vascular imaging

TRANSCRANIAL DOPPLER MONITORING OF PERFUSION ALTERATIONS IN ACUTE PERIOD OF ISCHEMIC STROKE

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Evaluation of cerebral blood flow with TCD is easy-to-use and comparatively inexpensive diagnostic method. Our aim was to monitor blood flow in the area of cerebral perfusion alterations within acute period of ischemic stroke.

The research involved 32 patients (64,3±4,9 years old) with anterior circulation atherothrombotic or cardioembolic ischemic stroke. T1, T2, DWI MRI was performed within the first 24 hours after the stroke onset. NIHSS examination and TCD were performed daily during the first week and than every 5-7 days within 30 days after the stroke onset.

The postischemic hyperemia TCD-signs (increase of linear blood flow velocities, systolic-diastolic ratio) were found in 19 patients (59%) up to 23 days after the stroke onset and were not accompanied by deterioration of neurological deficit.

The data shows, that cerebral perfusion alterations can last 23 days after the stroke onset, thus the informative period of TCD monitoring is within the 23rd day after the stroke onset. We propose that postischemic hyperemia can be promoted by reperfusion alterations of cerebral circulation.

580 Vascular imaging

COLOR DOPPLER IMAGING (CDI) OF RETROBULBAR VESSELS FINDINGS IN LARGE GIANT CELL ARTERITIS WITH EYE INVOLVEMENT

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Background: Giant cell arteritis is a primary vasculitis that predominantly affects extracranial medium-sized arteries, especially branches of the ECA.

Purpose: The main objective was to assess the role of CDI of retrobulbar (orbital) vessels in the study of three patients with giant cell arteritis with eye involvement.

Methods: We used a sonographer with 8-15 MHz linear probe for CDI of retrobulbar vessels.

Results: All patients presented malaise, temporal headache, tender temporal arteries and laboratory signs of inflammation. The first patient had a left central retinal artery obstruction, and the others had a left anterior ischaemic optic neuropathy. They presented a painless, severe loss of vision of the left eye. Temporal artery histology was positive in all cases. Ultrasound investigation was performed before corticosteroid treatement because prior corticotheraphy may be associated with loss of the histological features of active arteritis. CDI of retrobulbar vessels detected low blood velocities, especially end-diastolic velocities and high resistance index in all retrobulbar vessels in both orbits, for all patients (especially on the affected side with some peculiar ultrasound features). Typical sonographic features in temporal arteritis were "dark halo" sign (vessel wall thickening) associated with stenoses or occlusions of branches of ECA. Interestingly, in all cases the common carotid and the internal carotid arteries were also affected (large giant cell arteritis).

Conclusions: The ultrasound technique is a valuable diagnostic tool when investigating giant cell arteritis.

581 Vascular imaging

CAROTID ARTERY ANATOMY AND GEOMETRY AS RISK FACTOR FOR CAROTID ATHEROSCLEROTIC DISEASE

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Background and Aim: The traditional risk factors for carotid atherosclerotic disease do not account for the asymmetrical nature of carotid atherosclerosis and racial difference in site of atherosclerosis. The aim is to determine if carotid artery anatomy and geometry are independently associated with carotid atherosclerotic disease.

Method: This is a retrospective study of subjects who had CTA between 2006-2007. Demographic variables (age, sex) and traditional risk factors (hypertension, diabetes, hyperlipidaemia and history of smoking) were collected. Cluster logistic regression was used to account for the paired nature of carotid artery disease.

Results: The average age was 69±14 years. The prevalence of vascular risk factors was: hypertension (70%), male (65%), hyperlipidaemia (55%), smoker (34%), ischemic heart disease (34%), stroke (29%) and Diabetes (25%). In the model, the following were found to be independently associated with carotid artery stenosis: radius of internal carotid artery (OR 0.20, 95% CI: 0.14-0.29), ICA angle (OR 1.05 per degree change, 95% CI: 1.04 to 1.07), age (OR 1.05 per year, 95% CI: 1.03 to 1.07), male sex (OR 1.72, 95%CI: 1.08 to 2.8) and smoker (OR 1.85, 95%CI: 1.15 to 2.96).

Conclusion: Carotid artery anatomy and geometry are independently associated with carotid artery stenosis.

582 Vascular imaging

COLOR DOPPLER IMAGING (CDI) OF RETROBULBAR (ORBITAL) VESSELS FINDINGS IN ANTERIOR ISCHEMIC OPTIC NEUROPATHY (AION)

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Background: AION is a segmental infarction of the optic nerve head where structural crowding of nerve fibers and reduction of the vascular supply may

combine to impair perfusion to a critical degree. It may be associated with giant cell arteritis (arteritic AION). Nonarteritic AION is the most common acute optic neuropathy in patients over 50 years.

Purpose: The main objective was to assess the role of CDI of retrobulbar vessels in the study of five patients with anterior ischemic optic neuropathy (AION).

Methods: We used a sonographer with 8-15 MHz linear probe for CDI of retrobulbar vessels.

Results: All patients presented an unilateral painless severe loss of vision with a normal anterior segment examination of both eyes. Only the two patients with arteritic AION presented associated signs: temporal headache, tender temporal arteries and laboratory signs of inflammation. CDI of retrobulbar vessels in their cases supported the evidence of involvement of the entire trunck of the short posterior ciliary arteries (SPCA) in arteritic AION (low blood velocities, especially end-diastolic velocities and high resistance index in SPCA). In contrast, in the nonarteritic AION of the other three patients the impaired flow to the optic nerve head was distal to the SPCA themselves at the level of the paraoptic branches (only one third of the flow of the SPCA) with relatively conservation of the choroidal perfusion (blood velocities and resistance index relatively preserved in SPCA).

Conclusions: CDI of retrobulbar vessels is a valuable diagnostic tool when investigating anterior ischaemic optic neuropathy.

Vascular surgery and neurosurgery/interventional neuroradiology

617 Vascular surgery and neurosurgery/interventional neuroradiology

WALL CHANGES IN CAROTID STENTED ARTERIES: A DUPLEX ULTRASOUND STUDY OVER 2 YEARS
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Objective: We hypothesize that carotid stenting (CAS) could compromise long-term durability inducing a foreign body reaction leading to wall growth, plaques and restenosis, our aim is to compare the morphological characteristics of carotid stented arteries respect to the contralateral native arteries.

Material and Methods: We collected demographic data and risk factors of patients undergoing CAS. Carotid ultrasound was obtained at 6-12-24-36 months. Those patients with at least 24 months ultrasound follow-up were selected. Morfological measures were: intima-media (IMT) in 1 cm to the start of the stent and the distal third of the contralateral common carotid and the presence of new in-stent plaques. We analyze differences between carotid treated/untreated and possible relationships with risk factors.

Results: We included 215 patients (175 men and 40 women) with mean age 68,6±8 a. The IMT measured in the surrounding area of the stent was 0.89±0.30 mm and the contralateral carotid 0.91±0.27 mm, (ns dif). At 24 months only CAS had significant increased 0.092±0.31 (p=0.02). New plaques in-stent appeared in 60 cases (28%) and the presence of HTA and contralateral plaques seems to be related (p=0.031 and 0.027).

Conclusions: Growth of ITM seems to increase faster in the neighborhood of the stent than contralateral carotid artery. In this context, the presence of carotid arteriosclerosis and hypertension may accelerate the development of new in-stent plaques.

Vascular surgery and neurosurgery/interventional neuroradiology

619 Intracerebral/subarachnoid haemorrhage and venous diseases

MOLSIDOMINE TREATMENT IN THE PROPHYLAXIS OF DIND AND DELAYED BRAIN INFARCTION FOLLOWING SUBARACHNOID HEMORRHAGE (SAH)

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Purpose: To investigate the effect of molsidomine on delayed vasospasm-associated DIND and brain infarctions as well as outcome in patients with spontaneous SAH.

Objective: The delayed cerebral vasospasm (CVS) in micro- and macrocirculation is the most important reason for delayed neurological deficits (DIND), brain infarction and bad outcome in patients after SAH. Preventive as well as symptomatic therapies have not been proven to be satisfactory. Molsidomine is a well known NO-donor, and we hypothesized that it would have a positive influence on outcome parameters after SAH.

Materials Methods: N=27 patients with SAH and CVS were treated with molsidomine and compared with n=49 patients with SAH in the ICU under standard nimodipine therapy with or without CVS. Main inclusion criterion was: CVS as demonstrated by TCD (mean flow >120 cm/sec) and/or angiographically under continuous nimodipine therapy. Molsidomine in the highest possible dosage maintaining a MAP > 65 mmHg was used in addition to standard therapy. CCT at the beginning and after treatment were used to assess the frequency of infarction. Clinical outcome was determined at least 3 months after discharge by modified NIHS and Rankin Scales (mRS).

Results: 3/27 molsidomine patients and 25/49 standard patients developed CVS-associated brain infarctions (p=0.0005). At follow up, mean mNIHSS/mRS scores were significantly better in the molsidomine (4.58/1.85) than in the standard (10.26/3.83) treatment group (p=0.017/p=0.0004). Benefit was especially in patients with higher Hunt and Hess grades. Patients died (not due to bleeding) significantly less in the molsidomine (n=1) than in the standard (n=14) treatment group (p=0.014). Except acceptable hypotension there were no serious adverse effects.

Conclusion: Treatment of patients with SAH and CVS with molsidomine in addition to standard care has a significant impact on (a) the occurrence of brain infarction and (b) long term clinical outcome including (c) death.

Vascular surgery and neurosurgery/interventional neuroradiology

620 Vascular surgery and neurosurgery/interventional neuroradiology

PREDICTION OF CEREBRAL HYPERPERFUSION AFTER CAROTID ARTERY STENTING BY PERFUSION CT WITH ACETAZOLAMIDE CHALLENGE

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Background: Cerebral hyperperfusion (HP) is an uncommon but serious complication of carotid artery stenting (CAS). We assessed the efficacy of perfusion CT (PCT) with acetazolamide challenge to identify patients at risk for HP after CAS. **Methods:** We retrospectively analyzed 100 patients (mean age 71 years old, male 91) who underwent PCT before CAS between 2008 and 2010. The average of stenosis rate was 72% and 69 patients had symptomatic stenosis. All patients had pretreatment PCT with rest and acetazolamide challenge to assess hemodynamic compromise. HP was defined as remarkable increase of CBF assessed by PCT or transcranial color sonography after CAS. Cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) were calculated at region of territory of the middle cerebral artery. Changing rate in PCT parameters were calculated in corresponding region on resting and postacetazolamide PCT maps. Perfusion parameters were compared with HP group (n=9) and non-HP groups (n=91). Receiver-operating characteristic curve analysis was performed to determine the most accurate PCT parameter. **Results:** We had 6 patients (6%) with asymptomatic HP and 3 patient (3%) with symptomatic. There were significant differences for mean CBF (36.7 vs 47.5 ml/100g/min, p=0.013), CBV (2.88 vs 2.49 ml/100g, p=0.002), and MTT (5.33 vs 3.77 sec, p<0.001) between HP and non-HP groups. After acetazolamide challenge, mean CBF increased (35.9 vs 57.0 ml/100g/min, p<0.001) and MTT decreased (5.59 vs 3.64 sec, p<0.001) significantly. There were significant differences for changing rate of CBF (-2.0 vs 21.9%, P=0.003) and CBV (2.81 vs 14.6%, P=0.004). The PCT parameters that accurately identified patients at risk for HP was the resting MTT (optimal threshold at 4.75 sec), postacetazolamide MTT (5.00 sec), and changing rate of CBF (3.2%). **Conclusion:** Pretreatment PCT with acetazolamide challenge could identify patients at risk for HP after CAS.

621 Vascular surgery and neurosurgery/interventional neuroradiology

DRUG ELUTING BALLOONS IN THE TREATMENT OF INTRA- AND EXTRACRANIAL INSTENT RESTENOSIS: PRELIMINARY RESULTS

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Background: Intracranial stenosis is a frequent cause of major stroke. For symptomatic stenosis, stents are the favorable therapy, but instent restenosis rates are as high as 30%. Recently drug eluting balloons (DEB) for intracranial use were introduced and are now a therapeutic option. This study assessed technical success rate and mid-term follow up of DEB-treatment for instent restenosis. **Methods:** All patients treated at our university hospital for intra-, or extracranial instent restenosis who were treated with a DEB were included. Follow-up examinations were performed with transcranial and cervical ultrasonic at 1 day, 6 weeks, 3 months after PTA in all patients, after 6 months in 4/7 and after 12 months in 1/7. MR/MRA was performed in selected patients if necessary.

Results: Seven patients were treated with Paclitaxel coated drug eluting balloons (mean age 62 years). Two patients had a restenosis after stent placement in the intracranial vertebral artery, one in the proximal middle cerebral artery, two in the proximal right internal carotid artery, one in the proximal left internal carotid artery and one in the proximal right vertebral artery. The mean stenosis rate after stent placement was 21%. Median time from stenting to the diagnosis of the instent restenosis was 4 months. Mean restenosis rate at time of diagnosis was 68%. PTA with a DEB was feasible in all patients and no intraprocedural complications occurred. The mean residual stenosis rate was 36%. At follow up (mean 6 months) no restenosis was detected. 4/7 showed improvement of residual stenosis grade during follow-up period after PTA. No clinical symptoms related to residual stenosis were observed. **Conclusion:** PTA with drug eluting balloons seems to be a promising therapeutic option of intra-, extracranial instent restenosis.

622 Vascular surgery and neurosurgery/interventional neuroradiology

SNAPSHOT OF TIMING AND DELAYS FOR CAROTID ENDARTERECTOMY IN AN ACUTE GENERAL HOSPITAL IN UK

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Introduction: Carotid endarterectomy is probably the most important and commonly performed definitive procedure for preventing stroke in patients with significant carotid artery occlusion. In recent years, it has been established that the earlier it is done the better. UK NICE guideline recommends surgery within 14 days of symptoms, and more optimistic National Stroke Strategy (UK) suggests for intervention within 48 hours. We wished to find out the level of compliance and reasons for delay in performing surgery at our centre. **Methods:** Medway Hospital is an associated teaching hospital in the Southeast of England serving nearly 0.5 million people. Three of the vascular surgeons regularly carry out endarterectomies at the centre. We looked at the essential surgical data bank, patients case-notes and interviewed the physicians/surgeons, and found that 31 carotid endarterectomies were performed in one year (06.10.09–05.10.10). **Results:** Referrals to surgical team were predominantly through stroke physician (24/31 i.e. 77%). Of the total 31 cases, 25 were symptomatic: 12 non-disabling stroke, 10 TIA, 2 amurosis fugus and 1 other. Five (5/25 i.e. 20%) were referred within two days of their symptoms, and sixteen (64%) within 14 days. Eleven (36%) underwent surgery within 14 days of referral. Eight (32%) had endarterectomy within 14 days of symptoms (none had surgery within 48 hrs). The causes for delay were: lack of theatre time 10, delay in referral 10, delay in presentation 4, delay through patient preference 4, unavailability of surgeon 3, and other emergency cases taking priority 2. **Conclusion & Recommendation:** The Results were better (cf. 27% within 2 wks) than the previous year. The main avoidable reason for delay was lack of theatre time followed by delay in referral time. It was recommended that theatre management team would look into this urgently, and increased liaison between stroke team and surgeons were suggested with a view to immediate referral after imaging.

623 Vascular surgery and neurosurgery/interventional neuroradiology

PREDICTIVE FACTORS OF SUCCESSFUL RECANALIZATION FOLLOWING PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY IN ACUTE ISCHEMIC STROKE PATIENTS

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Background: Successful recanalization with endovascular treatments is the most important factor influencing a good clinical course in acute ischemic stroke patients with intracranial artery occlusion. This study investigated predictive factors of successful recanalization with endovascular treatments using percutaneous transluminal angioplasty (PTA).

Methods: The study comprised 117 acute ischemic stroke patients with intracranial artery occlusion who underwent endovascular treatment using PTA and/or adjuvant therapy between August 2005 and June 2010. Patients with angiographic achievements of Thrombolysis in Myocardial Infarction (TIMI) grade 2 or 3 were classified as the recanalized group (n=72; 62%), and patients with TIMI grade 0 or 1 were classified as the non-recanalized group (n=45; 38%). Clinical features and outcomes were compared between the two groups.

Results: A modified Rankin scale score of 0 to 2 at 90 days was found more frequently in the recanalized group than in the non-recanalized group (50% vs 13%; p<0.001). Univariate analysis showed that atherothrombotic stroke was more frequent in the recanalized group than in the non-recanalized group (32% vs 4.4%; p<0.001). Levels of d-dimer (1.3±1.4 vs 3.4±5.3 ug/mL; p=0.002) and BUN (16.3±6.8 vs 20.3±9.3 mg/dL; p=0.015) were lower in the recanalized group than in the non-recanalized group. Multivariate analysis showed that atherothrombotic stroke, hypertension, and the pretreatment National Institutes of Health Stroke Scale were independent factors associated with successful recanalization (OR=19.8, 0.27, and 0.94, respectively). An Alberta Stroke Program Early CT Score ≥7 was an independent factor associated with successful recanalization in patients with anterior circulation stroke (OR=4.9).

Conclusion: PTA is a useful modality for recanalizing acute atherothrombotic occlusion of the intracranial artery. Lower levels of d-dimer and BUN may be associated with successful recanalization.

624 Vascular surgery and neurosurgery/interventional neuroradiology

TIME-DEPENDENT CHANGES IN VARIOUS STENT DIAMETERS AFTER CAROTID ARTERY STENTING

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Background: Self expanding carotid stents are widely used to treat symptomatic and asymptomatic carotid artery stenoses. We aimed to study postinterventional intraarterial stent remodeling by analysing time-dependent changes in the proximal, middle and distal part of carotid stents.

Methods: Thirty-one carotid stents in 29 consecutive patients (18 men, 11 women) were analysed using duplex ultrasound scanning at days 1-3 and 3, 6, and 12 months after stent angioplasty of an internal carotid artery stenosis. Stent diameters were measured at the proximal and distal end and in the mid-section (at 2-4 points including the minimal diameter) of the stents. Statistical analysis of time-dependent stent diameter changes in the different sections was performed using repeated-measurement ANOVA.

Results: Mid-section and minimal stent diameters increased significantly over time with the highest increase occurring already within the first 3 months after stent placement. In contrast, distal stent diameters showed a significant decrease over time with the highest decrease to be observed within 6 months following stent placement. Proximal stent diameters did not significantly change during the 12-month observation period.

Conclusion: Following endovascular treatment of a carotid artery stenosis, stent diameters undergo differential and time-dependent changes with increasing diameters in the mid-section and decreasing diameters at the distal end of stents. Further analyses will determine the effect of other factors (e.g. gender, symptomatic vs. asymptomatic stenosis) on time-dependent postinterventional carotid stent remodeling.

625 Vascular surgery and neurosurgery/interventional neuroradiology

IDENTIFYING NOVEL MARKERS OF CAROTID ATHEROSCLEROTIC PLAQUE INSTABILITY USING WHOLE-GENOME EXPRESSION MICROARRAY CAN PREVENT STROKES

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Background: The objective of this study was to use Human Whole-Genome microarray analysis to compare the gene expression signature of unstable carotid atherosclerotic plaques. Instability was independently defined using the criteria of; (1) patient symptomatology (symptoms within 2 weeks) (2) evidence of spontaneous embolisation during pre-operative Transcranial Doppler (TCD) monitoring and (3) histological grade 3 & 4 plaques.

Methods: 24 patients undergoing Carotid Endarterectomy (CEA) were recruited; Asymptomatic n=9, Symptomatic n=15. Seven patients had TCD evidence of spontaneous embolisation. Seven plaques were graded as unstable by an independent histopathologist blinded to clinical details. RNA extracted from plaques harvested during CEA were hybridised onto the array. Analysis was performed using GenomeStudio (v1.0). Results of 4 genes chosen due to hierarchical significance and gene ontology processes were validated using TaqMan qRT-PCR.

Results: Three independent analyses were performed, and differentially expressed genes (>1.3 fold, P<0.05 after multiple correction testing analysis) were sought for; (1) recency of symptoms – 177 genes (2) evidence of embolisation – 2294 genes (3) histological grading – 134 genes. A total of 54 novel genes not previously associated with carotid plaque instability were identified in at least 2 of the 3 analyses stated. Genes of interest include motif-chemokine 19 (CCL19), Ephrin Type-B Receptor (EPHB1), Mitogen activated protein kinase 4 (MAPK4), Ubiquitin-Conjugating enzyme E2 (UBE2T).

Conclusions: The differential expression of 54 genes not previously associated with carotid atherosclerotic plaque instability has been demonstrated in plaques that have been independently shown to be histologically and phenotypically unstable. These genes related to apoptosis, cell signalling and inflammation, could represent novel markers i.e. making them targets for pharmacotherapeutic interventions or biomarker discovery.

626 Vascular surgery and neurosurgery/interventional neuroradiology

OUTCOME OF ENDOVASCULAR INTERVENTION FOR SYMPTOMATIC INTRACRANIAL VERTEBROBASILAR STENOSIS

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Background: The risk of recurrent events in patients with symptomatic stenosis in the vertebrobasilar (VB) arteries is high. Angioplasty and stenting are now possible, but carry a significant risk, particularly for intracranial stenosis. Further data on procedural and longer-term risks are needed to assess the feasibility of trials against medical therapy alone. We report our experience with endovascular treatment for intracranial VB stenosis over a 5-year period.

Methods: We followed up all patients who had stenting or angioplasty for symptomatic intracranial posterior circulation stenosis in our institution from 2006-10. We determined the occurrence of procedural complications, recurrent TIA or stroke, and the presence of restenosis or vessel occlusion on imaging (MRA, CTA, DSA).

Results: 27 patients [19 men, mean (SD) age 67 (11) years) were treated from Feb 2006 - Nov 2010. 19 patients (70%) had had recurrent TIA or stroke despite full medical treatment, and 10 patients (37%) had contralateral vertebral artery (VA) occlusion limiting collateral flow. Interventions were done by an experienced neuroradiologist on 22 distal VA and 5 basilar artery stenoses: 12 angioplasty, 8 stents, 5 angioplasty and stent, 2 abandoned (poor access). Periprocedural stroke (1) or death (1) occurred in 2 patients (7%). 3 patients (11%) had periprocedural TIAs. During follow-up [median (range) 14 (1-58) months] 4 patients (15%) had further posterior circulation events (2 strokes, 2 TIAs). The risk of stroke or death within 6 months of the procedure was 15%. The clinical recurrences were not associated with restenosis or vessel occlusion on i.a. angiography.

Conclusion: Our series highlights the risk of ischaemic events during and in the first 6 months after endovascular intervention in patients with intracranial VB stenosis. Trials comparing the outcome of intervention versus best medical treatment alone in this high-risk patient group will be essential and are now under way.

627 Vascular surgery and neurosurgery/interventional neuroradiology

PREDICTIVE FACTORS OF CLINICAL OUTCOMES IN PATIENTS WITH ACUTE ISCHEMIC STROKE UNDERGOING MECHANICAL REVASCULARIZATION WITHOUT THROMBOLYTIC AGENTS

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Background and purpose: Thrombolytic agents can increase the risk of intracerebral hemorrhage in patients with ischemic stroke beyond 3 hours after the onset. We sought to clarify the predictive factors of clinical outcomes in patients ineligible for intravenous thrombolysis undergoing mechanical revascularization without thrombolytic agents.

Methods: We analyzed data from consecutive patients treated with endovascular mechanical revascularization for major cerebral artery occlusion. Patients treated with thrombolytic agents were excluded. Successful recanalization was defined as criteria of Thrombolysis In Myocardial Ischemia 2 to 3 flow at the end of procedure. Favorable and poor outcome defined as a modified Rankin Scale score (mRS) of ≤2 and ≥5 at 3 months.

Results: 116 patients (68 men, 70±13.4 years old) were included in this study. Onset-to-puncture time was 11.4±20.5 (median 6.0) hours, and mean baseline National Institutes of Health Stroke Scale (NIHSS) score was 17.1±8.5. Balloon angioplasty was performed in 100 patients (86.2%), of those, 6 carotid artery stenting and 4 intracranial artery stenting were combined. Nine patients (7.8%) were treated with only microcatheter passing through lesion and seven (6.0%) were treated with thrombus aspiration. Successful recanalization was observed in 72 patients (62.1%). Symptomatic intracerebral hemorrhage occurred in 5 patients (4.3%); 3 (2.6%) of these were parenchymal hematoma type II. Favorable and poor clinical outcomes occurred in 35.3% and 38.8%, and mortality was 13.8%. In multivariate analysis, baseline NIHSS score (OR 0.80, P<0.001) and successful recanalization (OR 4.71, P=0.02) were independent predictive factors for the favorable outcome. Also, baseline NIHSS score (OR 1.11, P=0.003), occlusion of internal carotid artery or basilar artery (OR 5.39, P=0.005), successful recanalization (OR 0.24, P=0.01), and serum creatinine level (OR 4.03, P=0.03) were the predictors of poor outcome.

Conclusion: Endovascular mechanical revascularization without thrombolytic agents can be a feasible treatment in patient with acute ischemic stroke, and can avoid risk of intracerebral hemorrhage.

628 Vascular surgery and neurosurgery/interventional neuroradiology

PRIMARY STENTING FOR ATHEROSCLEROTIC STENOSIS OF VERTEBRAL ARTERY ORIGIN: CLINICAL RESULTS AND RESTENOSIS RATE

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Purpose: To report safety, and efficacy of primary stenting for atherosclerotic vertebral artery origin stenosis with follow-up angiogram to determine the incidence of restenosis.

Material and Methods: 49 patients (mean age: 68years, range: 42-87, M:F=26:23) with symptomatic vertebral artery origin stenosis were treated by using endovascular stent insertion in our institution between March 2005 and March 2010. Follow-up angiogram (mean 13months, range 3-34months) was available in 20 patients. We evaluated restenosis divided into insignificant (0-25%), mild (26-50%), moderate (51-75%), and severe (76-100%).

Results: Technical success (<20% residual stenosis) was in all 49 patients (100%) including 3 cases of double stent. Symptom improvement achieved in 47 patients (96%). Three patients (5%) had subacute in-stent thrombosis with posterior circulation infarction on DWI. There was no procedure-related mortality. On follow-up angiogram, insignificant restenosis noted in 55% (n=11) of patients, mild restenosis in 15% (n=3), moderate restenosis in 10% (n=2) and severe restenosis in 20% (n=4). Four patients with recurred dizziness and restenosis on follow-up angiogram underwent successful additional stenting (n=3).

Conclusion: Primary endovascular stenting is safe and effective treatment option for atherosclerotic vertebral artery origin stenosis. Relatively high recurrence rate was noted but treatable by additional stenting. Especially, drug eluting stent seem to be effective in reducing restenosis rate.

629 Vascular surgery and neurosurgery/interventional neuroradiology

THE RELATIONSHIP BETWEEN MRI/PWI FINDINGS AND 3-MONTH CLINICAL OUTCOME OF THE ACUTE ISCHEMIC PATIENTS WHO UNDERWENT ENDOVASCULAR REPERFUSION THERAPY FOR IC OR MCA OCCLUSION

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Purpose: To investigate relationship between MRI/PWI findings and 3-month clinical outcome following endovascular reperfusion therapy in acute ischemic stroke patients with occlusion of ICA or MCA.

Method: We retrospectively analyzed the patients 1) who were admitted to our institution from 2004 to 2010, 2) with serious neurological symptoms of NIHSS score of 8 or more, 3) who had total occlusion of the ICA or MCA displayed by MRA, and 5) who underwent emergency endovascular reperfusion therapy within 8 hours from stroke onset. We investigated patient's baseline features, MRI findings and 3-month modified Rankin scale (3M-mRS). We used DWI-ASPECTS for DWI findings and time-intensity-curve (TIC) types for PWI findings. Region of interests were set at symmetrical positions of the bilateral MCA territories and time-intensity-curves (TICs) were calculated and the type of TICs were classified into four patterns with time to peak (TP) and value of the peak signal (PV). Comparing the affected side with the contralateral side, we defined type 1 as TPa>TPc and PVa<PVc/2, type2 as TPa>TPc and PVc/2≤PVa<PVc, type 3 as TPa>TPc and PVa≥PVc, and type 4 as TPa=TPc. The primary outcome was mRS of 0-2 at 3 months, and secondary outcome was death within 3 months from onset. We assessed pre-treatment predictors for these outcomes by using logistic regression analysis.

Results: Seventy nine patients were analyzed. Their median age was 77 years, mean admission NIHSS was 17.9, successful recanalization (TICI 2B or 3) was achieved in 38 patients (54.0%).Twenty three patients (32%) had 3M-mRS of 0-2 and 11 patients (37%) died within 3 months. PWI-TICs of type 1,2,3 and 4 were in 13, 37, 21 and 0 patients, respectively. Logistic regression analysis demonstrated that independent predictors of 3M-mRS of 0-2 were DWI ASPECTS and age, whereas independent predictors of death within 3months were type of PWI-TIC (OR, 8.20; 95%CI,1.15-58.30, P=0.035) and admission NIHSS.

Conclusion: In ischemic stroke patients who underwent endovascular reperfusion therapy for the ICA or MCA occlusion within 8hours from onset, type of PWI-TIC was the significant predictor for death within 3months from onset.

630 Vascular surgery and neurosurgery/interventional neuroradiology

A DIVERSE ONE-YEAR ANGIOGRAPHIC OUTCOME OF INTRACRANIAL SELF-EXPANDABLE STENTING

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Objective: Registry studies reported in-stent restenosis (ISR) in 25-37% of patients 6 months after intracranial self-expandable stenting. Longer-term data from a protocol-driven study is lacking.

Methods: Patients who had Wingspan stenting for high-grade (60%-99%) intracranial symptomatic stenoses were recruited to receive a standardized medical regimen. Pre-specified therapeutic targets were low-density lipoprotein (LDL) ≤70 mg/dL, HbA1c ≤6.5%, systolic blood pressure ≤140mmHg, and abstinence from smoking. Dual anti-platelet therapy was begun from 3 days pre-stent until 8 weeks post-stent. Primary end-point was ISR (≥50% luminal diameter loss) at 12 months by digital subtraction angiography. Secondary end-point was progression >20% from immediate residual stenosis.

Results: Of 59 patients (66 stenoses), Wingspan stenting was technically successful in 58 patients. Mean stenosis was reduced from 76% (inter-quartile range (IQR) 70-83%) to 26% (IQR 17-36%). Mean LDL, HbA1c and systolic blood pressure all reached target levels during follow-up. At one year, mean stenosis was 33.6% (IQR 15-45%). ISR was evident in 14 lesions (21.2%); and totally, 18 stenoses (27.3%) had progressed >20%. By contrast, 16 lesions (24.2%) were static, 14 (21.2%) minimally progressed, and 17 (25.7%) regressed with positive remodeling. The risk factor profile in patients with ISR was comparable to those without ISR (Mann-Whitney U test). In a mean follow-up of 40.3 months, the frequency of any TIA, fatal or non-fatal stroke in the treated vascular territory was 6.6%.

Conclusion: Despite a uniform target in risk factor modification, we observed a diverse angiographic outcome at one year. An intensive control of atherosclerotic risks might improve overall stent patency but could not abolish ISR.

631 Vascular surgery and neurosurgery/interventional neuroradiology

STENTING IMPROVES CEREBRAL AUTOREGULATION IN STROKE PATIENTS WITH INTRACRANIAL LARGE ARTERY HIGH-GRADE STENOSIS

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Background: Intracranial stenting is an adjunctive treatment option in symptomatic intracranial large artery stenosis. External counterpulation (ECP) is a non-invasive technique to augment diastolic cerebral blood flow by inflation of pneumonic cuffs placed on the lower extremities, and could be used to assess cerebral autoregulation. We aimed to explore the intermediate-term effects of stenting on cerebral autoregulation.

Methods: In this subgroup study of a randomized controlled study of intracranial stenting, we assessed 14 ischemic stroke patients (8 patients received stenting) 2 years after randomization, who had symptomatic high-grade (≥70%) intracranial internal carotid artery or middle cerebral artery (MCA) stenosis. We performed ECP and transcranial Doppler monitoring of both MCAs. MCA mean blood flow velocities before and during ECP were recorded for 3 minutes. The increase in mean blood flow velocity induced by ECP (cerebral augmentation index [CAI]) was evaluated and compared based on the presence of infarction (symptomatic vs asymptomatic side).

Results: Baseline NIHSS and demographics were comparable between 2 groups. All patients had no stroke recurrence after randomization. MCA mean flow velocities significantly increased during ECP in both groups (stenting group: symptomatic side baseline 57.65 vs ECP 59.85, asymptomatic side 55.90 vs 57.20; non-stenting group: symptomatic 47.90 vs 53.05, asymptomatic 46.15 vs 49.4; all p<0.05). CAI on the symptomatic and asymptomatic sides of stenting group was significantly lower than that of non-stenting group (3.35 ± 3.37 vs 8.43 ± 3.43, p=0.028; 2.22 ± 1.97 vs 7.38 ± 3.25, p=0.01 respectively). CAI was not different between symptomatic and asymptomatic sides in both groups.

Conclusion: Stenting of intracranial atherosclerosis may improve the cerebral autoregulation and ability for the ischemic brain to accommodate flow augmentation in long term.

632 Vascular surgery and neurosurgery/interventional neuroradiology

NEW BRAIN LESIONS AFTER CAROTID REVASCULARIZATION ARE NOT ASSOCIATED WITH COGNITIVE PERFORMANCE

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Purpose: Carotid angioplasty and stenting (CAS) is a potential alternative to endarterectomy (CEA) for patients with significant carotid stenosis. However, diffusion-weighted imaging (DWI) has indicated that CAS is associated with a significantly higher burden of microemboli. The purpose of this study was to assess the potential effect on cognitive functions of new DWI lesions after CEA or CAS.

Methods: This prospective study analyzed the neuropsychologic outcomes after revascularization in 24 CAS and 31 CEA patients with severe carotid stenosis compared with a control group of 27 healthy individuals. All patients underwent clinical examinations, magnetic resonance imaging scans, and an extensive neuropsychologic test battery that assessed six major cognitive domains performed immediately before CEA or CAS, <72 hours after, and at 3 months.

Results: New DWI lesions were detected among 15 of 21 (71%) of the CAS patients immediately after treatment but in only 1 of the 28 CEA patients (4%; P<0.01). All patients with new DWI lesions showed a decline in their performance in the cognitive domains attention, and visuoconstructive functions within 72 hours after treatment.

Individually, however, in none of the cognitive domains did the decreases reach a clinically relevant threshold of z<1.5. Moreover, the cognitive performance did not differ significantly between patients with and without new DWI lesions 3 months after carotid revascularization. The cognitive performance was similar between CEA and CAS patients at all points.

Conclusions: The findings support the assumption that new brain lesions, as detected with DWI after CAS or CEA, do not affect cognitive performance in a long-lasting or clinically relevant manner. Despite the significant higher embolic load detected by DWI, CAS is not associated with a greater cognitive decline than CEA.

633 Vascular surgery and neurosurgery/interventional neuroradiology

CAROTID STENTING CARRIES HIGHER RISKS IN RECENTLY SYMPTOMATIC WOMEN

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Objective: Carotid Endarterectomy confers greatest benefit when performed within 2 weeks of symptoms onset. We investigated the effect of timing on the outcome of patients undergoing carotid angioplasty stenting (CAS).

Methods: This is a retrospective analysis of a cohort of 211 symptomatic patients who underwent CAS in a single tertiary center between 1997 and 2007. The effect of time on the 30-day risk of stroke, death was investigated. Outcomes were compared using the chi-square test and important factors were adjusted for using a logistic regression model.

Results: Among the 211 patients (56 females), 55 underwent CAS within 2 weeks of symptoms onset. Stroke was the qualifying event in 47.3% of the early group vs. 32.1% in the late (p-value 0.04). Fewer patients in the early group presented with retinal TIA (7.3% vs. 24.4%, p-value 0.006). There was no difference in the 30-day risk of stroke or stroke and death in the early vs. late CAS groups. However, females who underwent early CAS had a higher risk of 30-day stroke (23.1%) compared to those who had delayed procedures (2.5%, p-value 0.014). Similarly, higher 30-day risk of stroke occurred in females in the early group compared to males who underwent early CAS (23.1% vs. 2.4%, p-value 0.012). There was no difference in the 30-day risk of stroke or death in females who had early vs. late CAS (23.1% vs. 7.3%, p-value 0.12). Neither age nor the nature of qualifying event modified or confounded the effect of gender on CAS timing. Females had a risk ratio of 30-day stroke = 9.5 (95% CI 1.6 to 57, p-value 0.01) when CAS was performed within 2 weeks of symptoms onset.

Conclusion: Overall, early CAS was not associated with different 30-day risks of stroke, death, or stroke and death. However, females had a significantly higher 30-day risk of stroke if underwent CAS early. This observation need to be further explored by sub-analyses of large carotid revascularization randomized trials.

634 Vascular surgery and neurosurgery/interventional neuroradiology

VERTEBRAL ARTERY OSTIUM STENOSIS: TREATMENT WITH VERTEBRAL ARTERY STENTING – LONG-TERM CLINICAL AND ANGIOGRAPHIC RESULTS

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Background: The optimal management of patients with symptomatic severe vertebral artery ostium (VAO) stenosis is still unclear. Although stent-assisted angioplasty is thought to be a safe treatment option, the main concerns related to treating VAO stenosis with stents have been the rate of restenosis and the uncertain long-term Results. We analyzed the long-term outcome of patients with VAO stenosis who received vertebral artery stenting (VAS).

Methods: From April 2004 to August 2010, the authors performed 210 cases of VAS. 119 of them (M:F, 44:75; mean age 64 with a range of 38 to 82) underwent follow-up conventional angiography or computed tomography angiography with maxium intensity projection image, and were enrolled in this study. All patients were retrospectively analyzed. The indication criteria for this treatment protocol were symptomatic severe VAO stenoses (> 70%) and asymptomatic severe VAO stenoses (> 70%) with incidentally detected infarction in the posterior circulation or with severe bilateral VAO stenosis, contralateral VA occlusion, or contralateral hypoplastic VA.

Results: Technical success was 100%. Angiographic evaluation at a mean 12.2 months (range from 3-68 months) uncovered restenosis in 10 vessels (8.4%) (5 in bare-metal stent group, 5 in drug-eluting stent group) and occlusion in 3 vessels (2.5%) (1 in bare-metal stent group, 2 in drug-eluting stent group). Two patients (1.7%) had recurrent stroke in stented-vessel territories at 3 months with angiographic evidence of in-stent occlusion and 48 months without angiographical evidence of in-stent stenosis after the procedure, respectively.

Conclusion: VAS can be safely and effectively performed with a low rate of recurrent stroke in the territory of the treated vessel.

635 Vascular surgery and neurosurgery/interventional neuroradiology

SUPERFICIAL TEMPORAL ARTERY- MIDDLE CEREBRAL ARTERY BYPASS IN PATIENTS WITH SEVERE STENO-OCCLUSIVE DISEASE OF INTRACRANIAL CAROTID AND MIDDLE CEREBRAL ARTERY

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Background: EC/IC bypass in patients with symptomatic carotid occlusions did not show reduction in risk of stroke recurrence. Subsequent studies found that superficial temporal artery-middle cerebral artery (STA-MCA) bypass could be beneficial in patients with impaired cerebral vasodilatory reserve (CVR). We evaluated CVR in patients with symptomatic & severe steno-occlusive disease of intracranial carotid (ICA) or MCA and selected patients who could benefit from STA-MCA bypass surgery.

Methods: Patients with severe steno-occlusive disease of intracranial ICA or MCA were screened with transcranial Doppler (TCD) for their CVR by using breath-holding index (BHI). Breath-holding index (BHI) <0.69 constituted impaired CVR. Patients with impaired BHI were evaluated with acetazolamide-challenged HMPAO-SPECT imaging. We excluded artery-to-artery embolization by extended TCD monitoring for spontaneous emboli. Patients with significantly impaired metabolic perfusion/CVR on SPECT were offered STA-MCA bypass surgery. CVR was reevaluated in all patients at 6 months and they were followed up for cerebral ischemic events.

Results: 112 patients (79 males, mean age 57yrs; range 23-79yrs) fulfilled our TCD criteria of inadequate CVR. 35 (31%) patients demonstrated intracranial steal phenomenon (reversed Robin Hood syndrome) with a median steal magnitude of 17% (inter-quartile range, IQR 10). Acetazolamide-challenged SPECT demonstrated impaired CVR in 63 (56%) patients and 39 of them underwent STA-MCA bypass surgery. There were no perioperative complications. TCD and SPECT repeated at 5±2months showed significant improvement in CVR in patients who underwent STA-MCA bypass surgery. During follow up (mean 17months; range 3 to 37months), 34/73 (47%) cases managed with best medical therapy developed cerebral ischemic events. After STA-MCA bypass, only 4 of the 39 (10%) cases developed subsequent events (absolute risk reduction 37%, p=0.002).

Conclusion: Symptomatic severe intracranial steno-occlusive disease with impaired CVR carries high risk of cerebral ischemic events. STA-MCA bypass in carefully selected patients Results in significant reduction in stroke recurrence.

636 Vascular surgery and neurosurgery/interventional neuroradiology

STENT-ASSISTED ANGIOPLASTY IN PATIENTS WITH MOYAMOYA SYNDROME: MID-TERM CLINICAL AND ANGIOGRAPHIC FOLLOW-UP RESULTS

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Background: To report mid-term clinical and angiographic follow-up Results of stent-assisted angioplasty for patients with moyamoya syndrome.

Methods: Between May 2002 and May 2010, stent-assisted angioplasty was performed in ten patients (M:F=3:7, mean age: 44 years). They were all symptomatic (transient ischemic attack (TIA) in eight and ischemic stroke in two patients). Drug-eluting stent was used in all patients except one. We retrospectively analyzed technical success, the procedure-related complication, and the clinical and angiographic follow-up results.

Results: Technical success was achieved in eight patients. There were two vessel ruptures during procedure. One patient was rescued without neurologic complication using temporary balloon occlusion and another stent insertion. The other patient was rescued without neurologic complication after intentional middle cerebral artery occlusion using induced thrombosis. There was no procedure-related mortality or morbidity. There was no more TIA in all patients immediately after procedures. Angiographic follow-up was available in seven patients (mean: 14.7 months, range: 3-33). Instent restenosis developed in three patients and all were symptomatic. One patient showed instent restenosis on 7, 13, and 19 month after initial stenting and after 4th angioplasty, restenosis did not develop. Another patient showed restenosis on 7 month after initial stenting and after angioplasty, restenosis did not develop on serial angiographic follow-up up to 33 month after initial stenting. The other patient showed restenosis on 6 month after initial stenting and after angioplasty, restenosis did not develop on 3 month follow-up angiogram. Clinical follow-up was available in all patients (mean: 31.7 months, range:8-72). There were TIAs in three patients with restenosis. There was no bleeding or stroke in all patients.

Conclusion: Stent-assisted angioplasty in patients with moyamoya syndrome showed higher rates of vessel rupture and restenosis. However, stent-assisted angioplasty could be another treatment option for some patients with moyamoya syndrome in the future. Further study should be necessary.

637 Vascular surgery and neurosurgery/interventional neuroradiology

ENDOVASCULAR TREATMENT IN ACUTE BASILAR OCCLUSION: EXPERIENCE IN STROKE CENTER HOSPITAL GERMANS TRIAS I PUJOL-HOSPITAL DEL MAR (BARCELONA)

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Background: Acute basilar artery thrombosis is a severe stroke subtype with a high case fatality rate. Early recanalization is the most important prognostic factor for good outcome. Recanalization strategies include intravenous and intra-arterial thrombolysis. Patients must be admitted to specialized stroke centers although the superiority of endovascular treatment is not clear. It seems that intravenous thrombolysis followed by on-demand endovascular mechanical thrombectomy is the best option.

Methods: Between March 2008 and November 2010, we analyzed Results of endovascular treatment in patients with acute basilar occlusion in Stroke Center Hospital Germans Trias i Pujol-Hospital del Mar. Demographic data, stroke subtypes, clinical data, occlusion site, treatment administered and outcome were registered.

Results: 23 patients were treated. Mean age was 63.5±11.2, 69.6% were male. Median initial NIHSS was 13.5 (8,25). Mean initial symptoms-groin puncture time was 8.55 hours. 9 patients received intravenous thrombolysis prior to endovascular therapy (39.1%). Overall recanalization was achieved in 16/23 patients (70%). Independence (mRS≤2) was achieved in 40.9%. Mortality rate was 38.1%. Only one patient suffered a symptomatic intracranial hemorrhage (4.3%). Patients with previous endovenous treatment had better outcome that primary endovascular therapy, with more recanalization (88.9 vs 57.1, p=ns), more independence rates (75 vs 21.4%, p=0.014; OR 3.1) and less mortality (0% vs 57.8, p=0.01; OR 0.42).

Conclusion: Results in our center are similar to other series. Low complication rate was observed. Outcome is better if endovascular treatment is preceded by intravenous thrombolysis. In stroke centers is important not to delay the endovenous fibrinolytic therapy. It is necessary to increase the number of patients to confirm these results.

638 Vascular surgery and neurosurgery/interventional neuroradiology

PERIPROCEDURAL OUTCOME IN PATIENTS TREATED WITH CAROTID ARTERY STENTING: HOW MUCH DOES EXPERIENCE MATTER?

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Background and purpose: To evaluate periprocedural efficacy, safety and predictors of outcome in a single-center series of patients treated with carotid angioplasty +/- stenting (CAS).

Methods: Data about 486 consecutive patients (mean age ± standard deviation: 71,3±7,8 years; 366/486, 75% male) and 524 procedures, practiced between 1996 and 2010 by three interventional neuroradiologists of the Department of Neuroscience of Pisa, were retrospectively analyzed. Efficacy was defined as the absence of significant residual stenosis (lower than 30% according to NASCET criteria) at the end of the procedure. Safety was assessed through a combined endpoint (stroke/death), referring to events occurred within 30 days after CAS. As predictors of outcome, the presence of symptoms related to stenosis and procedural features (degree of stenosis, plaque ulceration, controlateral carotid occlusion, angioplasty alone vs angioplasty and stenting, use of cerebral emboli protection device, centre experience) were considered.

Results: CAS was successful in 504/524 cases (96.2%); unsuccessful procedures occurred more frequently in case of angioplasty alone rather than angioplasty and stenting (13/61, 21.3% vs 7/463, 1.5%; odds ratio 17.64 with 95% confidence interval 6.69-46.06). 17/524 (3.2%) CAS met the combined safety endpoint: stroke in 2.4% (including 4 cases with disabling strokes) and death in 0.8%; the rate of disabling stroke/death was 1.5%. Symptomatic stenoses were more prone to stroke/death than asymptomatic (9/178, 5% vs 8/346, 2.3%; odds ratio 2,25 with 95% confidence interval 0.86-5.87); disabling stroke/death occurred in 4/178 (2.2%) symptomatic and in 4/346 (1.2%) asymptomatic stenoses. Centre experience was inversely related to the rate of stroke/death (R2=0.9375), passing from 5.5% after 100 CAS to 2.8% after 500 CAS; as for disabling stroke/death (R2=0.9386), the rate was 4% after 100 CAS and 1.6% after 500 CAS.

Conclusions: Our data support the hypothesis that CAS is an effective and safe revascularization procedure both in symptomatic and in asymptomatic patients, if effected in experienced centres.

639 Vascular surgery and neurosurgery/interventional neuroradiology

BEYOND IV RTPA: ENDOVASCULAR TREATMENT OF ACUTE ISCHEMIC STROKE BY MECHANICAL MEANS IS SAFE AND EFFICIENT

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Background: To report interim data of a prospective single center database aiming at detailing the safety and efficacy of the endovascular treatment in patients with acute stroke due to occlusion of large extra- or intracranial arteries, considered unsuitable for intravenous thrombolysis.
Methods: Between January and December 2010, 93 patients (44 women, 49 men, mean age 67.4±13.6 years, mean ± SD), underwent an endovascular treatment of acute ischemic stroke in a single center. We analyzed time intervals from clinical onset to first DSA run and to recanalization, NIHSS scores pre, and post treatment, and mRS scores post treatment and at 90 days. Further we recorded the extent of collaterals, Thrombolysis in Cerebral Infarction (TICI) score for target vessel, and procedural complications.
Results: The interval from clinical onset to first DSA run was 357±284 minutes; the interval from stroke onset to recanalization was 484±278 minutes. Early recanalization after treatment (TICI 2a or higher) was achieved in 91% of patients. Mean pre intervention NIHSS score was 13.1±6.7. In 43 patients (46%) NIHSS improved by >3 points. 11 patients deteriorated by more than 3 NIHSS points. So far, 71 patients have completed 90-day follow up. An excellent outcome (mRS of 0 or 1) was reached by 41%, correlated with age (p = 0.59), NIHSS pre (p = 0.58), extend of collaterals (p = 0.42) and TICI (p = 0.18). 30 day mortality rate was 7.5% which correlated with NIHSS pre intervention > 20, severe non cerebral comorbidity, missing collaterals and failure to recanalize the target vessel.
Conclusion: Patients with acute occlusion of large extra- and intracranial vessels are suitable candidates for endovascular treatment. In our series, a >90% rate of target vessel recanalization could be achieved. The rate of procedural failures and complications is low. Good collaterals are a key prognostic factor outweighing even timing of treatment.

640 Vascular surgery and neurosurgery/interventional neuroradiology

REPERFUSION INJURY AFTER STENTING FOR INTRACRANIAL ARTERY STENOSIS

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Background: Cerebral hyperperfusion injury (CHI) is often seen with revascularization of large extracranial vessels such as extracranial carotid artery stenting or endarterectomy. With the advent of revascularization strategies of intracranial vessel stenosis, reperfusion injury is also noted in this group. It is important to outline angiographic predictors and clinical parameters of CHI in this group. We describe four patients with severe intracranial arterial stenosis due to atherosclerotic disease (3 patients) and vessel dissection (1 patient) and hyperperfusion injury after revascularization with stenting and angioplasty.
Methods: Database for patients undergoing intracranial stenting at our institution was reviewed. Patients with CHI were identified and a review of the records was performed.
Results: 196 patients underwent intracranial stenting with angioplasty or angioplasty alone between August 2006 and May 2010. Four patients (4/196; 2.06%) with subsequent CHI were identified. Three were men; mean age was 60.7 years (range 41-77). 3 patients had intracranial hemorrhage as a complication. One patient had cerebral edema and seizure. All patients had arterial stenosis greater than 90%. Residual stenosis was between 20% and 26% for all lesions. All patients underwent stent placement with balloon angioplasty. No intra-operative complications occurred. Symptoms of CHI were noted within 24 hours of the procedure in all four patients. Three of the four patients had systolic blood pressure exceeding 140 mmHg in the postoperative period of 24 hours. Permanent neurologic deficit occurred in 2 patients. There were no mortalities.
Conclusion: Cerebral hyperperfusion injury is an uncommon complication of stent placement and angioplasty for intracranial vessel stenosis and occurs within

24 hours of the procedure. However, it can have severe morbidity when it occurs. Inability to maintain strict blood pressure management goals may be a contributing factor in CHI.

641 Vascular surgery and neurosurgery/interventional neuroradiology

ASSESSMENT OF THE CEREBRAL VASOMOTOR REACTIVITY RESTITUTION USING THE TCD SONOGRAPHY AFTER EXTRA-INTRACRANIAL BYPASS IN PATIENTS WITH ISCHEMIC STROKE DUE TO CHRONIC INTERNAL CAROTID ARTERY OCCLUSION

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Background: Extra-intracranial (EC-IC) bypass may be of benefit in patients presenting with ischemic stroke due to chronic internal carotid artery (ICA) occlusion with impaired cerebral vasomotor reactivity (CVR). Several Methods are being used to assess CVR, including transcranial Doppler (TCD) sonography. The aim of the study was to assess (1) the restitution of CVR using the TCD after EC-IC bypass in patients presenting with ischemic stroke due to chronic ICA occlusion, (2) time interval surgery-CVR restitution and (3) the dependency of CVR restitution on patient age.
Methods: Study group consisted of 12 patients (11 males, 1 female; age 60-68, mean 60.7±5.1 years) presenting with ischemic stroke due to chronic ICA occlusion with impaired CVR according to the TCD examination, who underwent EC-IC bypass surgery. CVR was assessed in a 3-month intervals after surgery, using the TCD examination, including breath-holding/hyperventilation test (BH-HV) and breath-holding index (BHI). Complete CVR restitution was defined as a normal result of both BH-HV and BHI test and partial as a normal result of at least one of these TCD tests. Mann-Whitney U-test was applied when assessing statistical significance.
Results: Complete CVR restitution was found in 7 (58.3%) patients 3-27 (mean 6.0±8.4) months after the EC-IC bypass and partial CVR restitution in 5 (41.7%) patients 3-14 (mean 3.0±4.9) months after the surgery. The mean age of patients with achieved complete CVR restitution was 60.0±5.9 years versus 60.0±4.2 years in patients with achieved partial CVR restitution (p>0.05).
Conclusions: In the presented study, at least partial CVR restitution was found using the TCD in all ischemic stroke patients with chronic ICA occlusion and impaired CVR, who underwent EC-IC bypass surgery. The level of CVR restitution was not dependent on patient age.

642 Vascular surgery and neurosurgery/interventional neuroradiology

THE INFLUENCE OF THE MEDICAL PRETREATMENT FOR POSTOPERATIVE COMPLICATIONS AFTER CAROTID ARTERY STENTING

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Background and Aims: Previous studies have indicated that using antiplatelets and statins has resulted in benefit on cardiovascular outcome after carotid surgery. We aimed to study the influence of the medical pretreatment for postoperative complications after carotid artery stenting (CAS).
Methods: We investigated 63 patients with significant carotid stenosis (47male; mean age 61±9 years). All of them were suffered from arterial hypertension, and coronary artery disease was revealed in 38 (60%), congestive heart failure in 52 (82%), previous stroke in 32 (50%), intermittent claudicating in 11 (17%) ones. The lipids profile, 24-hour blood pressure (BP) monitoring and brain DW-MRI were performed before and at 1-2 days after CAS. Postoperative cardiovascular events were recording during 1 month.
Results: Despite on multiple atherosclerotic lesions only 49 (77%) patients had pretreatment with antiplatelet agents, 16 (25%)–statins, 26 (41%) – ACEI, 19 (30%) – beta-blockers. At baseline mean value BP was 138±14/81±9 mmHg, total cholesterol level was 5,8 (4,7;7,0) mmol/l. At 30 days we recorded 3 TIA, 2 minor stroke, 3 cardiovascular events. Postprocedural silent ischemic brain lesions

(PSIBL) are detected in 26 (41%) patients, its formation correlated with triglycerides and LPHD plasma levels (p=0,04). Moreover PSIBL associated with increased variability of systolic and diastolic BP in day-time and nocturnal variability of diastolic BP: respectively, 17,9 (16;18);12,4 (9,5;14,3) and 11,7 (11;12) vs 13,3 (10,7;16), 9 (7,2;11) and 7,4 (6,7;9) in patients without PSIBL (p<0,04).

Conclusions: While new clinical cerebro- and cardiovascular events are infrequent, PSIBL are detected on MRI in more than 40% patients after CAS. Routine medical treatment patients with multiple atherosclerotic lesions aren't in accordance to current guidelines for management of those. Improving of medical pretreatment to achieve lipids and BP target levels may benefits outcomes of CAS.

643 Vascular surgery and neurosurgery/interventional neuroradiology

OUTCOME AND RESTENOSIS AFTER MICROSURGICAL CAROTID ENDARTERECTOMY IN 586 PATIENTS

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Background: Carotid endarterectomy (CEA) can reduce the risk of stroke for >60% asymptomatic and for >50% symptomatic carotid stenosis.

Methods: We report the Results of 586 consecutive patients treated with CEA over an eleven-year period (1998-2009).CEA was performed microsurgically without routine patch implantation under general anesthesia with continuous transcranial Doppler and somatosensory evoked potential monitoring. Cross clamping was performed under EEG burst-suppression and adaptive blood pressure increase. Follow up was performed by an independent neurologist. Mortality at 30 days and morbidity such as major and minor stroke, peripheral nerve palsy, hematoma and cardiac complications were recorded. Restenosis rate was routinely assessed using duplex sonongraphy 1 year after surgery.

Results: 411 (70.1%) of the 586 patients were men, and 49.7% stenoses were on the right side. 439 patients (75%) had symptomatic and 147 (25%) asymptomatic stenoses. Median age was 69.7 years in symptomatic and 68.8 years in asymptomatic patients. A major perioperative stroke occurred in 5 patients (0.85%), 4 (0.91%) in symptomatic and 1 (0.68%) in asymptomatic patients. Minor stroke was recorded in 6 patients (1.0%), 4 (0.9%) in symptomatic and 2 (1.3%) in asymptomatic patients. Two patients with symptomatic stenoses died within 1 month after surgery. Reversible peripherial nerve palsies occurred in 9 (1.5%) patients and perioperative myocardial infarction in 9 (1.5%) patients as well.

High grade re-stenosis >70% at one year was observed in 3.2% (19/586): 2.7% (12/439) in symptomatic and 4.7% (7/147) in asymptomatic patients.

Conclusions: Carotid endarterectomy when performed in a team using a standardized operative and anesthesiological management has a low morbidity and mortality rate. The re-stenosis rate was low in comparison with other surgical series and carotid artery stenting.

644 Vascular surgery and neurosurgery/interventional neuroradiology

OUR DEPARTMENT'S STRATEGY AND AN IMPROVED SURGICAL TECHNIQUE FOR THE TREATMENT OF PARACLINOID ANEURYSM

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Background: Operations for paraclinoind aneurysms involve removal of the anterior clinoid process (ACP); however, the conventional method of drilling for removal of the ACP could cause major complications, such as damage to the optic nerve or internal carotid artery (ICA). In addition, the surgical strategy varies depending on the direction of the aneurysm. We present an improved surgical technique using videography and the Results of the operations conducted at our department.

Subjects: Thirty-nine patients with paraclinoid aneurysm, in whom surgical treatment of the aneurysm with extradural removal of the ACP was performed between May 2004 and December 2010 (direction of the aneurysm as seen from

the operative field: upward, 11 patients; inward, 14 patients; downward, 12 patients; outward, 3 patients).

Methods: A lumbar drain was inserted in all cases. The proximal segment of the ICA was secured in the neck. Opening of the superior wall of the optic canal, excision of the optic strut, and removal of the ACP were performed using the microrongeur. In cases where the aneurysm was facing inward, outward, or downward, the anterior clinoid process was removed by epidural manipulation alone. In cases where the aneurysm was facing upward, the ACP was removed while observing the aneurysm from inside and outside the dura mater. In regard to the handling of the aneurysm, we ablated the optic nerve sheath as distally as possible and then moved the whole optic nerve. Visual evoked potential monitoring was used preferentially for patients with a high risk of superior hypophysial artery occlusion, and the blockade of blood flow into the aneurysm was confirmed by indocianine-green angiography or intraoperative angiography.

Results: Effective clipping was possible in all cases, and there were no complications or cerebrospinal fluid rhinorrhea caused by the removal of the ACP.

Conclusion: Our method not only made it possible to avoid damage to the optic nerve, but also made safe removal of the ACP and clipping of the aneurysm possible, even in cases where the aneurysm faced upward and was fused with the ACP.

645 Vascular surgery and neurosurgery/interventional neuroradiology

WHICH TREATMENT DO YOU SELECT FIRSTLY FOR UNRUPTURED CEREBRAL ANEURYSMS? A COMPARATIVE STUDY OF CLIPPING AND COILING IN A SINGLE HIGH-VOLUME CENTER

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The more rapid evolution of techniques and device materials of neurointervention than microsurgery has changed the indication of clipping and coiling for cerebral aneurysms, especially unruptured. Then, which treatment do you select firstly for unruptured aneurysms? There may be so many different reported Results from different population of patients and from operators with different level of skill and experience. So, we retrospectively reviewed our experience with both treatment modalities of only unruptured aneurysms in a homogeneous population of patients of high-volume single center. During 5 years, 199 patients with 230 unruptured aneurysms were treated. Patients were divided into 2 groups (group I: clipping, group II: coiling). The group I and II were compared with the pretreatment variables and aneurysmal characteristics, clinical outcomes, complications and so on. Among 230 unruptured aneurysms in the study, 111 were treated by clipping and 119 were treated by coiling. The location of unruptured aneurysms in both group was similarly distributed in anterior circulation but most of MCA aneurysms were clipped and most aneurysms were coiled in posterior circulation. Three-month outcome of all patient was shown. 98% of all patients had no or mild disability and were not restricted for daily functioning or work. The excellent outcome was similarly 97.2% noted and 97.4% in each group I and II. The average of admission day was about two times higher in group I than group II, but the day of ICU was the same. Our incomplete occlusion rates in group I (3%) was much lower than group II (8%) after follow-up although both were better than usually reported. The rate of complication 7% in group I and 3% in group II. Most of complication were embolic infarction and ICH in both group. The Results of treatment of unruptured aneurysms have improved compared with previous reports and there was no significant difference in the outcomes between clipping and coiling. The location, immediate or complete occlusion, and complication, etc have to be studied and taken into consideration for selecting patients for clipping or coiling.

646 Vascular surgery and neurosurgery/interventional neuroradiology

BIFRONTAL DECOMPRESSIVE CRANIECTOMY IN CEREBRAL VENOUS AND SINUS THROMBOSIS

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Cerebral venous and sinus thrombosis (CVST) is a pathological condition characterized by thrombosis of the dural venous sinuses and deep cerebral veins; it predominates in young adults. Prognosis from this disease is highly variable but the mortality rate appears to be falling and approximately 13% of patients with the above condition have a poor clinical outcome with death or dependency. Death is often due to transtentorial herniation from cerebral oedema and mass effect of haemorrhage. Neurosurgery is indicated in selected patients with CVST whose con-

dition is deteriorating because of intractable intracranial haemorrhage and impending brain herniation. We report a 25 year old women, who presented with saggital sinus thrombosis and signs of brain herniation who subsequently underwent bifrontal decompressive craniectomies and made an excellent recovery with modified rankin score of 1. Until now there is no single published case report on usage of bifrontal decompressive craniectomy in severe CVST. Bifrontal decompressive craniectomy relieves intracranial pressure immediately in severe cases of CVST and can be life-saving.

647 Vascular surgery and neurosurgery/interventional neuroradiology

SHOULD THE EVIDENCES OF CREST TRIAL LEAD TO AN INCREASED USE OF CAS FOR THE TREATMENT OF ASYMTOMATIC CAROTID DISEASE OR DOES THE FIGHTING BETWEEN SURGERY (CEA) AND STENTING(CAS) CONTINUE?

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Background: CREST trial showed equivalence of CEA&CAS in symptomatic/asymptomatic pts. Mixture of two dissimilar patient groups violates principle of CETERIS PARIBUS. Controversies still exist.
Aim: To compare CEA and CAS and present critical overview on both possibilities after CREST trial.
Material & Methods: Data from Cochrane, Pubmed, Medline, EMBASE (1993-2010), ovn studies (CEA=312, CAS=155).
Results: Some risks resulting from surgery still exist, therefore increasing enthusiasm for CAS is seen. Recent RCTs of CEA/CAS provided controversial evidence: 30-day CI/death rates was unacceptably high-10% (CAVATAS), CAS was safer than CEA in high-risk asymptomatic pts (SAPPHIRE), increased 30-day CI/death rates with CAS:CEA (9.6%:3.9%-EVA-3S, 8.5%:5.1%-ICSS). CREST showed no significant difference between CAS:CEA in primary end points (CI, death, nonfatal MI). More MIs in CEA (2.3%:1.1%).
There is no equivalence between CEA and CAS. Comparing medical management with CEA, complication rates from CEA must be <3% and NNT to prevent one stroke is between 67-83.Medical management of asymptomatic ICA stenosis using statins markedly reduced annual CI risk to <1%, compared to CREST (4.5% for CAS, 2.7% for CEA). There is limited long-term follow-up of CAS.

Conclusions: 1. CAS is still associated with higher peri-procedural risk of CI/death than CEA. 2. In pts >70-years of age, CEA is clearly superior to CAS. 3. CEA should remain the gold standard for absolute RR in pts with severe ICA stenosis, and CAS may be alternative in symptomatic pts with major comorbidities, restenosis after previous CEA, and related to neck radiation. 4. More data are needed on medical management of asymptomatic ICA stenosis before CAS or CEA is recommended. 5. Both procedures may trigger MI, they cannot prevent it, both require preliminary cardiac evaluation. 6. CREST trial doesn't produce evidence for increased use of CAS in asymptomatic carotid disease, it is technically feasible but risky.

648 Vascular surgery and neurosurgery/interventional neuroradiology

COMPLICATIONS OF ANGIOPLASTY AND STENTING IN CERVICOCEREBRAL ARTERIES IN IRAN

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Background: Angioplasty and stenting of cervicocerebral arteries is a novel management of atherosclerotic stenosis which has periprocedural complicatiuons.
Methods: Retrospective assessment of neurointerventional archives of 9 Iranian interventionalists working in 5 university hospitals and 7 perivate hospitals during June 2003-June 2009 and review of their published articles is the basis of this national multicenter survey.
Results: 581 patients (73% males) with mean age 63.4±7 years underwent 592 extracranial internal carotid artery angioplasty and stenting. TIA, stroke, ICH, and death occurred in 1.7%, 1.7%, 0.34% and 1.52% of these 592 endovascular procedures respectively. 114 extracranial vertebral artery angioplasty and stenting was performed in 110 patients (68% males) with mean age 65.3±6 years. TIA and stroke each developed in 0.92%, while ICH and death did not occur during procedure. Seventy intracranial angioplasty and stenting was performed in 67 patients with mean age 68.5±8 years. TIA, stroke, ICH and death was observed in 1.4%, 8.6%, 1.4% and 2.9% of the procedures respectively.
Conclusion: The frequency of periprocedural complications of angioplasty and stenting of brain arteries in Iran is similar to the developed contries.

Management and economics

664 Management and economics

CAUSES OF READMISSION AFTER FIRST-EVER STROKE IN TAIWAN BY FUNCTIONAL DEPENDENCE AT DISCHARGE

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Background and purpose: Identification of preventable readmission after stroke could not only improve quality of care but also substantially lower costs. It is known that patients with functional impairment at discharge have a higher risk of readmission. However, the causes and the patterns of readmission are not well characterized. We aimed to evaluate the association of functional status at discharge with the causes of the first readmission in 1 year.
Methods: Patients hospitalized for first-ever stroke in two study hospitals in Taiwan were prospectively followed up for all-cause readmissions in 1 year. Functional status at discharge was classified as independent (modified Rankin Scale (mRS) score of 0 to 2) and dependent (mRS 3 to 5). Causes of readmission were verified from chart review and categorized as recurrent stroke, cardiovascular event, infection, and others. Baseline characteristics and outcome at discharge were tabulated among the major causes of first readmission. Kruskal-Wallis tests were used to compare continuous variables, and Pearson's chi-square analysis for categorical variables. Kaplan-Meier curves were used to estimate the probabilities of readmission.
Results: At discharge, of the 2584 study patients, 1199 (46.4%) were functionally dependent. The risk of readmission in the dependent group was greater than the independent: at 30 days (10.3% versus 5.8%), at 90 days (20.0% versus 10.8%), at 180 days (26.3% versus 16.1%), and at 360 days (36.6% versus 26.0%). The most frequent cause of readmission in the dependent patients was infection (32.6%), followed by recurrent stroke (13.0%). Conversely, recurrent stroke was the most common cause in the independent patients (22.4%), followed by infection (17.3%).
Conclusions: First-ever stroke patients with functional dependence at discharge had higher risk of readmission in 1 year than independent patients, with nearly twofold greater risk at early phases. Causes of readmission were also affected by functional dependence at discharge. This implies that functional status could be used for risk stratification as well as a target for early modification to reduce the burden of readmission after stroke.

665 Management and economics

"GETTING RESEARCH INTO PRACTICE IN STROKE CARE – HOW DO SWEDEN AND THE UK COMPARE?"

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Background: Despite significant investment in health research, challenges remain in translating this research into policies and practices that improve patient care. As part of a EUFP7 funded Programme, the researchers conducted comparative case studies of stroke research implementation in England, Sweden and Poland. Early findings from Sweden and the UK are presented here.
Methods: Comparative case studies were conducted, consisting of semi-structured interviews with key stakeholders in acute and primary care settings. Informants included a range of clinical and managerial staff involved in stroke services. The interviews examined barriers and facilitators to implementing stroke research into practice. The data was analysed using the interview schedule as a framework for content analysis.
Results: A number of emergent themes relating to the management of the implementation of research into practice in stroke care are discernable. These
include role played by leadership and the strength of the evidence in promoting uptake of research findings across professional groups. The importance of adequate and targeted funding for stroke care is emphasised, so too are issues of integration between acute and community providers.
Conclusion: These early Results highlight broad similarities in the UK and Sweden relating to implementing research into practice in stroke care. However, there are apparent contextual differences between the challenges faced in each country; the reasons for, and significance of which, need to be explored in greater detail.

666 Management and economics

DERIVATION AND VALIDATION OF A CLINICAL SYSTEM FOR PREDICTING READMISSION AFTER FIRST-EVER STROKE

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Background and purpose: Readmission after hospitalization for acute stroke is common. Valid prognostic models identifying stroke patients who are at high risk of readmission are useful for improving efficiency and quality in stroke care. We aimed to derive and validate a clinical prediction rule based on information at discharge typically available to physicians to identify patients at high risk of all-cause readmission during the first year following hospitalization for first-ever stroke.
Methods: The derivation cohort consisted of consecutive hospitalized first-ever stroke patients in the Chi-Mei Medical Center in Taiwan between August 2006 and December 2008. We used a Cox proportional hazards regression model to assess risk factors associated with the first readmission after the index hospitalization. The 1-year risk of readmission was derived by summing up the number of independent predictors with or without proper weights. The resultant score was externally validated in another similar hospital-based cohort, the Landseed hospital, during the same period.
Results: Predictors of readmission included age ($\geq$70 years), atrial fibrillation, coronary artery disease, any complication during index hospitalization, and functional dependence at discharge (modified Rankin Scale score>2). This five-point score was moderately predictive of risk of readmission (area under the ROC curve [AUC] = 0.62 to 0.67) in the derivation cohort (n=2005), which was less predictive when applied to a separate cohort of 579 patients (AUC = 0.55 to 0.66). Scores developed by predictors weighted by their corresponding hazard ratios did not improve the prediction performance.
Conclusions: Risk of readmission after first-ever stroke might not be easily predictable, neither consistent across hospitals with different characteristics. Further validations and refinements are needed.

667 Management and economics

RATIONALE APPROACH OF HEART IMAGING TO SPARE HEALTH CARE RESOURCES FOR SECONDARY STROKE PREVENTION

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Background: Hospitalization costs for stroke are continuously rising due to the ageing of populations. Since health care resources become more restricted, etiologic investigations including heart imaging should be selected according to a stepwise, rationale, decision process.
Methods: In a population of consecutive patients with TIA or stroke, we retrospectively compared the performance of a virtually "restricted" model of heart imaging to a "standard" model in 1) the identification of stroke etiology (TOAST) and 2) the final therapeutic decision. The "standard" model consisted in a very systematic use of cardiac imaging in the studied population. In the "restricted" model, transthoracic echocardiography (TTE) would have been performed exclusively in the absence of a significant extra-cranial or intra-cranial arterial

stenosis, atrial fibrillation, or lacunar infarct and transesophageal echocardiography (TEE) would have been requested only after TTE failed to demonstrate any cardiac source of embolism or expanded left atrium.

Results: Of 107 stroke/TIA patients (62 men; mean age, 70±13 years), 95 had TTE in the "standard" model compared to 42 patients only in the "restricted" model (56% reduction). TEE was performed in 85 patients in the "standard" work-up and would have been requested in 32 patients only in the "restricted" model (62% reduction). Stroke etiology did not change between the 2 models in 81 patients (76%), but a secondary etiology was found in 26 patients (24%) in the "standard" model. The final therapeutic decision did not differ between the 2 models. In the context of the Belgian healthcare system, the amount of money spared when using the "restricted" rather than the "standard" model would have been 10,000 € in these 100 patients.

Conclusions: A stepwise decision process for cardiac imaging leads to a significant reduction in the use of TTE and TEE and their related costs, without affecting the discharge treatment for secondary stroke prevention.

668 Management and economics

STAR: STROKE ANNUAL REVIEW AFTER STROKE: DEVELOPMENT AND FEASIBILITY PILOT

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Background: Significant proportions of stroke survivors report long-term needs. The UK National Stroke Strategy advocates annual follow-up of survivors to address unmet needs but provides little information about appropriate and effective service models. This study aimed to develop and pilot an innovative method of providing an annual review for stroke survivors.

Methods: Intervention development drew on analysis of unmet need 1-10 years post stroke in 3723 cases recruited to the South London Stroke Register (SLSR); qualitative interviews with 35 stroke survivors (1 year + post stroke) and 31 community based health and social care providers. A pilot study using observational Methods, interviews and self report was conducted to assess feasibility, acceptability and to identify relevant outcomes.

Results: Long-term unmet needs were medical, psychological and related to social participation and finances. Perceived constraints on service provision included resources, inadequate information, lack of clarity about responsibility and lack of stroke specialism. To address needs and overcome constraints, a model of group annual review delivered by stroke specialists in a community setting was devised, in consultation with professionals and patients/carers.17% of SLSR participants (1-2 years post stroke) accepted an invitation to take part in the group annual review. Reasons for refusals included inability to leave the house (32%), prior commitment (19%), and no unmet needs (17%). In addition to 3 group question-and-answer sessions, 23 individual consultations were provided leading to information provision (6/23), advice on self referral (10/23) and actual referrals (10/23). High levels of participant satisfaction were reported.

Discussion: The pilot group annual review was acceptable and feasible but not appropriate to all stroke survivors. Future work will aim to refine the model of intervention and test ist efficacy and cost effectiveness.

669 Management and economics

INEQUALITIES IN ACCESS TO MEDICAL REHABILITATION AFTER STROKE?

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Background: Access to medical rehabilitation after stroke seems to vary depending on sociodemographic factors like age and sex and on comorbidities. We sought to identify factors influencing access to rehabilitation after acute stroke treatment using data from a large German stroke registry.

Methods: Data were collected within the Berlin Stroke Registry (BSR), a network of 14 acute care stroke units, documenting about 80% of stroke patients in Berlin. We analysed the influence of sociodemographics, clinical characteristics and comorbidities on access to medical rehabilitation after acute stroke treatment. Multivariate logistic regression was used to assess the relation of age, sex, functional deficits, comorbidity and nursing care dependency before stroke with discharge to rehabilitation treatment.

Results: Between 2007 and 2009, 15 300 patients with ischaemic stroke were documented; mean age was 72 years, 49.4% were women. 36% of all patients and 70% of those showing relevant functional deficits (Barthel Index (BI) < 70) received medical rehabilitation. Functional deficits (p<.001), older age (p<.001), history of diabetes (OR, 1.15; 95% CI, 1.04-1.27) and atrial fibrillation (OR, 1.20;

95% CI, 1.08-1.34) were associated with higher odds of discharge to rehabilitation. Compared to patients living independently at home pre-stroke, patients receiving institutional care (OR, 0.09; 95% CI, 0.07-0.12) and patients receiving nursing care at home prior to the event (OR, 0.62; 95% CI, 0.53-0.73) were less likely to receive medical rehabilitation.

Conclusion: Discharge to medical rehabilitation after stroke strongly depends not only on the strength of the patients' functional deficits, but also on their living situation before stroke. Access to rehabilitation is especially limited for patients living in institutional care.

670 Management and economics

CIRCADIAN VARIATION OF ACUTE STROKE CODE EFFICACY

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Background: "Time is brain" means stroke should be considered as an emergency. Little is known about circadian variation of its performance and this could improve acute stroke code organization. We aimed to evaluate the circadian variation of the efficacy of acute stroke code referrals.

Methods: Consecutive data from our hospital in 2009 was analysed by gender, median age, initial NIHSS, diagnosis, thrombolysis treatment and median time of symptoms onset (ST), symptom-door (SDT), door-imaging (DIT), door-needle (DNT) and symptom-needle (SNT). Efficacy was measured as percentage of correct diagnosis, percentage of thrombolysis and time delays. ST was categorized into 4-hour periods.

Results: Data included 605 patients, with 417 confirmed strokes or TIA, and known hour in 383. Stroke or TIA were more frequent in the morning period and then decreased over time (4-hour periods, n=115, 96, 76, 56, 16, 24). Gender and age did not shown circadian variation. NIHSS showed tendency to higher scores during the night (12 pm to 8 h am). Percentage of correct diagnosis was higher from 8 to 12 am and 4 to 8 am and lower in the 8 to 12 pm period (80%, 96% and 63%, respectively, total=73%, p=0.005).

Thrombolysis rate was similar during all the time. (p=0.312) and there was no significant difference in time delays. However, there was tendency for higher SDT in periods from 8 to 12 am [86 (IQR 55-140)] and from 4 to 8 pm [84 (IQR 60-137)] and in thrombolysis subgroup, DNT and SNT recorded the higher values after midnight.

Conclusion: Stroke is known to have circadian variation peeking in the early morning. This was also reflected in acute stroke code and seemed to justify higher yield of diagnosis in this period against lower frequency of stroke mimics.

671 Management and economics

EFFICACY OF DIFFERENT PRE AND INHOSPITAL ACUTE STROKE CODES

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Background: "Time is brain" means stroke should be considered as an emergency. Understanding performance of pre and inhospital stroke protocol activation could improve organization.

Aim: Comparing efficacy between stroke code activated by non-physicians in direct presentation (DP) at emergency department and in pre-hospital emergency medical system (EMS).

Methods: EMS and DP screens for face-arm-speech-time protocol but the later extends to other neurological symptoms such as motor other than arm, sensitive, visual and incoordination deficits. Consecutive data from our hospital in 2009 was analysed by gender, median age, initial NIHSS, diagnosis, thrombolysis treatment, median time of symptom-door (SDT), door-imaging (DIT), door-needle (DNT) and

symptom-needle (SNT). Efficacy was measured as percentage of correct diagnosis, percentage of thrombolysis and time delays.

Results: Data included 605 patients. DP and EMS had similar number (305 vs 300) and gender (male 54%); the former were younger (65 vs 71y, p=0.002) and had lower NIHSS (2 vs 7, p<0.0001). EMS had more correct diagnosis (75% vs 63%, p=0.001) but similar thrombolysis rate (38 vs 33%, p=ns). EMS patients arrived earlier (SDT, 73 vs 94 min, p=0.0003) and in thrombolysis subgroup EMS had shorter DIT (32 vs 38 min, p=0.003), DNT (66 vs 71 min, p=ns) and SNT (135 vs 170 min, p=ns).

Conclusion: EMS was more efficacious in stroke diagnosis and transport to hospital, and their patients were more rapidly signalised for imaging as a possible stroke. DP with extended protocol included more stroke mimics lowering diagnostic yield but contributed with the same number of acute stroke admissions and thrombolysis in our institution.

672 Management and economics

DIFFERENCE IN KNOWLEDGE ABOUT STROKE AMONG HIGH AND LOW QUALIFIED AMBULANCE SERVICE MEMBERS

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Background: The knowledge of risk factors, early signs and physical examination of stroke is important in early period of stroke. The adequate early diagnosis and treatment may reduce the mortality and complication of stroke. In this process the ambulance service members have essential role. In our study we examined the knowledge of differently qualified ambulance service members about stroke.

Methods: In our cross sectional study we studied 150 ambulance service member from different regions of Hungary. Their knowledge was assessed with a self-fill-in questionnaire about risk factors, signs and physical examination Methods of stroke. Chi-square and Student-t test was used for comparison of variables. P-values less than 0.05 were considered statistically significant.

Results: The ambulance workers were assigned to two groups according to qualification (high qualified (HQ) - Ambulance Officer and Emergency Physician - (n=35) and low qualified (LQ) - Emergency Medical Technician - (n=115)). Significantly higher part of HQ have known exactly the risk factors of stroke, especially atrial fibrillation (p<0.001), and kidney failure (p=0.003). The precise information of Cincinatti Preshospital Stroke Scale (CPSS) was 56.7%, which was independent from qualification. Only 66.1% of ambulance workers have known that what is the exact onset of a potential stroke which was not shown difference between qualifications. The exact knowledge of special physical examination Methods of stroke as Babinski' sign (p=0.021), facial paresis (p=0.015) among LQ members was significantly lower than HQ members. More precise knowledge about stroke is associated with active participation of a previous (within 1-2 years) training.

Conclusion: The Results of present study underline that the theoretical knowledge of ambulance service members, especially EMT is not sufficient. The inaccurate knowledge about onset of the stroke and special skills relating with stroke may reduce the chance of early and adequate treatment of stroke. The regular training of all prehospital employees may increase the proficiency associating with stroke.

673 Management and economics

THE IMPROTANCE OF THE FIRST RESPONDER FOR ACUTE STROKE PATIENTS

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Objectives: The first responder plays an important role in order to transfer the stroke patient to the hospital in time. The purpose of the study was to describe the timing of stroke care delivery in a Hungarian sample.

Methods: a cross-sectional analysis has been performed among stroke patients' medical records (n=185) reported to the National Ambulance Service in two cities of Hungary. We analyzed care delivery from the onset of the first stroke symptoms. Beside socio-demographic data, characteristics of stroke symptoms, care delivered

in prehospital phase and admittance to the hospital were collected. Data collection was carried out in the last quarter of 2010 and statistical analysis (chi-square test, ANOVA) was performed with SPSS18.0.

Results: Gender-distribution of stroke patients was 46,5% male and 53,5% female. The average age was 66,8. The first experienced salient symptoms were: dizziness (43,2%); difficulties to speech (41,1%); hemiparesis (41,1%); obdormition (34,1%); limitation to move (27,6%); limitation of the visual field (26,5%); facial paresis (18,9%), dysphagia (13,5%). The time interval between first symptoms and first help seeking was around 1 hour in average, although 34,1% of patients experienced it more than 3 hours earlier. Almost in two third (62,2%) of all cases the patients were transported into hospital in 3 hours after the first encounter with health care provider. The majority of patients called their GP first (49,7%). Ambulances were called in 31,4% only and some called the hospital directly (18,9%). Those who got into the hospital later than 3 hours called their GP first (p=0,01). The patients living alone or widowed preferred to call the ambulances first (p=0,044). The time between the first symptoms and the first care also correlated with the type of first care provider (p=0,00).

Conclusions: After the first symptoms patients should know who to call in order to get adequate treatment in time. Not taking the first symptoms seriously and calling the GP first means time wasting in stroke care. Patients who already had milder symptoms and are at risk of stroke should be educated more on stroke symptoms and on first steps.

674 Management and economics

DEVELOPING A STROKE-SKILLED WORKFORCE

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Background: In the wake of the English National Stroke Strategy (2007) the UK Forum for Stroke Training (UKFST) was established to work towards achievement of recognised, quality-assured and transferable education programmes in stroke. In order to achieve this goal, the UKFST aimed to develop an Education Framework that would outline the stroke-specific knowledge and skills that health, social, voluntary and independent care staff need in addition to the generic skills that already possess.

Methods: A Steering Group and four Task Groups were convened with representation from the four UK countries, professional bodies, health and social care providers, voluntary organisations and service users. The groups identified 16 Elements of Care. These Elements of Care reflected the Quality Markers, Standards and Recommendations found in the stroke strategies of the four UK countries. Subsequently, the groups identified the "knowledge and understanding" and "skills and abilities" that staff should possess if they care for people affected by stroke within that Element of Care.

Results: A series of meetings and a targeted Stakeholder Engagement led to the development of The Stroke-Specific Education Framework (SSEF). The SSEF spans the whole of the stroke pathway and consists of 16 Elements of Care. For each Element a list of competency-based items was developed for "knowledge and understanding" (between 7 and 26 items) and "skills and abilities" (between 7 and 23 items).

Implications: The SSEF can be used by course providers to ensure that the content of their course reflects the contents of the SSEF. The SSEF underpins the new UKFST website where staff who care for people affected by stroke can search for suitable stroke-specific courses.

675 Management and economics

USE OF ORAL ANTICOAGULATION AMONG STROKE PATIENTS WITH ATRIAL FIBRILLATION IN CHINA

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Background and purpose: International guidelines recommend oral anticoagulation (OAC) in patients with atrial fibrillation (AF) according to their level of stroke risks. This study aimed to determine OAC use in AF patients with recent ischemic stroke and investigate factors that impact such management in China.

Methods: Among the patients with acute ischemic stroke (n=4782) from the China QUEST (QUality Evaluation of Stroke Care and Treatment) study, a multicenter, prospective, 62-hospital registry in China, there were 499 (10%) (mean age 70±12 years, 49% female) with documented AF with outcome data over 12 months of follow-up. Logistic regression analysis was used to identify the independent predictors of OAC use in these patients.

Results: Of the 499 stroke patients with AF, OAC use was 20% overall, but varied from 8% pre-stroke and 11% in-hospital (post-stroke), to 13% and 10% at 3 and 12 months, respectively. OAC use was independently associated with younger age (Odds ratio [OR] 0.95, 95% confidence interval [CI] 0.93-0.97, p<0.001), non-manual occupation (OR 0.44, 95%CI 0.25-0.80, p=0.006), and less cardiovascular risk factors (OR 0.81, 95%CI 0.68-0.96, p=0.02).

Conclusions: These data indicate OAC use is lower in stroke patients with AF in China than that in western countries, being applied more often in those of younger age, non-manual occupation, and having less cardiovascular risk factors.

676 Management and economics

REGIONAL DIFFERENCES IN PREHOSPITAL TREATMENT OF STROKE PATIENTS IN HUNGARY

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Background: The early prehospital and hospital diagnosis as well as the necessary prehospital therapy of stroke increase the chance of effective trombolysis and improvement. The mortality and morbidity of cardio- and including stroke may differ by localization in Hungary. The distance from a stroke center is also different which is usually shorter in the capital of Hungary (Budapest). In our study we examined the regional differences of the prehospital treatment of stroke.

Methods: In our retrospective study between 2003 and 2007 we studied 276 patients with the diagnosis: transient ischemic attack and stroke. The patients were divided 2 groups according to the localization. 104 patients were treated in Budapest (BUD) and 172 patients were treated in smaller cities in the western region (WR) of Hungary (Sopron and Szentgotthard). The patients' vital and diagnostic signs and their therapy were collected from prehospital documentations. Chi-square and Student-t test was used for comparison of variables. P-values less than 0.05 were considered statistically significant.

Results: The time of therapy in place of event and the transfer (from ambulance to hospital staff) of the stroke patient was significantly higher in BUD than WR (31.9 vs. 21.1 min and 20.3 vs. 10.9 min, respectively, all p<0.001). The duration of the transport to stroke center was significantly shorter in BUD (p<0.001). The primer transport of patient with symptoms of stroke to the computer-tomography was 21.1% in BUD and only 1.1% in WR (p<0.001). The characteristics of the patients and the treatment during prehospital period were not shown difference.

Conclusion: The regional difference in Hungary may diminish the chance of early and adequate treatment of a patient with stroke. In BUD the duration of prehospital therapy in place of event and the transfer time were longer than recommendation of the stroke protocol.

677 Management and economics

THE CONTROLLED STROKE PATIENT JOURNEY: DO WE ACT IN TIME? A PREHOSPITAL EMERGENCY PATIENT CARE STUDY

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Objectives: Our aim is to examine and subsequently follow up whether the prehospital providers consider the controlled patient journey in stroke care. We investigated, whether they are aware of this, furthermore whether they are capable to make the convenient professional decision at the offset points. Our study is capable to working out a quality assurance analysis that examines the effectiveness of the stroke care protocol.

Methods: During this pilot study self-fill-in questionnaires were administered to air ambulance and EMS doctors and BSc paramedics in 3 counties of Hungary in 2009-2010. 67 assessable questionnaires arrived back from the total of 153 that had been sent to every employee of the areas. Statistical analysis (chi-square test, Fisher's exact test and ANOVA) was performed with SPSS17.0.

Results: The questioned emergency providers - independently of their qualifications - consider the control of care at those patients who suffer from stroke important (100% of doctors, 95.92% of the BSc paramedics). The opinions are independent from whether the provider experienced difficulties in patient care because of the non-regulation (p=1.00), so the opinions are not based on observation but on confidence. In the studied regions altogether 86.36% of the providers know properly the existence (or non-existence) of a regulated patient journey. During the questions that examined the application of the protocol, it turned out that only 2/3 of the responders would leave for a further hospital with their patient from the scene, which could offer a definitive care. We established that the BSc paramedics compared to the specialists (1.70 average points), to the doctors (1.71), furthermore to the main average (2.06) overestimated (2.18) the patient care determining opportunities of the hemorrhagic and ischemic differential-diagnostic forms.

Conclusions: The quality assurance follow up of the stroke care protocol is practical. Our survey showed that a questionnaire worked out and applied in this field could be a convenient base.

678 Management and economics

FACTORS RELATED TO QUALITY OF LIFE OF STROKE SURVIVORS

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Stroke survivors may be dependent and need additional attention. We aim to determine factors that related to quality of life of stroke survivors. A hospital-based, analytical study was performed between January 1st, and March 31st, 2008 at Srinagarind hospital, Khon Kaen province Thailand. Factors related to quality of life using Thai SF-36 rating scale were studied. There were 237 stroke survivors participated. The age range of participants was between 20 and 91 years of age (mean = 63.7±12.8, median = 65.0). For physical heath summary scale, factor related with better scale were male gender (p<0.001, 95% CI= 6.3-21.9), aged under 50 (p<0.001, 95%CI=6.3-21.9), educational level higher than bachelor degree (p<0.001, 95% CI=8.1-22.3), unemployed status (p<0.001, 95%CI=6.4-19.8). For mental health summary scale, the education level (p<0.001 95%CI=7.3-20.1), employment status (p=0.007, 95%CI=2.3-14.5), household income (p<0.001), and severity of the disease (p<0.001, 95%CI=15.5-27.7) had statistically significant difference. Overall, the age, level of education, employment status, monthly household income and the Modified Rankin Score related to the quality of life. In Conclusion, the factors related to quality of life were age, educational level, occupation, monthly household income and the Modified Rankin Score.

Meta-analysis and reviews

700 Meta-analysis and reviews

LONG-TERM FUNCTIONAL OUTCOME AFTER SUBARACHNOID HEMORRHAGE: A SYSTEMATIC REVIEW ON PROGNOSTIC DETERMINANTS

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Background and purpose: To systematically review the literature on prognostic determinants of long-term functional outcome after subarachnoid hemorrhage.
Methods: The Pubmed, Embase and Psy-info databases were searched between 1994 and November 2009 for studies on prognostic determinants of long-term functional outcome measured by the Glasgow Outcome Scale and/or (Modified) Rankin Scale in patients with subarachnoid hemorrhage. Two reviewers independently performed study selection based on preset eligibility criteria. In total 38 articles were included in this review. Data on patient and study characteristics, inclusion and exclusion criteria, prognostic determinants, outcome measurements, univariate and multivariate Results were extracted by one reviewer and randomly checked by a second reviewer. A best-evidence synthesis was performed to determine the strength of each of the 24 prognostic factors evaluated.
Results: Strong evidence of prognostic value on outcome was found for the Glasgow Coma Scale (GCS), the Hunt&Hess Scale, age, cardiac history, smoking, hypertension, new-onset seizures and mean S100B-protein levels. Strong evidence of no association with outcome was found for gender, aneurysm site, coiling versus clipping and the occurrence of vasospasm. All other possible prognostic factors showed inconclusive Results. Age, GCS and WFNS show different levels of evidence at 6 and twelve month outcome.
Conclusions: Functional outcome after SAH is predicted by the GCS, the H&H Scale, age, cardiac history, smoking, hypertension, new-onset seizures and mean S100B-protein levels. Gender, aneurysm site, coiling versus clipping and the occurrence of vasospasm do not predict long-term functional outcome significantly.

701 Meta-analysis and reviews

ANIMAL MODELS OF FOCAL CEREBRAL ISCHAEMIA – THE INFLUENCE OF HYPERTENSION?

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Background: The failure to translate efficacy from bench to bedside in stroke has been attributed in part to the poor external validity in reports of animal experiments. Although the prevalence of hypertension in patients with stroke is high, animal data reporting its influence are limited. The efficacy of putatative interventions in hypertensive animal models may have important implications in translating their effect. Here we assess the relationship between hypertensive and normotensive controls in models of focal cerebral ischaemia and the impact of study characteristics and quality.
Methods: The CAMARADES database comprises information from over 500 publications involving more than 23,000 animals and testing 21 interventions in animal models of focal cerebral ischaemia collected in the context of systematic reviews. From this dataset we indentified studies reporting outcome as infarct volume comparing a hypertensive strain and a normotensive control. We used DerSimonian and Laird random effects meta-analysis.
Results: We indentified 61 publications reporting outcome in hypertensive animals of which 11 carried out a comparison with normotensive controls. The presence of hypertension increased infarct volume by 49% (95%CI 21.1-64.8, 29 experiments and n=525 animals). The spontaneously hypertensive rat (SHR) and stroke prone SHR were used. The change in infarct volume was increased in studies where control rats were Wistar (-81.3%; -112.9 to -19.7, n=346), compared to Fisher (-31.9%; -78.8 to 0.65, n=72) and Sprague-Dawley (7.3%; -5.2 to 19.8, n=107).
Conclusions: The use of hypertensive animals in stroke modelling is limited; more data describing efficacy in the presence of hypertension are required. The control strain used had a significant impact on outcome. However, SHRs differ from other rat strains in factors other than blood pressure; the use of animals with pharmacologically induced hypertension may therefore be of benefit in translational stroke research.

702 Meta-analysis and reviews

DEVELOPMENT, EXPANSION AND USE OF A STROKE CLINICAL TRIALS RESOURCE FOR NOVEL EXPLORATORY ANALYSES

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Background: Practical and financial barriers hinder the pace of stroke research and implementation of promising approaches to treatment. Exploratory analyses of reliable data may supplement Conclusions from randomised trials, and could improve future trial design. We aimed to extend an acute stroke trial archive to related areas of stroke research.
Methods: Using procedures developed by the Virtual International Stroke Trials Archive (VISTA) for acute stroke, we invited trialists to lodge data on rehabilitation, secondary stroke prevention, intracerebral haemorrhage (ICH), imaging, and observational or population studies in new specialist archives.
Results: We extended VISTA into 6 sections: VISTA-Acute (n=28,071 patients' data), VISTA-Rehab (n=9,787), VISTA-ICH (n=1,829), VISTA-Prevention, VISTA-Imaging (n=1,300) and VISTA-Plus (n=6,573). Data on age, stroke type, medical history, mRS, BI, NEADL, EQ-5D, discharge destination, mortality, adverse events and concomitant medications are available for analysis. Data from VISTA have been used to investigate thrombolysis in elderly patients, post–stroke atrial fibrillation and predict outcome after acute ischaemic stroke, facilitating 32 peer-reviewed research publications and 33 conference presentations.
Conclusion: Well managed trial archives can extend the value of clinical research at low cost, without threatening commercial or intellectual property interests. VISTA independently delivers valuable research output on a wide range of stroke topics. VISTA is not a meta-analysis dataset; rather it is used to investigate epidemiology, stroke outcomes and endpoints, pilot trial design elements and conduct exploratory analyses. We provide young researchers with access to specialised committees for collaboration and offer them competitive funding to build research portfolios using VISTA. We encourage collaboration with VISTA and development of similar databases in other disease areas.

THERAPEUTIC INR PROMOTES SURVIVAL AND REDUCES DISABILITY IN ATRIAL FIBRILLATION AND STROKE – A META-ANALYSIS

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Atrial Fibrillation (AF) is associated with increased risk of severe stroke. The use of anticoagulation therapy in AF for stroke prevention targets a goal International Normalised Ratio [INR] of 2-3, but many anticoagulated AF patients have low INR (<2) at stroke onset. We performed a meta-analysis of data addressing the relationship of INR at stroke onset to early and late outcome.
Methods: We performed a systematic review and meta-analysis of published and unpublished literature. Observational studies were included where outcomes in AF-associated stroke were reported categorized by pre-stroke antithrombotic category, with documented INR for those anticoagulated. Primary outcomes were survival and good functional outcome (mRS 0-2) at 30 days post-onset or hospital discharge. Secondary outcomes included survival at 1 year.
Results: 8 studies met our pre-defined inclusion criteria (n=2238, mean age 78 years). 30% had prior stroke, 68% had hypertension.
Compared with all other antithrombotic categories (INR<2 or no warfarin, n=1965), INR≥2 (n=273) was associated with improved survival at 30 days or discharge (pooled odds ratio (OR) for early death 0.47 (95% Confidence Interval (CI) 0.3-0.7, p<0.001). Similarly INR≥2 (n=225) was associated with good early functional recovery as compared with all other categories (n=1360) with an OR for mRS 0-2 of 1.8 (95% CI 1.4-2.5, p<0.001).
When compared with INR<2 at 30 days or discharge, INR≥2 at onset was associated with improved survival (pooled OR for death 0.48 (95% CI 0.3-0.8, p=0.004) and good functional outcome (pooled OR 1.8, 95% CI 1.1-2.7, p=0.01).
At one year when compared with all other categories, INR≥2 had an OR for death of 1.0 (95% CI 0.6-1.6, p=1.0). INR<2 compared with INR ≥2 had an OR of 0.8 (95% CI 0.4-1.4, p=0.4) for death at one year.

Figure 1. Forest plot showing pooled analysis of fatality at 30 days or discharge (INR≥2 compared to all other antithrombotic categories)
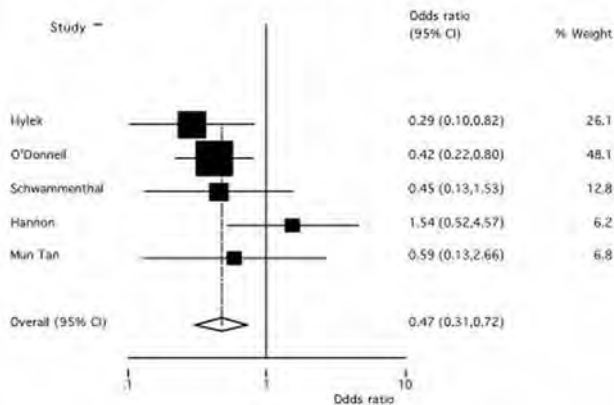
Conclusion: Available evidence indicates that maintaining INR ≥2 for stroke prevention in AF confers a benefit towards survival and functional recovery at early time-points post-stroke.

MATHEMATICAL IMAGE PROCESSING ALGORITHMS IN DETERMINING STROKE TISSUE STATUS AND PREDICTING ITS FATE: SYSTEMATIC REVIEW REVEALS UNTAPPED POTENTIAL

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Background: Acute ischemic stroke lesions are complex with no ideal method to differentiate dead/at risk/not at risk tissue to guide treatment. Basic thresholding Methods have limitations. Computational models and image processing Methods developed to map tissue morphological changes in other disorders (eg growth in tumors) might work in stroke to determine the acute tissue status and predict spatio-temporal evolution.
Methods: We searched the literature from 1995 to 2010 for computational and image processing studies aimed at identifying any tissue state at one timepoint and dynamic temporal changes in strokes. We classed these Methods into 5 groups: 1) static population-based, 2) static individual-based, 3) microscopic dynamic, 4) macroscopic dynamic population-based and 5) macroscopic dynamic individual-based Methods. Each group was sub-categorized according to the data used for testing: a) MR animal, b) MR human and c) synthetic.
Results: We found 35 studies describing 24 different models (1a 11%; 1b 26%; 1c 6%; 2a 3%; 2b 37%; 3c 17%), total sample size 530 patients, 88 animals. 65% of human studies had less than 20 patients. No models considered the mass effect induced by acute infarct swelling. Most studies suffered from numerous parameters to adjust (esp. group 3), lacked validation criteria, clinical evaluation, and 37% of the models have not been tested yet on stroke patient data. The most promising Results were obtained for groups 1 and 2. We found no models in groups 3-a, 3-b, 4 or 5.
Conclusion: The best computational model of acute ischemic tissue dynamics is as yet unclear. The considerable potential of MR imaging for identifying tissue state and fate in acute stroke remains largely untapped. A macroscopic dynamic model is needed to mathematically describe the spatio-temporal evolution of key tissues but has not yet been tried. The microscopic models (group 3) could be the basis for encouraging mathematical approaches to define validated stable and efficient models in stroke.

ASSOCIATIONS BETWEEN POST-STROKE FATIGUE AND BIOLOGICAL FACTORS: A SYSTEMATIC REVIEW

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Background: Fatigue is a common and distressing consequence of stroke, affecting around 40% of stroke survivors. Its aetiology is unknown and no treatments are available. Neuroanatomical abnormalities, neuroendocrine dysregulation and inflammation are associated with fatigue in conditions other than stroke. The purpose of this systematic review was to identify and critically appraise published studies which described associations between post-stroke fatigue (PSF) and these biological factors.
Methods: We searched Medline, EMBASE, CINAHL, PsycINFO, AMED and PubMed, and included studies in English that recruited and retained > 10 patients aged > 18 years old, after stroke or transient ischaemic attack (TIA) if latter was compared to stroke, assessed fatigue and described its relationship with biological factors of interest.
Results: Of 4916, we identified 20 publications (n=6337) which met inclusion criteria for this review. There was no association found between white matter disease, brain atrophy and pathological type of stroke and PSF. Eight studies found no association between site of stroke lesion and fatigue, whilst three studies (total n=341) found relationship between infratentorial lesion location and PSF, and one study (n=334) reported that basal ganglia was associated with fatigue. Although two studies suggested that PSF could be more common after right-hemisphere strokes, nine - found no association between lesion side and fatigue. One (n=28) reported an association between C-reactive protein levels and fatigue. No studies related PSF to neuroendocrine dysregulation were found. Two studies showed that the prevalence and severity of fatigue after stroke were significantly higher than after TIA.
Conclusion: The relationship between PSF and biological factors is uncertain. Further studies are required to determine the pathophysiology of fatigue after stroke. This work was supported by EFNS Scientific Fellowship to MK.

ULTRASOUND-ENHANCED THROMBOLYSIS FOR STROKE: A COMPARATIVE ANALYSIS OF IN VITRO, IN VIVO, AND CLINICAL STUDIES

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Background: There is growing evidence from in vitro, animal and clinical studies that ultrasound (US) at various frequencies and intensities may be beneficial for patients with acute ischemic stroke. This analysis will summarize our current knowledge about the use of ultrasound in enhancement of thrombolysis.
Methods: We searched Medline for English-language literature published in peer-review journals. We included papers that specified acoustic parameters, studied objects/subjects, treatment modalities, and efficacy outcome measures.
Results: We identified 55 papers from 1991 till 2010 comprising 73 experiments/studies, sourced to 40 lead authors. Of these studies, 58% (42/73) used in vitro models, 30% (22/73) in vivo animal models, and 12% (9/73) were clinical studies. Frequency range studied was 20 kHz to 3.4 MHz (43% used low-frequency [<1 MHz], 57% used high-frequency [$\geq$ 1 MHz]), spatial peak intensity range was 0.07 to 40 W/cm^2 (31% used high-intensity [$\geq$ 0.72 W/cm^2]), 44% used pulsed-wave US, 56% continuous-wave US. Fourty-one percent had tPA, 19% urokinase/streptokinase, 12% combined tPA/urokinase and microbubbles, 14% microbubbles, and 14% had ultrasound alone. Across all frequencies and intensities any ultrasound-accelerated thrombolysis effect was confirmed in 81% (59/73) of studies (51% by clot mass loss/degradation; 44% recanalization/reperfusion; 5% histology/microscopy and others). Detailed analyzes of the relationship between mechanical indices, frequencies, intensities and peak rarefactional pressures are explored.
Conclusion: The literature reports argue efficacy of ultrasound-enhanced thrombolysis regardless of frequency, intensity, and context of this adjuvant treatment element. This may reflect either publication bias or the fact that any ultrasound frequency and any ultrasound intensity can make a difference.

707 Meta-analysis and reviews

PREVALENCE OF UNRUPTURED INTRACRANIAL ANEURYSMS: AN UPDATED SYSTEMATIC REVIEW WITH EMPHASIS ON SEX, AGE, COUNTRY, INDICATION FOR STUDY AND TIME-TREND

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Background: We updated our 1998 review on the prevalence of unruptured intracranial aneurysms (UIAs), with the aim to describe subgroup specific data and risk factors.
Methods: Through PubMed and EMBASE searches we updated our set of studies on UIA until October 2010. Prevalences and prevalence ratios (PR) with corresponding 95% confidence intervals (95%CI) were calculated with a random-effects binomial meta-analysis and adjusted for sex, age and indication for study. A time-trend was assessed with year of study as continuous variable.
Results: 66 studies (80 study populations), with 1248 UIAs in 86,838 persons. For patients without a known risk factor the prevalence was 0.5% (95%CI:0.5-1.3). Prevalences were higher in patients with ADPKD (PR 25.6; 95%CI 6.2-106), a family history of subarachnoid haemorrhage (SAH) or UIA (PR 9.3; 95%CI 2.4-36), atherosclerosis (PR 3.1; 95%CI 1.1-8.7), a brain tumour or metastasis (PR 4.3; 95%CI 1.2-16) and a pituitary adenoma (PR 8.3; 95%CI1.8-39). Prevalences were elevated in women compared with men (PR 1.9; 95%CI 1.0-3.5) and for patients <30 years (PR 0.00; 95%CI 0.00-0.12) compared with patients >80 years. No gradual increase of the prevalence with age was found. Compared with the US, the PR for Japan was 0.8 (95%CI 0.3-1.9) and for Finland 0.9 (95%CI 0.3-2.6). Between 1948 and 2007 there was no significant change in prevalence (-3.7% per year; 95%CI -7.8 to 0.5).
Conclusions: For adults without risk factors the prevalence of UIAs is 0.5%. Prevalences are higher in women, patients >30 years, patients with ADPKD, atherosclerosis, a brain tumour or metastasis or pituitary tumour, or a family history of UIAs of SAH. The prevalence of UIAs did not change over time.

708 Meta-analysis and reviews

BALANCE BETWEEN PREVENTING PULMONARY EMBOLISM AND CAUSING SYMPTOMATIC INTRACEREBRAL HAEMORRHAGE WITH ANTICOAGULATION THROMBOPROPHYLAXIS IN EARLY ISCHAEMIC STROKE: A SYSTEMATIC REVIEW AND METAANALYSIS OF RANDOMISED CONTROLLED TRIALS

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Background: Anticoagulation has no role in the treatment of acute ischaemic stroke but is used for the prevention of venous thromboembolic events. We undertook a systematic review and metaanalysis to assess the balance between preventing pulmonary embolism (PE) and causing symptomatic intracerebral haemorrhage (SICH) in participants with recent stroke who were randomised to antithrombotics in trials.

Methods: We systematically searched the Cochrane Library, Medline, Embase and Science Citation Index for prospective randomised controlled trials assessing the effect of heparin and other antithrombotics in patients with acute/early ischaemic stroke. Included trials had to record information on PE and SICH. Risk ratios (RR) were calculated for SICH per PE for each trial using a random effects model.
Results: We identified 33 trials (50,415 participants) with 453 SICH and 175 PE events. The trials studied low dose subcutaneous (sc) anticoagulation (15 trials), medium/high dose sc anticoagulation (11 trials), intravenous (iv) anticoagulation (3 trials), oral antiplatelets (10 trials), and intravenous antiplatelets (3 trials). The ratio of SICH to PE approximated unity with low dose subcutaneous anticoagulation (RR 1.21, 95% confidence interval, CI, 0.85-1.73), but was increased with high dose subcutaneous (RR 3.33, 95% CI 2.31-4.8) and intravenous (RR 4.99, 95% CI 1.04-23.83) anticoagulation.
Conclusion: Prophylactic/low doses of subcutaneous anticoagulation have similar rates of PE and SICH. Since previous studies have not found anticoagulation to improve functional outcome, and administration is expensive in time and financial cost, there is no indication for the routine use of anticoagulation for VTE prophylaxis.

709 Meta-analysis and reviews

A SYSTEMATIC REVIEW OF INTRAVENOUS THROMBOLYSIS AND INTRA-ARTERIAL TREATMENT IN WAKE-UP STROKE

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Background: Symptoms of stroke present on waking in 15-20% ischaemic strokes. Treatment options for wake-up stroke (WUS) are limited as RCTs of iv rt-PA only included patients with known symptom onset or last seen well within the treatment time window. We undertook a systematic review of intravenous thrombolysis (IVT) and intra-arterial treatment (IAT) in WUS aiming to conduct a meta-analysis and narrative review.
Methods: We ran a PubMed search using the terms: wake, awake, sleep, asleep, unclear-onset, unclear onset AND stroke. Two authors independently assessed studies deemed potentially eligible. Main treatment outcomes of interest were modified Rankin Score (mRS) and symptomatic intracerebral haemorrhage (sICH).
Results: 631 articles were identified of which 17 were potentially eligible. Five (one RCT, 2 case series and 2 case studies described WUS treatment, n=82), 3 described treatment outcomes in broader "uncertain onset" groups, 7 were observational studies of untreated WUS, and 2 did not refer to WUS. Meta-analysis was not feasible. Median NIHSS ranged from 10-16. The3 case series/RCT WUS treatment studies compared treated with untreated WUS patients and 2 compared treated WUS with treated stroke whilst awake (SWA). Treatment including IV tPA, IAT, or both. The RCT studied iv abciximab. Outcomes of interest were not reported in all studies. Good outcome mRS 0-2 was reported in 38% (26/79) treated WUS. One found favourable outcome was more likely in treated than untreated WUS; the RCT had the opposite finding; another study found no difference. sICH was reported in 9% (6/70) treated WUS patients. The abciximab RCT found an increased rate of sICH in treated WUS than in SWA.
Conclusion: Published data on outcomes following reperfusion treatment for WUS are very limited. Effectiveness is unclear but IVT and IAT may be associated with an acceptable rate of sICH. RCTs of reperfusion therapies for WUS are lacking and urgently needed.

710 Meta-analysis and reviews

A COMPARISON OF DUAL ANTIPLATELET THERAPY WITH MONO THERAPY IN PATIENTS WITH ACUTE ISCHAEMIC STROKE OR TIA: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

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Background: Clinical guidelines recommend antiplatelet therapy for patients with non-cardioembolic stroke or transient ischaemic attack (TIA). This study assessed the safety and efficacy of dual antiplatelet therapy in comparison with mono therapy in reducing recurrent vascular events in acute ischaemic stroke or TIA.
Methods: Completed randomised controlled trials investigating the effect of dual versus mono antiplatelet therapy in patients with acute ($\leq$3 days) ischaemic stroke/TIA were identified using electronic bibliographic searches. The primary outcome was recurrent stroke (ischaemic, haemorrhagic, unknown, fatal, non fatal). Secondary outcomes included: combined stroke, TIA, acute coronary syndrome (ACS); all death; stroke; myocardial infarction (MI); vascular death; MI; fatal

stroke; severe stroke (mRS 2-6); TIA; intracerebral haemorrhage; major bleeding; death; and vascular death. The comparison of binary outcomes between treatment groups was analysed with random effect models and described using odds ratios (95% confidence interval).

Results: 12 completed randomised trials involving 3,766 patients were included. Further 14 studies (3,879 patients) were excluded, largely because these had no acute patient data. In comparison with mono-antiplatelet therapy, dual therapy significantly reduced stroke recurrence (OR 0.67, 95% CI 0.48 to 0.94; 11 studies 3,614 patients), and the composite of stroke, TIA, ACS and all death (OR 0.69, 95% CI 0.52 to 0.9; 8 studies 3,004 patients). Dual antiplatelet therapy showed non significant trends for lowering combined stroke, MI, vascular death, fatal stroke, MI, and TIA. Severe stroke (mRS 2-6), death, vascular death, bleeding events was not altered by dual antiplatelet therapy. There was no heterogeneity in the Results.

Conclusions: Dual antiplatelet therapy appeared to be safe and effective in reducing stroke recurrence in patients with acute ischaemic stroke or TIA than mono therapy. The lack of heterogeneity suggests that the composition of dual antiplatelet therapy was not important. The limited number of studies and patient data may have contributed to some of the non significant trends in the present study.

711 Meta-analysis and reviews

INFLUENCE OF LIPID PROFILES ON THE RISK OF HAEMORRHAGIC TRANSFORMATION IN ISCHAEMIC STROKE PATIENTS: A SYSTEMATIC REVIEW

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Background and purpose: It has been suggested that low cholesterol levels are associated with a slightly increased risk of haemorrhagic transformation (HT) in patients with cerebral ischaemia. We systematically reviewed published studies to determine the influence of lipid profiles on the HT risk.

Methods: We searched PubMed from 1966 and Embase from 1980 for studies that investigated the association between lipid profiles and HT. We performed a meta-analysis separately for the comparison between HT vs. no-HT, for total-, LDL-, HDL-cholesterol and triglycerides (weighted mean difference method). This analysis was performed for any-HT and symptomatic-HT.

Results: Eight studies gathering 1763 patients were eligible. No study recruited consecutive acute ischaemic stroke patients irrespective of the cause and treatment received. No study was designed specifically for this question. The meta-analysis showed that (i) LDL-cholesterol levels were significantly lower in patients with any-HT (p = 0.008), but not total cholesterol (p = 0.129) and triglycerides (p = 0.900), while HDL-cholesterol tended to be higher (p = 0.066); and (ii) total cholesterol levels were significantly lower in patients with symptomatic-HT (p = 0.035), while LDL-cholesterol levels (p = 0.056) and HDL-cholesterol levels (0.138) tended to be lower, but not triglycerides (p = 0.851).

Conclusion: LDL-cholesterol levels are lower in HT patients, but Results are not conclusive for HDL-cholesterol. There is no association with triglycerides levels. The next step will be to focus on the mechanisms of this association, especially in patients treated by rtPA who are those with the highest risk of HT in practice.

712 Meta-analysis and reviews

SYSTEMATIC REVIEW OF BICUSPID AORTIC VALVE AND SPONTANEOUS STROKE

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Background: Bicuspid aortic valve (BAV) is the commonest congenital cardiac abnormality, affecting 1-2% of the population. Many people remain asymptomatic although premature aortic stenosis, aortic regurgitation, proximal aortic dilatation or dissection and increased risk of infective endocarditis are all recognized complications. Calcific emboli have been documented frequently at extracranial sites, but spontaneous ischemic stroke has rarely been associated with BAV. We systematically reviewed the literature for an association between BAV and spontaneous ischemic stroke.

Methods: Medline and Ovid databases were searched using the terms bicuspid aortic valve and stroke. Bibliographies of citations were examined. Inclusion criteria required reports of at least one patient with ischemic stroke attributed to the presence of a BAV. Cases were collated to determine mean age, sex ratio and

frequency of single and multiple cerebrovascular events (transient ischemic attack and stroke) as well as aortic valve morphology.

Results: Nine patients (one woman and eight men) with BAV and ischemic cerebrovascular disease were identified, mean age 40.8 (SD 16.1) years. Two of the nine patients had a transient ischemic attack, seven had stroke. Three of the nine patients had multiple cerebrovascular events. There was little information on BAV morphology.

Conclusion: Although rarely reported, the literature suggests that BAV may be a risk factor for stroke. Better characterization of BAV morphology may identify reasons for this association. Stroke investigation, particularly in young patients with apparent cryptogenic stroke, should always include careful aortic valve examination.

713 Meta-analysis and reviews

DOES PRETREATMENT WITH STATINS IMPROVE STROKE OUTCOME?

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Background: Statins have shown to be effective in the primary and secondary prevention of stroke. Recent studies demonstrated that statin use before stroke onset may reduce stroke severity. On the other hand, studies mention an influence of statin therapy on the risk of hemorrhagic transformation.
The purpose of this review is to evaluate if pretreatment with statins improves stroke outcome, and if they increase the risk of hemorrhagic transformation after tissue plasminogen activator (tPA) treatment.

Methods: Medline/Pubmed was searched for relevant articles on stroke, stroke outcome and statins. We included studies who reported as outcome either functional outcome assessed by the modified Ranking Scale at 3 months, in-hospital mortality and/or the risk on a symptomatic hemorrhagic transformation after tPA.

Results: Ten studies met the inclusion criteria. In four studies patients had an IV or IA-thrombolysis. In the other 6 studies no thrombolytic treatment was given. We could not find a significant difference for good functional outcome after 3 months in tPA treated patients, the pooled OR was 0.94 (95% CI: 0.66 to 1.33, P = 0.72).Six studies, who included patients who didn't have tPA treatment, reported data on in-hospital mortality. Statin therapy before stroke-onset significantly decreased in-hospital mortality in this patient group, with a pooled OR of 0.48 (95% CI: 0.36 to 0.65, P< 0.00001). We found a significant increase in the risk of developing a hemorrhagic transformation after thrombolytic therapy, when taking statins before stroke onset. The pooled OR is 2.34 (95% CI 1.31 to 4.17, P = 0.004).

Conclusion: Pretreatment with statins may decrease in-hospital mortality in stroke-patients who didn't had tPA treatment. There was no significant difference between statin users and no statin users for functional outcome in patients who had tPA treatment. We found that statins may increase the risk of hemorrhagic transformation in the tPA patient group.

714 Meta-analysis and reviews

RELATIONSHIP BETWEEN CAROTID BRUIT AND STENOSIS: META-REGRESSION AND META-ANALYSIS IN OVER 15,000 ARTERIES

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Background: Uncertainty exists over whether listening for carotid bruits as part of the clinical examination is informative in terms of predicting the presence of carotid stenosis. We sought to undertake a comprehensive meta-analysis of all studies to date that have assessed the relationship between carotid bruit and stenosis.

Methods: Electronic databases were used to identify all published studies in humans evaluating the association between bruit and stenosis published until and including July 2010. The odds ratio (OR) and 95% confidence intervals (CI) were calculated for each group using fixed and random effects models. Meta regression, using random effects (method of moments estimator), was performed in order to determine the association between the presence of a carotid bruit and the degree of stenosis.

Results: We identified 26 studies evaluating the association between carotid bruit and stenosis, in 15,117 arteries. There was a significant association between carotid bruit and carotid stenosis at all degrees of severity (overall pooled OR, 4.84; 95% CI, 3.64-6.44; p<0.00001) apart from stenoses greater than 80% (OR, 2.41; 95% CI, 0.56-10.27; p=0.23) making it a poor discriminator of clinically relevant (or non-relevant) carotid disease. Meta-regression showed a (non-significant) inverse relationship between carotid bruit and stenosis.
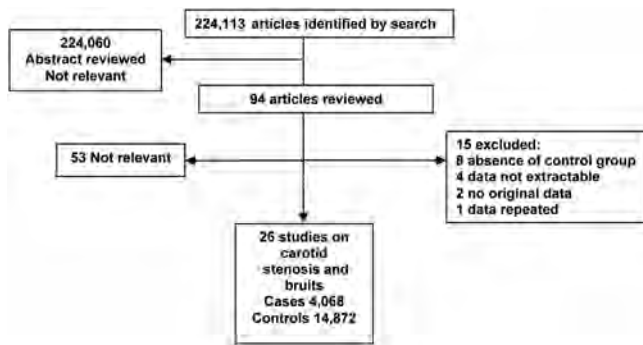
Figure 1. Summary of studies on carotid bruit and stenosis.
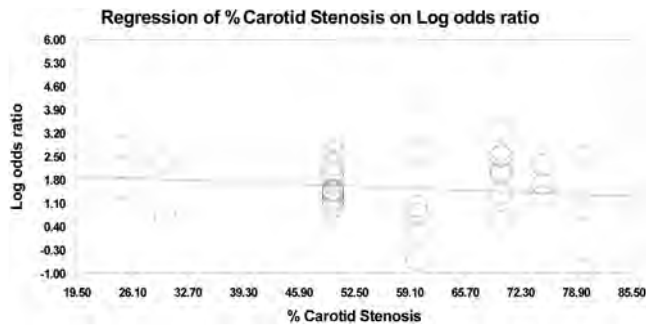
Figure 2. Weighted linear regression of log odds ratio of bruit against % carotid stenosis.

Conclusion: Carotid bruits are poor predictors of stenosis severity. However their detection should prompt the implementation of cardiovascular risk reduction strategies.

715 Meta-analysis and reviews

META-ANALYSIS OF OBSERVATIONAL STUDIES FOR THE RISK OF RECURRENT STROKE WITH PFO CLOSURE OR MEDICAL TREATMENT AND COMPARISON TO THE RESULTS OF THE CLOSURE I TRIAL

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Background: Percutaneous closure of patent foramen ovale (PFO) in patients with cryptogenic stroke is commonly considered as a secondary prevention measure based on observational evidence, but no published randomized data are available.

Methods: Meta-analysis of observational primary studies examining the incidence of recurrent stroke in cryptogenic stroke patients after PFO closure or medical treatment and comparison of effect size estimates to those reported for the CLOSURE I trial at the AHA Scientific Sessions.

Results: Data from 59 articles (69 separate cohorts, 2020 patients on medical treatment and 7104 undergoing closure) were synthesized. Of studies investigating closure-treated patients, 27/50 (54%) had no stroke outcomes on follow-up. The summary incidence rate (IR, 95% confidence interval) of recurrent stroke in closure studies was 0.4 (0.2-0.6) per 100 person-years, whereas in the medical studies it was 2.7 (1.8-3.9). By meta-analysis of 9 non-randomized comparative studies, a dramatic effect of 89% reduction in the IR of stroke with closure was shown (IR ratio = 0.11 (0.03-0.48)), which was highly discordant to the non-significant effect size observed in the CLOSURE I trial (0.76 (0.45-1.28)). Among closure-treated patients, the estimated IR for stroke was about three times higher in the CLOSURE I trial than the summary estimate from observational studies (1.3 (0.7 to 2.3) vs 0.4 (0.2-0.6)). Meta-regression analyses by study-level variables did not identify any patient characteristics as modifiers of the treatment effect.

Conclusion: Observational evidence based on large numbers of case series suggests that stroke recurrence after closure is extremely rare and PFO closure is very efficacious, but randomized data do not support such an effect. This evidentiary discrepancy highlights the necessity of randomized evidence to inform clinical decision making and the importance of continuation of enrollment of patients in the ongoing PFO closure trials.

SURGICAL DECOMPRESION FOR CEREBRAL EDEMA IN ACUTE ISCHEMIC STROKE

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Introduction: Large hemispheric cerebral infarction has a high case fatality, largely due to brain edema. The outcome remains poor despite medical treatment. Decompressive surgery is performed although evidence of clinical benefits was not available until recently. We performed a meta-analysis to compare the effects of decompressive surgery plus medical therapy with medical therapy alone in patients with large hemispheric cerebral infarctions.

Methods: Using the Cochrane methodology we searched the Cochrane Stroke Group Trials Register. We also searched the Cochrane Central Register of Controlled Trials, The Cochrane Library, MEDLINE (1966 to October 2010), EMBASE (1980 to October 2010), and Science Citation Index (October 2010).

We sought randomised controlled studies of decompressive surgery plus medical treatment vs. medical treatment alone in patients with cerebral infarcts complicated with cerebral edema. Outcomes of interest were Death at the end of follow-up, Death or moderately severe disability defined as mRS >3 at 6 and 12 months, and Death or severe disability defined as mRS >4 at 12 months. The Results are given using the Peto odds ratios with 95% confidence intervals (95% CI).

Results: We identified 5 completed randomised controlled trials, three had available published Results. These studies included 134 patients. The time window for intervention was 30 hours from stroke onset in two studies and 96 hours from stroke onset in one study. Surgical decompression decreased the risk of death at end of follow-up [OR= 0.19 (95% CI 0.09, 0.37)]. Death or disability defined as mRS >3 was not significantly different between the two treatment arms at end of follow-up [OR= 0.56 (95% CI 0.27, 1.15)]. Surgical decompression decreased the risk of death and severe disability defined as mRS >4 at 12 months [OR= 0.26 (95% CI 0.13, 0.51)]. Surgical decompression was associated with a non significant trend to survival with disability defined as mRS of 4 or 5 [OR= 2.45 (95% CI 0.92, 6.55)].

Conclusion: Surgical decompression lowers the risk of death and death or severe disability (mRS >4). Survival may be at the expense of severe disability.

POSTERIOR INFERIOR CEREBELLAR ARTERY (PICA) INFARCTION: CLINICAL OBSERVATIONS AND PROGNOSIS IN 81 PATIENTS

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Background and purpose: Since the magnetic resonance imaging appearance, diagnose cerebellar stroke and define involved territories has become easier. The aim of the present study is to describe the clinical characteristics and prognosis of patients with PICA infarction.

Methods: We retrospectively analyzed data from 81 consecutive patients with PICA infarction during a five-year period (March 2005-March 2010). All the infarcts were documented on computed tomography scan and/or magnetic resonance imaging. Other vascular territories could be involved.

Results: The mean age of our serie was 64.6 years, 69.1% in male.

PICA infarction was isolated in 61 patients and was accompanied by other territories in 20 patients (11 with other cerebellar territories, 9 with supratentorial infarctions). **Differently to other studies, atherothrombotic disease was the most important etiology in PICA (p:**0.02) and cardioembolism if other territories were involved (p:0.01).

Clinically, gait disturbance and other cerebellar signs were the prominent presenting features (81.5%), followed by long tract signs/symptoms (53.1%) and cranial nerves involvement (44.4%).

As main complications, there was hemorrhagic transformation in 23 patients (28.4%) and hydrocephalus appeared in 14 patients (17.3%). The mean day of appearance was 2.87±1.5 from stroke onset.

Considering Rankin scale (mRS), prognosis at discharge was worse if there were more than one vascular territories involved (mRS>3 in 65% VS 36%; p:0.057). Four patients were exitus (3.2%).

Conclusions: The etiology of isolated PICA infarction is frequently atherotrombosis. PICA infarctions may develop severe complications during the first week of stroke evolution, but their prognosis don't depend on it, it rather depends on the number of territories involved.

INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE IN ASIA: A META-ANALYSIS

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Background: Despite proven benefits of intravenous tissue plasminogen activator (IV-TPA) in acute ischemic stroke (AIS), treatment rates remain low. Data on thrombolysis in Asia are scarce & only a small percentage of patients are thrombolyzed. Dose of IV-TPA in Asia remains a controversial issue. Previous trials in Asia included only Japanese patients & suggested the efficacy and safety of low-dose IV-TPA (0.6mg/kg body weight; max 60mg) as comparable to standard-dose (0.9mg/kg body weight; max 90mg). Reduced treatment cost, lower symptomatic intracerebral hemorrhage (SICH) risk & comparable efficacy encouraged many Asian centers to adopt low or even variable-dose IV-TPA regimens. We aimed at evaluating various Asian studies on thrombolysis as compared to the SITS-MOST registry & NINDS trials.

Methods: We searched the published literature on AIS thrombolysis in Asia. We included studies published in English, with at least 10 patients, reported functional outcomes at 3months and SICH rates. Unadjusted relative risks and 95% Confidence intervals were calculated for each study. Pooled estimates from random effects models were used as tests for heterogeneity were statistically significant.

Results: We found only 17 publications on AIS thrombolysis in Asia. Of the 44 countries in Asia, only 9 (total number of patients1808) reported their Results. Owing to ethnic differences, stroke severity, small number of cases, outcome measures & TPA dose-regimens, it is difficult to compare these studies. In general, the functional outcomes were almost similar (to Japanese studies) when low-dose TPA was used in non-Japanese populations across Asia. Interestingly, with standard-dose IV-TPA regimen, considerably better functional outcomes were observed, without increasing SICH rates.

Conclusions: Variable dose-regimens of IV-TPA are used across Asia without any reliable or established evidence. Based on Japanese studies, recommending low-dose TPA across Asia is difficult as there has never been a head-to-head comparison of variable dose regimens. Perhaps, an Asia-wide large randomized controlled trial can address the prevailing confusion about IV-TPA dose.

Rehabilitation and reorganisation after stroke

788 Rehabilitation and reorganisation after stroke

EFFICACY OF HYBRID CONSTRAINT-INDUCED MOVEMENT THERAPY

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Background: Constraint-induced movement therapy (CIMT) is a rehabilitation technique for upper extremity (UE) hemiplegia resulting from stroke and other brain injuries. Its efficacy is now well established. We previously demonstrated that CIMT more effectively treated the distal function of the affected arm compared to the proximal function. Here, we describe a hybrid procedure that involves CIMT in combination with robotic therapy (HCIMT: Hybrid Constraint-induced movement therapy) to address the shortcomings with respect to efficacy on proximal function. The purpose of this study was to evaluate the efficacy of HCIMT in chronic rehabilitation.

Methods: The study was a prospective, multicenter clinical trial conducted at two rehabilitation facilities between 2008 and 2010. Subjects were 28 individuals (21 men, 7 women; mean age, 57.4 ± 12.0 years) who met the CIMT inclusion criteria. Subjects were allocated to one of two interventions that spanned 2 weeks (5 days/week). Subjects in the HCIMT group underwent 4 hours of CIMT and 1 hour of robotic therapy, whereas those in the control group underwent 5 hours of CIMT. In both groups, CIMT was carried out in accordance with the EXCITE protocol. UE function was assessed using the three subcomponents of the Fugl-Meyer Assessment (FMA; Category A, shoulder/elbow/forearm; Category B, wrist; Category C, hand) at baseline and post-intervention. Analysis of covariance (ANCOVA) was used to examine the effects of HCIMT for all variables. $p<0.01$ was considered significant.

Results: HCIMT showed significant improvements in all three subcomponents of the FMA compared to the control group (score change for HCIMT group vs. control; Category A: 5.73 ± 5.12vs. 1.06 ± 2.68, $p<0.01$; Category B: 1.36 ± 1.56 vs. 0.94 ± 1.14, $p<0.01$; Category C: 3.54 ± 3.33 vs. 1.06 ± 1.43, $p<0.01$).

Conclusion: HCIMT improved the function of the affected arm in chronic post-stroke patients to a greater degree than that achieved by CIMT. HCIMT is also expected to reduce the burden on therapists because it includes one hour of self-training per session.

789 Rehabilitation and reorganisation after stroke

EVIDENCE FOR EFFECTIVENESS OF INTERVENTIONS FOR EYE MOVEMENT DISORDERS IN STROKE PATIENTS: RESULTS FROM A COCHRANE SYSTEMATIC REVIEW

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Background: Eye movement disorders (EMD) may affect over 70% of stroke patients, resulting in difficulty maintaining a normal ocular position, moving eyes appropriately and subsequent functional disabilities. Treatment interventions for EMD are inconsistent, including eye movement training, compensatory head postures, prisms, eye patches, pharmacology. We aimed to systematically review randomised trials of interventions for EMD in people with stroke.

Methods: We searched the Cochrane Stroke Group Trials Register, the Cochrane Eyes and Vision Group Trials Register and nine electronic bibliographic databases including: The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, AMED, and PsycINFO. We searched reference lists and trials registers, hand searched relevant journals and contacted experts. We included randomised controlled trials (RCTs) of adults with stroke (or with mixed aetiology including stroke), which investigated interventions targeted at improving an eye movement disorder or the ability of participants to cope with an eye movement disorder. Our primary outcome was functional ability in activities of daily living. Two authors independently screened abstracts, extracted data and appraised trials. Assessment of methodological quality considered sources of bias including allocation concealment, blinding of outcome assessor, method of dealing with missing data.

Results: We considered 7357 titles, 373 abstracts and 81 full papers. Two studies including participants of mixed aetiology (n=38, 5 with stroke) met the inclusion criteria. Both studies investigated pharmacological interventions. It was not appropriate to pool data. We also identified two studies with which require further assessment, and one ongoing study.

Conclusion: There is an absence of evidence relating to the effectiveness of interventions for patients with EMD after stroke. Well-designed and conducted RCTs are urgently required.

790 Rehabilitation and reorganisation after stroke

TOLERANCE OF REHABILITATION USING TILT-TABLE WITHIN THE FIRST 48 HOURS AFTER STROKE ONSET

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Background: The aim of this study was to assess the predictors of tolerance of early rehabilitation using tilt-table in acute stroke patients.

Methods: We prospectively included AS 40 patients (67.5% males; mean age 59.8, 75% ischemic; 25% hematomas) during the first 48 hs after stroke onset. Patients with arrhythmias, severe internal diseases and damages of peripheral nervous system were excluded. All patients received the standard medical and physiotherapy. Patients were tilted using tilt table under blood pressure (BP), heart rate (HR) and SpO2 control. Respiratory probes with apnea and hyperventilation were investigated at patients without aphasia. The analysis of HR variability (HRV) using short-term recordings (5 minutes) was performed. Total power (TP; ms2), standard deviation of the NN intervals (SDNN; ms), low frequency component (VLF; ms2), low frequency component (LF; ms2), high frequency component (HF; ms2), ratio LF/HF were investigated.

Results: Twenty five (62.5%) patients didn't present orthostatic hypotension. The analysis of HRV revealed ratio LF/HF 3.39 ± 2.99 in these patients. Twenty one patients were able to perform respiratory tests and the adequate probe with apnea was demonstrated in 15 patients (78.9%). Fifteen patients (37.5%) presented significant decreasing of BP during session on the first day. These patients presented ratio LF/HF 7.69 ± 7.84 (p=0.026). The adequate probe with apnea was demonstrated in 4 (21%) of 12 patients without aphasia (p=0.033) in this group.

Conclusion: Stroke may lead to hyperactivity of sympathetic and central pathways of HR regulation even in horizontal position of patient. It occurs due to decreasing role of parasympathetic influence and can disturb the response on physiological test such as respiratory test and tilt. It is possible that inadequate respiratory probes and increasing of LF/HF ratio might be predictors of orthostatic hypotension during early rehabilitation sessions using a tilt-table.

791 Rehabilitation and reorganisation after stroke

WHEN DAUGHTERS BECOME CAREGIVERS TO A PARENT WHO HAS SUFFERED A STROKE: A QUALITATIVE EXPLORATION OF HOW THE PARENT-CHILD RELATIONSHIP INFLUENCES CAREGIVER WELL BEING

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Background: Approximately 50% of stroke survivors with disability live in the community and are cared for by the family. Currently, 55% of North American caregivers are adult children with daughters becoming caregivers more often than sons. Since the "child" and "parent" roles develop prior to stroke, changes to the parent-child relationship can influence the caregiving experience of adult daughters. Thus, the relationship's influence on the well being of adult daughter caregivers (ADC) warrants further attention.

Method: A qualitative descriptive approach was taken to gain insight into which aspects of the relationship interact with well being and how this interaction arises. 21 ADCs participated in one in-depth interview, which was transcribed, reviewed, coded and categorized to generate themes.

Results: Data analysis revealed four key themes: 1)Becoming a caregiver: Predispositions to caregiving included geographic proximity to parent and gender considerations; 2)Having too little time: Time constraints due to high demands of parent care and conflicts with other roles. To cope, ADCs changed their lifestyle (e.g. reduced work hours); 3)Changing relationships: Relationship with parent became closer post-stroke while relationships with others were more strained. ADCs were upset that cognitive and physical limitations prevented parent from interacting with them as they did pre-stroke. Parent care was compared to child care with mention of role reversal; 4)Needing support: ADCs desired peer support and found parent care stressful when spousal support was absent.

Conclusion: This study helps health care professionals understand the context and experiences of adult daughters who assume the stroke caregiving role. Findings reveal: 1) Who is likely to take on the caregiving role and why; 2)Some of the challenges ADCs face (e.g. time, relationship changes, population-specific support needs); 3)That programs could incorporate peer support, relationship counselling and respite.

792 Rehabilitation and reorganisation after stroke

IMPLEMENTING EARLY SUPPORTED DISCHARGE: BEYOND THE EVIDENCE BASE

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Background: As part of our research into Early Supported Discharge (ESD) services for stroke patients, we are investigating what services exist across a predefind area of approximately 2 million people in the UK, and how they are organised and delivered in practice. A main objective is to identify key factors influencing the ESD service models implemented. We also explore team working issues identified as needing further Discussion, such as: multidisciplinary roles; access to stroke specialist knowledge; and interaction with carers.

Methods: Our work adopts a multi-method, qualitative approach to data collection and analyses, employing; semi-structured interviews, observation of relevant meetings, and the collation of documentary data. The findings are based on a thematic qualitative analysis of interviews with 35 professionals working in and around two ESD services. We elicited the views and experiences of service commissioners, service managers, physicians, therapists, nurses and allied healthcare professionals.

Results: Preliminary analysis has generated several themes, which illustrate the challenges of implementing ESD services. Firstly, patient eligibility decisions require collaborative work between ward staff and ESD team members. One enabling mechanism relies on job roles that span acute and community organisational boundaries. Ensuring stroke specialist knowledge is made available can also be critical to effectiveness. In terms of a multidisciplinary model, ESD teams respond to changing local patient needs, and the existence of other services. A final theme is how ESD interventions may raise carer stress and burden, so increasing the demand for support and education for this group.

Conclusion: These findings suggest that ESD functioning is complex, with team working a critical element. Our ongoing research will provide insights into how to deliver effective ESD services within an integrated stroke care system, for the benefit of patient and carer groups.

793 Rehabilitation and reorganisation after stroke

EVOLUTION OF CARDIORESPIRATORY FITNESS AFTER STROKE: A 1-YEAR FOLLOW-UP STUDY. INFLUENCE OF PRE-STROKE PATIENTS' CHARACTERISTICS AND STROKE-RELATED FACTORS

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Background and Objectives: Cardiorespiratory fitness is poor after stroke; however its evolution has hardly been investigated. We examined changes in cardiorespiratory fitness between 3, 6 and 12 months post-stroke and explored the effect of pre-stroke patients' characteristics and stroke-related factors on this evolution.

Methods: Thirty three patients performed a symptom-limited graded cycle ergometer test at 3, 6 and 12 months post-stroke. Age, gender, pre-morbid physical activity level, clinical history (smoking, diabetes mellitus, chronic pulmonary diseases, cardiovascular diseases, overweight and hypertension), stroke type and area, side of lesion and assessments of stroke severity were evaluated at intake.

Results: Peak oxygen uptake (VO2 peak) was 18.1 ± 6.6 mL/kg/min, 19.8 ± 8.0 mL/kg/min and 19.7 ± 8.4 mL/kg/min at 3, 6 and 12 months post-stroke. Values were 1575.3 ± 638.3, 1710.7 ± 710.3 and 1687.2 ± 777.5 for the Oxygen Uptake Efficiency Slope (OUES) respectively. Mixed models showed no significant difference over time for VO2 peak (p=0.10), nor for the logarithm of OUES (p=0.09). Stroke survivors at risk of deconditioning were pre-morbid less active at work or in sport activities, diabetic or initially more severely impaired. Combination of factors revealed that older stroke patients with diabetes were less likely to improve on VO2 peak and older, female, diabetic non-smokers improved less on log OUES.

Conclusions: Cardiorespiratory fitness is reduced during the entire first year post-stroke and showed no evolution. Further studies should clarify how to increase cardiorespiratory fitness during stay in the rehabilitation centre and how community based aerobic exercise training post-rehabilitation can be organised.

794 Rehabilitation and reorganisation after stroke

ALTERNATIVE MEDICINES FOR STROKE TREATMENT IN NORTHWEST INDIA

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Background: Alternative medicines (AM) are commonly used by stroke patients in India. Patients often discontinue secondary prevention measures while on AM. Our objectives were to study the spectrum of AM use and also to explore the factors that predict the use of AM in stroke patients.

Methods: This study was done in the Stroke Unit of Christian Medical College, Ludhiana from June 2010 to December 2010. Stroke patients were interviewed using a structured questionnaire ≥ 6 months post stroke. Demographic details and stroke characteristics were documented. Outcome was assessed using modified Rankin scale (mRs). Statistical analysis were done using SPSS version 16.0.

Results: 214 stroke patients were interviewed. The mean age was 57.1 ± 13 years and 145 (67.7%) were men. Out of 214 patients, 104 (48.5%) had used AM treatment. They are as follows; ayurvedic massage 59 (57.3%), intravenous fluids 22 (21.4%), herbal medicines 15 (14.6%), homeopathy 14 (13.6%), witchcraft 3 (2.9%), acupuncture 3 (2.9%), opium intake 10 (9.7%) and other indigenous treatments 10 (9.7%). Most of the patients 94 (93.1%) heard about AM treatments from their friends or relatives. Patients who had residual limb weakness (p=0.02), ischemic stroke (p=0.01) and poor outcome (mRs >2, p<0.0001) often utilized AM treatment. Thirty five (33.6%) patients noticed significant improvement and 8 (7.7%) patients experienced side effects after taking AM. The mean cost and duration of treatment was approximately Indian rupees 7972 ± 17149 (Euro 136 ± 292) and 3.6 ± 4.6 months respectively. Patients who received AM treatment were less likely to discontinue secondary prevention measures as compared to patients who did not receive AM treatment (32.6% vs. 67.4%, p=0.01).

Conclusions: Nearly half of our patients opted for AM. Residual limb weakness, ischemic stroke and poor outcome predicted the use of AM. Patients who use AM were more likely to adhere to secondary prevention strategies.

795 Rehabilitation and reorganisation after stroke

OBSERVATIONS WITH A NEW MOVEMENT-MONITORING DEVICE IN REHABILITATION OF STROKE PATIENTS

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Background: Our team developed a small, wireless device for easy measuring of 3-d acceleration and movement-duration of paretic limbs. The Aims were to validate its usefulness and compare the data with stroke scales on bedridden, hemiparetic, acute stroke patients.

Methods: Data of 50 acute, severely hemiparetic, bedridden acute stroke pts. (mean age: 59 yrs min: 29, max 76, mean NIHSS on admission: 6,8 min: 1, max: 21) will

be presented. The small, battery driven devices were attached to the paretic and non-paretic limbs and any movements and movement-durations were registered (24/7), wireless and analyzed by our program: spectra of daily and night movements, increasing or decreasing trends of movement-amounts, quantitative comparison of changes of paretic and non-paretic limbs. The data of movement-monitors were compared also with the changes of NIHSS, European Stroke Scale and Barré-Mingazzini, wrist extension tests etc).

Results: The device sensitively detected the movement-differences between paretic and non-paretic limbs, daily and night periods (meals, round visit, visitors) including the sudden, unexpected events (fall, excitation etc.). The subclinical paresis could be detected and the intensity and duration of passive and active physicotherapy controlled not only real-time but also retrospectively.

The data collected by the movement-monitor showed significant correlation with the changes of stroke scales both for the improving and non-improving patients (P 0.01).

Conclusion: Our device has multipurpose applications. Besides alarm-function, it can be used for quantitative evaluation of improvement/worsening of paresis and efficacy of physicotherapy and also for elaboration of individualized rehabilitation strategy.

796 Rehabilitation and reorganisation after stroke

EARLY SUPPORTED DISCHARGE: WHAT PROPORTION OF PATIENTS BENEFIT?

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Introduction: There is a robust evidence base for Early Supported Discharge (ESD) of stroke patients and an increasing policy drive to implement ESD services across the UK and internationally. ESD services can reduce long term dependency and admission to institutional care as well as reducing the length of hospital stay. A meta-analysis of ESD trial data showed that ESD is most effective for mild to moderate stroke patients. Whereas research literature suggests around 40% of stroke patients would benefit from ESD, it remains unclear what the proportion of patients would be eligible in practice.

Methods: Barthel scores provide a reliable means to assess stroke severity of a population of patients. A recent ESD consensus activity established that most patients eligible for ESD would have a barthel score of between 10-17. This permitted calculation of the percentage of stroke patients that would have been eligible for ESD, using retrospective data from Nottingham University Hospital NHS Trust (NUH), a large acute trust in the UK.

Results: Of the 3,169 stroke patients admitted during 2007-2009, barthel scores were recorded for 2,143 patients (68%) on admission. Of these, 53% were severe strokes (barthel score of 0-9), 15% were moderate (barthel 10-14) and 32% were mild (barthel 15-20). Using ESD consensus guidelines, only 27% of patients would have been eligible for ESD.

Conclusion: Data suggest that, at least for NUH, only around 27% of patients would be eligible for ESD. This is less than the 40% target featured in a UK accelerated Stroke Improvement Programme initiative, and trial based data. Attempts to meet the 40% target may result in more severe or too mild patients taking up places in the ESD service or hospitals waiting for patients to improve before referring them to ESD. This could compromise the benefit of ESD, which is to significantly reduce length of stay in hospital, realise cost savings and provide early and effective rehabilitation in patient's homes.

797 Rehabilitation and reorganisation after stroke

REHABILITATION GAMING SYSTEM (RGS): THE IMPACT OF VIRTUAL REALITY BASED TRAINING ON UPPER LIMB RECOVERY IN THE ACUTE AND CHRONIC PHASE OF STROKE

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An estimated 30-60% of adult patients do not achieve satisfactory motor recovery after stroke despite intensive rehabilitation. Novel interventions such as Virtual Reality (VR) and robotics have been developed for upper limb treatment without a clear consensus on their effectivity. We present the Results of three studies including both acute and chronic patients for upper limb motor rehabilitation with a VR based system called Rehabilition Gaming System (RGS).

Between October 2007 and December 2010, 103 volunteer stroke patients with hemiparesis were recruited for this study. Different patient groups: acute (< 2 weeks post-stroke), first-year post-stroke (> 2 weeks and <1 year) and chronic (>1 year) underwent RGS therapy. In the acute group we conducted a randomized study comparing intervention to a control group. The intervention group underwent RGS therapy (20 min/day for 3 weeks or 12 weeks) + standard therapy. The control group received standard therapy + 20 additional extra min. The first-year post-stroke and chronic groups received RGS therapy during 3 weeks 20 min/day + standard therapy. Assessment was conducted at baseline, post-treatment and follow-up using a set of standard clinical scales.

In the acute group patients allocated to the RGS group showed improvements as compared to controls with significant differences in the Fugl-Meyer and Chedoke Arm and Hand Test. The comparison between the 3 week and 12 week acute groups showed that patients benefit from extensive training. The first-year post-stroke group as well as the chronic group improved significantly from baseline to end of treatment at most of the standard clinical scales. Comparing the three different groups shows that is favorable to start RGS therapy early after stroke.

Overall, the different studies show that both acute and chronic stroke patients benefit from RGS based VR therapy.

798 Rehabilitation and reorganisation after stroke

COGNITIVE ABILITIES AND MOTIVATION IN VIRTUAL REALITY-ENRICHED ARM TRAINING WITH INCREASED COGNITIVE DEMAND IN SUBACUTE STROKE PATIENTS

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Background: Virtual Reality (VR) has been applied successfully in neurorehabilitation of movements and applications have become highly sophisticated. Despite technical innovations, it is crucial that virtual tasks are therapeutically effective and engage patients adequately. Stroke patients often exhibit reduced cognitive abilities causing VR-games to be very challenging. Difficulties in task fulfillment can lead to reduced motivation and less effective therapy.

This study investigated the relationship between cognitive abilities, motivation and task performance at different levels of cognitive demand in a VR-enriched arm training.

Methods: 12 stroke patients with moderate to severe motor impairment in the arm performed a training session using the passive arm orthosis Armeo. In a "pick-and-place"-game a bottle had to be put into a basket. Three increasingly demanding versions were played: an arrow (1), a picture puzzle (2) or a question (3) indicating the goal. For each, patients rated enjoyment, motivation, physical and cognitive effort. Task performance and average grasp time (from pick till drop) were calculated. As measures of cognitive abilities a crossmodal integration, a divided attention test and the ACE-R were used.

Results: A decrease in performance across version 1-3 corresponded to an increase of grasp times across versions (both p<0.01), mirroring an extended need for cognitive resources. Divided attention score correlated negatively with number of caught bottles for all versions. Correlation strength increased across version 1-3 (r=-.485 to -.621) and reached significance (p<0.05) in version 3. Moreover motivation scores differed significantly across versions (p<0.05) with the highest values for version 2 followed by 3 and 1.

Conclusion: Results show that the cognitive demand of a motor exercise in VR is crucial to maximize motivation and movement success. When developing VR it is important to consider individual capabilities to design appropriate applications.

799 Rehabilitation and reorganisation after stroke

VALIDATION OF THE EXTENDED ICF CORE SET FOR STROKE FROM THE PATIENT PERSPECTIVE USING FOCUS GROUPS

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Background: The Extended ICF Core Set for Stroke is an application of the International Classification of Functioning, Disability and Health (ICF) of the World Health Organisation (WHO) with the purpose of representing the typical spectrum of problems in functioning of persons with stroke. The objective of the study was to add evidence to the validation of the Extended ICF Core Set for Stroke from the

perspective of patients using focus groups to explore the aspects of functioning and health important to persons with stroke.

Methods: Qualitative study using focus groups. The sampling of the participants followed the maximum variation strategy. Sample size was determined by saturation. The focus groups were audio recorded and transcribed verbatim. After qualitative data analysis the resulting concepts were linked to ICF categories and compared to the categories included in the Extended ICF Core Set for Stroke.

Results: Sixty persons with stroke participated in 15 focus groups. One hundred and twenty-one out of 166 ICF categories contained in the Extended ICF Core Set for Stroke were reported by the participants. Thirty-one additional categories that are not covered in the Extended ICF Core Set for Stroke were raised.

Conclusion: The existing version of the Extended ICF Core Set for Stroke could be confirmed almost entirely from patient perspective.

800 Rehabilitation and reorganisation after stroke

BRAIN PLASTICITY AFTER ISCHEMIC STROKE. A SEQUENTIAL BIOELECTRIC BRAIN IMAGING STUDY WITH A NEW METHOD OF SINGLE CHANNEL ACTIVITY LAPLACIAN MAPPING

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Background: Reorganisation of neuronal networking in the course of functional recovery after stroke is still not fully understood. For mapping the sequentiqal activity of different cortical areas in preparation and execution of motor activity and their reorganisation in the time of stroke rehabilitation, the BOLD fMRI was used even though its low temporal resolution. Using finger tapping paradigm, high power EEG based brain mapping with a 0.5 ms temporal resolution promises a new insight on brain plasticity.

Methods: 128 channels EEG studies were carried out on 9 stroke patients with right hemiparesis (5 male, 4 female, age 63.7±11.0 yrs; 6 with subcortical; 3 with motor cortex lesion). The first investigation was performed on average 10.4 days after stroke, follow-up measurement was carried out 6 months later in 4 of the patients. For motor cortex activation, the finger tapping paradigm was used with a visual cue. Laplacian maps and Single Channel Activity (SCA) were calculated by taking the surface Laplacian maps 200 ms before and 100 ms after tapping. Selecting the appropriate level of absolute radial current strength (above 2x SD calculated in every moment of registration) was considered as brain activation. SCA was calculated from 1-400 Hz spectral activity.

Results: Finger tapping with the paretic hand differed from the nonparetic tapping in showing greater activation in the ipsilateral motor, ipsilateral posterior parietal, and bilateral prefrontal cortex. In most of the cases we found smaller or no activity in the contralateral motor cortex in the subacut phase, this activity has appeared over time with the recovery of function, with larger than normal extention in all cases.

Conclusion: SCA Laplacian mapping, a new functional brain imaging method promises new possibility in understanding reparative processes following stroke. Repeated measurements can characterise the organisation of the preparative phase and the extent of the execution.

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802 Rehabilitation and reorganisation after stroke

PARTICIPATION IN EVERYDAY ACTIVITIES ONE YEAR AFTER STROKE

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Background: Participation in everyday life after stroke is considered to have a positive influence on well-being and is an important outcome in rehabilitation. The aim of this prospective longitudinal study was to explore and describe factors associated with participation in everyday activities (i.e. occupational gaps) and to identify factors at 3 months that predict restrictions in participation in everyday activities one year post stroke.

Methods: The Occupational Gaps Questionnaire was administered to 200 persons 1 year post stroke. Occupational gaps data (i.e. gaps in ADLs, work, social and leisure activities) was used as the dependent variable in a regression analyses. Demographic variables, the Stroke Impact Scale and reported life satisfaction were used as independent variables in a 12 month association model and a three month prediction model.

Results: The mean number of occupational gaps was 4.6 and 10% of the persons did not experience any gaps. Five factors were associated with occupational gaps at 12 months: social participation, not born in Sweden, recovery, life satisfaction, and stroke severity. The three factors; social participation, not born in Sweden, and

ADL ability at 3 months predicted the extent of occupational gaps at one year and explained 27% of the variance.

Conclusion: Participants perceived restrictions in participation in everyday activities one year post stroke. Predicting participation in everyday activities one year after stroke is possible early in the rehabilitation process and can facilitate identification of persons that risk restrictions in participation. This in turn can enable effective preventative rehabilitation interventions.

803 Rehabilitation and reorganisation after stroke

ACUTE STROKE COMBINED WITH EARLY NEUROREHABILITATION TREATMENT (ASCENT): A PILOT SAFETY-FEASIBILITY STUDY

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Background: There is debate whether rehabilitation in the first few days after stroke is safe, despite evidence of a unique early treatment window in which neuroplasticity is facilitated by altered inhibition/disinhibition. Obstacles to early rehab include cardiovascular comorbidity, coordination of acute stroke and rehab management, and poor patient knowledge about rehabilitation, leading to low participation. We aimed to test safety and feasibility of very early rehabilitation on an acute stroke unit in an urban, racially diverse, tertiary referral hospital.

Methods: Using an adaptive design stepwise sequential probability ratio test (sSPRT) we assessed safety during dose-escalation of a gait training intervention 24-96h after stroke onset. A licensed PT delivered interventions focused on progression to upright mobility and walking. The study team consisted of an acute stroke neurologist, physiatrist, study PT, and bilingual patient educator who communicated goals of rehab to patient and family prior to PT. The team reviewed daily cardiac/neurological outcomes. Inclusion criteria were stroke or ICH, NIHSS leg motor or ataxia ≥1, NIHSS consciousness ≤1, ability to consent, prestroke Rankin ≤3, and admission to the Stroke service <24h after stroke.

Results: The sSPRT algorithm included 6 tiers of rehabilitation intensity, from 30 min at 72-96h to 60 min at 24-48, 49-72, and 73-96h. After 28 patients (age 45-97, baseline NIHSS 1-20) the study met dose-escalation criteria at the highest tier. All patients received education intervention. Safety outcomes were 3 withdrawals for cardiac concerns (2 pts at tier 3, 1 at tier 6), and 3 withdrawals due to fatigue (1 at tier 4, 1 at tier 5, 1 at tier 6). One patient did not complete his assigned dose due to sedation for diagnostic testing.

Conclusion: These preliminary data suggest that very early rehabilitation with gait training may be safe and feasible beginning 24-48h after stroke onset An integrated acute stroke/rehabilitation team was critical to feasibility. Further study is required to validate safety and efficacy of very early rehabilitation in acute stroke.

804 Rehabilitation and reorganisation after stroke

SOCIAL RGS: THE INFLUENCE OF A MULTIPLAYER VIRTUAL REALITY SYSTEM ON MOTOR REHABILITATION PERFORMANCE AND MOTIVATION

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Depression affects approximately one third of stroke patients. Social factors and motivation are strongly linked to the development of depression [1]. The goal of this study is to evaluate the effects of including social interaction in Virtual Reality (VR) based stroke rehabilitation.

We hypothesize that a multiplayer competitive context will have a positive effect on the involvement of the patients in the therapy and thus also on the rehabilitation process. We test this hypothesis using the Rehabilitation Gaming System (RGS), an ICT virtual reality (VR) tool for upper extremities motor rehabilitation [2]. We developed a dedicated RGS scenario where the player has to match pairs of cards from a stack of playing cards. This task trains cognitive (memory) and motor tasks (grasping and reaching). The stroke patients (N=8, Male = 4, mean time post stroke = 7 months) participated in two sessions lasting 20 minutes, one using a single player VR environment and another using a multiplayer version of the same game.

Our Results show that the upper limbs exercises performed by the patients in multiplayer mode reached wider elbow flexion/extension movements than the ones performed during the single-player game session (p = 0.036). Considering that the presence of spasticity is very common in patients affected by an ictus and it causes an ongoing level of contraction, the these Results suggest that the patients affected displayed more effort in reaching in a social task.

Our study shows that the social engagement in multiplayer environments positively affects the patients' performance and enjoyment during the task. Although the long term impact of this enhanced motivation needs to be further assessed, our Results do suggest that the inclusion of social factors such as multi-player capabilities is an important factor for the rehabilitation process in VR based therapy and might have an impact on both performance and mood of stroke patients.

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805 Rehabilitation and reorganisation after stroke

GIVING ADVICE TO PATIENTS ON DRIVING AFTER TIA/STROKE: A SURVEY OF HEALTH CARE PROFESSIONALS

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Background: In Scotland driving regulations, including those specific to TIA/stroke, are set by the Driver and Vehicle Licensing Agency (DVLA). Many patients are keen to return to driving following TIA or stroke. Healthcare professionals are often asked to give advice on returning to driving.

We wanted to find out if members of the multidisciplinary stroke team (MDT) at Ayr Hospital are confident in giving advice on driving to patients. As we operate a Rapid Access TIA clinic accessible to local GPs we also wanted to assess the advice given by GPs on driving.

Methods: We designed two short surveys, one aimed at local GPs and one at healthcare staff. We distributed the survey to 102 local GPs and 50 staff members. Surveys were completed and returned anonymously.

Results: 27 local GPs who had made a recent referral to our Rapid Access service completed the survey. 20 (74.1%) regularly give advice on driving to patients suspected to have had TIA. 18 (66.7%) correctly advise all such patients to abstain until further notice. 23 (85.2%) are aware of DVLA regulations. 13 (48.1%) were asked by our team to advise the patient to abstain until further notice.

47 MDT members completed the survey. 34 (72.3%) were aware of DVLA regulations and 18 (38.3%) were confident in advising on driving after TIA/stroke. 13 (27.7%) were aware that regulations differ according to vehicle driven, 18 (38.3%) knew that all patients should abstain immediately following the event and 14 (29.8%) knew which patients could safely return to driving. 17 (36.2%) knew how to organise further assessment of driving if required.

Conclusions: There is a lack of awareness of DVLA regulations and the correct advice to give to patients on driving after TIA/stroke among local GPs and particularly MDT members. We plan to institute an educational program for all healthcare professionals in order to improve the quality of advice given to patients and increase confidence in giving this advice.

806 Rehabilitation and reorganisation after stroke

THE COMPLEX ASSESSMENT OF THE PATHOLOGICAL WALKING PATTERN AND THE EFFICACY OF REHABILITATION IN ACUTE STROKE PATIENTS

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Purpose: Assessment of the rehabilitation's efficacy at stroke gait disorders.
Methods: We examined 97 patients in an acute period of ischemic and hemorrhagic stroke, including deep neurologic examination; ADL-scales (standing balance - SB, functional ambulation categories - FAC, Bartel index - BI); stabylometry with the open and closed eyes; stimulating electromyography (EMG); tests for the evaluation of movement's vegetative maintenance. 1st examination spent before the beginning of gait's training (in average at 13 ± 3 days from stroke onset); 2nd - before discharge from a hospital (30 ± 2 days). Patients of 1st group (n=38) received the standard rehabilitation program on the ontogenetic caused kinesitherapy method; patients of 2nd group (n=59) in addition trained on the robotic device Gait Trainer I (GT).
Results: Complex examination has shown that gait's disturbance in acute stroke patients is defined mainly by a condition of vegetative nervous system, severity of a paresis and intensity of an ataxy. From ADL-scales the most adequate was complex use of SB and FAC scales; BI has shown the least suitability. Dynamic EMG-data (increase of H/M ratio, realizations of F-waves) is positively correlated (p<0,05) with rehabilitation's efficiency reflected the recovery of reflex spinal segmentary activity. Prognostic in aspect of the gait independence recovery was stabylometry. Complex parameter Stab at 1st examination positively correlated (r=0,52; p<0,001) with an evaluation on FAC at 2nd examination. The patients of 2nd group trained on GT at 2nd research have shown the best recovery of muscular force, sensitivity and independence (p<0,01).
Conclusions: For the integrated evaluation of gait's function in stroke patients use of separate scales is ineffective, but complex clinical and physiological examination is necessary. Use in acute stroke period of robotic devices allows to accelerate a recovery and is safe for a patient.

807 Rehabilitation and reorganisation after stroke

DISORDERS OF CONSCIOUSNESS AFTER SEVERE VASCULAR BRAIN INJURY: INFLUENCE OF CLINICAL CHARACTERISTICS AND EARLY REHABILITATION ON FUNCTIONAL OUTCOME

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Background: Vegetative state (VS) and Minimally Conscious State (MCS) may be the result of large strokes or strategic vascular lesions which cause a disconnection syndrome leading to consciousness breakdown. Information about the recovery and the long-term outcome of these patients is scanty.
Methods: All patients admitted to the Post-Coma and Rehabilitation Care Unit in a 1-year period were assessed along a six months period by means of the Coma Recovery Scale Revised (CRS-R), the Level of Cognitive Functioning (LCF) scale, the Extended-Glasgow Outcomes Scale (E-GOS) and the Disability Rating Scale (DRS). ANOVA and Tukey's post-hoc comparisons were used to compare groups.
Results: Out of 83 patients with a severe brain injury 29 (64%) had an hemorrhagic stroke and 16 (36%) an ischemic stroke. On admission, the most frequent diagnosis was VS (56%), followed by locked-in syndrome (LIS) (15%), coma (11%), MCS (9%) and residual cognitive impairment (9%). Time from brain injury to admission was less than 15 days in 2 patients (4%), from 16 to 30 days in 16 (36%), from 31 to 60 days in 21 (47%) and more than 60 days in 6 (13%). At the 6-month follow-up 13 patients died (29%), 9 had a good recovery (20%), 7 a residual cognitive impairment (16%), 4 a persistent VS (9%) and 4 a MCS (9%), 7 a LIS (15%), and 1 a subtentorial coma (2%). Patients with ischemic stroke improved less than patients with hemorrhagic stroke. Patients who started rehabilitation within a shorter time interval from the acute event had a higher degree of improvement in terms of LCF (rho=0.27; p=0.039) and DRS (rho=-0.29; p=0.032) scores.
Conclusions: Recovery of consciousness is the prerequisite for any rehabilitative goal and represents the major divide between patients who recover and patients who do not. Encouraging early rehabilitation and tailoring the management of patients to their individual needs may improve long-term recovery.

808 Rehabilitation and reorganisation after stroke

POST-STROKE VISUAL DEFICIT: CLINICAL COURSE AND CHANGES IN CEREBRAL ACTIVATIONS

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Background and purpose: Little is known about the outcome and recovery mechanisms of visual perception after a focal lesion of the occipital lobe in humans, especially after stroke. In this study, we aimed to describe the clinical course and the neural substrates of conscious perceptive visual deficit after posterior cerebral artery infarct.
Methods: We prospectively included eight patients (7 men and 1 woman; mean age = 64.6 years ±18) with visual deficit induced by partial damage of the striate cortex related to acute posterior cerebral artery infarct. Conscious perception of colour and motion was assessed from the acute phase to the third month. Functional Magnetic Resonance Imaging (MRI) was performed to investigate neural substrates of visual recovery.
Results: In the acute phase of stroke, visual deficiency was global (3/8 patients), selective to colour (4/8 patients) or selective to motion (1/8 patients). During the follow-up, visual performance increased with respect to colour (from 29% to 70%; p<0.005) and with respect to motion (from 47% to 74%; p<0.005). Despite a lack of ipsilesional V1 area activation in the acute phase, activations in this area and in the contralesional extrastriate cortex were obtained during follow-up. Both ipsi- and contralesional V4 activations were correlated with better outcome.

Conclusions: Extensive visual recovery occurs early after partial acute posterior cerebral artery infarct. Spared islands in ipsilesional V1 area and transcallosal pathways might be involved in post-stroke visual recovery.

809 Rehabilitation and reorganisation after stroke

VIRTUAL REALITY NAVIGATION AND VISUOSPATIAL NEGLECT AFTER STROKE

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Background: Virtual reality integrates real-time computer graphics, body tracking devices and visual displays that may assess visuospatial skills and navigation abilities. A preliminary study in right brain damaged patients has proven the applicability of virtual reality device. We propose the extension of this study with more subjects so as to verify that virtual reality assessment does discriminate stroke patients from matched control in a navigation task.
Methods: In this prospective study, right hemispheric stroke patients and matched controls were proposed a head-mounted-display virtual reality system. Subjects were asked to navigate through a virtual town, to count the targets (bus-stops) and to find one single target (swings in a park). Number of omitted bus-stops and their location (right or left from the subject's point of view) and the ability to locate the swings were compared with the Results of matched controls with the sign test. All patients sustained also an assessment for visuospatial neglect with the Bells Test and Catherine Bergego Scale. MRI analysis was proposed. We have searched correlation between paper and pencil test, behavioural assessment, virtual reality task and MRI data for all patients with group and individual analysis.
Results: Nineteen right brain-damaged patients and nineteen matched controls have been included. Patients differed significantly from controls in the virtual reality task for the number of omitted targets (p:0.01) and for the ability to locate the swings (p:0.03). Concordant Results between standardized and virtual reality task were observed for 60% of the patients. Overlap of stroke lesions and the right inferior frontal fasciculus was observed for all patients who underwent MRI.
Conclusion: Navigation impairment after right brain damage could be assessed by a virtual reality task. We now propose the assessment to all right brain-injured patients and propose a virtual reality therapy.

810 Rehabilitation and reorganisation after stroke

ANKLE FOOT REHABILITATION IN STROKE USING BIOMECHANICAL ASSESSMENT

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Background: We think that is important to monitoring gait rehabilitation using the biomechanical evaluation by force plate.
Material and Methods: Our study included 100 patients shared in 2 lots-lotA began the rehabilitation in first month, lot B-began after 1 month from stroke. Biomechanic assessment of foot included lateral heel (HL), medial heel (HM), midfoot (M) by force plate RSScan. Parameters- load rate (LR), maxim force (MaxF) during gait. Funcitonal assessment for gait and balance (Tinetti, Berg, Fugl Mayer). Evaluation at 3 weeks, 3months, 6months. Rehabilitation goals, developemnt of ankle foot mobility, rehabilitation of muscle force and motor control, of static and dynamic balance.
Results: Tinetti scales for balance shaw a evolution from 1,84 to 11,52 (lotA), 3,8 to 10 (lotB); Tinetti scales for gait from 1,34 to 9,98 (lotA), 3,08 TO 8,06 (lotB); Berg scale from 4,6 to 46,12 (lotA), 15,66 to 41,56 (lotB); Fugl Mayer scales for lower limb shaw a evolution from 10 to 33 (lotA), 9 to 23 (lotB) Biomechanical assessment shaw for HL, MaxF had a good evolution at lotA even if the begining we observed at lotB a higher value. LR had an increase at lotA because it is correlate with muscle spasticity. At HM we observed a decrease of MaxF at lotB and increase at lotA.The same evolution had LR. This evolution can be explain by decrease of foot inversion and plantar flexion at lotA. At M region all parameters had a good evolution at lot A the lotB.
Conclusions: Biomechanic assessment shaw that early begin of foot rehabilitation and monitoring it can increase motor control and force progression during gait phases.We consider that we have explication regarding gait pattern and to build rehabilitation program using physical therapy. Rehabilitation foot allows: body weight sustain by lower limb, body weight propulsion, improvement of dynamic balance, control of knee joint position and ankle foot position during gait, optimizing of rithm and coordination of ankle foot system.

811 Rehabilitation and reorganisation after stroke

ISCHEMIC STROKE AND STRIATAL LESIONS IN HUMANS – IMPLICATIONS FOR STEM CELL THERAPY

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Background: Stem cell therapy is a potential treatment for functional improvement beyond the acute phase of ischemic stroke. Experimental studies have often focused on striatal infarctions and replacement of striatal neurons by endogenous or grafted neural stem cells, and have reported benefits in animal models. Before translation to the bedside can be made, more data on striatal lesions in the clinical setting is needed. We examined frequency as well as clinical and neuroradiologic features of striatal infarcts in humans from a stem cell therapy perspective.
Methods: Patients aged 20-75 years, with first-ever supratentorial ischemic stroke between July 7, 2009 and January 7, 2011 were included. Patients were examined within 4 days of stroke onset with brain dw-MRI. We analyzed location, size, number of focal ischemic abnormalities and involvement of the subventricular zone, i.e. the area containing the endogenous neural stem cells. NIHSS was used to assess severity.
Results: 104 patients were included. 24 patients had any involvement of striatum, 8 of whom had predominantly striatal lesions, i.e. > 50% of the total ischemic lesion volume located in caudate nc and/or putamen. Among the 24 patients with striatal involvement, 62% had multiple lesions. Patients with predominantly striatal lesions had relatively mild strokes with a NIHSS median of 3. Among the 104 patients, the distance from the margin of the ischemic lesion(s) to the subventricular zone was ≤ 2 mm in 46%.
Conclusion: Predominantly striatal infarcts are relatively rare in the clinical setting. However, areas of endogenous neurogenesis seem to be involved in a relatively high proportion of patients with supratentorial ischemic stroke.

812 Rehabilitation and reorganisation after stroke

BASELINE CHARACTERISTICS AND BOTULINUM TOXIN TYPE A (BONTA) DOSING PATTERNS FOR PATIENTS WITH ADULT FOCAL SPASTICITY IN A PROSPECTIVE OBSERVATIONAL COHORT STUDY: MOBILITY

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Background: The MOBILITY study database provides the opportunity to characterize adult patients with focal spasticity in Canada and to evaluate variations in BoNTA dosing patterns in such patients.
Methods: In this study, demographic, diagnostic and treatment data were collected from newly-treated (naïve) patients and previously-treated (maintenance) patients who received at least one dose of BoNTA. In this interim analysis we describe the baseline characteristics and dosing patterns of 360 patients with focal spasticity (AFS).
Results: The most common etiologies of AFS reported were stroke (n=177, 49%), multiple sclerosis (n=40, 11%), spinal cord injury (n=37, 10%), and traumatic brain injury (n=19, 5%). Eighty-six percent (86%) were Caucasian, 49% female and 51% male. The mean age of females (54yr) and males (55yr) was similar, as was the mean BMI of females (26) and males (27). 130 patients (36%) were naïve and 229 (64%) were on maintenance therapy. Of patients on maintenance therapy, 12%, 16%, 33%, 38% and 1%, respectively, had received 1, 2, 3, 4 and >4 BoNTA injections in the previous year. For those who received >1 BoNTA injections, the mean time interval between injection cycles was 131 days. The mean BoNTA dose at the first treatment visit was lower in all naive patients (254U±137U vs 343U±161U in maintenance patients, p<0.0001, Wilcoxon rank sum test), and remained lower at the subsequent treatment cycle (297U±153U vs. 354U±156U in maintenance patients, p=0.004). BoNTA dose did not vary significantly when each AFS etiology was analyzed by BMI, weight, gender, or age. The majority of patients (84%) received electromyographic and/or electrostimulation guided injections.
Conclusion: In Conclusion the Results suggest that naïve patients receive lower BoNTA doses than maintenance patients and that baseline characteristics and AFS etiology do not significantly influence BoNTA dose selection.

THE INFLUENCE OF THE SEQUENCE OF STIMULI, SOUR AND TASTE, ON DEGLUTITION PHARYNGEAL TRANSIT TIME IN INDIVIDUALS AFTER ISQUEMIC STROKE

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Background: The influence of stimuli, taste and temperature, on the swallowing biomechanics has been investigated in the scientific community, in both health individuals and in after neurological disease individuals. However, there are some questions that could be better explained, as well as, the sequence of offered stimuli and if they influence the pharyngeal response in different way. The present study had as general proposes to verify the influence of the sequence of stimuli, sour taste and cold temperature, on deglutition pharyngeal transit time in individuals after stroke.

Methods: Participated this research 60 individuals after isquemic stroke, unilateral, 29 males and 31 females, aged from 41 to 88 years (mean age of 66,2 years), ictus from 0 to 50 days (median of 6 days) and oropharyngeal dysphagia from mild to moderate. These 60 individuals were divided in two groups. The Group 1 (G1) received nonrandomized sequences of stimuli and Group 2 (G2) received randomized sequence of stimuli. To analyze the deglutition pharyngeal transit time it was realized the videofluoroscopic deglutition exam. It was offered four different stimuli, the G1 received nonrandomized sequences of stimuli (natural, cold, sour and sour cold) and the G2 randomized sequence. Afterward the images were digitalized and specific software was used to measure the pharyngeal transit time.

Results: The G1 individuals presented shorter pharyngeal transit time with sour cold stimulus and with statistical difference than other stimuli. The G2 individuals do not presented statistical difference in pharyngeal transit time among stimuli. There was statistical difference in pharyngeal transit time in all stimuli comparing the both offer sequence.

Conclusion: The Results showed that the sequence of offered stimuli influences in different way the pharyngeal transit time in individuals after stroke. And, it suggests that, maybe, when the sour cold stimulus is offered in randomized sequence can influence the other stimuli response.

EXPLORING READINESS TO ASSESS FITNESS TO DRIVE AFTER STROKE

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Background: In the absence of complete resolution of all symptoms, readiness to undergo assessment of fitness to drive and the optimum timing of such assessment remains nebulous for people recovering from stroke.

Methods: A prospective clinical study among a sample of sub acute stroke patients comprising of an occupational therapy off-road assessment followed by an on-road assessment was conducted. Off-road assessment findings were examined using non-parametric analysis.

Results: Over a 22 month period 46 stroke patients (mean age 64 years, mean time post onset 3.8 months) completed OT off-road assessment and were referred for on-road testing. Subsequently 35 participants successfully completed an on-road test. Eleven participants did not take the on-road test because of self-perceived unreadiness (5), further rehabilitation needed (2), unsafe to be assessed on-road (2), medical deterioration (1), refused (1).

Scores for the subgroup who did not take the on-road tests were significantly lower than those of the group who passed the on-road test on the MMSE (P=0.042), ACER (P=0.027), FAB (P=0.006), selective (P=0.023) and divided (P=0.018) attention tests. Time taken to complete the star cancellation test was slower (P=0.025). Overall OT impression of readiness to return to drive was significantly lower for the group who did not take the on-road test (P=0.000).

Conclusion: Impaired performance on some commonly used and easy to administer clinical screening tools appeared to be sensitive in identifying stroke patients who may not yet be ready to undergo an on-road driving assessment. Speed of processing also appeared to be indicative of readiness to return to driving. Further exploration of the clinical reasoning used by therapists in forming their opinion on readiness to return to drive may assist the development of a clinical pathway in relation to determining appropriate timing of commencing fitness to drive assessment post stroke.

COMPREHENSIVE ASSESSMENT FOR STROKE REHABILITATION: A NEW AUSTRALIAN MODEL

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Background: The Australian Stroke Coalition is an organisation of members representing all major groups, agencies and professions involved in stroke care in Australia. One of the key priorities identified by this coalition was to investigate rationales and models of assessment for rehabilitation that could be used across Australia. It had been identified that assessing stroke survivors for rehabilitation (eligibility, where and in what form) was often ad hoc, inequitable and more often determined by the variable capability of the rehabilitation unit rather than the capacity of the individual stroke survivor to benefit.

Method: A Rehabilitation Working Group was established with representation and expertise from relevant institutions, professions and consumers across Australia. This group convened regular meetings and conducted a national survey of current assessment practice as well as an extensive review of the literature regarding best practice.

Results: The findings from the survey (52 sites) and review (104 retrieved papers) revealed a radical basis for rehabilitation eligibility. A simple assessment algorithm was devised, along with explanatory notes and tools for documentation. Piloting of the process resulted in further refinement.

Conclusion: This national project combined expert opinion, consumer values and current literature to produce a simple set of processes to assess stroke survivors for rehabilitation. This has resulted in procedures and tools that: ensure clear and accountable decision-making, focus on the person with stroke and their family and involve all stroke team members.

HEALTH UTILITY AMONG PATIENTS WITH ADULT FOCAL SPASTICITY TREATED WITH BOTULINUM TOXIN TYPE A (BONTA) IN A PROSPECTIVE OBSERVATIONAL COHORT STUDY: MOBILITY

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Background: The goals of spasticity-related interventions are focused on improving health and quality of life. The ongoing MOBILITY study will prospectively measure the impact of BoNTA at regular intervals on patient-reported health utility in both newly-treated (naïve) and previously-treated (maintenance) patients.

Methods: The SF12v2 Health Survey was administered at baseline, week 4 post-BoNTA treatment (W4) and subsequent injection visits (SV). Physical (PCS) and mental (MCS) component summary scores were derived from self-reported SF12v2 and health utility was measured via the SF-6D. In this interim analysis, we examine the change in SF6D, PCS and MCS scores at W4 and SVs in 360 adults with focal spasticity (AFS).

Results: Most frequently reported etiologies of AFS were stroke (n=177, 49%), multiple sclerosis (n=40, 11%), spinal cord injury (n=37, 10%), and traumatic brain injury (n=19, 5%). The proportion of patients with maintained or increased scores from baseline was compared to those with decreased scores using a Chi-square test for equal proportions. Of patients for whom data were available at the baseline visit and at least one other study visit, 130 (36%) were naive and 229 (64%) were on maintenance therapy. At W4, no significant difference in the proportion of patients with maintained/improved vs decreased health utility scores was observed. In contrast, significantly more patients had maintained/increased SF6D scores at both SV1 (63%; p<0.001) and SV2 (60%; p=0.032). This trend was associated with increased SF6D, PCS and MCS scores, and was consistent in the naïve cohort at SV1 (66%; p=0.005) and SV2 (65%; p=0.032), and in the maintenance cohort at SV1 (61%; p=0.006) and SV2 (58%; p=0.100).

Conclusions: These interim data suggest that improvements in health utility develop over time with BoNTA treatment in patients with AFS. Future analyses of the MOBILITY database will examine whether these early trends will continue over the longer term.

CORRELATIONS AMONG IMPAIRMENT, THINKING OPERATIONS AND DAILY ACTIVITIES AFTER STROKE

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Background: there is a great need to find valid, reliable measures of cognitive outcome after stroke. Measures of higher cortical function developed for other disorders, are im-practical for many stroke victims. On the other hand, there are tests of Activities of Daily Living (ADL) that require intact performance in categorization, sorting and reasoning. We tested the hypothesis that ADL tests dependent on cortical functions could be used to assess outcome in stroke patients.
Method: 27 right-handed stroke patients were evaluated on National Institute of Health Stroke Scale (NIHSS), Barthel Index (BI), Instrumental Activities of Daily Living (IADL) Scale and thinking process items of Lowenstein Occupational Therapy Cognitive Assessment (LOTCA).
Results: We found significant correlations between thinking process subtests of LOTCA and different items of NIHSS such as consciousness, arm movement, aphasia, ataxia and inattention. Spearman correlation of thinking process and BI tasks showed no relation-ship, although Structured Risca of thinking process evaluation was correlated to both self-care and mobility areas of the BI. Thinking process was strongly related to IADL total score (p=0.004). The total NIHSS correlated significantly with BI and IADL total scores.
Conclusion: higher-order functions, such as categorization, sorting and reasoning, are related to IADL performance which depend on complicated cognitive abilities. In con-trast, the BI depends heavily on motoric function, and does not correlate with higher-order functions. Further confirmation is needed, but our data suggest that commonly used IADL tests could serve to as valid, reliable tests of cognitive impairment and recov-ery in stroke victims.
Keyword: activities of daily living, categorization, reasoning, sorting tasks, stroke

HIGH-INTENSITY INTERVAL TRAINING IMPROVES ENDURANCE AND WALKING DISTANCE FOR PATIENTS 3 TO 9 MONTHS AFTER STROKE. A SAFETY AND FEASIBILITY STUDY

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Background: Motor impairments are one of the barriers to conduct high-intensity training after stroke. A treadmill with body-weight support (BWS) can help overcome this. The aim of this study was to assess the safety and feasibility of a six-week high-intensity interval training program performed on a treadmill with BWS for patients after stroke.
Methods: Acute stroke patients treated in our stroke unit were screened for inclusion 3-9 months after onset. Inclusion criteria were; independent walking with or without walking aid, able to perform VO2max test. Patients were excluded if they suffered from unstable pulmonary or cardiac disease or severe cognitive impairments. The intervention consisted of 4x4 min intervals at 85-95% of maximum heart rate (Borg Scale=17), interrupted by 3 min active breaks. This training protocol was repeated twice a week for six consecutive weeks. Compliance, Borg Scale and adverse events were used as measures of safety and feasibility. Other outcomes were VO2max, 6 minute walk test (6MWT) and muscle strength assessed before and after the intervention and 12 weeks later.
Results: Ten men and 5 women (mean age; 71, range; 61-85), were included. Mean Scandinavian Stroke Scale score at inclusion was 56.1 (range; 51-58). All patients completed all training sessions. No adverse events occurred during training. Mean (SD) Borg Scale score at end of intervals was 16.5 (2.3). Mean (SD) change from pre-test to end of follow up was; 28.6 (4.0) to 30.6 (3.6) ml/kg/min, p=0.053, on VO2max, 413 (99) to 481 (91) meter, p=0.000, on 6MWT and 107 (42) to 116 (44) Newton meter, p=0.087, on muscle strength of affected leg.
Conclusion: This study shows that it is safe and feasible to perform a high-intensity training program for a selected group of stroke patients. The intervention gave a slight improvement in endurance and a clinically highly significant improvement in walking distance. This protocol should be tested out in a randomized controlled trial.

CHEST INFECTION AMONG STROKE PATIENTS ON NASO GASTRIC TUBE FEEDING

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Background: Dysphagia after stroke is very common and its detection is an important part of acute stroke management. Dysphagia is seen in more than 65% of post stroke patients, and is a marker of poor prognosis, increase risk for chest infection, malnutrition, persistent disability, prolonged hospital stay and increase cost burden on NHS, institutionalisation and increase mortality.
Aims and Objectives: To evaluate the safety of Nasogastric tube feeding in stroke patients suffering from dysphagia. A prospective study designed to evaluate the appropriateness of the Nasogastric tube feeding in Stroke patients.
Methods: The study is randomised prospective study of Stroke patients in age group of 50-94 years that was completed within 04 months. 43 patients for this short study randomly and followed them for 04 months in different wards at King George hospital. We looked for

- Mortality/morbidity among diff age group of patients.
- Type of stroke and disability.
- Duration of stay in hospital
- Nasogastric tube feeding duration
- Incidence of chest Infection while being fed via NG tube.
- Deaths among patients fed via NG tube.

Result: 85% of post stroke patients develop swallowing problems on presentation. 93% of patients on NG tube feed developed Pneumonia, out of these 63% scummbled to chest infection. Maximum incidence of chest infection was seen among 60-90yrs+ age group who were chosen for NG Tube feed and maximum deaths were among 70-90yrs+ age group directly due to aspiration pneumonia.
Conclusion & Recommendation: Increasing awareness of "dysphagia" post stroke as common complication and specific training to identify dysphagia on admission. Recognise "silent aspiration" which is seen among 40-50% among these patients during their initial presentation. Simple water swallow test is most convenient and easy method to assess patient when they present in A&E. Proper documentation in the notes with date & time of Assessment. Identifying high risk patients early is the key to prevent chest infection and early speech and language referral. Dysphagia and nutritional chart to identify patients at risk of developing malnutrition.

PHYSICAL ACTIVITY IN THE FIRST 6 MONTHS AFTER STROKE

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Background: Physical activity (PA) may be an important factor for recovery and secondary prevention after stroke and should therefore be encouraged. Knowledge about PA after stroke is very limited. The aim of this study was to investigate how PA changed across the first 6 months after acute treatment in a stroke unit, and how PA was associated to function in this group of patients.
Methods: This prospective study with follow up assessments at 1, 3 and 6 months after stroke included patients admitted to our stroke unit with the diagnosis of acute stroke if time from onset were less than 14 days. Patients receiving palliative care were excluded. A single-axis accelerometer with a switch tilt (PAL2) was used to measure PA. PAL2 data are presented as the total number of transitions (changes in position) and total amount of minutes in lying, sitting and upright (standing/walking) position across 24 hours. Function was measured using Berg Balance Scale (BBS) and Barthel Index (BI). Appropriate random effect regression models were used to investigate the associations between time since stroke, patients' activity levels and functional ability.
Results: 15 male and 13 females (mean age; 79, range; 62-93) were included. The median time in upright position increased from 92 min at baseline to 144 min 6 months later, while the median number of transitions changed from 50 to 59 over the same time period. Time in an upright position increased by 0.22 min for every 1% change in time since stroke (p<0.001), adjusted for age and stroke severity. Adjusted for time since stroke, a single point increase on BBS was associated with extra 4.1 min spent in upright position (p<0.001), while a single point increase on BI was associated with extra 1.8 min spent in upright position (p<0.000).
Conclusion: We have shown that in the first 6 months after stroke there are a significant increase in PA. Whether these activity levels help reduce further cardiovascular risk still needs to be determined.

WHAT IS THE RELATIONSHIP BETWEEN WEIGHT-BEARING ASYMMETRY AND SUBJECTIVE VISUAL VERTICAL (SVV) FOLLOWING STROKE?

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Background: The evidence base for effective rehabilitation techniques following stroke is limited. This is especially true for perceptual and postural disorders.
A pilot study was designed to investigate the relationship between weight-bearing asymmetry and subjective visual vertical (SVV) following stroke in order to inform rehabilitation in this area.
Design: A pilot, correlational design.
Setting: A stroke unit in South East England.
Participants: 14 patients admitted to the stroke unit with radiologically diagnosed first stroke who could stand unsupported for 30secs.
Interventions: SVV and weight-bearing symmetry in standing were measured on one occasion.
Results: There was no relationship between presence of weight-bearing asymmetry and presence of SVV tilt ($p = 0.067$). There was a correlation between magnitude of weight-bearing asymmetry and magnitude of SVV tilt ($R = 0.640$, $p = 0.018$). The numbers of participants with abnormal SVV was low. Direction of SVV tilt is not consistently related to direction of asymmetry.
Conclusions: Weight-bearing symmetry following stroke is determined by a number of factors that alter depending on context and environment. There are only small numbers of participants with abnormal SVV who were able to stand independently in the acute stage post-stroke. It could be proposed that the asymmetrical weight-bearing seen in the people with a greater SVV tilt could be a compensation for the feeling of instability that these individuals experience. This suggests perceptual disorders following stroke need to be addressed during rehabilitation in order to normalise stance symmetry. Further research is required into the relationship between SVV and weight-bearing abnormality following stroke.

A NOVEL INTERVENTION TO SUPPORT RETURN TO WORK AFTER STROKE: DEVELOPMENT AND FEASIBILITY PILOT

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Background: Clinical guidelines and health policies call for improved access to vocational rehabilitation after stroke. However, there is little evidence to inform what should be provided, or evidence of effectiveness of such interventions. This study aimed to develop and test the feasibility of a novel intervention to support return to work after stroke.
Methods: Phase 1: intervention development included analysis of 2874 incident stroke cases recruited to the South London Stroke Register; survey of 217 specialist neuro-rehabilitation providers to investigate provision of care to working age adults with stroke; qualitative interviews with 31 stroke survivors aged 24-62 years; consultation with stakeholders to devise a pilot intervention. Phase 2: a pilot study using observational Methods, interviews and self report was conducted to assess feasibility, acceptability and identify relevant outcomes for future evaluations.
Results: Phase 1 studies indicated the need develop a novel intervention to support preparation for return to work or other meaningful activity. The proposed intervention aimed to improve participants' confidence through the provision of relevant training and information. It comprised a structured course conducted over two weeks with additional self-directed study; it was led by an employment professional, herself a stroke survivor. Participants reported satisfaction with the course and improved confidence in how to attempt to re-enter the work force. They also reported that the course provided social support and peer learning. Suggested changes to the delivery method included shorter sessions and offering the course to stroke caregivers.
Discussion: The pilot intervention was feasible and acceptable to participants. Future work will aim to refine the model of intervention and test ist efficacy.

VISUAL PROBLEMS IN PATIENTS WITH STROKE

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Background: Visual problems are common after stroke and can have a major impact on rehabilitation, mobility, daily activities, ability to drive, psychosocial wellbeing and discharge destination. The aim of our study was to determine whether patients with acute stroke were screened for visual problems and whether the ones with impairment were referred to orthoptist and received driving advice.
Methods: Retrospective study of medical records of admissions to the Stroke Unit at University Hospital Coventry in April and May 2010.
Results: Total population was 60 with age range of 44-96 years. Diagnosis was ischemic stroke in 45 patients (2 hemorrhagic transformations), intracerebral hemorrhage in 12, and 3 had TIA. 7 patients died. Results are summarised in Table 1.

Table 1. Results

	Yes	No	Not documented	Unable to assess	Comments
Visual impairment in history	11 (18.3%)	12 (20%)	35 (58.3%)	2 (3.3%)	Reduced GCS
Double vision in history	2 (3.3%)	5 (8.3%)	51 (85%)	2 (3.3%)	Reduced GCS
Does the patient drive? (documented in the notes)	15 (25%)	20 (33.3%)	25 (41.7%)		
Eye movements Impairment	2 (3.3%)	29 (48.3%)	29 (48.3%)		
Visual field defect	13 (21.7%)	22 (36.6%)	25 (41.7%)		
Visual neglect	8 (13.3%)	15 (25%)	37 (61.7%)		
Orthoptic assessment	2 (3.3%)	58 (96.7%)			1 in a patient who does not drive
Driving advice in the notes	11 (18.3%)	24 (40%)			25 (41.7%) did not drive or died. (2 non-drivers died)
Driving advice in the discharge letter	3 (5%)	32 (53.3%)			25 (41.7%) did not drive or died. (2 non-drivers died)

23 patients had documented visual problems and Table 2 shows their outcome. Visual assessment was mainly done in A&E and Hyperacute Stroke Unit and only 5 patients had reassessment of vision after the acute stage.

Conclusion: Almost half of stroke patients were not screened for visual problems. Out of 23 patients with visual problems, only 1 had orthoptic assessment, and only 4 received driving advice. Prevalence of visual problems can be higher as many were not reassessed after the acute stage. High pressure atmosphere of A&E and Hyperacute Stroke Unit, time constraints and patient's clinical condition limit the accuracy of screening for visual problems and it is essential that all patients be reassessed on the Stroke ward by trained staff.
The following measures can improve patients' care:
1. Education of members of the stroke team regarding the importance of:
   • Screening for visual problems in all patients, and repeating it after the acute stage.
   • Referring patients with suspected visual problems to orthoptist.
   • Driving advice in patients with visual problems.
2. Establishing links with orthoptic department with a streamlined referral system.
3. Regular audits.

Table 2. Patients with visual problems

	Number	Orthoptic assessment	Driver	Non-driver	Not documented	Driving advice	Comments
Documented eye movement problems	2	0	0	1	1	0	The patient with no documented driving status died.
Documented visual field defects	13	1	5	5	3	3	
Documented visual neglect	8	0	3	3	2	1	
Total number of patients with documented visual problems	23	1 (4.3%)	8	9	6	4	

824 Rehabilitation and reorganisation after stroke

INDIVIDUALIZED ASSESSMENT OF STROKE IMPACT ON RESTING-STATE FUNCTIONAL CONNECTIVITY

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Background: Resting-state functional Magnetic Resonance Imagery (rs-fMRI) allows the study of functional networks, known as resting-state networks (RSN), that exhibit synchronized spontaneous activity even in the absence of specific task performance. It is particularly suitable for disabled patients as it does not require task-related patient cooperation. The present study assessed the pattern of impact from ischemic stroke on seven major RSN and focused on individual analysis by comparing each patient to a control group.
Methods: 13 first ever stroke patients (8 males, age range 36 to 72 years, mean 55 years) were recruited at the Pitié-Salpêtrière University hospital stroke center (Paris) and a control group was recruited to match patients for age.
All subjects underwent two rs-fMRI scanning sessions. Before undergoing MRI, patients had a neurological exam including classical global clinical scores (NIHSS, mRS, Barthel).
33 regions of interest (ROIs) were defined with seeds in seven major RSN. Matrices of resting state functional connectivity between the 33 ROIs were computed for every subject and we compared that of each patient with that of the control group. Results were analyzed in relation to the clinical pattern and the lesion location of each patient.
Results: The control group's RSN were in keeping with literature data. In patients, two types of abnormality in functional connectivity between pairs of ROIs were identified. The first involved ROIs damaged by stroke and is trivial, but the second implicated pairs where neither ROI was affected by the lesion. The disrupted networks were consistent with the clinical pattern of the patient.
Conclusion: This study assesses not only direct consequences of stroke on resting-state connectivity but also remote dysfunctions which may be more accessible to new therapies such as non-invasive brain stimulation as they occur in biologically healthy tissue. Resting-state fMRI is hence a feasible approach in individual stroke patients.

825 Rehabilitation and reorganisation after stroke

EFFECTS OF AN ANTERIOR ANKLE-FOOT ORTHOSIS ON STATIC STANDING POSTURAL CONTROL, FUNCTIONAL BALANCE ACTIVITIES, AND FEAR OF FALLING IN STROKE PATIENTS

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Background: Gait and balance disorders are common in stroke subjects and are a major cause of falls in this population. In Taiwan the Anterior Ankle-foot orthosis (A-AFO) is commonly prescribed for post-stroke subjects to stabilize the ankle by compensating for the inadequate dorsiflexion and mediolateral subtalar instability during walking. There is substantial evidence showing that the A-AFO improves walking ability. However, the information on the effects of the A-AFO on balance or postural control is limited and inconclusive. The aim of this study was to investigate the effects of an A-AFO on: (1) static standing postural control, (2) functional balance activities, and (3) fear of falling in hemiplegic stroke patients.
Method: Fifty-one stroke patients, who had been wearing an A-AFO for at least 5 months were enrolled. Static standing postural control was evaluated using the posturography: Tetrax Interactive Balance System. Timed up and go, one-leg stand, and forward reach tests were used to assess functional balance activities. The Falls

Efficacy Scale-International questionnaire was used to investigate the change in balance confidence resulting from the use of an A-AFO.
Results: A-AFO had significant positive effects on the following postural parameters of the posturography: (1) general stability (p = 0.01); (2) synchrony between affected heel and toes (p < 0.01), unaffected heel and toes (p < 0.01), and between bilateral heels (p < 0.01); (3)forward weight shifting (p < 0.01); and (4) reduction of medium-high frequency sway (p < 0.01). The A-AFO did not increase weight loading on the affected leg during bipedal standing. Subjects with A-AFO demonstrated improved performance in the one-leg stand (p = 0.04), forward reach (p = 0.016), up and go (p < 0.01) tests, and had less fear of falling (p < 0.01).
Conclusion: Stroke subjects using an A-AFO showed better posture and balance control in the physiological, functional, and psychological aspects.

826 Rehabilitation and reorganisation after stroke

ACTIVITY CHANGES IN PRIMARY SENSORY CORTEX ARE ASSOCIATED WITH SUCCESSFUL MOTOR REHABILITATION AFTER STROKE

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Background: The role of the primary sensory cortex (S1) in recovery is till now controversially discussed. Previous studies showed a posterior shift of activation toward S1 following stroke but the expected relationship to the test of the affected hand function was unverifiable. Therefore, some authors suggested that the posterior shift of activation has no clinical relevance.
Objective: We were interested in the role of S1 in the process of recovery.
Methods: Assuming that previous studies had an inhomogeneous group of patients, we selected chronic stroke patients with moderate hand paresis but normal sensory examination and SEP as well as no lesion within S1, thalamus or brain stem. To force hand function improvement, constraint-induced movement therapy (CIMT) was used. To relate fMRI activation changes (between baseline and post CIMT) to hand function test change, a correlation analysis between those was evaluated.
Results: We found a close relationship between hand function improvement and activation changes within ipsilesional S1. With better outcome the activation changes within S1 increased.
Conclusion: The current data supports the notion that in pre-selected patients the sensory network has influence on motor recovery.

827 Rehabilitation and reorganisation after stroke

USING GOAL ATTAINMENT SCALING AS AN OUTCOME MEASURE IN INPATIENT NEUROREHABILITATION

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Background: It is sometimes difficult to find outcome measures that reflect the complex, individualised and multidisciplinary work that is carried out in a neurorehabilitation setting. Goal Attainment Scaling (Kiresuk & Sherman, 1968) is one way in which success of an intervention is measured within this setting. GAS allows calibration of degree of success, rather than just a binary decision between "achieved" and "not achieved". It also allows individualised goals to be standardised into a single system of measurement. A recent systematic review of

the use of goal setting as an outcome measure in adult physical and neurological rehabilitation (Hurn, Kneebone & Cropley, 2006) concludes that there is evidence to support goal attainment scaling as having inter-rater reliability, congruent validity, predictive validity and sensitivity.

Previous papers have provided practical guides to introducing GAS and some have suggested using a simplified version of GAS goal writing to save time (e.g. Turner-Stokes, 2009; Bovend'Eerdt, Botell & Wade, 2009). This paper explores the potential to introduce full Goal Attainment Scaling to a routine, NHS clinical setting in order to maximise validity and reliability.

Methods: GAS was introduced to a pre-existing goal planning process in 2008. A full year's data is available for patients discharged from a tertiary neurorehabilitation centre during 2010.

Results: Full Goal Attainment Scaling has been successfully introduced to this setting. Some of the data gathered in this way will be explored.

Conclusion: The successful incorporation of GAS into a pre-existing goal planning process will be discussed. In particular, how centres can introduce more structured, quantitative collection of outcomes using GAS. Issues around the different approach to GAS used in different centres will be explored.

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828 Rehabilitation and reorganisation after stroke

ICONS: IDENTIFYING CONTINENCE OPTIONS AFTER STROKE: FINDINGS FROM THE CASE STUDY PHASE

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Background: Urinary incontinence following acute stroke is common, affecting between 40%-60% of people admitted to hospital. It is related to poor outcome and poorly managed in many cases.

We conducted a case study of the Introduction of a systematic voiding programme in one stroke service to inform a Phase II randomised controlled trial.

Methods: Critical path analysis. Urinary incontinence was measured as (i) number of incontinence episodes in last 5 days prior to discharge (ii) Barthel UI item. Incontinence at discharge was analysed descriptively and factors affecting discharge incontinence were investigated using multiple logistic regression.

Health professionals' views of the algorithm. We conducted six taped focus group interviews with a purposive sample of health professionals delivering the programme (n=21) at monthly intervals throughout the case study.

Whole systems analysis: A soft systems approach (Checkland, 1981), comprising four group interviews with clinical staff and managers (n=17), was used to identify system requirements for the trial algorithm to be embedded in mainstream stroke practice.

Results: At discharge, the mean (SD) number of incontinence episodes (over 5 days) was 6.8 (6.8), a reduction of 3.2 from baseline. Twenty-three (53.5%) patients remained incontinent at discharge.

The systems analysis highlighted that responsibility for decision-making was diffuse, with considerable distances between aspects of practice, assessment, care planning and organisational aspects of continence care.

Conclusion: The presentation will focus on how learning from the case study has informed and shaped the design of the Phase II trial.

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829 Rehabilitation and reorganisation after stroke

EFFECTIVE MOOD MANAGEMENT AFTER STROKE (EMMAS): PATIENT SATISFACTION WITH A CONTEMPORARY PSYCHOLOGICAL INTERVENTION PROGRAM IN A REHABILITATION UNIT IN SINGAPORE

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Background: Depression is one of the most prevalent psychiatric sequelae of stroke. However there is no psychological intervention program incorporated into existing healthcare system of any rehabilitation unit in Singapore. The purpose of this program is to provide early screening and intervention for depressive symptoms among stroke patients admitted into a rehabilitation center.

Methods: Stroke patients who were admitted to the Department of Rehabilitation Medicine, Tan Tock Seng Hospital were included in this program. These patients were screened for depressive symptoms at admission, one month post admission, and at three months post discharge before they exit from the program. A total of 59 patients completed a program satisfaction tool that contains seven questions

scored on a six-point Likert scale ranging from 1 (strongly disagree) to 6 (strongly agree) at the end of the program. Out of these patients, 24 patients who displayed depressive symptoms received treatment interventions such as: individual session with psychologist or psychiatrist, medication, and psychotherapy group.

Results: A total of 93.2% of the sample was satisfied with the program in overall. In addition, 81.4% of the sample felt that information that was given to them was useful. Of those who received individual psychologist session, 70.8% of them reported that the program not only helped with the prevention and alleviation of depression, it also makes them feel less anxious about their life after stroke.

Conclusion: The existence of a mood management program appears to be beneficial in helping stroke patients in coping with depressive symptoms following stroke in a rehabilitation setting.

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830 Rehabilitation and reorganisation after stroke

RELATIONSHIP BETWEEN OROPHARYNGEAL DYSPHAGIA GRADE AND NATIONAL INSTITUTES OF HEALTH STROKE SCALE (NIHSS)CX IN PATIENTS WITH ACUTE STROKE

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Background: Oropharyngeal dysphagia is a common deficit in patients with ischemic Stroke, occurring more than 50% of cases. Studies have been tried to understand the relationship between clinical founds of swallowing evaluation and the severity scale stroke by the National Institutes of Health Stroke Scale (NIHSS). However, more researches are required to validate this interaction in clinical routine. The aim of this study was to describe the relationship between oropharyngeal dysphagia and NIHSS score in patients with acute Stroke.

Methods: It was studied 54 patients with acute ischemic Stroke, 34 male and 20 female, aged 48 to 88 years (median of 71 years). They were submitted to the NIHSS scale and divided in 3 groups according to NIHSS score: G1 (0-8), G2 (9-16), G3 (>17). Following, swallowing (clinical) evaluation was performed, and a standard scale which classifies the oropharyngeal dysphagia in mild, moderate and severe was used.

Results: It was established a relationship between the severity dysphagia and the NIHSS score. Patients that not present symptoms of dysphagia (7.4%) are in group G1. Mild dysphagia (27.7%) was seen in the groups G1 (93.3%) and G2 (6.6%). Moderate level (31.4%) was present in groups G1 (58.8%) and G2 (41.1%). Severe dysphagia (33.3%) was only found in groups G2 (33.3%) and G3 (66,6%).

Conclusion: There is association between the severity oropharyngeal dysphagia and NIHSS score. Group 3 frequently suggest severe swallowing disturbs (severe dysphagia). Furthermore, despite groups 1 and 2 present a variety of dysphagia level (without, mild, moderate and severe), they also need a specific clinical evaluation. Therefore, due to this variability, it is necessary to increase the number of patients to determinate the safest manner to better understand this relationship.

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831 Rehabilitation and reorganisation after stroke

THE TIMING IT RIGHT STROKE FAMILY SUPPORT PROGRAM: PHASE 1 INTERVENTION DEVELOPMENT

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Background: Family caregivers play a central role in the recovery, rehabilitation, and community re-integration of individuals who have experienced a stroke. Currently, it is not standard clinical practice to prepare and support family members who take on this care-giving role. We developed the Timing it Right (TIR) framework to determine the specific types of support stroke families need at specific times during the stroke survivors recovery. The objective if this presentation is to describe the development of our TIR Stroke Family Support Program.

Methods: Qualitative interviews with family caregivers and health care professionals (HCPs) that explored caregivers' needs for education, emotional support, training, and tangible assistance informed intervention content and delivery Methods. A multi-disciplinary committee of HCPs from acute and rehabilitation care environments reviewed the content of the intervention to ensure it accurately reflected stroke care delivery in our region.

Results: Interviews with 24 caregivers and 14 HCPs were used to create an outline for each phase of the intervention. We then leveraged existing resources, tailored it to caregivers, and prepared new materials as needed to create the educational tool.

Participants' recommendations for intervention delivery lead to two Methods: 1) one individual, stroke support person, providing support over time in person during acute care and then by telephone thereafter and 2) self-directed intervention where caregivers are instructed by the stroke support person on how to use the intervention guide to self-manage their support needs. We incorporated the suggestions of 8 HCPs into the final version of the intervention.

Conclusions: We created the TIR Stroke Family Support Program to support stroke families from acute care through to community re-integration. After completion of a pilot evaluation (separate abstract), we are now conducting a multi-site randomized controlled trial of the intervention.

833 Rehabilitation and reorganisation after stroke

HOW DO HEALTHY PEOPLE MOVE IT? BIOMECHANICAL FEATURES OF NOVEL STROKE REHABILITATION PROGRAMME IN HEALTHY INDIVIDUALS

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Introduction: A novel ontogenetic based stroke rehabilitation programme was investigated for its biomechanical and EMG muscle activation patterns in 10 healthy adult volunteers. Even though, there are many concepts in neurorehabilitation biomechanical studies could contribute to understanding of key factors of physical activities and movements patterns.

Methods: A novel ontogenetic based rehabilitation programme was investigated in healthy adult volunteers. The study protocol included neurological and physiotherapy clinical examination and biomechanical and EMG assessment of programme exercises, by Qualysis motion capture system 8 of OQUS-500 cameras and EMG by ME 6000.

Results: Several phenomena were revealed. Movement patterns could vary in different exercises for the same joint or muscle.

1. In healthy controls any exercise movement cycle shows time symmetry. The maximal ROM is reached at 50% of the motion cycle.
2. There are fore-movement and endplay movement phenomena present in all complicate movements. A trigger fore-movement is a specific trigger small amplitude movement in a direction opposite to a targeted movement. Endplay movement is small amplitude overdo of a targeted movement with consequent reverse movement to the target.
3. Any simple movement in shoulder and hip joints would occur in all 3 of 3D planes.
4. There is kinematic asymmetry between right and left side in right-handed individuals. The left side demonstrates greater range and less selectivity in EMG pattern of phase motion.
5. There are different patterns of trunk and extremity muscle activation in different individuals. In some it would activate distal muscles and reach the core, in others it would occur within the core and extend to extremities.

Discussion: Phenomena of fore-movement and endplay movement, which are prerequisite for any movement of any body part, and patterns of core and extremity activation desire further research.

834 Rehabilitation and reorganisation after stroke

HOW COMMON IS IMPAIRED ARM AND HAND FUNCTION IN PATIENTS WITH FIRST OCCASION OF STROKE? AN UNSELECTED POPULATION FROM A STROKE UNIT WITH A GEOGRAPHICAL CATCHMENT. PART OF THE SALGOT STUDY

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Background: The upper extremity function is reported affected in around 2/3 of the cases. However, these reports are based on data > 10 years back and stroke care has changed. We started a study (SALGOT) to follow recovery of unction longitudinally after stroke in non-selected population with first stroke. As part of this we investigated the frequency of impaired arm and hand function in all patients on the ward.

Methods: All patients at a stroke unit at Sahlgrenska University Hospital were assessed during 090201-100826. From the hospital records, the patients were identified, the patient charts were read and first stroke diagnosis was confirmed. Upper extremity function was assessed with M-MAS UAS -99; impaired defined as reduced score on F, G or H. This corresponds to a Grasset test, a grip test and a pinch test. If missing data, physical therapist or occupational therapist documentation was assessed.

Results: 676 patients were admitted to the stroke unit with first occasion of stroke; (average age 72 years, 52.8% were men). 58 patients had impaired upper extremity function prior to the stroke, 65 were too severely ill with live expectancy shorter than a year (SALGOT follow up time). Eleven patients were discharge before day 3 and 44 had unclear onset of symptoms.

At day 3, 10 patients were at an intensive care unit, 29 at another ward and 459 (97% ischemic stroke) at the stroke unit. Of these, 41.6% had impaired arm and hand function.

Conclusion: The frequency of impaired upper extremity function in this unselected population of first occasion of stroke is lower than previously reported. The Copenhagen stroke study noted 69% impaired at admission and 43% at one week and the South London Stroke registry 78% at on week. This indicates that today's stroke patients present less frequent with impaired motor function in the upper extremity. However, they may have difficulties in functional activities which may influence content of rehabilitation process.

835 Rehabilitation and reorganisation after stroke

BIOMECHANICAL FEATURES OF NOVEL STROKE REHABILITATION PROGRAMME IN ACUTE STROKE PATIENTS

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Introduction: Movement impairment is a common outcome of cerebral stroke. It develops within acute period and could often persist in some form for the rest of life. Even though, there are many concepts in neurorehabilitation, onotogenetic based and others, biomechanical studies could contribute to understanding of key factors of physical activities and movements patterns.

Methods: A novel ontogenetic based rehabilitation programme was investigated in acute stroke patients. The study included 10 acute stroke patients with hemiplegia of varying degrees and 10 healthy adult volunteers. The study protocol included neurological and physiotherapy clinical examination and biomechanical assessment of programme exercises (motion capture and EMG), by Qualysis motion capture system 8 of OQUS-500 cameras and EMG by ME 6000.

Results: Several phenomena of movement patterns were disclosed. There is a marked difference in performance of the same test movement, performed in different test positions, in symmetrical and asymmetrical movements for the same joint or muscle. There is a deviation in time of maximal ROM towards the end of the cycle in cyclic movements.

Poor muscle strength is often compensated by substitutional trunk movement.

Symmetric movements would boost performance on paretic side, compared to unilateral movements. EMG muscle response demonstrates at least 2 patterns of activation: hyperactivity on the side of lesion, compared to non-paretic side, and reduced EMG activity on the side lesion. The hyperactivity pattern demonstrates an increased number of muscles peak activation on the side of lesion.

Discussion: We have found few publications concerning at this matter. So, it needs more data for an opportunity to compare our Results with other studies. However, we could assume that movement control has more complicate nature when was expected.

836 Rehabilitation and reorganisation after stroke

LONGITUDINAL STUDY ON QUALITY OF LIFE, FUNCTIONING AND DISABILITY IN STROKE PATIENTS

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Background: The study carried out in the Italian National Neurological Institute "Carlo Besta" in 2009-2010 aimed to get a better understanding about the quality of life, functioning and disability of patients with stroke and to see possible changes over time. are among those that cause the greatest impact on society and health systems and a better understanding of quality of life, functioning and factors that have the facilitating or hindering role for persons with stroke is still needed to plan interventions.

Methods: The biopsychosocial model of ICF, defining disability as an interaction between a person's health condition and the environment, was used. WHO-DAS II, SF-36 and ICF Brief Core Set for Stroke were administered to evaluate the quality of life and functioning of patients with stroke. Out of 111 patients enrolled in the study 49 patients were assessed in two time points: baseline and after six months.

Results: Quality of life in patients with stroke resulted worse than in general population. Patients who perceived worse health status, also perceived lower quality of life and stronger disability. Most frequently reported problems in activities and participation were in walking, speaking and understanding. The main differences between capacity and performance (representing the impact of environment in performing the activities) were found in activities of self-care, such as washing oneself or dressing. Immediate family and health professionals resulted to be the main facilitators. Slight differences between two time points were found.

Conclusions: Stroke patients report lower quality of life compared with general population. The difficulties in functioning and activities partially are resolved with the presence of facilitating environmental factors.

Acute stroke: clinical patterns and practise including nursing

837 Acute stroke: clinical patterns and practise including nursing

AN EXPLORATION OF THE FORMAT AND KEY MESSAGES USED TO INFORM STROKE AWARENESS CAMPAIGNS

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Background: The dissemination of health information is becoming more dynamic through the utilisation of approaches such as mediation, message placement and community level outreach. These approaches are now common and often involve the delivery of key messages to a targeted audience. However, no studies have suggested the type of content, messages or specific approaches that would be needed to tackle the complex area of stroke awareness and action. The aim of this study was to review and discuss existing material that is currently used to raise the public's awareness about stroke, in order to inform future public awareness campaigns.
Methods: A convenience sample was identified through the stroke research team at a University. Twelve participants were identified, providing perspectives from academia (n=4), patients (n=3), carers (n=1), health professionals (n=2) and a patient charity (n=2). Participants discussed ways of raising the public's awareness about stroke in a focus group.
Results: Four themes emerged in relation to the format in which information should be provided: information should be tailored for different groups; information should be informed by stroke survivors; messages should be suitable for everyone; messages should be conveyed through pictures and images. Four further themes around the content of public awareness campaigns for stroke also emerged: a range of stroke symptoms should be described; stroke as a medical emergency; treatments for stroke; hope, fear and the consequences of stroke.
Conclusion: This study provided the opportunity to explore public awareness materials and messages for stroke. The Results provided information on the content of stroke information and how it should be disseminated. The findings will inform the development of educational information aimed at raising awareness of stroke and the action that should be taken when stroke is suspected.

838 Acute stroke: clinical patterns and practise including nursing

MODELLING TRANSITIONS OF CARE FOR STROKE PATIENTS AND THEIR FAMILIES

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Background: Stroke survivors and their family caregivers view transitions between care environments as one of the most stressful aspects of recovery. Effective stroke care requires a collaborative team approach where stroke patients, their families and caregivers are active participants. Emerging evidence on the needs and burden of patients, families and caregivers concerning transitions has led the Canadian Stroke Strategy to expand their stroke best practice recommendations to incorporate this important topic.
Methods: A structured review of the literature and an environmental scan were undertaken which included published reports and case studies on patient, family and caregiver needs during their transitions throughout the stroke care continuum. An expert task group reviewed the literature and developed stroke best practice recommendations targeting seamless transitions of care, which were then vetted through an external consensus panel. They also completed a mapping exercise to develop a model of care transitions for stroke.
Results: The new Canadian stroke recommendations for transitions of care focus on timely flow of communication and discharge planning to ensure that stroke survivors and family caregivers' needs for information, skills training (including self management techniques), psycho-social support, and community linkages are met. These recommendations support transitions between care environments and return to the community. A comprehensive model to demonstrate key transition points was also developed for use by the interprofessional stroke team.
Conclusions: Nurses and rehabilitation professionals play a critical role throughout the transition process. The adoption of these new recommendations by healthcare professionals will raise the bar in addressing needs of patients, families and caregivers in the weeks and months following stroke. Ultimately, application of these recommendations will increase stroke survivors' and family caregivers' abilities to cope with transitions between care environments and reduce negative outcomes that result from breakdowns in communication and ongoing monitoring of stroke patients.

839 Acute stroke: clinical patterns and practise including nursing

BRINGING PALLIATIVE CARE INTO BEST PRACTICES

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Background: Palliative Care is defined by the World Health Organization (WHO) as "the active total care of patients whose disease is not responsive to curative treatment" (i.e. chronic disease). Palliative care is comprehensive care that Aims to control pain, provide comfort, improve quality of life and effectively manage patients and their families' psychosocial needs during advanced or chronic illness, such as stroke. Patients and families are often unsure about recovery following stroke and the possibility of dying from stroke. The palliative approach, attending to physical, social, psychological or spiritual needs of patients and their families need not be reserved for those imminently dying. Palliative care can be provided in acute care hospitals, long-term care facilities, hospice facilities, or in home settings. Palliative care was recognized as an important component of care for patients with stroke. This led to the development of a new set of recommendations in the 2010 update of the Canadian Best Practices for Stroke Care. The purpose of this presentation is to discuss the process of developing palliative care best practice recommendations within the Canadian guidelines that are applicable to stroke patients around the globe.
Methods: National, inter-professional task group formation, Review of the current literature, Draft recommendation for BPG based on literature and consensus.
Results: Evidence was summarized related to palliative care, advance care planning and end-of-life care and a set of best practice recommendations were drafted by an interprofessional expert task group. These recommendations were discussed, amended, and approved at a Canadian Consensus Panel held in 2010. In addition, a set of targeted performance measures were developed to support uptake and monitoring of this best practice implementation.
Conclusion: The inclusion of palliative care recommendations has increased awareness of the importance of providing expert services in this area. Stroke programs and Accreditation programs across Canada have begun to integrate these services more formally into stroke care plans.

840 Acute stroke: clinical patterns and practise including nursing

PROFESSIONAL DEVELOPMENT RESOURCES: BRINGING BEST PRACTICE RECOMMENDATIONS TO PRACTICE

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Background: Canadian Best Practice Recommendations for Stroke Care, first issued 2006, are intended to reduce variations in stroke care and facilitate closing gaps between evidence and practice. A mandate of the Canadian Stroke Strategy for professional development is use of multi factorial approaches to facilitate uptake and implementation of guidelines. A three-pronged model targeting pre-professional education, professional development, and systems change is used.

Significant focus on professional development, led to creation of point-of-care tools for interprofessional teams across care settings. These resources are used by teams to facilitate awareness, understanding and application across the care continuum, including pre-hospital, acute stroke, stroke units, prevention and long term care.

Methods: An environmental scan and inventory of existing resources completed in 2005, identified priority areas for development. Ongoing consultations and feedback from clinician stakeholders provided direction and identification of priority needs. The process of resource development, such as the EMS Implementation Resource, used an interprofessional,evidence based approach.

Results: Since 2006, development of resources to facilitate knowledge transfer of stroke care evidence to practice has occurred including: Secondary Prevention Toolkit; Acute Stroke Nursing Management Workshop; EMS Implementation Resource; pocket reference cards; and Canadian Best Practice Recommendations Toolkit for teams to examine recommendations and practice.

Conclusion: National professional development resources are highly credible, cost-efficient and facilitate increased standardization leading to reduced variations in care. The province of Ontario has a well-developed stroke system and has been a leader in developing and mobilizing education resources to facilitate awareness and utilization of Canadian Best Practice Recommendations for Stroke Care. For example, a comprehensive Emergency Medical Services Resource was jointly developed with the Ontario Stroke Network and serves as a key driver for revisions to paramedic acute stroke protocols, training and continuing education.

841 Acute stroke: clinical patterns and practise including nursing

WHAT IS DATA MINING SAYING ABOUT STROKE AWARENESS IN A US POPULATION-BASED SURVEY?

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Background: Stroke is common cause of mortality and leading cause of disability in the U.S. Health care providers agree that the awareness of stroke symptoms by his/her family or friends is the most important factors of positive outcome of care. Further, stroke education is mandated among many acute care settings in the U.S. Despite of the striving, research including a recent systematic review suggests that the awareness remains poor. Rigorous evidence-based approaches should be applied to identify the exact status of awareness and target population for the education. Data mining of existing data collected in 2010 may be useful to address current knowledge gaps.

Methods: We conducted a secondary data analysis of the Behavioral Risk Factor Surveillance System (BRFSS), the world's largest, ongoing telephone health survey system, tracking health conditions and risk behaviors in U.S., to examine the awareness level and to identify potential target population for the stroke symptom awareness education after their hospital discharge. To explore BRFSS, various data mining techniques were applied using WEKA 3.7.1 software and PASW STATISTICS 18.

Results: Descriptive statistics including demographics and the status of awareness of stroke symptoms were visualized with graphs. Further, nursing framework and strategies to improve the awareness of stroke symptoms were identified by experienced stroke nurses from multicenter based on evidence from BRFSS database. We designed educational materials for the target population.

Conclusion: We conducted data mining of BRFSS U.S. large data base to identify epidemiological information and the level of awareness of stroke symptoms among stroke population. Nursing care strategies for stroke nurses to improve the awareness of stroke symptoms were recommended as a result and educational materials were developed.

842 Acute stroke: clinical patterns and practise including nursing

NEUTRAL POSITIONING - WHAT MATTER DOES IT MAKE?

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Introduction: In stroke patients sleep disturbances are often seen and may be responsible for the wellbeing and rehabilitation of the patients. Experience shows, that some patients benefit from neutral positionin.

Aim: To describe the characteristics of acute hemiplegic or restless stroke patients after neutral positionin.

Method: The study was descriptive, explorative, and qualitative and involved 12 observations of 10 stroke patients within 3 days after stroke onset. The observations included patient movements, sleep latency, awakenings after sleep onset, and respiration during the first two hours after positionin.

Results: Neutral positioning made it difficult for the patients to turn on the other side, some patients may have stayed awake due to stimulation from a compact diaper or compact bedding, or due to broken sleep habits. Neutral position was difficult to keep in lateral position, and it was characteristic that the patients fell asleep either within 12 minutes – or not until after 80 minutes. Neutral positioning possibly prevented some patients from obstructive apnea in lateral positio.

Conclusion: When using neutral positioning the nurse is encouraged to bee conscious of defining the patients need for rehabilitation and sleep, because patients laying on the affected side slept les than patients laying on the non-affected side. Further more the nurse is encouraged to bee conscious of lowering the temperature in the room, reduce bedding and diaper, and to see the patient roughly 12 minutes after positioning to, if necessary, adjust the bedding or to turn the patient on the other side.

843 Acute stroke: clinical patterns and practise including nursing

STRESS AS A PSYCHO-PHYSICAL RISK FACTOR FOR ICTUS

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Background: Chronic psycho-physical stress is associated with cardiovascular diseases. The relationship is not so well established in stroke. Stress is influenced by vital life events, personality type, quality-of-life (QoL), and level of distress and anxiety.

Objective: To assess the influence of prior psycho-physical stress as a stroke risk facto.

Material and Methods: Case-control study (conducted between Mar 2007 and Mar 2010), paired by age ($\pm$5y), of residents in the Community of Madrid. Cases: patients consecutively admitted in the Stroke Unit of the Hospital Clínico San Carlos, diagnosed as incident stroke. Controls: 2 neighbours per case recruited from the same population census. Sample size: 150 cases, 300 controls. Study variables: socio-demographics, risk factors, psycho-physical scores: Holmes and Rahe, ERCTA, SF12, GHQ 28.

Statistical analyses: A multiple conditional regression model was applied for each score using the STATA 9.0 statistical package.

Results: Significant associations between stroke and stress (patients vs. controls) after adjustment for age, gender, diabetes, hypertension, hypercholesterolaemia, alcohol, smoking, and alterations in cardiac rhythm were: Holmes and Rahe >150 (OR 4.9; 95%CI: 2.5-9.7; p<0.001), ERCTA score >24 (OR 2.6; 95%CI: 1.5-4.7; p<0.001), mental SF12 score >50 (OR: 0.4; 95%CI: 0.2-0.7; p=0.005), psychical SF12 score >50 (OR: 0.5; 95%CI: 0.3-0.8 p=0.008), GHQ28 score >8 (OR: 1.3; 95%CI: 0.7-2.4; p=0.34).

Conclusion: Psycho-physical stress related to vital events, Type A behaviour and low QoL were associated with a higher risk of stroke compared to healthy individuals. Conversely, levels of anxiety and distress did not appear significantly associated with ictus.

844 Acute stroke: clinical patterns and practise including nursing

DETECTION, WORK-UP AND MANAGEMENT OF ACUTE ISCHEMIC STROKE PATIENTS APPROPRIATE FOR THROMBOLYSIS BY EXTENDED NURSING SERVICE IN RAMBAM HEALTH CARE CAMPUS

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Background: Emergent and immediate assessment of acute ischemic stroke patients is extremely important in the achievement of the best Results in the treatment and outcome of stroke. This is especially imperative in patients treated with either intra-arterial (IA) or intravenous (IV) thrombolysis. For the better identification of patients appropriate for thrombolysis two nurses and stroke coordinator were defined as nursing stroke team in neurology department and ER in 2009. Also, it was considered that such reinforcing will increase the number of diagnostic tests such as CT angiography (CTA) and CT perfusion of brain performed in ER and through the hospitalization.

Patients and Methods: All patients diagnosed as acute ischemic stroke in Emergency Room (ER) in 2009-2010 were included in the study. The number of IV treatments was 25 in 2009 versus 26 patients in 2010 (NS). However, the number of IA treatments increased from 8 in 2009 to 14 in 2010. Also, the number of the imaging procedures increased significantly - totally 510 exams of CTA of carotid, CTA of brain and CT perfusion in 2009 versus 706 in 2010 (p<0.007).

Conclusions: The organization of the nursing stroke team improved early detection, work-up and management of acute ischemic stroke patients.

Acute stroke: treatment concepts for physiotherapists and nurses

845 Acute stroke: treatment concepts for physiotherapists and nurses

NURSES' AND REHABILITATION PROFESSIONALS' ROLES IN MEASURING AND MONITORING STROKE QUALITY OF CARE

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Background: Nurses and Rehabilitation Professionals (RP) play a pivotal role in the assessment and management of stroke patients throughout the stroke continuum from prevention through acute care, rehabilitation, long-term care and return to the community. Current performance indicators available to monitor the quality of stroke care are often broad and non-specific. The purpose of this presentation is to examine stroke best practices where both nursing and RP sensitive outcomes are defined and measurable. Best practices and corresponding indicators in preventing acute complications and to facilitate seamless transitions of care will be explored.
Methods: Structured reviews of the research and grey literature were conducted to identify evidence for both best practice recommendations and validated performance measures for all topics included in the 2010 update of the Canadian stroke best practices. A further search was conducted on nursing and RP sensitive outcomes and performance measures. Both were reviewed through a Modified-Delphi process.
Results: Several performance measures were identified in the areas of prevention of complications and transitions of care. Among these a small subset were identified as being nursing-sensitive. No rehabilitation professional specific indicators were identified in the literature; however, the expert reviewers saw several of the nursing indicators as being relevant to both groups.
Conclusions: Demonstrating the impact that nursing and rehabilitation professionals have on stroke patient care through ongoing measurement and monitoring is key to sustaining and improving best practice initiatives within clinical settings.

846 Acute stroke: treatment concepts for physiotherapists and nurses

GAIT RECOVERY AFTER STROKE: A PHYSIOTHERAPY PROTOCOL BASED ON CLINICAL AND FUNCTIONAL CRITERIA

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Introduction: Improved walking is one of the main goals of rehabilitation after stroke, however, due to the complexity of stroke and its after-effects it is difficult to create treatment protocols tailored to each individual patient. The aim of this study is to validate a reproducible physiotherapy protocol for gait recovery after stroke based on functional criteria.
Methods: We have performed a randomized double-blind controlled trial. Inclusion criteria were: patients over 60 years old who had suffered a single stroke episode with residual hemiparesis, ability to walk before stroke and to be clinically stable enough to begin physiotherapy. Exclusion criteria were: blindness, prosthetics or significant osteoarthritis of the lower limbs, serious cardiac disease and severe cognitive impairment. Control and target groups were treated with conventional physiotherapy for stroke, but we added specific techniques to the target group depending on patient's functional level. Hospital de Sagunto (HS) Functional Scales have been used to determine the functional level of each patient. The outcome measures were balance on Berg Balance Scale, walking ability on gait speed and HS Functional Ambulation Classification (FACHS), and functional ability on Barthel Index. Assessment was done at baseline, on the fourth and the twelfth week.
Results: 25 patients (mean age 77.20 ± 7.88) were included in the study and 11 completed the protocol (control group n=4, target group n=7). ANOVA suggested no significant differences between groups. However, the effect size of the variables suggested differences between both groups: gait speed ($\eta2=0.042$), FACHS ($\eta2=0.146$), Berg Balance Scale ($\eta2=0.168$) and Barthel Index ($\eta2=0.125$); and all patients improved significantly their gait ability after rehabilitation (p<0.01).
Conclusions: Treatment protocols after stroke should consider the individual characteristics of each patient and should include training techniques of postural control and balance.

847 Acute stroke: clinical patterns and practise including nursing

A CLINICAL EPIDEMIOLOGICAL STUDY IN 187 INPATIENTS WITH VERTIGO

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A retrospective study to investigate the clinical epidemiological characteristics of vertigo was carried out on 187 patients with vertigo. A clinical history for each patient was recorded precisely about the attack, frequency, and development of vertigo, its duration, intensity, and the accompanied symptoms including the risk factors for cerebrovascular disease, etc. All the patients were subjected to physical examination with special attention to neurologic systems and Dix-Hallpike maneuver, computed tomography/computed tomography–angiography (CT/CTA) and MRI scan were performed when necessary. Majority of the patients in this study suffered with posterior circulation ischemia (59.89%) and benign paroxysmal positional vertigo (16.04%). Other ailments that affected these patients included migraine, Meniere's disease (1.6%), sudden hearing loss (1.07%), vestibular neuronitis, multiple sclerosis, acute viral encephalitis, meningioma, neurosis, post-traumatic vertigo, acute myocardial infarction (0.53%), and neurosis (14.97%). It appeared that in comparison to younger patients the elderly population is likely to be more susceptible to vertigo. Vertigo attacks patients with various diseases, which pre-dispose the patients to this disease. Presentation of vertigo can be clinically diagnosed in most cases of patients suffering from posterior circulation ischemia.

Physiotherapy and early rehabilitation including intensive care and artificial respiration

848 Physiotherapy and early rehabilitation including intensive care and artificial respiration

MIRROR THERAPY FOR IMPROVING MOTOR FUNCTION AFTER STROKE - A SYSTEMATIC REVIEW CARRIED OUT USING COCHRANE METHODOLOGY

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Background: During mirror therapy, a mirror is placed in the patient's midsagittal plane, thus reflecting movements of the non-paretic side as if it were the affected side. The aim of this systematic review is to summarise the effects of mirror therapy on motor function, activities of daily living, pain and visuospatial neglect in patients after stroke.
Methods: We searched the Cochrane Stroke Group Trials Register, CENTRAL, MEDLINE, EMBASE, CINAHL, AMED, PsycINFO and PEDro up to March 2010. We also handsearched relevant conference proceedings, trials, and research registers, checked reference lists, and contacted experts in our field of study. We included randomised controlled trials and randomised cross-over trials. Two review authors independently selected trials based on inclusion criteria, documented methodological quality using the PEDro Scale, and extracted data.
Results: We included 11 studies with a total of 330 participants that compared mirror therapy to other interventions. The median possible PEDro score of all included studies was seven points. Based on our analysis, mirror therapy has a significant effect on motor function, activities of daily living, pain, and visuospatial neglect compared to all other interventions. Furthermore, the effects on motor function were stable at follow-up assessment after six months. Based on a subgroup analysis, we found evidence that the effects might have been corrobated by the type of control treatment.
Conclusions: The Results indicate evidence for the effectiveness of mirror therapy for improving motor function, activities of daily living, pain, and visuospatial neglect for patients after stroke. Therefore, mirror therapy could be recommended at least as an adjunct to routine stroke rehabilitation. Limitations are due to small sample sizes of included studies, control interventions that are not used routinely in stroke rehabilitation, and some methodological limitations of the studies.

849 Physiotherapy and early rehabilitation including intensive care and artificial respiration

SPINAL POSTURE WHILE STANDING IN PEOPLE WITH CHRONIC STROKE AND THE RELATION WITH IMPAIRMENT, ACTIVITY AND PARTICIPATION

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Background: Trunk posture and movement is a prerequisite for activities of daily living and an independent and significant predictor of motor and functional outcome after stroke. Clinical scales to assess trunk control are available in the literature but little is known about underlying trunk deficits such as thoracic and lumbar curvature, sacral position and trunk inclination. The aim of this study was to examine these parameters between people after stroke and healthy controls and to investigate its relation with impairment, activity and participation.
Methods: People with chronic (>6 months) stroke (PwS) and age-matched healthy controls (HC) were recruited for an observational, cross-sectional study. Thoracic, lumbar, sacral and total spinal inclination were measured with the standardized SpinalMouse® while standing upright, flexed forward and extended backward. Clinical measures included the Trunk Impairment Scale (TIS), Barthel Index (BI) and Stroke Impact Scale (SIS).
Results: We assessed 16 PwS and 17 HC. When standing upright, PwS had significantly greater forward spinal inclination (p=0.006) in comparison with HC. When flexed forward, PwS demonstrated less anterior sacral inclination (p=.017) and less total spinal inclination (p=0.023). When extended backward, PwS showed less posterior sacral inclination (p=0.016) and less total spinal inclination (p=.004). All these variables correlated significantly with the TIS. Total spinal inclination in the upright and extended backward position as well as sacral inclination in the extended backward position correlated also significantly with the Barthel Index (r=-0.55 to -0.65).
Conclusion: Total spinal inclination is impaired in the chronic phase after stroke and related to deficits at impairment and activity level. Furthermore, we observed decreased sacral movement when bending forward and backward which was also related to independence after stroke and could become a specific target of rehabilitation.

Poster Session Red
Physiotherapy and early rehabilitation including
intensive care and artificial respiration

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203

Stroke care problems

850 Stroke care problems

IRANIAN EXPERTS' EXPERIENCE OF REHABILITATION SERVICES FOR STROKE SURVIVORS

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Background/Aim: Stroke is a global burden that can cause significant health care problems. Stroke sufferers and their family caregivers experience that the rehabilitation care in Iran needs to be developed. In order to understand the broader picture of stroke rehabilitation, even the experiences of stroke rehabilitation experts is needed. The aim of this study was to explore the experiences of Iranian rehabilitation experts about rehabilitation services in community for stroke survivors and their points of view on how to develop these services.
Method: A qualitative research using grounded theory approach with purposive and theoretical sampling was used. Data were gathered through two focus group Discussions and four individual interviews with ten Iranian rehabilitation experts. Constant comparative analysis method was used.
Findings: Non-integrated rehabilitation service emerged as core concept of the study. The explored concepts were identified as "deficiently allocated budget", "inadequate social insurance", "lack of availability of rehabilitative care", "public views", "lack of consistency of care", "split services and professional separation", "need for changing policymakers attitudes", "needs for re-defining rehabilitation in health care system", "needs for establishing a registration system", "needs for providing information and skills" and "needs for seeing family as a whole".
Conclusion: The experts experienced that the rehabilitation services are not profoundly integrated within the health system in Iran and refinements need to be done. Adequate budgets for implicating discharge plan should be allocated to make opportunities for rehabilitation team working. These efforts could bring opportunities for stroke survivors and their family caregivers to gain knowledge and skills and to participate in rehabilitation teams and also to help reduce their problems.

851 Stroke care problems

ETHICAL PROBLEMS IN STROKE CARE DUE TO SUDDEN AND UNEXPECTED DEATH BY ACUTE STROKE - A STROKE UNIT TEAM APPROACH

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When people die suddenly and unexpectedly caused by acute stroke ethical issues often come to the fore and staff at stroke units have to deal with ethical problems in care.
We aimed at describing stroke teams' staffs' experiences of ethical problems in care and how the teams managed the situation when caring for patients faced with sudden and unexpected death from stroke.
Data were collected through four focus group interviews with nineteen team members, enrolled nurses, registered nurses and physicians in stroke-unit teams.
The result show three themes: To give information when conditions are unstable; To decide on care when the situation is changing and To support when uncertainty prevails.
To give information was experienced as central and related to several ethical problems since the situation was experienced as unstable. Difficulties in making ethical decisions for example about treatment, nutrition and drip for those patients suffering from severe stroke were experienced because of the changing and uncertain situation. In striving to support next-of-kin in the changing and uncertain situation the teams said they felt the patients slipped into the Background and the focus moved to the next-of-kin and questioned who's needs that should guide the care, the next of kin's or the patients.
Mutual trust, both within the stroke team and with next-of-kin, emerged as the core and was seen as a way of handling ethical problems when giving care with the patient's best at heart. Issues experienced as ethically problematic require reflection and cooperation with next-of-kin and other team members. A mutual exchange of information forms the basis for decisions that need to be made when uncertainty prevails. Through trust, a relationship can be constructed that enables the stroke-team members to support the next-of-kin. It is a challenge for the stroke-teams to create mutuality, which is the basis of trust, when conditions are changing.

852 Stroke care problems

FORMEL DIALOG MEETINGS WITH THE CHILDREN OF PARENTS WITH ACUTE STROKE

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Background: Children of parents with stroke express themselves as forgotten and kept away in connection to the illness of their parents. At the same time the healthy parent is often going through a psychological crisis and may be unaware of how to react toward the children.
In the Stroke Unit of Aalborg Hospital, Denmark, we decided to concentrate on these children by organizing formal dialog meetings with the participation of children between 6 and 18 years, nurses, social workers, and neurological psychologists. Parents were allowed to participate, but the children and their interests were in focus.
Aim: To describe our experiences with dialog meetings with children of parents with stroke.
Method: A qualitative semi structured interview was completed with the participation of nurses, a social worker, and a neurological psychologist.
The interview dealt with the reaction of the children, how to make the children open up for a talk, which remedies were needed, the reaction of the parents, the wishes of the children and which information the children were given.
Results: The poster shows our experiences with these dialog meetings.

853 Stroke care problems

THE PREVALENCE OF MOOD DISORDERS AMONG STROKE PATIENTS ADMITTED INTO A REHABILITATION CENTER IN SINGAPORE

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To study the prevalence of mood disorders among stroke patients who were transferred to a rehabilitation center from acute hospitals. A total of 214 stroke patients were admitted into Tan Tock Seng Rehabilitation Center from acute hospitals over a period of six months. Patients with apparent cognitive or hearing impairment, aphasia, dysphasia, Abbreviated Mental Test (AMT) score<6 and those who refused to participate were excluded from our study. Patient demographics were collected. Diagnosis of major depressive episode and adjustment disorder was conducted by psychiatrists, based on Structured Clinical Interview for DSM IV (SCID) criteria. 162 patients met our inclusion criteria and were seen by psychiatrist within the first week of admission into rehabilitation center and at one-month post admission. The mean age of this population was 59.2 (SD ±11.67) years. The ratio of male to female patients was 2:1. The percentage of SCID positive cases was 20.99% in our sample. Of these patients, 29 were clinically diagnosed with adjustment disorder or major depression within the first week of admission while another 5 patients met SCID criteria at one-month post admission. The occurrence of mood disorders was highest among Chinese stroke patients (25.86%) as compared to Malay (7.4%) and Indian (15.4%). From our sample, we also found that married patients having the least percentage of mood disorders in comparison to patients with other marital status such as divorced, single and widowed. In Conclusion, mood disorders such as depression and adjustment disorder are common among patients who suffered from stroke.

IMPROVING THERAPY DISCHARGE HANDOVER FROM INPATIENT ACUTE STROKE UNIT TO COMMUNITY SERVICES - A SERVICE IMPROVEMENT PROJECT

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In 2010 East Kent Hospitals University Foundation Trust Therapy services began a Department of Health supported Allied Health Professional service improvement project which looked at the transition of Stroke patients' Physiotherapy and Occupational therapy from the Acute stroke unit teams to the Intermediate Care Team (ICT) therapists in the community.This project has been ongoing since July 2010 and has aimed to improve communication between hospital and community therapists by initiating early referral and Acute to Community Outreach Handover Visits for patients with complex rehabilitation needs on leaving the stroke units. Criteria for those patients who were to receive a handover visit were set out to include those with complex therapy needs where communication of those needs would be inadequate on paper or by telephone. Patients were referred to ICT therapists up to seven days prior to discharge and the outreach handover visit was booked for the next working day after discharge wherever possible. Following the handover visit a report was compiled within one working day and a copy sent for filing within ICT notes.Information from service users and staff was gathered by questionnaire and data was collected against the standards set and on length of stay and readmission rates.Pre-service improvement 71% of patients waited 7 days or more for community therapy.77% of outreach patients had their visit within 1 working day.This was also first contact with community services.83% of outreach patients reported being either very confident or reassured by being present at the handover of their care. 90% of staff in both acute and ICT teams felt that outreach was beneficial to both patients and staff. Outreach patients are those with complex needs who are likely to have a longer length of stay. On average length of stay for these patients was 11.6 days below maximum.Thirty day readmission rates for the outreach patients was reduced from 10.7% to 0.

PREDICTORS OF FAILURE IN STROKE EDUCATION DURING ADMISSION: A STROKE-CENTER BASED STUDY

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Background: Stroke survivors are often not aware of the warning signs and risk factors for stroke. Patient education following a stroke can help prevent future strokes. Predictors of failure in achieving successful stroke education after a stroke admission are not well established.

Methods: Retrospective analysis of prospectively collected data of patients admitted to a tertiary hospital with stroke. Clinical and demographic findings were analyzed. Stroke education followed an institutional protocol and educational status was obtained from nursing reports.

Results: from October 2008 to October 2010, 279 patients were evaluated, of which 25 were excluded, because they died (n=15) or had been transferred from outside hospitals (n=10). A total of 229 (90%) patients had ischemic stroke, and 25 (10%), hemorrhagic stroke. The mean age was 71±28 yo (57% males). The median NIHSS at admission was 5 [1 9] and the median length of stay was 9 days [4 17]. Most patients (79%) received stroke education. The median time from admission to the educational intervention was 5 days [3 9]. Patients who received stroke education and those who did not were similar in age (71±15 vs 69±18, p=0.3), stroke severity (NIHSS 5 [1 9] vs 4 [1 10], p=0.79), and the prevalence of aphasia (28% vs 31%, p=0.3). Patients who received stroke education had a trend towards shorter length of stay than those who did not (6 [6 13] vs 9 days [5 18], p=0.16). Univariate predictors of failure in achieving stroke education were being a smoker (OR=1.7, p=0.10), having a history of coronary artery disease (OR=1.6, p=0.10), length of stay (OR=0.99, p=0.10), and discharge during the weekend (OR=1.7, p=0.11) After multivariate logistic regression analysis, none of the variables evaluated remained an independent predictor of educational failure.

Conclusion: Studies that help identify predictors of educational failure might help plan successful post stroke patient education and have an impact upon stroke recurrence.

Epidemiology of stroke

1   Epidemiology of stroke

NEUROLOGIC PHENOTYPE ASSOCIATED WITH HEREDITARY HAEMORRHAGIC TELANGIECTASIA IN A MONOCENTRIC COHORT OF 154 PATIENTS

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Introduction: Hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant disorder that leads to the formation of vascular malformations in mucocutaneous tissues, visceral organs, and central nervous system. The most frequently reported neurologic injuries are cerebral vascular malformations (CVM), especially cerebral arteriovenous malformations (CAVM). Neurologic manifestations secondary to a right-to-left shunt through pulmonary arteriovenous malformations (PAVM) are less known.
Methods: All patients with HHT collected between 1991 and 2010 in a prospective registry in a tertiary teaching hospital were included in this study. Neurologic data and brain imaging were assessed by 2 neurologists and 1 neuroradiologist.
Results: In our cohort of 154 patients with HHT, 27 (17.5%) had a symptomatic neurologic injury, while symptomatic neurologic injury was present in 27 (29%) patients among the 93 patients with a PAVM. Prevalence of stroke or TIA was 14.2% in the overall group and 23.6% in the subgroup with PAVM. At 3 months, patients with stroke had good recovery (modified Rankin Score ≤ 2). Aetiological work-up for stroke or TIA revealed a right-to-left shunt through PAVM in 94.6% cases, including 13.6% of cases occurring during PAVM embolization. Ischemic events occurred in 4.5% of cases during cerebral AVM embolization. No cerebral ischemic recurrence occurred in patients with complete PAVM embolization. Four patients (0.03%) had cerebral abscesses. One patient had a symptomatic cerebral haemorrhage caused by a brain cavernoma. Various and asymptomatic CVMs were found on MRI in our study population: CAVM with small niduses (n=10), capillary telangiectasias (n=8), venous developpmental anomalies (n=7), and cavernomas (n=3).
Conclusion: Neurologic symptoms related to HHT affect more than 1 patient in 6. Our Results underline the high prevalence of stroke or TIA in HHT, especially in those with a PAVM. Cerebral vascular anomalies are common and atypical in HHT patients.

2   Epidemiology of stroke

THE BUDAPEST DISTRICTS 8-12 PROJECT: LIVING STANDARS AND STROKE - STUDY METHODS AND BASELINE DATA

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Background: Stroke mortality in former Central-Eastern European countries has been consistently higher in the last 30 years than in the West. According to WHO data smoking and heavy alcohol consumption is more frequent, whereas GDP per capita is smaller in these countries. To test whether differences in living standard has an influence on stroke characteristics in a smaller geographical scale as well, we set forth to compare 2 Budapest districts.
Methods: District-12 is a wealthy district in Buda, whereas District-8 has one of the lowest living standard on the Pest side of Budapest. Residents of these Budapest districts hospitalized with a major diagnosis of stroke during year 2007 were listed from the register of the National Health Insurance Fund. Survival status of these patients as well as their registered general practitioners (GPs) in 2010 were identified.

A standard case report form was developed. Anonym patient data were used. Personal visits to GPs by the research staff is organized to obtain data of interest regarding risk factors, stroke characteristics and outcome at 3 years after stroke.
Results: For District-8 and District-12 population are 82.000 and 56.000, and population density 12.003/km^2 and 2.120/km^2. In District-8 489 stroke cases belong to 148 GPs, whereas in District-12 364 stroke patients are covered by 103 GPs. Mean age at stroke is 5 years younger in the less wealthy district (69±14 vs. 74±12 years, p<0.001). Of all stroke patients 27.2% are below 60 years of age in District-8, whereas this rate is 14.0% in the more wealthy district (p<0.001).
Conclusion: baseline data show that even within one city, in the less wealthy district stroke not only hits 5 years earlier, but affects twice frequently the working age group.

3   Epidemiology of stroke

STROKE AWARENESS IN THE GENERAL POPULATION: KNOWLEDGE OF STROKE, RISK FACTORS AND WARNING SIGNS IN OLDER ADULTS

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Background: Stroke is a leading cause of death and functional impairment. While older people are particularly vulnerable to stroke, research suggests that they have the poorest awareness of stroke warning signs and risk factors. This study examined knowledge of stroke warning signs and risk factors among older adults.
Methods: The study was conducted between June 2009 and October 2009. The subjects were selected through a system of double randomization based on census units and conglomerates. The previously trained medicals students face to face interviews in selected households using a structured questionnaire with open and closed questions. Questions assessed knowledge of stroke warning signs and risk factors, and personal risk factors for stroke. Adequate knowledge was previously defined.
Results: 2411 subjects were interviewed during the study period (59.9% women; mean age, 39.0 years; age range, 16.4 to 93.8 years). Overall, 538 (38%) were aged 65 years or older. Fifty-nine percent of respondents over 65 years correct named at least one established stroke warning signal vs 78.7% in the young group (p <0.0001), and 46,8% correctly named at least 1 established stroke risk factor vs 62,8% (p< 0.0001). When participants were asked what action they would take if they suspected the symptoms of stroke, 63,1% in older adults have a hypothetical ideal attitude to the disease vs 84,4% in the youngest (p< 0,0001). A 20,6% of this older population had adequate general knowledge of stroke compared with 45% of the population aged under 65 years (OR 3,2; 95%CI 2,5-3,9; p< 0,0001).
Conclusion: Many older adults may not recognize early symptoms of stroke in themselves or others. Thus, they may lose vital time in presenting for medical attention. Lack of public awareness about stroke warning signs and risk factors must be addressed as one important contribution to reducing mortality and morbidity from stroke.

4   Epidemiology of stroke

EFFECT OF STROKE CLASSIFICATION SYSTEMS ON A SERIES OF STROKE IN YOUNG ADULTS

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Introduction: A large number of stroke series in younger adults have been reported and in recent years the majority have used the TOAST criteria. A phenotypic stroke classification system has been suggested with the potential to provide significant additional information (ASCO criteria). It is possible that stroke may be classified

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differently using the 2 schemes. In particular, given the higher level of evidence required in particular in the cardioembolic stroke category, we hypothesised an increase in those coded as undetermined stroke by ASCO criteria.

Methods: We recorded all stroke presentations in those ≤55 years over an 18 month period. All cases-notes were reviewed and stroke subtype by TOAST and ASCO recorded. ASCO grading was grouped by level 1 (ASCO1) and level 2 (ASCO2) evidence for comparison with TOAST. Proportion of cases classified as undetermined by TOAST and ASCO was compared (using McNemar's test).

Results: 316 cases ≤55 years (145 inpatient, 171 outpatient) presented to the stroke service in the time period. Of these, there were 124 confirmed strokes (107 infarcts and 14 haemorrhages); 29 TIAs, 157 mimics and 9 with incomplete data were excluded.

By TOAST criteria, there were 6%, 11%, 28%, 22% and 34% of large artery atherosclerosis, small vessel occlusion, cardiac embolism, other determined cause and undetermined cause respectively. Considering the same groups, there were 6%, 9%, 11%, 22% and 52% by ASCO1 and 6%, 16%, 16%, 22% and 41% by ASCO2 (Figure). The proportion of cases classified as undetermined by ASCO1 was significantly greater than by TOAST (52.3% v 33.6%; p=0.0002).

For those with a cardiac cause of stroke by TOAST criteria, the majority had a PFO (60.0%), which were not coded as cardioembolic by ASCO1 criteria.
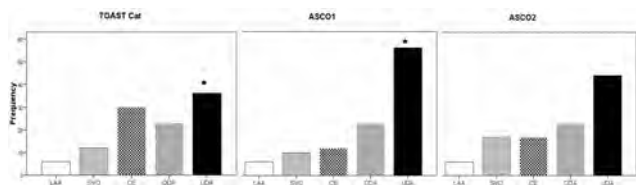
Figure 1. Bar charts of stroke subtype under different classification schemes. LAA Large artery atherosclerosis; SVO small vessel occlusion, CE cardiac embolus; ODA other determined aetiology; UDA undetermined aetiology (*p<0.001).

Conclusion: In a younger stroke cohort, significantly more cases are classified as undetermined with ASCO1 than with TOAST. This is largely due to the exclusion of lower risk cardiac lesions from the cardiac embolus group.

5   Epidemiology of stroke

STROKE IN PATIENTS AGED 100 OR MORE. CASE-FATALITY AND RISK FACTOR PROFILE

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Background: The oldest old is the fastest growing segment of the elderly population. We studied stroke severity, risk factor profile and case-fatality in a Danish cohort of 39 stroke patients aged ≥100 years comparing these to patients aged 70-79 years, 80-89 years and 90-99 years.

Methods: A registry aimed at registering all hospitalized stroke patients in Denmark 2002-2010 holds 61 935 patients. The patients underwent an evaluation including stroke severity (Scandinavian Stroke Scale (SSS), 0 (worst) – 58 (best)), CT-scan and a cardiovascular risk factor profile.

Results: Of the 39 patients age range was 100-107 years; 13% men, 87% women; mean SSS: 25. Single living 92%, nursing home residents 31%, own home 69%. Hemorrhagic/ischemic stroke 8%/92%, atrial fibrillation 24%, previous myocardial infarction 6%, diabetes 3%, hypertension 48%, intermittent arterial claudication 0%, previous stroke 15%, daily alcohol consumption > 3 drinks per day 0%, current smoking 9%. One-week case-fatality 13%, 30-day case-fatality 39%. Compared to patients aged 70-99 years risk factor prevalence was generally lower in patients aged ≥100 years. In particular prevalence of previous myocardial infarction, previous stroke, diabetes, intermittent arterial claudication and current smoking was much lower in patients ≥ 100 years of age. Strokes were more severe in patients aged ≥ 100 years (SSS 25) compared to patients aged 70-79 years (SSS 42), 80-89 years (SSS 37), 90-99 years (SSS 32). One-week/30-day case-fatality was higher in patients ≥ 100 years (13/39%) compared to patients aged 70-79 years (6/10%), 80-89 years (8/16%), 90-99 years (12/28%), ≥ 100 years (13/39%).

Conclusion: Prevalence of cardiovascular risk factors were lower in stroke patients aged ≥ 100 years compared to younger patients. Case-fatality was higher but strokes are also more severe in patients aged ≥ 100 years. Two thirds are living in own home.

6   Epidemiology of stroke

PRESTROKE CHADS2 SCORE: RESULTS FROM THE LUDWIGSHAFEN STROKE STUDY (LUSST), A POPULATION BASED STROKE REGISTER

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Background: Cardioembolism appeared to be the main source for ischemic stroke in the Ludwigshafen Stroke Register (LuSSt). The CHADS2 score is a clinical stratification tool for estimating the risk of cardioembolic stroke in patients with nonvalvular atrial fibrillation (AF). We investigated prestroke CHADS2 score in patients with first-ever ischemic stroke (FEIS).

Methods: The Ludwigshafen Stroke Study (LuSSt) is a prospective ongoing population-based stroke registry among the 167.906 inhabitants of Ludwigshafen am Rhein, Germany. Between January 1, 2006 and December 31st, 2007, 1.231 patients with residency in Ludwigshafen who suffered from acute stroke or transient ischemic attack (TIA) were consecutively registered. For the present analysis, only patients with FEIS were included.

Results: 626 patients suffered a first-ever-in-a-lifetime ischemic stroke. AF was present in 191 (31%) patients, being newly diagnosed in 68 patients. The mean age of the AF-patients was 77 + 10 years, 57% were female. In 154 patients (79%) prestroke CHADS2 score indicated moderate or high risk for cardioembolism (CHADS2 score > 2). In patients with an increased CHADS2 Score > 2 and previously diagnosed AF, only 34% were on anticoagulation therapy at the time of stroke occurrence.

Conclusions: The majority of patients with cardioembolic FEIS (79%) had a prestroke CHADS2 Score > 2, and only every 5th patient with FEIS presented with a low prestroke CHADS2 Score of 0 or 1. Despite an increased CHADS2 Score of > 2, only a third of patients with AF received oral anticoagulation before stroke.

7   Epidemiology of stroke

DIFFERENCES IN STROKE SUBTYPE BETWEEN FIRST-EVER AND RECURRENT STROKE: THE SOUTH LONDON STROKE REGISTER (SLSR)

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Background: Data reporting long-term patterns of cumulative risk of stroke recurrence between different aetiological and pathological stroke subtypes are lacking. Furthermore, information regarding transition in subtype of first and recurrent stroke is not widely available.

Methods: Data were collected from the SLSR, a population-based stroke register in South London. Patients were followed up for a maximum of 12 years. Kaplan-Meier estimates were performed to assess cumulative risk of stroke recurrence and this was stratified using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) and Oxford Community Project Classification (OCSP) classifications. Initial and recurrent stroke subtypes were cross-tabulated to calculate transition probabilities.

Results: Between 1995 and 2009, 4023 patients with first-ever stroke were included in the SLSR. Mean follow-up period was 3.0 years. In 11981.7 person-years of follow up, 394 recurrent strokes were documented. The overall cumulative risk of stroke recurrence was 6.7% at 1 year, 15.1% at 5 years, 21.5% at 10 years and 23.5% at 12 years after first stroke. Between 1999 and 2009, the cumulative risk of stroke recurrence 1 year post stroke ranged from 4.0% in the small vessel occlusion (SVO) group to 6.5% in the large artery occlusion (LAA) group. These Results were lower than 1 year recurrence rates for both intracerebral (PICH) and sub-arachnoid (SAH) haemorrhages which were 8.6% and 8.8%. Transition in aetiological subtype between initial and recurrent stroke was seen in 51.0% at 1 year, increasing to 61.9% 10 years after first stroke.

Discussion: The cumulative risk of stroke recurrence is wide-ranging between aetiological and pathological subtypes. Further research is needed to identify predictors for increased risk of recurrence amongst different stroke subtypes and to investigate whether implementation of intensified secondary prevention strategies in high risk patients can reduce the long-term risk of stroke recurrence.

LONG TERM SURVIVAL: PREDICTORS AND TRENDS IN THE SOUTH LONDON STROKE REGISTER FROM 1995 TO 2009

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Aim: To estimate survival up to 15 years after a first-ever stroke and the influence of year of stroke, sociodemographic, case-mix, stroke subtype and acute stroke care factors on survival.

Methods: Population based stroke register registering first in a lifetime strokes between 1995 and 2009. Baseline data collected on sociodemographic factors, subtype, case mix, risk factors prior to stroke, and acute stroke care variables. Survival curves were estimated with Kaplan-Meier Methods and multivariate survival analyses were undertaken using Cox Proportional-hazards models.

Results: Among 4037 patients with a first-ever stroke between 1st January 1995 and 31st December 2009, 2514 (62.3%) have died (all causes) by 31st May 2010. Survival gradually improved over this 15-year period as shown in Kaplan-Meier curves for patients registering in each consecutive 3-year period (P-value<0.0001). The significant factors influencing all-cause mortality were age, year of stroke, ethnic group, case-mix, subtype, stroke unit admission, and risk factors prior to stroke such as MI (myocardial infarction), AF (atrial fibrillation), diabetes and smoking. Recent stroke (calendar year of stroke), being black Caribbean or black African, non-manual employment and stroke unit admission were shown generally associated with better survival after adjusting for age, gender, case mix, stroke subtype and other potential confounders. Patients with PICH (Hazard ratio: 1.15[1.01, 1.32]) and SAH (Hazard ratio: 1.40[1.09, 1.79]) had worse survival than those with Cerebral infarct. Of the risk factors prior to stroke, MI, AF, diabetes and current smoker were associated with reduced survival.

Conclusions: Survival has gradually improved for patients from South London Stroke Register between 1995 and 2009. Recent stroke (calendar year of stroke), infarct subtype, being black Caribbean or black African, non-manual employment and stroke unit admission were associated with better survival.

RISK FACTORS, NOT ETHNICITY, DETERMINE STROKE RISK AMONG ASIANS: FOLLOW-UP OF THE COMMUNITY-BASED MULTI-ETHNIC SPEEDS STUDY

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Background: Previously published studies of inter-ethnic differences in stroke incidence in "Western" populations showed higher risk among some ethnicities even after adjusting for vascular risk factors (RF). The only multiethnic Asian studies, both from Singapore, showed a higher incidence among Malays compared to Chinese and Indians. Neither study explored the confounding effect of differing RF profiles.

Methods: Singapore is a tropical island city-state of 5 million people, predominantly Chinese, with large Malay and Indian minorities. Heavily-subsidised healthcare is widely available to all. The Stroke, Parkinson's disease, EpilEpsy and Dementia in Singapore (SPEEDS) study was a tri-ethnic community-based prevalence survey of neurological diseases among 14906 randomly-selected Singaporeans aged above 50yr. A self-report of vascular risk factors was obtained at baseline. For this incidence study, subjects stroke-free at baseline were contacted by telephone 4 years after their initial participation and asked by a trained interviewer if they have had a stroke. Medical records of non-respondents were retrieved. The study was approved by the IRB.

Results: Of the original 14906 study subjects, 606 had had a stroke at baseline, yielding a population of 14300 for this incidence study; 59.6% Chinese, 20.7% Malay, 19.7% Indian. Mean age was 63.1yr (+9.0), 55.2% female. 34.1% had hypertension (HT), 21.2% hyperlipidemia (HL), 18.1% diabetes (DM), 9.4% heart disease (HD), 26.6% ever smoked (SM), 10.8% family history of stroke (FH). Over the 4 year period, 125 developed an incident stroke (IS): crude IS rate 220/100000/yr, 0.87%, 95%CI 0.72-1.02), 0.96% among Malays, 0.94% Chinese, 0.64% Indians. On univariate analysis, IS was significantly associated with increasing age, HT, DM, HD, SM, but not gender, ethnicity, HL, FH. On multivariate analysis, significant association remained only for age (OR 1.08, 95%CI 1.06-1.1), DM (OR 1.86 95%CI 1.24-2.79), HT (OR 1.75, 95%CI 1.20-2.55).

Conclusions: Stroke risk among Asians is independent of ethnicity; it is higher among those with HT, DM and increasing age. More studies in multiethnic populations are needed.

TEMPORAL TRENDS IN THE EPIDEMIOLOGY OF ADULT RESPIRATORY DISTRESS SYNDROME (ARDS) AFTER ACUTE ISCHEMIC STROKE IN THE UNITED STATES

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Background: We sought to determine the epidemiology of ARDS, the prevalence of risk factors, and impact on hospital mortality after acute ischemic stroke (AIS) in the U.S.

Methods: Data were derived from the National Inpatient Sample from 1994-2008. We searched for admissions of patients >18 years, with a diagnosis of AIS and ARDS. Definitions were based on ICD9CM codes. Adjusted incidence rates for the U.S census were calculated and multivariate logistic regression models were then fitted to assess for the impact of ARDS on hospital mortality.

Results: Over the 15-year period, we identified 5,451,998 admissions that corresponded to a primary diagnosis of AIS of which 209,291 had ARDS for a cumulative incidence of 4%. The adjusted rate of AIS increased from 132/100,000 in 1994 to 142/100,000 in 2008 and the adjusted rate of ARDS after AIS increased from 4.7/100,000 in 1994 to 5.7/100,000 in 2008. ARDS was more common among old (OR 0.9; 95%CI 0.9-0.98), men (OR 1.2; 95%CI 1.2-1.21), blacks (OR 1.2; 95%CI 1.1-1.2), urban-academic centers (OR 1.4; 95%CI 1.3-1.5); and in sepsis (OR 8.0; 95%CI 7.6-8.4), cardiovascular dysf. (OR 3.5; 95%CI 3.3-3.7), renal dysf. (OR 2.3; 95%CI, 2.2-2.4), hepatic dysf. (OR 2.9; 95%CI 2.4-3.4), hematological dysf. (OR 1.9; 95%CI, 1.8-2.1), and thrombolysis (OR 3.8; 95%CI, 3.6-4.0). The total hospital mortality after AIS fell from 9% in 1994 to 5% in 2008. Mortality was highest among ARDS (adjusted (a) OR 17; 95%CI 16-18), old (aOR 1.03; 95%CI 1.03-1.03), whites (OR 1.2; 95%CI 1.1-1.2), sepsis (aOR 3.4; 95%CI 3.2-3.6); and thrombolysis (aOR 1.6 95%CI 1.4-1.7). A differential effect of ARDS on hospital mortality was found in those that received thrombolytics (aOR 0.5; 95%CI 0.4-0.6).

Conclusion: Our analysis demonstrates an increase in the incidence of AIS in the U.S. Despite a decline in overall AIS related mortality, ARDS increased the risk of in-hospital death but those that received thrombolytics were more likely to survive.

THE STROKE EPIDEMIOLOGY IN SIX REGIONS OF RUSSIA

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Background: The aim of the work is to study rates of incidence, attack, mortality and fatality cases from stroke in Russia, in order to organize treatment and acute stroke prevention.

Material and Methods: The research was executed with the Register method according to the uniform criteria of Methodological Instruction Russian National Association of Fight against Stroke.

Study of epidemiological stroke indexes was conducted in open population of men and women older than 25 years in six regions of Russia, the number of residents was 981 207, among them: men were 435 678 and women - 545 529. Those regions were the Republic of Bashkiria, Ivanovo region, Irkutsk region, the Republic of Karelia, Stavropol region, Sverdlovsk region. The number of stroke cases registered for 1 year was 3 411; 1 572 stroke cases and 1 839 stroke cases, among men and women, in accordance.

Results: According to the European standard, standardized stroke attack rate in 6 regions for 1-year study period (2009) was 3.48 per 1 000 population: 3.61 per 1 000 for men and 3.37 per 1 000 for women.

Incidence of first stroke was 2,65 per 1 000 population: 2.69 per 1 000 for men and 2.62 per 1000 for women.

Incidence of recurrent stroke was 0,85 per 1 000 population: 0.91 per 1 000 for men and 0.75 per 1 000 for women.

Non-fatal incidence first stroke (not finished with case fatality in a period within 28 days from the onset of the stroke) was 1.86 cases per 1 000 population. Non-fatal incidence recurrent stroke was 0.54 cases per 1 000 population.

A stroke case mortality rate within 28-days period of the stroke was 0.91 per 1 000 population: 0.82 - among men, 0.99 - among women.

Conclusions: Epidemiological study of stroke in the open population of Russia demonstrates the high rate of incidence, attack and case fatality and shows the necessity of further investigation of stroke risk factors.

12 Epidemiology of stroke

DIFFERENTIAL PROPENSITY OF MAJOR HAEMORRHAGIC EVENTS IN PATIENTS WITH DIFFERENT TYPES OF ARTERIAL DISEASES

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Aims: Atherosclerosis is the most frequent cause of coronary artery disease (CAD), cerebrovascular disease (CVD) or peripheral arterial obstructive disease (PAOD). We previously found that patients with CVD or PAOD had a two times higher risk of major haemorrhagic complications than patients with CAD. We investigated whether this difference was attributable to baseline risk factors or genetic variants involved in haemostasis.

Methods and Results: We included 2622 consecutive patients from a single university hospital who presented with non-disabling CAD, CVD or PAOD. All patients were followed for the occurrence of major haemorrhagic complications during a mean of 6.6 years. Major haemorrhagic events included intracranial haemorrhagic, fatal haemorrhagic event and any haemorrhagic complication requiring hospitalisation, irrespective of interventions. Major haemorrhagic complications occurred in 122 patients (annual event rate 0.77%). Patients with CVD or PAOD had more haemorrhagic complications than patients with CAD (HR: 2.05 (95%CI: 1.39-3.01). Hypertension, diabetes, renal failure and use of oral anticoagulants or antiplatelet therapy did not explain the difference (HR adjusted for all characteristics 1.74; 95%CI 1.14-2.61). Additional adjustment for genetic variants did not further change the HR.

Conclusion: Patients with CVD or PAOD are at higher risk for major haemorrhagic events than patients with CAD. This difference could not be explained by known risk factors, use of antithrombotic agents or genetic variants involved in haemostasis. Further research to find the reason for this difference and possible differences in pathogenesis is warranted.

13 Epidemiology of stroke

NATIONAL TRENDS IN STROKE ADMISSIONS, DENMARK 1997-2009

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Background: The aim of this nationwide register study is to analyze trends of incidence in hospitalized stroke events in Denmark from 1997-2009 and to provide projections on the number of stroke patients in Denmark in 2030.

Methods: Data from the Danish National Patient Register were used to identify all first-ever hospitalized stroke events in Denmark from 1997-2009. Persons aged 25 years and above were included. Incidence rates were calculated for all major stroke sub-types. Poisson regression analyses adjusting for age in 1-year intervals were used to examine trends in age-, gender- and subtype stratified IRs.

Results: During the observation period of $5.44*10^7$ person years-at-risk (PY) a total of 88,153 and 88,254 stroke events were registered in men and women, respectively. For all ages the total absolute unadjusted incidence rate (IR) in 1997 was 3.21/1000 PY (95% CI 3.15-3.26) and increased in 2009 to 3.73/1000 PY (95% CI 3.67-3.79). Incidence rate ratio adjusted for age in the time period 2007-2009 was statistically significant increased compared with the time period 1997-2000 in most 10-years age groups, see tables 1 and 2.

Table 1. Stroke incidence rate ratios for men for all types of stroke for 4 time periods (1997-2000 reference)

All types, men	1997-2000	2001-2003	p-value	2004-2006	p-value	2007-2009	p-value
<45 years	1.0	1.123 (1.02-1.236)	0.0183	1.216 (1.103-1.34)	<0.0001	1.492 (1.34-1.661)	<0.0001
45-54 years	1.0	1.189 (1.123-1.259)	<0.0001	1.133 (1.068-1.201)	<0.0001	1.296 (1.216-1.38)	<0.0001
55-64 years	1.0	1.038 (0.996-1.082)	0.0745	0.957 (0.918-0.997)	0.0356	1.077 (1.03-1.126)	0.001
65-74 years	1.0	1.05 (1.012-1.09)	0.0089	0.905 (0.872-0.94)	<0.0001	0.949 (0.91-0.989)	0.0133
75-84 years	1.0	1.036 (1.001-1.072)	0.041	0.94 (0.908-0.974)	0.0006	0.91 (0.874-0.947)	<0.0001
>84 years	1.0	1.053 (0.994-1.117)	0.0811	1.045 (0.991-1.102)	0.1029	1.129 (1.071-1.19)	<0.0001

Poisson regression model. 95% confidence interval.

Table 1. Stroke incidence rate ratios for women for all types of stroke for 4 time periods (1997-2000 reference)

All types, women	1997-2000	2001-2003	p-value	2004-2006	p-value	2007-2009	p-value
<45 years	1.0	1.116 (1.010-1.233)	0.0314	1.302 (1.178-1.440)	<0.0001	1.773 (1.591-1.975)	<0.0001
45-54 years	1.0	1.209 (1.126-1.298)	<0.0001	1.190 (1.108-1.279)	<0.0001	1.513 (1.403-1.63)	<0.0001
55-64 years	1.0	1.13 (1.071-1.193)	<0.0001	0.982 (0.93-1.037)	0.5213	1.113 (1.051-1.18)	0.0003
65-74 years	1.0	1.089 (1.045-1.135)	<0.0001	0.948 (0.909-0.99)	0.0145	0.958 (0.913-1.004)	0.0732
75-84 years	1.0	1.079 (1.047-1.112)	<0.0001	0.971 (0.941-1.003)	0.071	0.955 (0.920-0.990)	0.0131
>84 years	1.0	1.113 (1.068-1.159)	<0.0001	1.055 (1.012-1.100)	0.0111	1.094 (1.045-1.145)	<0.0001

Poisson regression model. 95% confidence interval.

The total unadjusted IR of unspecified strokes generally decreased from 1997-2009 whereas there was a steep rise in IR of ischemic strokes from 1997-2009.

According to estimates based on UN's population projections the number of hospitalized stroke events will increase from 14,186/year in 2010 to 19,055/year in 2030.

Conclusion: During the period 1997-2009 there has been an overall trend of an increase in hospitalized stroke incidence among the Danish population.

14 Epidemiology of stroke

A POPULATION-BASED STUDY OF TRANSIENT ISCHEMIC ATTACK INCIDENCE IN JOINVILLE, BRAZIL, 2010

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Background: There is no population-based on transient ischemic attack (TIA) in Latin America and many barriers are positioned between symptoms recognition by patients and ideal care. Based on symptoms specificity, we aim to define incidence of first ever TIA in Joinville, Brazil.
Methods: From JOINVASC, a community-based stroke data bank, in 2010, we registry incidence and risk factors of all first ever definite and probable TIA in overall population of 497329 residents in Joinville, Brazil. The rates were adjusted by direct method.
Results: In one year we registered 37 definite and 74 definite and probable TIA. The crude annual rate per 100000 residents was 7 (95% CI, 5 to 10) for definite cases and 15 (12-19) for definite and probable cases. These rates standardized to European populations were 12 (9-17) and 28 (22-35), respectively.
Conclusions: Using these diagnostic criteria, the rates found in Joinville are two to three times smaller than the rates published in some high income populations. The reasons for this remarkable finding need to be study.

15 Epidemiology of stroke

HIGH INCIDENCE OF STROKE IN THE BREST FRENCH STROKE POPULATION REGISTRY

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Background: Population registries on stroke are necessary to evaluate the precise burden of stroke on a defined population. Only one other population stroke registry is available in France (Burgundy).
Methods: A population based stroke registry recorded all stroke patients aged > 15 years. Data were collected prospectively since January 1st 2008. By using 5 referral sources, cases of stroke were identified in a defined area corresponding to 79 districts surrounding and including Brest (Brittany). The total population was 352319 according to 1999 census. Hospital surveillance of admissions for stroke included 2 teaching and 1 general hospital. Community surveillance of stroke included patients under private neurologists or radiologists care. Patients with transient neurological deficits vanishing within 1 hour (H) and normal brain imaging or with subarachnoid haemorrhage were excluded. Two stroke definitions were used: A new focal neurological deficit > 24 H or all neurological deficits lasting at least 1H or resolving within 1H but with an abnormal and clinically relevant brain imaging. Standardized incidences based on two definitions were calculated.
Results: For 2008, 1626 patients were identified, but only 851 were included. The number of sources per patient varied between 1 and 5 notifications sources: 61.4% had at least 2 sources. For more than 80%, the first source of identification was emergency wards (80.2%), for 10.9% it was hospital based electronic research using ICD 9, for 5.4% it was radiology, for 3.1% it was death certificate. Standardized overall incidence was 317/100 000 inhabitants (CI 95%: 296-339), first-ever-stroke (FES) was 234 (216-253). For patients with symptoms >24 H standardized incidence was 250 (231-269) and FES 188 (172-205). For 2009, a total number of patients of 899 was included.
Conclusion: Incidence of stroke in Brittany is almost the double compared to incidence in Burgundy. Reasons for such differences remain to be determined.

16 Epidemiology of stroke

ABCD2 SCORE VALIDATION IN ITALY. TIA INCIDENCE AND 2-, 7-, 30- AND 90-DAY STROKE RISK: A POPULATION-BASED PROSPECTIVE STUDY IN UDINE, ITALY

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Background and purpose: Transient Ischemic Attack (T.I.A.) have been proven to be a strong predictor of subsequent ischemic stroke: the aim of our study was to estimate a)T.I.A. incidence, b) 2-, 7-, 30- and 90-Day risk of stroke and c) to validate the ABCD2 score in Udine District, north-east Italy, with a total population of 153313 (2007 census). All cases were enrolled between April 1, 2007 and March 31, 2009.
Methods: patients were identified by active monitoring of overlapping sources, including general practitioners, hospital databases and death certificates; T.I.A. were classified according to the International Classification of Diseases, 9th Revision (ICD-9), WHO 2006 definition. The ABCD2 score was calculated for each patient (when all items were available). Vascular risk factors were identified according to WHO 2006 definitions.
Results: during the study period 178 patients (90 men and 88 women) suffered from a T.I.A. Crude annual incidence of T.I.A. was 0.52/1000 (95% confidence interval [CI], 0.44 - 0.61), 2-day, 7-day and 90-day stroke risk were respectively 3,1%, 6,2% and 11,8%.
Statistical analysis proved ABCD2 score to be an effective tool for risk assessment in our population (R.O.C. curve A.U.C. = 0,758, Asy. Sig. = 0,000) with a clear 4 points watershed as a cut-off, identifying patients at low risk (ABCD2<3), moderate risk (4<ABCD2<5) or high risk (ABCD2>6) of stroke after T.I.A.
Conclusions: This is the first validation of ABCD2 score in an Italian population. Our study further confirms that T.I.A. should be regarded as a strong predictor of short term stroke occurrence and provides stroke-risk stratification according to the ABCD2 score. Appropriate treatment and monitoring are mandatory for patients experiencing a T.I.A.

17 Epidemiology of stroke

DECELERATION AND DECLINE IN VERY EARLY CASE-FATALITY RATES IN FIRST-EVER-ISCHEMIC STROKE PATIENTS OF ADVANCED AGE

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Background: Mortality rates accelerate as age increases. However, at ages above 80 years deceleration of mortality rates takes place and at very advanced age even decline in mortality rates are reported in a number of species including man. With the aim of investigating prevalence of these phenomena also in case-fatality rates we studied age trajectories of stroke case-fatality rates at older ages.
Methods: A registry started 2001designed to include all hospitalized stroke patients in Denmark holds 26 818 patients with first-ever -ischemic stroke with evaluations of stroke severity (Scandinavian Stroke Scale, SSS), CT-scan and cardiovascular risk factors i.e. atrial fibrillation, ischemic heart disease, diabetes, hypertension, peripheral arterial disease, smoking and alcohol consumption. Data on mortality were obtained through the Danish Central Person Registry and used in constructing age trajectories of 3-day, 1-week, 1-month, 3-months and 1-year case-fatality rates.
Results: Of the patients 48.1% were women; 51.9% were men. Mean age 71.2 (SD 13.4) years; mean SSS score 43.9 (SD 15.2). Three-day case-fatality rates decelerated in the age of mid-seventies; decline of case-fatality rates was observed after the age of 85 years. Seven-day case-fatality rates steadily increased almost linearly with increasing age. One-month, 3-months and 1-year case-fatality rates, however, were all accelerating with increasing age.
Conclusion: We present the paradox that case-fatality rates in the very acute state of stroke instead of accelerating with increasing age decelerate and even declined in patients of very advanced age. Heterogeneity in regard to survival capacity and "survival of the fittest" may explain the phenomenon.

18 Epidemiology of stroke

SEX DIFFERENCES IN VERY YOUNG STROKE PATIENTS (<35Y) – RISK FACTORS, MECHANISMS AND CLINICAL PRESENTATIONS: THE STROKE IN YOUNG FABRY PATIENTS (SIFAP-1) STUDY

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Background and purpose: Data on gender variations in risk factors, stroke mechanisms and clinical presentation in very young stroke patients under the age of 35 years is limited. The purpose of this study was to analyze gender differences of very young stroke patients (<35y) regarding risk factors, clinical presentation and mechanisms of stroke.

Methods: Data from the multicenter European multinational prospective European sifap-1 (Stroke In young Fabry Patients) study was analyzed. The total cohort (n= 5024) of young aged (18–55 years) stroke patients was categorized into patients <35 (n=633) and >35 years (n=4391). Sex differences between the two age groups were analysed regarding stroke type and severity, clinical characteristics, etiology and risk factors.

Results: The proportion of female stroke patients in the very young group was higher compared to the population >35y (female 56.7% versus 38%, respectively). Stroke type differed significantly between age groups (p=0.02). Diagnosis of TIA was more frequent in very young female (23.7%) than in male (15.5%) patients (p=0.023) compared to the age of group >35 years (female 24.7 vs. male 21.3%; p<0.001). Very young patients showed as clinical presentation more frequently headaches (female 48.2; male 46.4%; p<0.001) and hemianopia 18.4; 12.4%;,m p=0.001) than patients 35-55 years old (38.0; 26.7% and 11.1; 10.5%). Other symptoms like paresis or sensory deficit showed no differences for sex or age groups. A sedentary life style was significantly more frequent in very young women (47.6 vs. 29.9%, p 0.001) but showed no sex-differences the age group >35y (49.9 vs. 46.2%, n.s.).

Conclusion: Stroke in the very young is more frequent in women. Sex differences in clinical presentation, stroke type, etiology and in risk factors exist.

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19 Epidemiology of stroke

STUDY ON EPIDEMIOLOGY AND RISK FACTORS OF ISCHEMIC AND HEMORRHAGIC STROKE IN NORTHWEST IRAN, 2009

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Background: Cerebral vascular events are the second cause of mortality worldwide. Considering the consequences of stroke including mortalities and morbidities, being aware of the epidemiology of stroke and the effects of various risk factors could help health system to improve curative, preventive and supportive majors.

Methods: This cross-sectional analytic population based study was performed in Iran, Northwest, since October 2009 until October 2010. The data were obtained from randomly selected people and related patients' records in hospitals. 214 non stroke age and sex matched healthy people neighboring each stroke cases were considered as control group to compare risk factors.

Results: Five thousands subjects were selected. Thirty four (0.68%) of them had stroke with the mean age of 68.7 (range 38-85 years). Thirty one patients (91.2%) had ischemic and 3 (8.8%) hemorrhagic stroke. Nineteen (55.9%) of patients were male and 15 (44.1%) were female. Risk factors were hypertension in 25 (73.5%), hyperlipidemia in 11 (32.4%), diabetes mellitus in 9 (26.5%), smoking in 10 (29.4%) and CAD in 6 (17.6%). Logistic regression showed significant relation of hypertension and age with incidence of stroke (p=0.02).

Conclusion: This report consistent with pervious studies showed remarkably high prevalence of stroke which should take into consideration and needs special health system strategies for educating people to further prevention. According to associated risk factors, hypertension, as a modifiable and most common risk factor must be controled to decrease cerebrovascular events.

Keywords: stroke, ischemic, hemorrhagic, hypertension.

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21 Epidemiology of stroke

DIABETES MELLITUS AND ISCHEMIC STROKE SUBTYPES

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Background: It has been suggested that stroke subtypes are different in diabetic patients with an overrepresentation of lacunar and vertebrobasilar strokes compared with non-diabetic ones; however the available information is scarce. The aim of this study is to analyze the TOAST and Oxfordshire stroke classification, comparing diabetic with non-diabetic stroke patients.

Methods: Prospective study of 1728 consecutive acute ischemic stroke (IS) patients included in the BASICMAR register. For this analysis, patients with undetermined cause of stroke due to insufficient study (n=94) or double possible etiology (n=91) were excluded. The final cohort was 1543 cases. Patients were classified and compared according to the TOAST and Oxfordshire classification.

Results: A total of 465 patients (34.7%) were diabetics. TOAST and Oxfordshire classification according to diabetes were as follows:

	Atherothrombotic	Lacunar	Cardioembolic	Inusual	Undetermined
DM	19.4%	26.0%	36.7%	2.7%	15.1%
Non-DM	14.2% 25.3%	36.2%	4.1%	20.2%	
	TACI	**PACI**	**POCI**	**LACI**	
DM	19.6%	35.9%	16.1%	28.4%	
Non-DM	20.6%	36.6%	12.7%	0.7%	

Conclusions: There are some differences between diabetics and non-diabetics patients, with a significant increase (p<0.001) in atherothrombotic subtype (TOAST) and a non-significant increase (p=0.163) in POCI (Oxfordshire) subtype in diabetics. Our Results do not confirm the overrepresentation of lacunar strokes in diabetics.

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22 Epidemiology of stroke

STROKE RECURRENCE: HIGHER RISK IN MEN AND PATIENTS WITH MINOR STROKES BUT NO ASSOCIATION WITH AGE

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Background: We studied risk of death and recurrent stroke based on a nation wide register of 29 599 patients admitted to Danish hospitals with stroke.

Methods: A registry designed to include all hospitalized stroke patients in Denmark is now including 29 599 patients (2002-2010). Evaluations included stroke severity (Scandinavian Stroke Scale, SSS 0-58), CT-scan and cardiovascular risk factors i.e. atrial fibrillation, ischemic heart disease, diabetes, hypertension, peripheral arterial disease, smoking and alcohol consumption. Data on mortality were obtained through the Danish Central Person Registry. Readmissions with recurrent strokes were registered. We applied the competing risk survival model proposed by Fine and Gray (FG) with recurrent stroke and death treated as competing events adjusting for age, stroke severity score, gender and cardiovascular risk factors).

Results: Mean age 69.3 years (SD 13.4), stroke severity 45.5 (SD 14.2), 91% ischemic strokes, 9% hemorrhagic strokes, 46% women. Median follow-up 2.6 years. During follow-up 26% had died and 10% had recurrent stroke. High age, severe strokes and all risk factors were significantly related to survival. Applying the FG model we find that men are at higher risk of dying after stroke, Hazard Ratio (HR) 1.17 (95% CI 1.10-1.24) compared to women. Recurrent strokes are significantly related to minor strokes but not to age. Most risk factors indicate association with recurrent stroke although not significantly. However, men are at significantly higher risk of recurrent stroke compared to women, HR 1.13 (95% CI 1.04-1.22).

Conclusion: Women are at lower risk of recurrent stroke and survive stroke better than men. Stroke recurrence is significantly related to minor strokes i.e. higher risk of recurrence in patients with initially mild stroke. Stroke recurrence is not related to age.

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23 Epidemiology of stroke

TRANSIENT GLOBAL AMNESIA – EPIDEMIOLOGY AND MRI FINDINGS

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Background: Transient global amnesia (TGA) is characterised by the sudden onset of amnesia without other focal neurologic deficits with usually complete remission within 24 hours. The pathogenesis remains still unknown, but the pathophysiological correlate seems to be a transient dysfunction seen by small signal abnormalities in the hippocampus on diffusion-weighted imaging (DWI). The objective of this study was to evaluate the prevalence of TGA in Wiesbaden, Germany and to examine the frequency of signal abnormalities seen by MRI.

Methods: We conducted a retrospective review of patients with symptoms of TGA admitted to the hospital in Wiesbaden, Germany between 1/2007 and 1/2010. Of 9334 patients in the neurologic department, 83 cases fulfilled the diagnostic criteria of TGA and were further analysed. We included cerebral imaging in all cases.

Results: The overall incidence was 6.7/100 000/year. In all patients the symptoms resolved within 24 hours. Women were slightly more often affected than men (57.3 vs. 42.7%). The mean age was 65.8±8.9 years. The frequency over the year showed no significant differences. However most patient were admitted from Tuesday to Saturday, whether Sundays and Mondays significantly less patients became

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affected. Most episodes started after some form of exercise (55%), followed by emotional distress (24%). A "hot bath" was taken before in only 8% of the cases. The mean duration of TGA was 3.5±2.7h. All patients underwent cerebral imaging (MRI 83%). Typical changes in the hippocampus of the temporal lobe in DWI were found in 15%, without any corresponding lesion in FLAIR sequence.

Conclusion: TGA is a syndrome of which physicians should be aware. The diagnosis is made clinically and the prognosis is good. Ischemic infarcts should be ruled out. Typical findings by MRI are changes in the DWI without corresponding lesions in FLAIR sequence, The underlying pathophysiologic mechanism requires further investigation.

24 Epidemiology of stroke

DISTRIBUTED PATTERNS AND OUTCOME OF SYMPTOMATIC STENO-OCCLUSION IN PATIENTS WITH ACUTE CEREBRAL ISCHEMIA

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Background: Symptomatic steno-occlusion (SySO) of cerebral arteries has significant impact on treatment options and prognosis of patients with acute ischemic stroke. However, we do not know well about its prevalence, distribution, clinical characteristics, and outcome, especially in the Korean population, where intracranial cerebral atherosclerosis is a major cause of stroke.

Methods: In this retrospective observational study, a consecutive 5395 patients, who were hospitalized with acute ischemic stroke between 2008/9 and 2010/3 to 9 participating centers scattered nationwidely, were identified based a prospective stroke registry. A total of 3181 patients were presented within 24 hours from symptom onset and had relevant lesions. Patients without MR angiography and outcome were excluded. SySO was defined as stenosis or occlusion of cerebral arteries with relevant ischemic lesions in the corresponding arterial territory.

Result: Among 3057 patients included, 1929 (63.1%) had SySO. Distribution of SySO with multiple involvements was present in Figure 1. SySO with multiple involvements were associated with older age, higher myocardial infarction history and glycosylated hemoglobin (P<0.05), but not high risk cardioembolism (P=0.14). SySO was an independent risk factor for poor outcome at discharge (≥ 3 of modified Rankin Scale) after adjusting for age, gender, stroke history, diabetes, initial stroke severity and thrombolysis. Multiple involvement SySO raised the risk of poor outcome (adjusted odds ratio (OR), 2.68; 95% confidence interval, 2.05-3.51). Degree of steno-occlusion was also associated with outcome (p<0.01 on the likelihood ratio test for trend). The effect of SySO on outcome did not differ by cerebral artery significantly (p of interaction term between SySO and a kind of cerebral artery>0.2).

Figure1. Distribution of symptomatic steno-occlusion (SySO) at acute stage of ischemic stroke and relationship with functional outcome at discharge
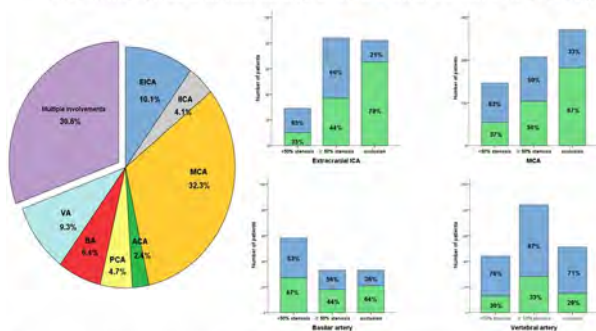
Pie graph showed distribution of SySO (N=1929). Bar graphs presented the relationship between degrees of steno-occlusion of EICA, MCA, BA and VA with single involvement SySO and outcome. Outcome was assessed by mRS at discharge and dichotomized as good (blue, mRS:0-2) and poor (green, RS:3-6). Abbreviations are EICA for extracranial ICA, IICA for intracranial ICA, BA for basilar artery and VA is vertebral artery.

25 Epidemiology of stroke

STROKE IN YOUNG NIGERIANS: A HOSPITAL-BASED STUDY IN NORTHEAST NIGERIA

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Background: There are no data available regarding strokes among young Nigerian adults in northeast Nigeria. To obtain an overall perspective and to assess the nature and magnitude of the problem, we aimed to determine the incidence, risk factors, stroke subtypes and case fatality among young Nigerian adults with first-ever acute stroke.

Methods: This prospective, multicentre, consecutive study ascertained first ever stroke on all 18- to 44-year-old patients admitted from January 2006 to December 2009. All patients were evaluated by clinical examination, brain computed tomography and/or magnetic resonance imaging.

Results: Initially 336 were enrolled, but 15 were subsequently excluded from the study when they were diagnosed with recurrent stroke and stroke mimics. Thus 321 individuals with confirmed first stroke were enrolled in the study; 60.2% were male. The majority of strokes (75.5%) were cerebral infarctions, with 15% primary intracerebral hemorrhages, 7.7% subarachnoid hemorrhages, and 1.8% strokes of unspecified type. Hypertension was responsible for most of the cases; other important risk factors were excessive alcohol intake, valvular heart disease, diabetes mellitus human immunodeficiency virus (HIV) and sickle cell anaemia. The case-fatality rate for all types of stroke was 29.9% (mortality within the first 4 weeks after the event, on average 6 days). The survival rate was 77.7% for cerebral infarctions, 41.7% for intracerebral hemorrhages, and 52% for subarachnoid hemorrhages; 66.7% of all survivors remained with an impairment resulting in a disability.

Conclusion: Stroke in the young Nigerian adult is not uncommon. Incidence and case-fatality rates and outcomes of stroke found in young adults in our study seem to be higher than those reported from most Western countries. Considerable percentage of survivors with a disability in a population at the beginning of their family, professional, and social lives indicate the magnitude of the problem.

26 Epidemiology of stroke

A 12 YEAR FOLLOW-UP OF A COHORT OF HOSPITALISED STROKE PATIENTS

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Background: There is a large body of literature describing the effects of stroke early after onset. Data on the longer term effects are available but relatively limited. We aimed to follow-up a cohort of patients 12 years after stroke.

Method: Consecutive patients were identified on the stroke registers of two hospitals over a six month period in 1996. Patients were initially followed up for a period of five years; ethical approval was subsequently gained for a 12 year follow-up. GPs were contacted for patient status; postal questionnaires were used for additional information. Here we present data on residence, function, and mood.

Results: We identified a cohort of 539 patients. Over the course of 5 years, 36 (7%) were lost to follow-up through moving out of area or refusing consent. At the start of the study the 503 patients had a median age: 75 years (Interquartile range 68 83 years); females: 269 (54%). At the 12 year follow-up 47 (9%) patients were still alive. Twenty of the 47 did not return their questionnaires. Of the remaining 27 patients, 25 (93%) lived at home. Fifteen (56%) patients had a Barthel score above 18 and 12/25 (48%) patients had a score of ≥5 on the GHQ-28.

Conclusion: This study contributes evidence about the longer term effects of stroke. Less than 10% of the cohort were alive at 12 years: most lived in their own home. Just over half of the respondents were independent, although half had low mood.

27 Epidemiology of stroke

SUBARACHNOID HAEMORRHAGE IN JOINVILLE, BRAZIL 2005 TO 2010: INCIDENCE AND CASE-FATALITY TRENDS

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Background: With aging population, the profile of subarachnoid hemorrhage (SAH) is likely to change. We aim to evaluate the trends for incidence and case fatality rates of SAH in the Joinville, Southern Brazil.
Methods: From JOINVASC, a community-based stroke data bank, we compare the age-sex adjusted incidence and 30-days case fatality rates after first ever SAH, between 2005-6 and 2010 in Joinville, Brazil.
Results: In 2005-6, 55 of SAH were identified and in 2010, 25 cases. The incidence per 100000 age-adjusted to the world population were 7.0 (95% CI 3.5 to 9.1) and 7.6 (4.9-11.2), in 2005-6 and 2010, respectively. The 30-day case- fatality was 36.4% (22.0-56.0) in 2005-6 and 40% (19.2-73.6) in 2010.
Conclusions: In the last five years the SAH incidence rate in Southern Brazil remains stable, higher than other Latin America population studies, and similar to high income populations. Howevwe, nearly half of patients continue to die in the first 30-days.

28 Epidemiology of stroke

EXPLORATORY FACTOR ANALYSIS TO IDENTIFY DETERMINANTS OF CEREBRAL WHITE MATTER DISEASE

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Background: Cerebral white matter lesions (WML) on MR imaging are common in the elderly and associated with significant morbidity and mortality. Their determinants, associations with vascular risk and systemic vascular disease are unclear. We tested a novel approach, factor analysis, to see whether confirmatory factor analysis and structural equation modelling would be valuable to determine associations between risk factor exposure, systemic and cerebral vascular damage.
Methods: We recruited subjects from the Lothian Birth Cohort 1936, who are generally health subjects born in 1936 and tested for mental ability aged 11 and 72 years. At age 72, we collected detailed vascular disease data, quantified carotid stenosis, intima media thickness (IMT) on ultrasound and WMLs on MR (Fazekas score). We obtained a correlation matrix and performed exploratory factor analysis.
Results: Of 820 subjects, mean age 72 years (SD 1 year), 49% had hypertension, 11% diabetes, and 29% ischemic heart disease. Mean carotid stenosis was 20% (SD13.7), IMT 0.8 (SD 0.2), and Fazekas score 1.3 (SD 0.6). Carotid stenosis and IMT measured on the same side were significantly correlated, (left side: r=0.16, p<0.001; right side: r=0.12, p<0.001), but not between sides. Deep and periventricular WMLs were highly correlated (r=0.53, p<0.001). Deep WMLs and carotid stenosis both correlated with hypertension (r=0.18 p=0.002; r=0.10 p=0.001 respectively) but not each other. Exploratory factor analysis identified 2 factors, one for vascular risk and one for large artery disease, that explained over 53% of the total variance of each.
Conclusion: Factor analysis shows promise for determining causal inter-relations between multiple features of vascular risk, large and small vessel disease. This will enable the development of structural equation models to explore the effects of susceptibility vs. exposure to vascular risk on cerebral WML.

29 Epidemiology of stroke

STROKE OUTCOME AND LIVING ENVIRONMENT: THE DISTRICTS 8-12 PROJECT – PRELIMINARY DATA OF A 3-YEAR COMPARATIVE FOLLOW-UP OF TWO DISTRICTS IN BUDAPEST

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Background: The most frequently considered stroke risk factors are lifestyle factors (smoking, physical activity, etc) and risk diseases (hypertension, atrial fibrillation, etc). Earlier data suggested that living standard is also associated with stroke morbidity and mortality. We further test this hypothesis by comparing stroke characteristics in 2 districts in Budapest.
Methods: residents of 2 Budapest districts with different living standard hospitalized with a major diagnosis of stroke during year 2007 were identified by the register of the National Health Insurance Fund. A 3-year follow-up was launched in 2010. Results of the first interim analysis of the project is presented.
Results: follow-up of 201 patients (District-8: n=108; District-12: n=93) has been completed at their general practitioners. In this initial sample the age at stroke was 6 years younger in those living in the less wealthy district (70.4±13.0 vs. 76.4±11.8 years, p<0.001). Both alcohol dependency and smoking were more frequent among stroke patients in the less wealthy district (17% vs. 7%, p=0.05; and 35% vs. 15%, p=0.006). Three years after stroke case fatality did not differ between the 2 districts (33% and 37.5%, p=0.48), but those who died were almost 10 years younger in the less wealthy district (73.1±14.6 vs. 82.4±8.4 years, p<0.0001).
Conclusions: Based on the data of less than one third of the total stroke population identified in the 2 districts, already large and statistically significant differences were found in risk factor distribution, and in age at stroke onset and at death.

30 Epidemiology of stroke

CLINICAL CHARACTERISTICS OF ISCHEMIC STROKES OCCURRING IN THE EARLY MORNING HOURS: RESULTS FROM A PROSPECTIVE STROKE REGISTRY

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Background: Impaired morning haemostatic activity, diurnal and wake-up blood pressure fluctuations, as well as circadian diversity in endothelial responsiveness have been previously related with increased risk of ischemic vascular events in the morning. However, we lack data concerning the specific clinical characteristics of ischemic strokes happening in the early morning, and their possible relation to stroke outcome.
Methods: Data arose from 1039 ischemic stroke patients prospectively included in the Hellas Stroke Registry from September 2008 to December 2010. Stroke risk factors, TOAST subtypes, severity on admission (measured by NIHSS), deaths and outcome at discharge and on month 1 (assessed with the modified Rankin Scale, mRS) were compared between ischemic strokes happening from 05:00 to 09.30, and all other events. Simple chi-square, t-test, as well as multivariable regression analyses were applied.
Results: We identified 310 (29.8%) ischemic strokes occurring in the morning. Mean age, sex, vascular risk factors, TOAST classification, stroke severity and dependency measured by mRS, did not significantly differ between morning strokes and all other cases. However, deaths during hospitalization were significantly fewer in the morning-stroke group compared to all other patients (9.4% versus 14.8%, p=0.019). This association remained significant even after adjustments for age, sex, vascular risk factors, TOAST categories and stroke severity [Odd Ratio (95% Confidence Intervals)= 0.58 (0.35-0.95)].
Conclusion: Ischemic strokes occurring in the early morning present similar burden of vascular risk factors, etiologic subtypes, severity, and dependency rates, with "other-time" strokes. However, morning strokes seem to be related with less mortality during hospitalization, independently of possible important confounders. Further studies are needed to elucidate the significance of this finding.

31 Epidemiology of stroke

THE EFFECT OF METEOROLOGICAL FACTORS IN CASE OF CEREBRAL HEMORRHAGE AND TRANSIENT ISCHEMIC ATTACK

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Background: The aim of our study is to investigate whether the time of onset of an acute cerebrovascular event demonstrates a seasonal variation, and it also examines the influence of certain meteorological factors on the occurrence of this event.
Methods: We have examined patients admitted to the Departments of Neurology in Hungary between 2005 and 2007 with the diagnosis of a cerebral hemorrhage

(n=11,604) or a transient ischemic attack (n=12,513). Data was collected from the database of the Hungarian National Health Insurance Fund on the basis of International Classification of Diseases (ICD). Meteorological data (temperature, atmospheric pressure, relative humidity) was retrieved from the National Meteorology Service. Statistical analysis was carried out with SPSS 14.0 for Windows.

Results: Analysis of meteorological data showed that an increase in average temperature on the previous day resulted in a notable drop of cerebral hemorrhage incidence during all seasons (p<0.05), while in case of transient ischemic attack such a decrease only occurred during Summer (p<0.05). Examining atmospheric pressure and relative humidity no detectable influence was found.

Conclusion: In summary, our Results indicate that the incidence of cerebral infarction, cerebral hemorrhage, and a transient ischemic attack show a typical variation depending on the season of the year and the values of the temperature may influence the development of different cerebrovascular events.

32 Epidemiology of stroke

MORTALITY AND OUTCOME AFTER ACUTE ISCHEMIC STROKE. A HOSPITAL REGISTRY STUDY

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Methods: Prospective cohort study of stroke patients from a hospital stroke registry. We included consecutive ischemic stroke patients who were admitted between 2009- 2010. Variables including demographics, history, clinical data, mRankin scale, Barthel Index, process measures, and outcome were analyzed. We used Kaplan-Meier analysis to estimate cumulative survival and logistic regression to study 30-day mortality and recurrence during follow-up and associated factors.

Results: We included 1023 patients, mean age 75 years (SD 12,85) 57,4% males. According to the TOAST subtypes of the ischemic stroke group cardioembolic was the most common 368, followed by undetermined 257, large artery disease 203 and lacunar 162. The 30-day mortality rate was 11.4%, and was independently associated with age > 78 y (OR=2,59; 95% CI 1,4-4,7), male (OR=2,68; 95% CI 1,48-4,85), previous mRankin (OR=2,30; 95% CI 1.18-4,49) NIHSS at admission (falta el Odds Ratio el IC) atrial fibrillation (OR=1,72; 95% 0,88-3,37) cardiac disease (OR=1,96; 95% 1,02-3,55). In the follow up, the mortality was 20,5%. The cumulative 1-year recurrence rate was 6% and with logistic regression was associated with atherotrombotic stroke.

Conclusion: In our cohort, and after adjusting for all variables, we found higher 30-day mortality in older subjects, males and atherotrombotic disease. The recurrence rate was associated with atherotrombotic stroke and virtually unchanged throughout the first year after stroke.

33 Epidemiology of stroke

CHARACTERISTICS OF TRAUMA IN STROKE PATIENTS –AN ANALYSIS OF 29663 TRAUMA PATIENTS IN JAPAN

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Background and Purpose: Little is known about the trauma risk in stroke patients. Our study purpose is therefore to assess the prevalence, gender-difference, anatomical characteristics and mortality of trauma in patients with prior stroke in Japan.

Subjects and Methods: The data source is Japan Trauma Databank (JTDB), a multicenter, nationwide and prospectively recruited trauma registry in Japan. We selected the hospitalized trauma patients who were older than 16 years old, recorded with confirmed trauma diagnosis and trauma severity and recorded with clear outcome. We excluded cases of cardiopulmonary arrest on arrival. Logistic regression analysis after adjustment for age and gender showed effects of having prior stroke for anatomical differences in severe trauma. Furthermore, logistic regression analysis after adjustment for age, gender and pre-existing medical conditions showed effects of having stroke for in-hospital trauma mortality.

Results: Of 29663 records from JTDB, 15023 cases matched the selection criteria and 445 (3.0%) cases had prior stroke. Trauma patients with prior stroke were frequent in female gender (35 versus 30%, P<.05), more elder (median 74 versus 47 years old, P<.001), similar in trauma severity (13 versus 14 in the Injury Severity

Score, NS) and higher in trauma mortality (14 versus 9%, P<.001). Trauma patients with prior stroke had higher risk for severe head trauma (Odds ratio [OR] 1.2, 95% confident interval [95%CI] 1.0-1.5, P<.05), however showed similar mortality in comparing with patients without prior stroke (OR 1.1, 95%CI 0.8-1.5, NS).

Conclusion: Our study demonstrated increased severe head trauma risk which may relate to fall. Further studies to aim the prevention of trauma on head are expected.

34 Epidemiology of stroke

SEX DIFFERENCES IN TYPE, SEVERITY AND RISK FACTORS OF STROKE IN THE HELLENIC STROKE REGISTRY

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Background: Previous studies have suggested that women may have a more severe presentation of stroke and a poorer outcome than men. This could be due to sex differences in risk factors and stroke types. We estimated sex differences in these variables across patients of the hellenic stroke registry.

Methods: Twenty centers all over Greece documented all stroke admissions in their clinics from September 2008, to December 2010, and recorded stroke severity on admission, stroke-type, risk factors and outcome at discharge, month 1 and month 6. Chi-square and t-test comparisons were used to determine sex differences in the above mentioned parameters.

Results: A total of 2903 stroke cases were documented. Women (1209, 41,6%) were older than men [mean (standard deviation) age = 74 (12,3) vs. 68 (13,5), p<0,001], had more severe strokes [NIHSS 10 (8,4) vs. 8 (7,4), p<0,001], and female mortality was higher during hospitalization (15,9% vs. 10%, p<0,001). They suffered more often from atrial fibrillation (36% vs. 20%, p<0,001), were more often on anticoagulation on admission (14% vs. 7%, p<0,001), and were diagnosed more often with embolic strokes (30% vs. 19%, p<0,001) than men. Outcome was worse for women at discharge, month 1 and month 6, but this association was statistically significant only for outcome at discharge (55% vs. 46%, p<0,001).

Conclusion: According to our study, women present with more severe and disabling strokes. This could be explained by their older age at presentation and the higher prevalence of embolic type of stroke, which in turn Results from the higher prevalence of atrial fibrillation in females.

35 Epidemiology of stroke

PROPOSAL FOR A GLOBAL CASE DEFINITION FOR STROKE USING ADMINISTRATIVE DATASETS WITH ICD9 AND ICD10

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Introduction: The Canadian Stroke Strategy (CSS) is a national coordinated effort to improve stroke care and stroke outcomes. Counting stroke events using administrative data is an important way of measuring performance. There is a broad need for a comprehensive single case definition of stroke, that allows comparison intra- as well as internationally. Over several years we developed a cohesive national definition of stroke by collaborating between government and the stroke community.

Methods: Our purpose was to identify a consensus single definition of stroke and stroke types that could be used for annual or bi-annual reporting of stroke rates in Canada. Definitions were based upon (a) literature review of published validation studies; (b) expert opinion from government surveillance agencies, c) consensus opinion from Canadian content experts in stroke medicine; (d) original work done in Canada using chart review to validate codes.

Results: We were constrained by the extent of available data and perceived uses. Only some provinces in Canada routinely collected and reported the 4th and 5th digits of the ICD9 codes. ICD9 code 433 may represent stroke or not depending upon the 4th and 5th digits. There was an inherent trade-off between sensitivity and specificity. Our definition of stroke is provided in Table 1. We used the first position or most-responsible diagnosis only. We considered type 1 diagnoses only,

and excluded in-hospital stroke or stroke as a procedural complication. We excluded ICD9 code 433 when the 4th and 5th digits were unavailable.

Table 1

Canadian Stroke Strategy Stroke Case Definitions 2010			
Group	Acute Stroke Main Category	ICD-9 codes *	ICD-10 codes *
1.	Acute stroke	430	160 (excl 160.8)
		431	161
		433.x1ᵉ	163 (excl 163.6)
		434	164
		362.3ᵇ	H34.1
	Acute stroke plus transient ischemic attack	435	G45 (excl G45.4)
		362	H34.0
Acute Stroke Sub Categories			
2.	Ischemic stroke (includes acute but ill-defined cerebrovascular)	433.x1ᵉ	163 (excl 163.6)
		434	164
		436	H34.1
3.	Subarachnoid hemorrhage	430	160 (excl 160.8)
4.	Intracerebral hemorrhage	431	161
5.	Transient ischemic attack	435	G45 (excl G45.4)
		-	H34.0

Discussion: The administrative definition of stroke is complex because stroke is the final result of multiple possible underlying etiologies and conditions. This definition has been validated in Canada and should be considered for validation elsewhere in the world.

36 Epidemiology of stroke

TEMPORAL PROFILE OF TISSUE INHIBITOR OF METALLOPROTEINASE-1 (TIMP-1) IN ISCHEMIC STROKE – RESEARCH FOR BIOMARKERS IN ISCHEMIC STROKE (REBIOS)–

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Background and Purposes: It is thought that tissue inhibitors of MMPs (TIMPs) play an important role in ischemic stroke by counteracting matrix metalloproteinases (MMPs), critical factors for tissue remodeling, such as angiogenesis and tissue repair. We examined the temporal profile of plasma TIMP-1 and its significance in patients with ischemic stroke.
Methods: We designed Research for Biomarkers in Ischemic Stroke (REBIOS) study to find useful blood biomarkers, and 176 patients with ischemic stroke (atherothrombotic (AT) 34, cardioembolic (CE) 51, lacunar (Lac) 45, and unclassified 46) were recruited from the Fukuoka Stroke Registry, a prospective multi-centered study for acute stroke in Japan. Blood samples as well as clinical information were obtained from the patients at 5 points after the stroke onset, day 0 (within 24 hours), 3, 7, 14, and 90. Plasma TIMP-1 and other biomarkers, including MMP-9 and VEGF, were measured by HumanMAP® v 1.6 (Rules-Based Medicine, Inc.). Age and sex -matched healthy subjects were enrolled from the Hisayama study in Japan as the control group (n=171).
Results: Values of plasma TIMP-1 were higher even at day 0 in all the stroke subtypes, with statistical significance in AT (96.1 ± 4.0 pg/ml (mean $\pm$ SE), $p<0.01$) and CE (101.8 ± 3.3 pg/ml, $p<0.001$), compared with the control group (82.0 ± 1.8 pg/ml). The TIMP-1 values remained higher at least until day 90 in AT and CE. In contrast, plasma MMP-9 levels were significantly higher only at day 0 and 3 in CE than in the control. The temporal profile of TIMP-1 was very similar to that of VEGF, and there was positive correlation between VEGF and TIMP-1 throughout the observational period ($r=0.43$; $p<0.0001$ at day 0).
Conclusions: Plasma TIMP-1 may increase immediately after the onset and remain high at least for 3 months in ischemic stroke. Besides the role as an inhibitor of MMP-9, TIMP-1 may play some important roles cooperatively with VEGF after ischemic stroke.

37 Epidemiology of stroke

STROKE RISK IN THE CITY OF SAO PAULO – BRAZIL: STRATIFICATION ACCORDINGLY TO AGE AND SOCIOECONOMIC STATUS

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Background and purpose: Advanced age and low socioeconomic status are related to a high risk of ischemic stroke. We evaluated the relationship between socioeconomic status and ischemic stroke in different groups accordingly to age using a new socioeconomic stratification model.
Methods: With a new geographic socioeconomic segmentation tool, we evaluated incidence of ischemic stroke patients and control groups from two hospitals which serve different socioeconomic status population, in the city of São Paulo, Brazil. Patients were stratified by socioeconomic status and age groups (30 to 65 years, 65 to 79 years, 80 years or older). The ratio between ischemic stroke and control group was calculated.
Results: There was a greater number of older patients in the higher socioeconomic status hospital (χ^2obs= 28.7, g.l. = 2, p value < 0.0001). The ratio of ischemic stroke was significantly higher in patients with lower socioeconomic status (p value < 0.00001, with Zobs 5.03; 9.93 e 5.88 for groups of 30 to 64 years old, 65 to 79 years and 80 or older, respectively).
Conclusions: Our study showed that lower socioeconomic status is associated to a higher incidence of ischemic stroke independently of the age group.

38 Epidemiology of stroke

STROKE RISK FACTORS AND OUTCOMES AMONG VARIOUS ASIAN ETHNICITIES IN SINGAPORE

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Background: Limited data exists regarding inter-ethnic differences among Asian stroke population. We evaluated the relationship between various cardiovascular risk factors, stroke subtypes and outcomes in our multiethnic Singaporean population.
Methods: Consecutive ischaemic strokes patients presenting to our tertiary center over 1-year period were evaluated. Strokes were classified by Trial of Org 10172 in Acute Stroke Treatment (TOAST) and Oxforshire community stroke project (OCSP) criteria. Functional independence at hospital discharge was defined by modified-Rankin Scale (mRS grade 0-2).
Results: Ethnic distribution of the Singaporean population (n=481, mean age 64.1 ± 11.9years) was Chinese (74%), Malays (17%) and Indians (9%). Prevalence of risk factors was similar among the three Asian ethnic groups except for diabetes (Chinese 39.8%, Malays 67.5% Indians 52.3%; $p<0.001$). Hypertension and hypercholesterolaemia were the commonest cardiovascular risk factors. Lacunar strokes constituted the most frequent stroke subtype (47.9%). Large-artery atherosclerotic infarctions were more prevalent in Indians (25.0%) while lacunar infarctions occured more frequently in Chinese (51.8%, $p<0.01$). No differences were observed regarding in-hospital mortality and functional independence at discharge among three Singaporean ethnic groups.
Conclusion: Despite the differences in risk factors and the stroke subtypes classified by location or underlying aetiology, short-term outcome measures were similar among different Asian ethnicities in Singapore.

39 Epidemiology of stroke

SEVERE STROKE IN NEUROLOGICAL INTENSIVE CARE UNIT: EPIDEMIOLOGY, COMPLICATIONS AND OUTCOME

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Background: Severe stroke is the leading cause for admission in Neurological Intensive Care Units (NICU) worldwide. Our primary objective was to determine the rate of mortality and disability at short term follow up. Secondary objective was to assess the correlation between certain risk factors and outcome.
Methods: We included 189 patients, divided in three groups, based on type of stroke. Standardized scales were used for evaluation of clinical and neurological status. Furthermore, all patients were divided in two groups, based on clinical outcome at discharge (survivors vs lethal (unfavorable) outcome). Survivors were examined for functional outcome using modified Rankin scale at discharge.
Results: Basic demographic and clinical data at admission are shown in Table 1. Average overall NIH stroke scale rate at admission was 23.5, but with significant

differences when correlated to type and subtypes of stroke. Neurological complications were found in 82.5% of patients, rising to 90% in group with unfavorable outcome. Brain edema was the most prominent feature, registered in 108 patients, followed by onset of coma, brain stem disturbances and seizures, all being significantly more frequent in group with unfavorable outcome, in contrary to onset of agitation and delirium, findings more frequent in survivals. Overall mortality was 47.1%, with noteworthy variations depending of subtypes of stroke. Use of mechanical ventilation (MV) was strongly associated with highest mortality rate, longer hospitalization time and higher risk of complications. Onset of complications was significantly related with longer hospital stay, use of MV and more severe neurological impairment at admission.

Table 1. Basic demographic and risc factors data in correlation with outcome at discharge

	Survivers (n=100)	Lethal outcome (n=89)
Age	57.5	62,6
Age bellow 45 years (%)	22 (11.6%)	6 (3.2%)
Age over 45 years (%)	74 (39.2%)	69 (36.5%)
Length of hospital stay	13 days	20 days
Risc factors		
- Arterial hypertension, %	74	82
-Diabetes mellitus, %	20	24.7
-Lipids %	45	50.6
-Smoking, %	42	33.7
-Atrial fibrillation %	28	31.5
-Other important heart diseases, %	33	51.7
Other data		
-Previous ischemic stroke, %	11	16,7
-Previous haemorrhagic stroke, %	8	10.1
-Blood glucose level at admission , mmol/L	7,9	8.4
-GCS at admission - median value	10,1	7.6
-NIHSS at admission - median value	19.2	28.1

Conclusion: Severe stroke patients have high mortality rate, high incidence of all types of complications and high level of disability, but with significant improvement of neurological status at discharge in survivors, underlining benefits of specialized therapeutic approach applied in NICU.

41 Epidemiology of stroke

SEASONAL PATTERN OF CEREBROVASCULAR DISEASES IN TROPICAL AREA OF SOUTHWESTERN IRAN: A HOSPITAL-BASED STUDY
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Background: The aim of this study was to investigate the probable effect of the special tropical climate of Khozestan province on patterns of cerebrovascular accidents (CVA) and stroke types, based on admission records.
Methods: In a retrospective study, records of all admitted patients in Golestan hospital in the city of Ahvaz, the academic center of neurological diseases of Jundishapur University, during first to twelfth month of Persian calendar in the year 1388 (2009-2010 AD) was evaluated. Total numbers of admissions in each season in addition to the final diagnosis of CVA patients were determined. To assess the differences in the amount of admissions and CVA types, goodness of fit analyses by means of Chi-squared test were done. P-value less than 0.05 was considered as significant.
Results: According to the documents, of 932 admitted subjects to our neurology ward with the final diagnosis of CVA, the proportion of Ischemic, hemorrhagic and venous thrombosis events were 81.6%, 16.4% and 2% respectively. Analyses shown that we had a higher amount of admission in the winter because of significant higher count of ischemic stroke in this season (P=0.018). Interestingly, there was a significant lower patients of hemorrhagic CVA in the fall, compared with other seasons (P=0.009). There was not significant difference in venous thrombosis events between seasons.
Conclusion: In most previous studies, hemorrhagic events accounts for approximately 10% of stroke. Our study showed that we have significant higher hemorrhagic event (P<0.001) in comparison to the other area, probably due to poor hypertension control.
Results: indicated that by lowering the average of temperature in transient period of fall and concomitant increase in air pressure, a significant decrease in hemorrhagic events occurs. Nevertheless, it needs to be evaluated over years before considered as a fact. We expected venous thrombosis to be more in hot seasons in this area (spring and summer) because of the effect of inevitable dehydration, but Results indicated that changing the weather has no significant effect on such events.

42 Epidemiology of stroke

STROKE DURING ALCOHOL DRINKING –A REPORT FROM STROKE CENTER IN THE METROPOLITAN TOKYO AREA, JAPAN
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Background: We sought to clarify characteristics of acute stroke patients during alcohol drinking.
Methods: A retrospective analysis of 473 acute stroke patients admitted in the emergency department, Tokyo Medical and Dental University Hospital and 21 stroke patients had stroke symptoms during alcohol drinking. We compared basic characteristics, Glasgow Coma Scale (GCS) on arrival, stroke subtypes which is classified as acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), subarchnoid hemorrhage (SAH), and transient ischemic attack (TIA) and mortality between patients during alcohol drinking and the other.
Results: This analysis revealed a significant difference of constitution of stroke subtypes; AIS/ ICH/ SAH/ TIA were 38%/ 44%/ 10%/ 10% in patients during alcohol drinking versus 33%/ 46%/ 17%/ 4% in control (P<0.0001). However there was no significant difference in prevalence of ischemic (AIS and TIA) to hemorrhagic stroke (ICH and SAH). Onset to door time had a trend to be short in patients during alcohol drinking (median 73 minutes, Interquartile range [IQR] 47-137 minutes) versus control (median 134 minutes, IQR 55-477 minutes) (P=0.06). There were no significant differences in basic characteristics, GCS at arrival, and mortality.
Conclusions: Our study is maiden study to show the characteristics of stroke patients during alcohol drinking. The study failed to show significant difference between stroke patients during alcohol drinking and the other, however, constitution of stroke subtype might differ between both groups. Larger study is needed to show alcohol effects on stroke onset.

43 Epidemiology of stroke

EPIDEMIOLOGY STUDY OF ACUTE CEREBROVASCULAR DISEASE ABOUT 586 CASES
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Background: The stroke is frequent cause in neurology departement.The authors present a morrocan study and analyse epidemiology, clinical and aetiology aspect.
Method: the authors present a retrospective study of 586 cases who presented stroke, selected among the hospitalized at neurology service of military hospital Mohammed V during a period from january 1st 2000 until 31 december 2010.The patient may fulfil the criteria of the Ad Hoc committee of cerebrovascular disease and must have imagery which confirm stroke and a mimimum of aetiology's bilan.
Results: The patient are aged 24 to 96years.The authors note a male predominance (78%).The most frequency localization is territory of middle cerebral artery (76%). The aetiology are multiple, but it's dominate by angeiitis and cardiopathy before 45 years and by atherosclerosis over this age.
Discussion and Conclusion: the authors discuss all this Results and compare to litterature and concluse that the analyse of different result note no differnce.

44 Epidemiology of stroke

IN-HOSPITAL STROKE IN A SINGLE GENERAL HOSPITAL
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Background: There were many reports of ischemic stroke, but few reports of in-hostpital stroke. We assessed patients with in-hospital ischemic stroke in a single hospital in the era of rt-PA.
Methods: The study was retrospectively investigated by clinical recordings and consultions of my stroke department. In our hospital, 32999 patients were admitted from April 1 2007 to May 30 2009.
Results: Fifty-nine consecutive patients were enrolled during 2 years, of which 48 were admitted due to emergency problems. The mean age was 77 years, and females were 23. The main causes of hospitalization were malignant neoplasms in 15, infection in 14 and heart failure in 13 patients. The comorbidities were hypertension (n=41, 70%), diabetes (n=20, 34%), hyperlipidemia (n=26,44%). The most prevalent subtypes of stroke was cardioembolism (n=43, 73%). The commonest therapies for ischemic stroke were best supportive care (n=33). Only 4 patients were treated with rt-PA of which two achieved an mRS of 0 to 2.

At discharge, 11 patients achieved an mRS of 0 to 2, and 25 patients achieved an mRS of 6.
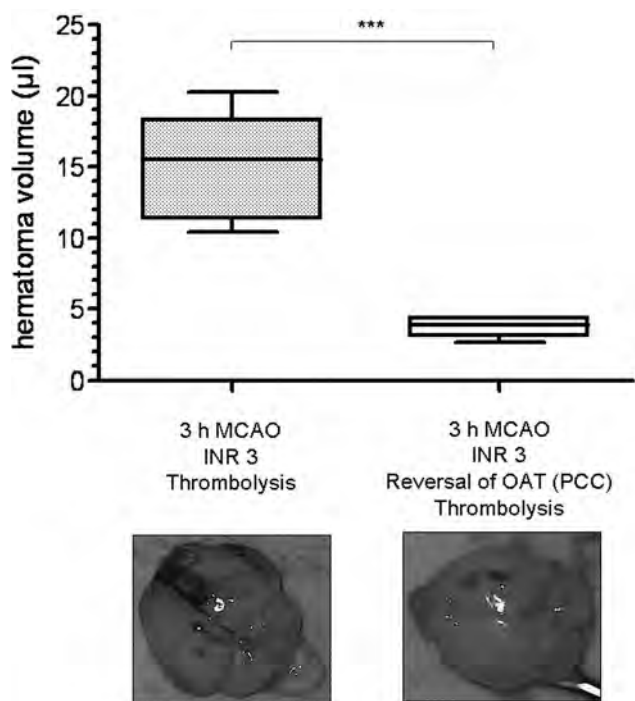
Conclusion: Patients with in-hospital stroke were elder, had no threapy in acute phase of stroke and bad outcome in mRS at discharge.

VARIATIONS OF CIRCLE OF WILLIS RELATED WITH HYPOPLASIA OF POSTERIOR COMMUNICATING AND ISCHEMIC STROKE

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Variations of circle of Willis related with hypoplasia of posterior communicating and ischemic stroke.

Background: One of the most frequent variations of circle of willis is hypoplasiaof posterior communicating artery (P.Co.A). This is a congenital variations that is founded in 7-20% of populations. P.Co.A is a risk factor of ischemic stroke in a cases with ipsilateral Internal carotid artery (I.C.A) or in grave stenosis.

Methods: In our study examinated 50 ischemic stroke patiens (mean age 40±20 years)with M.R.I in comparition with control group.The incidence of P.Co.A hypoplasia in our group was 17% (n=8.5) more than in control group 8% (n=4). In our cases with hypoplasia of P.Co.A (n=8.5) we have founded 32% (n=2.62) with occlusion of Ipsilateral I.C.A. The most locations of ischemic stroke in cases with hypoplasia of P.Co.A was seen in hipsilateral periventricular area (lacunar infarctions) 70% (n=5.95),and with occipital lobe involment 30% (n=2.55).

Results: In our study we have seen a correlation beetwen P.Co.A and ischemic stroke even in cases without occlusion of ipsilateral I.C.A. (17% in comparition with 8% in control group).

This risk was seen to be higher in the ipsilaterial periventricular penetrate arteries area, 70% of cases with P.Co.A hypoplasia.

Conclusion: Our comparative study has shown o signifcant correlation between the abnormalities of circle of Willis like his P.Co.A hypoplasia and ischemic stroke.

Acute stroke: emergency management, stroke units and complications

91 Acute stroke: emergency management, stroke units and complications

RTPA INDUCED FIBRINOGEN DEGRADATION COAGULOPATHY PREDICTS SYMPTOMATIC BLEEDING COMPLICATIONS IN 548 CONSECUTIVE ACUTE STOKE PATIENTS

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Background: Intravenous rtPA is associated with an increased risk of intracranial and systemic bleeding complications. Previous studies indicate that rtPA also cleaves fibrinogen sometimes resulting in fibrinogen depletion and impaired coagulation.

Material and Methods: A total of 548 consecutive stroke patients receiving intravenous rtPA were prospectively evaluated and fibrinogen levels, INR and aPTT were measured before thrombolysis and six and 24 hours thereafter. Intracranial hemorrhage was assessed in serial CT examinations (24, 72 hours and on demand) and symptomatic intracranial bleedings were defined according to the NINDS criteria. In addition systemic bleedings requiring transfusion therapy, leading to a hemoglobin drop >40 g/L or judged as medically important, were recorded.

Results: Symptomatic intracranial or systemic hemorrhage occurred in 42 patients (7.7%). Most of the 548 patients showed a modest decline in fibrinogen levels (median [IQR] Δ baseline-6h 91 mg/dl [118 mg/dl]) but in one fifth a prominent drop in fibrinogen was paralleled by an increase in aPTT and INR (r=0.40 and 0.49 p<0.001). This condition, previously termed as fibrinogen degradation coagulopathy, emerged as the strongest single risk predictor of intracranial and/or systemic bleedings (OR [95% CI] 6.0 [3.1-11.5] and 5.2 [2.6-10.2] after adjustment for pretreatment with warfarin, age, sex, diabetes, blood glucose and NIHSS upon admission) and was found in more than 50% of patients with symptomatic hematoma.

Conclusion: Fibrinogen degradation coagulopathy after rtPA treatment in acute ischemic stroke is much more common than previously assumed and represents the strongest risk predictor for bleeding complications in our series of 548 consecutive thrombolysis patients.

92 Acute stroke: emergency management, stroke units and complications

INSULAR STROKE INDUCES ACUTE SYMPATHETIC HYPERACTIVATION AND IMMUNODEPRESSION

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Background: Poststroke immunodepression has been related to brain lesion size but not a specific lesion location.

Methods: Clinical, brain imaging and laboratory data of 384 patients with acute ischemic stroke involving the middle cerebral artery (MCA) territory were prospectively studied (Clinical trial registration information: ClinicalTrials.gov, NCT00906542).

Results: Patients with acute lesion affecting >33% of MCA territory had increased serum metanephrine and normetanephrine levels, elevated neutrophil counts but decreased eosinophil and helper T lymphocyte counts. Considering only patients with non-lacunar infarction in <33% of MCA territory, those with insular infarction had higher levels of normetanephrine, higher neutrophil counts but lower eosinophil and lymphocyte counts than those with non-insular infarction (each, p<0.05). This coincided with an increased frequency of infections in patients with insular lesion compared to those with non-insular infarction (chest infection: 23 vs 8%, p=0.005; any infection: 36 vs 20%, p=0.028). While patients with right insular lesion showed significantly decreased heart rate variability compared to those with left insular lesion (p<0.05), lesion laterality had no impact on any laboratory finding or frequency of infections.

Conclusion: Findings suggest a specific role of insular lesion in the pathogenesis of stroke-induced sympathetic hyperactivation and immunodepression.

93 Acute stroke: emergency management, stroke units and complications

EARLY STROKE-RELATED DVT IS MORE THAN JUST EARLY DIAGNOSED POST-STROKE DVT

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Background: Deep vein thrombosis (DVT) is a serious complication of stroke. However, previous studies concentrated on the overall diagnosis of thrombosis after stroke, regardless the time point of examination. Our aim was to analyze the difference between patients diagnosed with DVT in the first 7 days post-stroke and those developing DVT during a few following days, using DVT free patients as an additional reference.

Methods: We enrolled 323 consecutive patients admitted to our center due to acute ischaemic (92.9%) or haemorrhagic (7.1%) stroke. We collected data on their stroke and DVT risk factors, baseline neurological status, CRP and fibrinogen serum level <24 hours of hospital stay and 3-month outcome. Ultrasound imaging was performed at the median 3rd (IQR: 2-4) and 9th (IQR: 8-9) day after stroke. Pre-stroke DVT was defined as already present in the first examination. Early stroke-related DVT was present exclusively in the second examination.

Results: Pre-stroke DVT was found in 28/323 patients. It was independently associated with CRP>10 mg/l (OR 3.15; 95%CI:1.31-7.60) and pre-stroke dependency (OR 2.89; 95%CI:1.19-7.05), but did not affect the outcome. Early stroke-related DVT was diagnosed in 9/299 patients. It was independently associated with CRP >10 mg/l (OR 10.1; 95%CI:1.93-52.9), fibrinogen >4 mg/dl (OR 0.18; 95%CI:0.04-0.74) and increased the odds for death at 3 months (OR 12.4; 95%CI:1.72-89.4). Despite small number of patients both groups differed in the ratio of patients with fibrinogen >4 mg/l (85.7% vs 44.4%; p=0.02) and pre-stroke dependency (44.9 vs 11.1%; p=0.12).

Conclusions: Pre-stroke DVT and early-stroke related DVT should be considered separate entities and the later one with non-equivalent impact on stroke outcome. The first one is most likely a pre-existing condition, but if the screening ultrasound evaluation is performed later than 1 week after stroke it may be impossible to distinguish between those groups of patients.

94 Acute stroke: emergency management, stroke units and complications

MANAGEMENT OF HYPERGLYCAEMIA AFTER STROKE

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Background: UK national stroke guidelines recommend screening patients for undiagnosed diabetes mellitus within one week of stroke onset, and intervening to moderate hyperglycaemia greater than 11mmol/l. We sought to determine the management of hyperglycaemia after stroke across an NHS Health and Social Care Trust in Northern Ireland.

Methods: In a multicentre retrospective study we reviewed the case records of patients admitted with stroke to three hospitals across the NHS Trust over 3.5 months (January 1 to April 15, 2008). Management was compared with the UK Intercollegiate Stroke Working Party's National Clinical Guidelines for Stroke, National Institute for Health and Clinical Excellence's National Clinical Guideline for diagnosis and initial management of acute stroke and transient ischaemic attack,

and the Scottish Intercollegiate Guidelines Network's Management of patients with stroke or TIA.

Results: We identified 94 patients with no prior history of diabetes mellitus, 16 patients with type 2 diabetes mellitus and two patients with type 1 diabetes mellitus. The prevalence of hyperglycaemia over 7.8mmol/l in the first five days of admission ranged from 24% to 34% of patients, but hyperglycaemia was under-monitored and undertreated. Of the 94 patients with no prior history of diabetes mellitus, there was evidence that 70% had fasting glucose tested, 5% had Haemoglobin A1C tested, and none received an oral glucose tolerance tolerance test.

Conclusion: Hyperglycaemia in hospitalised stroke patients is under-monitored and undertreated. Although acute stroke glcaemic control may not conclusively alter short term clinical outcome, the identification of undiagnosed diabetes mellitus and ist subsequent management represent an important opportunity for vascular disease protection.

95 Acute stroke: emergency management, stroke units and complications

MAGNETIC RESONANCE IMAGING PREDICTORS OF OUTCOME IN REPERFUSION THERAPY FOR UNCLEAR-ONSET STROKE

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Background: We examined whether analysis of multimodal MR imaging could find factors related to poor clinical outcome in MR-based thrombolysis for unclear-onset stroke study (RESTORE).

Methods: RESTORE study is a prospective multi-center MR based thrombolysis trial for patients with unclear onset stroke (UnCLOS). MRI-specific eligibility criteria of reperfusion therapy for UnCLOS were presence of perfusion-diffusion mismatch >20%. We analyzed multimodal MR images in term of volume of Diffusion-weighted imaging (DWI) lesion, DWI-ASPECT score, malignant pattern on DWI, focal FLAIR change within DWI lesions, Leukoariosis, microbleed, and occlusion site. We trichotomized the DWI-ASPECT score into 3 groups based on extent of early change (ASPECTS >7, 4 to 7, <4). All Patients received combined reperfusion therapy including IV rtPA, IA urokinase, mechanical clot disruption and/or stenting. Primary clinical endpoint was good outcome defined as modified Rankin Scale (mRS) 0-2 at 3 months.

Results: Of 83 received reperfusion therapy, 67 patients (80.7%) having steno-occlusion of artery in anterior circulation were studied. Median age was 66 years and median baseline NIHSS was 14. Four patients (6.0%) experienced SICH with any neurological decline. Good clinical outcome was observed in 32 (47.8%). Backward stepwise multiple logistic regression analysis showed that female (OR, 19.24; 95% CI, 3.17-116.7; p=0.001), initial NIHSS score (OR, 1.31; 95% CI, 1.09-1.60; p=0.004), occlusion of the distal internal carotid artery (OR, 11.53; 95% CI, 1.14-116.3; p=0.038), FLAIR change (OR, 0.90; 95% CI, 0.011-0.757; p=0.027), and <4 DWI-ASPECT score (OR, 13.06; 95% CI, 1.89-90.29; p=0.009) were independent predictors of poor clinical outcome.

Conclusion: We should consider that proximal vessel occlusion, focal FLAIR change, and bad DWI-ASPECT score as well as perfusion-diffusion mismatch are important in patient selection for MR-based reperfusion therapy in UnCLOS.

96 Acute stroke: emergency management, stroke units and complications

ICOOL (INDUCTION OF COOLING) PILOT: A RANDOMIZED TRIAL COMPARING 3 METHODS FOR RAPID INDUCTION OF THERAPEUTIC HYPOTHERMIA IN STROKE PATIENTS

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Background: Mild therapeutic hypothermia improves clinical outcome in patients with global cerebral ischemia after cardiac arrest and in newborns with hypoxic ischemic encephalopathy.

Hypothermia seems promising also in other acute hypoxic ischemic or in brain swelling associated cerebrovascular disease. Facing the fact that "time is brain", fast induction of hypothermia is a major issue. Different cooling systems are available, each with specific advantages and disadvantages. Regarding a rapid induction Methods should be easily applicable, transportable and effective in brain cooling. Unfortunately, few studies comparing different cooling Methods have thus far been performed, none comparing the effectiveness of induction techniques.

The goal of the iCool Pilot is to evaluate 3 different induction techniques in patients with ischemic or hemorrhagic stroke with regard to speed of brain cooling, feasibility and safety: (1) Cold infusions, (2) nasopharyngeal cooling with the RhinoChillTM device (BeneChill, USA) and (3) external head and neck cooling with the Sovika® helmet (HVM Medical, Germany).

Methods: Mono centric, prospective, randomized, controlled study (n=30). Intubated and ventilated stroke patients with combined ICP-temperature-probe are included. Main exclusion criteria are: Contraindications to hypothermia (vasospastic disorders or coagulopathies) and medical conditions likely to complicate therapy (e.g. uncompensated arrhythmia, severe heart, liver or renal failure). The intended core temperature is 34°C. Primary endpoint is speed of brain cooling during the first hour. Secondary endpoints are safety aspects: Intracranial bleeding complications, respiratory effects, co-medication. Furthermore the effects on ICP and cerebral auto-regulation are examined.

Results: Active trial. We will present preliminary Results and discuss the design of the study on the Background of the current available data.

97 Acute stroke: emergency management, stroke units and complications

OUTCOME OF ACUTE STROKE PATIENTS WITH AND WITHOUT RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR THERAPY: A JAPANESE MULTICENTER STROKE REGISTRY

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Background and purpose: Although several studies clarified the efficacy of 0.6 mg/kg alteplase therapy for ischemic stroke within 3 hours of onset in Japan (J-MARS, SAMURAI), comparison between patients who received and did not receive rt-PA has not yet been made. The goal of this study was to compare stroke outcome of patients with and without rt-PA therapy based on a multicenter, prospective, observational study.

Methods: This study involved prospective enrollment of 778 patients (477 men, 73.9±11.9 years old) with ischemic stroke who were admitted to 28 hospitals within 2.5 hours of onset from January 2008 through December 2009.The modified Rankin Scale (mRS) score 0-1 at the time of discharge from the hospital was rated as favorable outcome, and mRS score 4-6 was rated as poor outcome. The association between the rt-PA therapy and outcomes was assessed by logistic regression analyses adjusted for sex, age, and admission NIHSS score on admission.

Results: IV rt-PA therapy was done for 230 patients (29.6%, 143 men, 75.2±10.6 years old). Patients receiving rt-PA more commonly had atrial fibrillation (55.2% vs 34.7%, P<0.001) and cardioembolic stroke (65.2% vs 40.0%, P<0.001), and had a higher NIHSS score on admission (median 14 [IQR 8-20] vs 5 [2-14], P<0.001) than those without rt-PA (548 patients, 334 men, 73.4±12.4 years old). At discharge (median 25 days), favorable outcome was less common (30.9% vs 43.6%, P=0.001) and poor outcome was more common (48.7% vs 37.4%, P=0.004) in patients with rt-PA than the others. After multivariate-adjustment, however, favorable outcome was more common (OR 1.76, 95% CI 1.14-2.74, P=0.01) and poor outcome was less common (OR 0.57, 95% CI 0.37-0.86, P=0.008) in patients with rt-PA than the others.

Conclusion: Acute stroke patients who were eligible for rt-PA and received the therapy had relatively better outcome after adjustment for sex, age, and initial stroke severity, indicating the possible therapeutic effect of rt-PA.

98 Acute stroke: emergency management, stroke units and complications

PREHOSPITAL DELAY FACTORS AFTER STROKE AND PARAMEDIC IDENTIFICATION OF STROKE PATIENTS IN A METROPOLITAN CITY EMERGENCY MEDICAL SERVICE SYSTEM

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Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

219

Background and Objectives: Hospital admission delay is a main limiting factor for effective thrombolytic therapy in acute ischemic stroke patients. Accurate recognition of stroke victims by ambulance paramedics is necessary to ensure the rapid transfer of these patients to the hospital. We carried out a prospective study to characterize the cause of prehospital delays after stroke by the emergency medical service (EMS) and to determine the accuracy of identifying acute stroke by paramedics.

Methods: All paramedics in the Busan Metropolitan 119 EMS were asked to record the clinical presentations, time of dispatch, time of arrival of EMS personnel at the scene, and transport time to the hospital for suspected stroke patients for a month (February 1, 2010 to February 28, 2010). Neurologists in twenty four transferred hospitals reviewed the hospital records for the patients who were given a diagnosis of stroke or transient ischemic attack by the paramedics. The time intervals from symptom onset to various points along the patient's prehospital course were analyzed. We compared the diagnosis made by paramedics with the final diagnosis made by the neurologists of each hospital.

Results: Of the EMS on-scene evaluations, the diagnosis of stroke by ambulance paramedics was correct for 79 of the 186 (43%) patients. Positive predictive values for main suspected stroke symptoms were 95% in hemiparesis, 88% in speech disturbance and 44% in impaired consciousness. The prehospital personnel transferred the suspected stroke patients to each hospital at a mean of 25 minutes after the emergency 119 call. However, only 62% of the stroke patients called EMS within the first 2 hours of stroke. About 50% of patients with ischemic stroke who sought EMS early could receive intravenous thrombolytic therapy.

Conclusions: Public education for the need to seek EMS promptly after stroke as a medical emergency, and stroke-specific training for EMS personnel are essential so that stroke patients receive effective acute treatment.

99 Acute stroke: emergency management, stroke units and complications

FREQUENCY OF INCREASED BLOOD PRESSURE LEVELS DURING SYSTEMIC THROMBOLYSIS AND RISK OF INTRACEREBRAL HEMORRHAGE

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Background and purpose: Significantly increased blood pressure (BP) is common in stroke patients and guidelines suggest that patients with BP levels persistently above 185mmHg systolic and 110mmHg diastolic should be excluded from intravenous thrombolysis (IVT). We aimed to investigate the frequency of systolic BP levels >185mmHg and/or diastolic BP > 110mmHg before and during thrombolysis and its relation to intracerebral hemorrhage (ICH).

Methods: Data for patients treated with intravenous thrombolysis in the years 2007-2009 were extracted from our local stroke database. All documented BP levels from admission to follow-up imaging scan were analyzed. BP protocol violations were defined as systolic BP >185mmHg and/or diastolic BP > 110mmHg. Symptomatic intracerebral hemorrhage (sICH) was defined as ICH plus worsening of the National Institute of Health Stroke Scale ≥ 4 points.

Results: BP protocol violation before IVT emerged in 12.6% and in the course of IVT in 40.1% of 427 patients. SICH occurred in 10 (2.3%) and ICH in general in 51 (11.9%) of 427 patients. Proportions of BP protocol violations were similar in patients with ICH, without ICH, and with sICH (3.1 vs. 2.8% vs 3.2%). Systolic BP levels and mean arterial pressure did not differ between ICH-negative and ICH-positive patients. In the multivariate analysis, only early CT findings independently predicted sICH (OR, 2.39; 95% CI, 1.25 to 4.61; p=0.009).

Conclusion: We demonstrate a relevant incidence before and a substantial increase in BP protocol violations during the course of IVT. Neither the frequency of BP protocol violations nor BP levels predicted ICH or sICH in univariate or multivariate analysis in our patients.

100 Acute stroke: emergency management, stroke units and complications

TELEMEDICINE IN ACUTE STROKE: SYNTHESISING EVIDENCE ON IMPLEMENTATION

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Introduction: Delivery of rapid intravenous thrombolysis can be facilitated by audio-visual consultation with a neurologist or stroke physician i.e. telestroke. Establishing a system requires understanding of barriers, and efficient use of resources. We aimed to construct a standardised toolkit for telestroke implementation in the UK.

Method: We undertook a structured search of the main healthcare databases for research relating to telestroke and searched the Internet to identify telestroke projects. Projects were contacted and asked about resources to support implementation; group Discussions and interviews were undertaken with UK teams using telestroke systems. Findings relating to barriers and facilitators for successful use of telestroke were analysed using Normalisation Process Theory as a framework. Implementation resources were content analysed for variance.

Results: 14 telestroke projects were identified through published research. A further 61 projects were identified worldwide from the literature, Internet and telephone contact. Findings based on the formal and informal evaluation of barriers and facilitators identified in existing telestroke systems related to the parameters of technical and clinical systems, system governance, organisational support and staffing, telestroke pathways and procedures, competency assessment and training, and recording and evaluation. Findings and resources for implementation were synthesised into a pre-implementation checklist, and a standardised "toolkit" to guide telestroke implementation in the UK.

Conclusions: Formal evaluation of implementation of telestroke is limited, with most of the barriers identified relating to issues of organisational governance. Exhaustive searching and contact with existing projects identified sufficient information to support the construction of a standardised toolkit that now needs to be tested in practice, and the consequences evaluated for professionals and patients.

101 Acute stroke: emergency management, stroke units and complications

HEMORRHAGIC COMPLICATIONS AFTER SYSTEMIC THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE IN ANTICOAGULATED PATIENTS

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Methods: We assessed the safety of systemic thrombolysis in this patient population using a prospectively recorded database from 2006 to 2010. An intracerebral hemorrhage leading to a deterioration of ≥ 4 points on the National Institutes of Health Stroke scale (NIHSS) was classified as symptomatic. We also performed a systematic PubMed search to identify studies reporting on the risk of SICH in anticoagulated patients prior to thrombolysis.

Results: Among 687 patients (mean age, 72 years; median NIHSS, 11, median onset-to-treatment time, 135 minutes) 27 patients had taken oral anticoagulants leading to elevated INR values prior to treatment (median INR: 1.5; IQR 1.4-1.9 vs. median INR: 1.0; IQR 0.9-1,0; p<0.001). The rate of SICH did not differ significantly between patients with normal and elevated INR values (4.4% vs. 0%; p = 0.6). Although the outcomes of 4 previously published studies were not sufficiently homogeneous to allow a quantitative synthesis, an unadjusted meta-analysis including our registry data found no significant increase in the risk for SICH in patients taking oral anticoagulants prior to thrombolysis (OR 1.14; 95% CI 0.51-2.51).

Conclusions: The risk of SICH following intravenous thrombolysis after ischemic stroke does not appear to be increased in patients with elevated INR values.

102 Acute stroke: emergency management, stroke units and complications

THREE-MONTHS AND LONG-TERM OUTCOME AND ITS PREDICTORS IN ACUTE BASILAR ARTERY OCCLUSION TREATED WITH INTRA-ARTERIAL THROMBOLYSIS

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Background: Intra-arterial thrombolysis (IAT) can be used for treatment of basilar artery occlusion (BAO). Predictors of outcome before initiation of treatment are of special interest.

Methods: From 1992 to 2010, we treated 106 consecutive patients with BAO with IAT. Baseline characteristics, treatment, clinical course, 3-months and long-term outcome (>12 months) were assessed. Outcome parameters were vessel recanalization after treatment, complications, modified Rankin scale (mRS) and mortality after 3-months and in long-term.

Results: At 3-months clinical outcome was good (mRS 0-2) in 33.0% of the patients and moderate (mRS 3) in 11.3%. Mortality was 40.6%. Partial or complete recanalization was achieved in 69.8% of the patients, and symptomatic intracranial hemorrhage occurred in one patient (0.9%). Between 3-months and long-term follow-up 22 survivors (40.8%) showed clinical improvement of at least 1 point on the mRS score, 29 (53.7%) were functionally unchanged and 3 (5.7%) showed functional worsening (p<0.0001). Multivariate analysis identified diabetes as a predictor of poor vessel recanalization (p=0.028). Low baseline NIHSS was identified as a predictor of good or moderate clinical outcome (p<0.0001) and survival (p=0.001) at 3-months, and younger age as an additional predictor of survival (p=0.012). For prediction of long-term clinical outcome age was also an independent predictor (p=0.018).

Conclusions: In our series IAT as treatment of BAO was safe. NIHSS at admission and age were identified as predictors of outcome, and these predictors should be considered for treatment allocation in future randomized trials.

103 Acute stroke: emergency management, stroke units and complications

SHORT-TERM CLINICAL OUTCOME FOLLOWING MR-BASED ACUTE TREATMENT IN STROKE PATIENTS WITHIN 3 HOURS OF ONSET DUE TO ACUTE CAROTID ARTERY OCCLUSION

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Purpose: To investigate short-term clinical outcome following MR-based treatment in stroke patients admitted within 3 hours from sudden onset due to acute carotid artery occlusion.

Method: Criteria for retrospective analysis were stroke patients 1) who were admitted within 3 hours of stroke onset between Jan 2006 and March 2010, 2) who presented NIHSS score of 6 or more and 3) who underwent emergency MR imaging on admission, which suggested the affected carotid artery occlusion. NIHSS on admission (NIHSS adm), DWI-ASPECT score, MRI-PWI score (1,2,3 and 4), DWI+PWI score (ASPCT score plus PWI score), reperfusion therapy, NIHSS on the 7th day, and in-hospital death were investigated. MRI-PWI score was defined according to time-intensity-curve (TIC) types of PWI. Variables to predict reperfusion therapy or in-hospital death were assessed with multivariate analysis and in-hospital outcome was evaluated in patients with reperfusion therapy (group R) and without reperfusion therapy (group non-R).

Results: Fifty-six patients were analyzed. NIHSS adm (median) was 21, ASPECT, PWI and DWI+PWI score (median) were 7.5, 2 and 7.5, nineteen patients (33.9%: 19/56) underwent reperfusion therapy (one i.v. t-PA and eighteen endovascular therapy), 7-day NIHSS was 18.5, hospitalization period was 9 days, and in-hospital death rate was 35.7% (20/56). Multiple regression analysis showed that the most significant predictors for reperfusion therapy and in-hospital death were ASPECT score (p<0.005) and DWI+PWI score (p<0.005), respectively. In 36 in-hospital survivors, 19 of median NIHSS adm improved to 13 of median 7-day NIHSS (p<0.001). In group R, in-hospital death was 5 (26.3%). In 14 survivors (73.7%) of group R, NIHSS adm and 7-day NIHSS (median) were 20.5 and 9.26 (p<0.05). In group non-R, 15 patients (40.5%) died. In 22 survivors (59.5%) of group non-R, NIHSS adm and 7-day NIHSS (median) were 19 and 15 (p<0.005).

Conclusion: Emergency MR imaging for acute ischemic stroke is a powerful tool for decision of reperfusion therapy. MR-based acute appropriate treatment was able to improve 7-day NIHSS in survivors.

104 Acute stroke: emergency management, stroke units and complications

SIGNIFICANCE OF CEREBRAL MICROBLEEDS ON T2*-WEIGHTED MRI IMAGES FOR HEMORRHAGIC TRANSFORMATION IN ACUTE ISCHEMIC STROKE

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Background: Cerebral microbleeds (CMBs) detected by T2*-weighted MRI are considered as a risk factor of cerebral hemorrhage. We examined whether or not CMBs on T2*-weighted images at admission are a marker of future hemorrhagic transformation associated with antithrombotic therapy for acute-stage ischemic stroke, including thrombolytic therapy (recombinant tissue plasminogen activator, rt-PA).

Materials and Methods: Of 528 patients with acute ischemic stroke admitted between December 2007 and November 2009, 236 diagnosed as atherothrombotic or cardioembolic stroke were evaluated. We examined the relationship between subtypes of infarction, Alberta stroke programme early CT score on diffusion-weighted images (ASPECTS-DWI), National Institutes of Health stroke scale (NIHSS) score, CMBs on T2*-weighted images and hemorrhagic transformation on computed tomography (CT) or MRI performed after any antithrombotic therapy.

Results: Relative risk of hemorrhagic transformation was significantly increased 1.24-fold (95% confidence interval: 1.06-1.43) per 1 point decrease of ASPECTS-DWI, and 1.10-fold (1.03-1.17) per 1 point increase of NIHSS score. Odds ratio of thrombolytic therapy for hemorrhagic transformation was significantly increased 1.6-fold (1.12-2.45) per 1 point decrease of ASPECTS-DWI. But, the odds ratio of CMBs on follow-up CT or MRI for hemorrhagic transformation was not significantly increased.

Conclusion: CMBs on T2*-weighted images may not be predictive for hemorrhagic transformation associated with antithrombotic therapy for acute-stage ischemic stroke.

105 Acute stroke: emergency management, stroke units and complications

PATIENT OUTCOMES AFTER DEVELOPMENT OF HYPERACUTE STROKE UNITS (HASU) IN TWO DISTRICT GENERAL HOSPITALS

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Introduction: To facilitate the implementation of the stroke thrombolysis service in Ayrshire, we have developed hyperacute stroke units (HASU) within the two district general hospitals. These 6-bedded hyperacute areas allow rapid assessment and intensive monitoring of acute stroke patients. We evaluated the benefits of HASU and analysed patient outcome data, pre- and post-HASU from both hospital sites.

Methods: Data for each pre- and post-HASU period was collected over a duration of 18 months for Hospital A and 12 months for Hospital B, as this unit opened later. This information included patient demography, length of stay, timing of stroke assessment and treatment.

Results: For Hospital A, 346 stroke patients (male, n=172) were admitted during the pre-HASU period and 419 patients (male, n=199) during the post-HASU period. Comparing the pre- and post-HASU data, there were significant improvements in direct access to acute stroke care on day of admission (62% vs 79%; P<0.001), CT brain scanning within 48 hours (88% vs 96%; P<0.001) and aspirin administration within 48 hours for ischaemic stroke patients (64% vs 77%; P<0.001). There were also reductions in hospital length of stay (median=8 vs 5 days; P<0.001) and patient mortality (13% vs 10%; P=0.21).

For Hospital B, 342 stroke patients (male, n=166) were admitted during the pre-HASU period and 330 patients (male, n=155) during the post-HASU period. Comparing the pre- and post-HASU data, there were significant improvements in direct access to acute stroke care on day of admission (53% vs 82%; P<0.001), CT brain scanning within 48 hours (81% vs 93%; P<0.001) and aspirin administration within 48 hours for ischaemic stroke patients (67% vs 79%; P<0.001). There were also reductions in hospital length of stay (median=9 vs 6 days; P<0.001) and patient mortality (12.8% vs 8.8%; P=0.11).

Conclusion: Our Results show major improvements in stroke management and care, since development of HASU in both hospitals.

106 Acute stroke: emergency management, stroke units and complications

INCREASED AWARENESS OF THE ROSIER (RECOGNITION OF STROKE IN THE EMERGENCY ROOM) TOOL IN THE EMERGENCY CARE SETTING IMPROVES ACUTE STROKE PATIENT CARE

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Objective: We investigated the emergency care teams knowledge and use of the ROSIER (Recognition Of Stroke In the Emergency Room) tool before and after education. We further analysed whether increased use increased rates of admission to specialist care within 24 hours of Emergency Department (ED) presentation.

Methods: The emergency care teams knowledge of the ROSIER tool was analysed before and after an educational programme. We compared the number of ROSIER assessments performed on patients admitted to the acute stroke unit from the ED, and patients reaching specialist care within 24 hours of admission during two study periods.

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

221

Results: Knowledge of 96 doctors, nurses, and paramedics was assessed; 41 during 2009 and 55 during 2010. Education significantly increased ROSIER tool knowledge. This included; what the acronym ROSIER stands for (p<0.0001), in what setting the ROSIER tool should be used (p<0.0001), the purpose of the ROISER tool (p<0.0001), and the implications of a ROSIER assessment (p<0.0001). During the initial period 69 patients were admitted with stroke, with 17% (n=12) receiving a ROSIER test, of which 4 were admitted to specialist care within 24 hours of presentation. During the follow up period 59 patients were admitted with stroke, of which 80% (n=44) had a ROSIER score performed and 40 were admitted to specialist care within 24 hours of presentation, and four were not. Significantly more patients assessed with the ROSIER tool in ED were admitted to specialist care within 24 hours of presentation in 2010 in comparison to 2009 (p=0.002).

Conclusion: Education increased knowledge and the numbers of ROSIER assessments completed in the ED, and contributed to faster admission of stroke patients to the acute stroke unit. We advocate the ROSIER tool to be used in the ED as part of the acute stroke pathway to achieve faster access to specialist care.

107 Acute stroke: emergency management, stroke units and complications

DAY OF ASSISTANCE INFLUENCE (WORK DAY VS. HOLIDAY) IN THE TREATMENT OF ISQUEMIC STROKE WITH INTRAVENOUS THROMBOLYSIS

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Background: Previous studies suggest that the day of treatment (work day vs holiday) may affect the recovery and complications in patients with stroke. The influence of that fact in patients treated with intravenous thrombolysis (IVT) is not known. Our objective is to determine if such an influence does exist.

Methods: Prospective registry of patients treated with IVT in 5 stroke units sharing a common stroke code and care protocols (Madrid Stroke Network). We compared demographic, clinical and outcome (hemorrhagic transformation rate, mortality and functional status at 3 months) data according to the day IVT was administrated to the patient. We considered working day (WD) from Monday to Friday, holiday (HD) for week-end days and festivities. We also compared vacation period (V) –from July 1 to august 31, and non vacation period (NV) -rest of the year.

Results: We included 1147 patients (January 2004-december 2009). 802 (69.9%) were treated in WD while 345 in HD (30.1%). 988 (86.1%) received IVT in NV, and 159 (13.9%) in V. The data are similar to the distribution of days in the working calendar (67% WD, 33% HD, 83% NV, and 17% V). There were no differences between age, sex, and basal NIHSS between WD/HD, and V/NV. "onset-to-door time": 81,9 minutes in WD vs. 81.3 in HD (n.s.); 80.6 minutes in V vs. 81.9 in NV (n.s.). "door-to-needle" time: 63.5 minutes in WD, 62.3 in HD, 61.0 in V, 63.5 in NV. Functional recovery was similar in the different groups (modified Rankin scale at 3 months 0-2): 58.2% in WD, 59.2% in HD, 54% in V, and 59% in NV. There were no significant differences in total hemorrhagic transformations, symptomatic, or mortality.

Conclusions: HD or V does not affect negatively the efficacy or security of IVT. These findings suggest that in the Madrid Stroke Network, they are not evolution and complications differences in patients treated with IVT in function of work day or holliday treatment.

108 Acute stroke: emergency management, stroke units and complications

A SAFE AND EFFICACIOUS INTRAVENOUS INSULIN PROTOCOL FOR STRICT GLYCEMIC CONTROL IN ACUTE ISCHEMIC STROKE

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Background: There is a J-shaped association between post-stroke glycemia and outcome. We designed an intravenous insulin protocol aiming at rapid and strict glucose control in hyperglycemic ischemic stroke patients. Here, we describe the initial experience, safety and efficacy of this protocol to achieve and maintain euglycemia in the first 48 hours.

Methods: The protocol is based on parallel scales for adjustment of insulin infusion rate according to current glycemia and the rate of change of glycemia, and was implemented in our stroke unit in 4/2007. Acute ischemic stroke patients with glycemia >6mmol/l were eligible for the protocol. Capillary blood glycemia was measured hourly with fingerprick test at onset of treatment and after each scale change. Target glycemia was 4.0-6.0mmol/l preprandially (5.5–8.0mmol/l postprandially). Specific algorithms were employed during meals and for patients leaving temporarily the stroke unit for diagnostic or therapeutic work-up.

Results: In the 90 protocol patients, the first normoglycemia was achieved within 8hours of treatment in 91.1% of patients (median interval 4.6±2.7hours). During the median treatment duration of 29.3±10.7hours, median glucose reduction was 2.5±3.0mmol/l. The overall rate of hypoglycemias and hypokalemias was 4.5% and 18.5% respectively. There was a significant increase in the proportion of hypokalemias on the first on-treatment measurement compared to admission (24.4% vs. 8.9%, p=0.002).

Conclusions: The present analysis shows that the proposed intravenous insulin protocol safely and effectively controls acute post-stroke hyperglycemia. After the addition of potassium, this protocol may be suitable for use in larger, randomized controlled trial to explore its clinical effect.

109 Acute stroke: emergency management, stroke units and complications

SUBSTANTIAL QUALITY IMPROVEMENT & REDUCED VARIABILITY IN DELIVERY OF ACUTE STROKE CARE ACROSS WALES WITH THE USE OF CONTINUOUS QUALITY IMPROVEMENT METHODOLOGY

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Background: Following the Royal College of Physicians' Stroke Audit, which reported poor delivery of stroke care in Wales, a programme of work was announced by the Welsh Assembly Government in December 2007. An All Wales Stroke Service Improvement Collaborative was formed and it, in collaboration with National Leadership and Innovation Agency for Healthcare (NLIAH), adopted a continuous quality improvement methodology based on "Care Bundles" & "Intelligent targets" to drive the change, reduce variability and monitor progress.

Methods: Using Institute for Healthcare Improvement's continuous quality improvement ("care bundles")methodology, 4 evidence-based care bundles were designed for acute stroke care: 1.Diagnosis (< 3hrs) 2. Emergency treatment (< 24hrs). 3. Early specialist care (< 72 hrs). 4. Goal oriented care (< 7days). Local leads were identified & trained to deliver each bundle. The "Intelligent Targets" computerized data collection methodology, developed by NLIAH, was used to collect & monitor nationwide, real-time data, at patient level.

Results: Across Wales, 15 hospitals providing acute stroke care were included. In April 2010, zero % compliance was recorded in 8 sites for bundle 1, six sites for bundle 2, nine sites for bundle 3 and 12 sites for bundle 4. By October 2010, the compliance rates were 100% in 8 sites for bundle 1 (with 3 more sites over 87%), >75% in 5 sites for bundle 2, over 80% in 13 sites for bundle 3 (6 sites 100%), and > 92% in 12 sites (9 sites 100%) for bundle 4.

Conclusions: This project demonstrates that it is possible to achieve substantial improvements in stroke care and reduce variability in service delivery, at a national level, with the use of continuous quality improvement methodology.

110 Acute stroke: emergency management, stroke units and complications

INSULIN-LIKE GROWTH FACTOR-1 PREDICTS EARLY NEUROLOGICAL DETERIORATION IN ISCHEMIC STROKE: RESEARCH FOR BIOMARKERS IN ISCHEMIC STROKE (REBIOS)

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Background: Early neurological deterioration (END) often associates with poor outcome in patients with ischemic stroke, and there are no good predictors of END. Insulin-like growth factor-1 (IGF-1) has neuroprotective effects after ischemic stroke in animal models. High IGF-1 also has been shown to predict progression of ischemic heart disease. Thus, we examined whether IGF-1 could predict END in human ischemic stroke.

Methods: Blood samples and clinical information were obtained from the patients with ischemic stroke (n=171) (atherothrombotic 34, cardioembolic 49, lacunar 45, and unclassified 43 cases), who were registered to Research for Biomarkers in Ischemic Stroke (REBIOS) study, at 5 points after the onset [day 0 (within 24 h), 3, 7,14, and 90]. Age- and sex-matched healthy controls (n=171) were enrolled from the Hisayama study in Japan. END was defined as an increase in the National Institute of Health Stroke Score (NIHSS) within the first 72 h after the onset. Favorable improvement after END was defined as a decrease in NIHSS below that on admission by day 14.

Results: Age, sex, and NIHSS on admission were not different between patients with (n=31) and without END (n=140). IGF-1 levels at day 0 were higher in patients with END (17.6±4.7 ng/ml) (mean ± SE) than those without END (7.6±5.4) and controls (6.5±4.6) (p<0.05). IGF-1 levels were significantly higher in patients with END than in controls throughout the observation and in patients without END from day 0 to day 7. Increases in IGF-1 in the first 72 h after the onset were greater in patients showing favorable improvement after END (17.0±5.2) (n=15) than in patients without favorable improvement after END (2.5±4.3) (n=16) and in patients without END (6.8±1.1) (p<0.05).

Conclusion: High plasma levels of IGF-1 on admission could predict END after ischemic stroke. The increase in IGF-1 may reflect its endogenous protective response to limit brain injury after ischemic stroke.

111 Acute stroke: emergency management, stroke units and complications

MICROALBUMINURIA IS A PREDICTOR FOR POOR OUTCOME IN ACUTE STROKE PATIENTS

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Introduction: Over the past decade, the role of microalbuminuria (MA) as a risk factor for chronic diseases has become apparent. MA is associated with increased risk of cardiovascular events and all cause of mortality. There is little information regarding MA as an independent risk factor for stroke or as a predictor of stroke outcome. Aim of this study was to determine the prognostic value of MA in acute stroke patients.

Methods: We prospectively included patients with acute ischemic stroke admitted to our stroke unit. Clinical history and vascular risk factors were collected. Neurological examination and CT scan were performed upon admission. Severity of stroke and outcome were assessed by NIHSS and modified Ranking Scale. The urinary albumin excretion was measured in 24-h collection of urine.

Results: We enrolled 146 patients (mean age 67±11 years). Upon discharge the median NIHSS was 3 and the median modified Rankin Scale was 2. MA was found in 43% of subjects. MA was associated with CRP upon admission (p=0.008), HbA1c (p=0.005), diabetes mellitus (p=0.004), glucose at baseline (p=0.001); systolic blood pressure upon admission (p=0.046), atrial fibrillation (p<0.0001), age (p=0.002), premorbid mRS (p=0.019), NIHSS upon admission (p<0.0001), NIHSS upon discharge (p<0.0001) and mRS upon discharge (p<0.0001). At the multivariate analysis, MA (beta=0.218; p=0.004), CRP (beta=0.198; p=0.005), premorbid mRS (beta=0.386; p<0.0001) and NIHSS upon admission (beta=0.231; p=0.002) were independent predictor for poor outcome.

Conclusion: MA was found in approximately half of the patients studied with acute ischemic stroke. Patients with MA were shown to have severe neurological deficit upon admission and severe functional outcome upon discharge. MA was shown to be an independent predictor of poor outcome after ischemic stroke. Microalbuminuria can serve as useful, easy and inexpensive risk and prognostic marker for future stroke studies.

112 Acute stroke: emergency management, stroke units and complications

HAS EXTENSION OF T-PA THERAPEUTIC TREATMENT WINDOW TO 4.5-HOURS AFFECTED TREATMENT TIMES AND OUTCOMES?

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Background: In accordance with the publication of ECASS III Results in October 2008, our hospital extended the t-PA treatment window from 3 to 4.5 hours. The aim of this study was to examine whether this affected treatment times and patient outcomes.

Methods: Data was extracted from the hospitals t-PA database (commenced in 2003) for all patients receiving intravenous t-PA admitted via the emergency department. Before (n=208) and after (n=126) comparisons were made for: the proportion of ischaemic stroke (IS) treated; door-to-CT and door-to-needle times; outcome at three-months (modified Rankin Score (mRS) 0-2 and mortality).

Results: The proportion of ischaemic stroke patients treated increased from 11% to 14%, following extension of therapeutic window, but was not statistically significant (p=0.19). Patients presenting within two and three-hours of onset were treated later after timeframe extension to 4.5 hours (72 minutes vs 91 minutes, p<0.001 and 45 minutes vs 85 minutes, p=0.01, respectively). No statistical differences were seen in three-month outcomes (mRS 0-2 =51% vs 44%, p=0.16; mortality =14% vs 13.5%, p=0.91).

Conclusions: Following the extension of the treatment window, patients presenting to hospital within two-three hours of onset are being treated later. This is unacceptable given the time-dependant outcome seen with thrombolytic therapy.

113 Acute stroke: emergency management, stroke units and complications

SAFETY OF INTRA-ARTERIAL THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE IN A SERIES OF 116 PATIENTS TREATED IN A COMMUNITY HOSPITAL: EFFECT OF PROTOCOL VIOLATIONS

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Background: Intra-arterial treatment (IAT) is increasingly used in acute ischemic stroke (AIS) patients ineligible or unresponsive to intravenous thrombolysis. However selection criteria for IAT are not univocally defined. We assessed the safety of IAT protocol adopted in our Institution (Careggi Hospital, Florence).

Methods: According to our protocol, approved by the local Ethic Committee in 2004, patients with severe AIS, evidence of vessel occlusion and ASPECTS>7 are eligible for IAT within 6 hours (anterior circulation) or 12 hours (vertebrobasilar occlusion). Exclusion criteria are: coma with cerebral herniation; tumor or vascular malformations on cerebral CT; high hemorrhagic risk (uncontrolled hypertension, hemorrhagic diathesis, active bleeding, platelet count<50×10^9/L) and life expectancy <1 year. Data of patients were collected in an observational hospital registry. The predictive role of protocol adherence on 3-months mortality was evaluated with a multivariate logistic stepwise analysis.

Results: Out of 3254 patients with AIS arriving to Emergency Department from Mar 2004 to Jan 2010, 116 (M: 59%; median age: 71years; median NIHSS: 21) received IAT. Forty-four patients had a protocol violation: ASPECTS ≤7 (24), exceeding time window (14), high hemorrhagic risk (6). There were no differences in demographics, NIHSS, serum glucose level and occlusion location between "off" and "on protocol" groups. Despite a similar rate of symptomatic hemorrhage (5.3%vs7.0% respectively, p=0.62), "off protocol" patients were more likely to achieve a mRS>3 at 3-months (63.6%vs54.2%, p=0.30). The proportion of patients dead at 3-months was significantly higher in the "off protocol" group (38.6%vs20.8%, p=0.04). "Off protocol" treatment was an independent predictor of mortality (OR 3.36, IC95% 1.29-8.78) on multivariate analysis, adjusted for age and NIHSS.

Conclusion: In our experience the risk of death after IAT is significantly higher in presence of protocol violation.

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

223

EFFECT ON RENAL FUNCTION OF RADIOGRAPHIC DYE ADMINISTERED INTRAVENOUSLY FOR ACUTE STROKE CT STUDIES

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Background: Acute stroke patients often have emergent CT perfusion and angiogram studies requiring intravenous dye which can negatively affect renal function. Concerns have been raised regarding performing acute stroke CT studies with dye (ASCTSD) without knowing the pre-CT serum creatinine level (SCL). At Mayo Clinic Hospital Arizona (MCHA), we routinely perform ASCTSD without knowing the pre-CT SCL, so we reviewed SCLs pre and post-ASCTD to assess the impact of this practice on renal function.
Methods: The serum creatinine levels (mg/dl) performed prior to, and within 48 hours after ASCTSD, were recorded from the last 62 acute stroke patients at MCHA. Impairment in renal function due to the administration of intravenous dye was determined to have occurred if there was a rise in the SCL of 0.5 mg/dl or more within 48 hours of the ASCTSD.
Results: Among the 62 patients studied, 54 (87%) had a normal baseline SCL, and 8 (13%) had a mildly increased baseline SCL prior to ASCTSD. None of the 62 patients had dye related renal impairment. A mild increase in the SCL by as much as 0.3 mg/dl was observed in 15 (24%) patients; no SCL increase was seen in 10 (16%) patients; and a decrease up to 0.5 mg/dl was seen in 37 (60%) patients. Among the 8 patients with an increased baseline SCL, 3 (38%) had a post-CT SCL rise of 0.1 mg, and the remaining 5 (62%) patients had either no change or a decrease in the post-CT SCL.
Conclusion: In this observational study, patients with neither normal, nor slightly impaired renal function, had evidence of renal impairment after ASCTSD. While only 62 patients were evaluated, this study suggests that acute stroke patients can have CT studies with dye without having a significant impact on their renal function. Based on these Results, acute stroke patients at MCHA will continue to have ASCTSD without needing to know the pre-CT creatinine level.

THE EFFECT OF YOKUKANSAN (TJ-54) ON DELIRIUM FOLLOWING ACUTE ISCHEMIC STROKE AND HOSPITALIZATION

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Objective: It is reported that Yokukansan (TJ-54), a Japanese herbal medicine (kampo), may be safe and beneficial in the treatment of the behavioral and pychological symptoms of dementia. The aim of our retrospective study was to investigate the efficacy and safety of Yokukansan (TJ-54) in treating delirium follwoing acute ischemic stroke.
Method: We retrospectively analyzed the patients 1) who were admitted to our single stroke center from January to December 2010 due to acute ischemic stroke within 4 days from onset, 2) who presented delirium after admission, which was diagnosed according to DSM-IV-TR criteria, and 4) who received 2.5g of Yokukansan (TJ-54) three times a day for treating delirium and continued until discharge or possible adverse effects. We investigated patient's baseline features, stroke subtypes, stroke location, NIHSS score on admission (AD-NIHSS),and the 7th day (7D-NIHSS), period of hospitalization, period of Yokukansan treatment, a history of using of another psychotropic drug, and complications. We used Delirium Rating Scale (DRS) to access delirium state before and after Yokukansan (TJ-54).
Result: Four hundred eighty nine acute ischemic stroke patients admitted to our stroke center during the study period and 29 patients were included for analysis. Their median age was 85 years. Two patients had been diagnosed as dementia and three patients had used anticholinergic drugs before admission. AD-NIHSS (median) was 7 and 7D-NIHSS (median) was 5. Nine patients had aphasia, six patients had neglect symptoms. The median period of hospital stay was 9 days. DRS score (median) before and after Yokukansan was 18 (15-26) and 14 (13-23) (p<0.001). Median period of Yokukansan (TJ-54) treatment was 6 days. Twenty-six patients were controlled with Yokukansan (TJ-54) alone, but three patients received other psychotropic drugs in addition to Yokukansan (TJ-54). No patients developed oversedation due to Yokukansan (TJ-54).
Conclusion: Yokukansan (TJ-54) was safe and effective in treating delirium following acute ischemic stroke and hospitalization.

IMPROVEMENT OF KNOWLEDGE ABOUT CORRECT RESPONSE TO INDIVIDUAL STROKE SYMPTOMS IN THE GENERAL POPULATION BY A PUBLIC INFORMATION CAMPAIGN DURING THE WORLD STROKE DAY 2010

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Introduction: Increasing the knowledge of stroke symptoms and correct action following a stroke event in the general population might reduce time between stroke onset and seeking medical advice. We investigated the influence of a public information campaign on improvement of stroke action knowledge.
Methods: During the world stroke day 2010 public information campaigns were organised in 15 centres across Germany by local hospitals, the German Stroke Society, and the German Stroke Foundation and evaluated by the Center of Stroke Research Berlin. A standardized set of slides was used for informing the public on stroke symptoms. Action knowledge among participants was measured before and after the information campaign by presenting specific symptoms including paresis, headache, gait-disturbance, impaired vision and aphasia. As potential influencing factors on knowledge, age, sex, risk factors, stroke experience and education were analysed by multivariable logistic regression.
Results: Overall 565 people in 15 centres participated in the study. Before the information campaign, correct action knowledge was observed in 69% for the symptom paresis, 65% for aphasia, 51% for gait-disturbance, 37% for visual impairment and 24% for headache. After the information campaign the correct action knowledge increased for all symptoms. The highest increase of knowledge was found in paresis (78%), followed by gait-disturbance (69%), aphasia (66%), visual impairment (63%) and headache (59%). Logistic regression analyses revealed that correct action knowledge before the information campaign was associated with higher age (p=0.001) and higher education (p=0.005) whereas previous stroke experience (p=0.02) and higher education (p=0.003) were the most relevant factors for improvement of knowledge after the campaign.
Conclusion: Education seems to be of particular importance for stroke action knowledge. This data provide a basis, on which lay information can be adjusted to population group needs.

DECOMPRESSIVE SURGERY FOR MALIGNANT SUPRATENTORIAL INFARCTION REMAINS UNDERUTILIZED AFTER GUIDELINE PUBLICATION

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Background: Decompressive surgery <48 h from stroke onset reduces the prevalence of mortality and morbidity from malignant supratentorial infarction. We investigated if utilization of decompressive surgery changed in the Czech Republic (CZ) after the release of new guidelines regarding treatment of malignant brain infarction.
Method: The volume of decompressive surgery in 2006 and in 2009 in all centers in the CZ was assessed.All neurosurgery departments in the CZ were asked to complete a questionnaire and asked to identify all cases of surgery for malignant brain infarction through combination of discharge codes for "brain infarction" and "decompressive surgery" from electronic hospital charts. To estimate the number of candidates of decompressive surgery for malignant infarction, all admissions for ischemic stroke in one participating Comprehensive Stroke Center were reviewed, and the number of candidates assessed based on published guidelines for decompressive surgery.

Result: Data for 56 patients were obtained from 15 of the 16 neurosurgery departments in the CZ. The average age was 53±13; number of males 20; median time to surgery was 48 h (range 24-62); median NIHSS score was 25 (IQR, 20–30); median infarct volume was 300 cm³ (IQR, 250–350); mean shift on CT was 10.6±3.6 mm and size of hemicraniectomy was 125 cm² (IQR, 110–154). A favorable outcome was achieved in 45% patients. The number of procedures increased from 39 in 2006 to 56 in 2009. Based on data from one stroke centre, 10% suffered from malignant supratentorial infarction and 2.3% met the criteria for decompressive surgery.

Conclusion: In 2009 as compared with 2006, the volume of decompressive surgery carried out moderately increased. However procedures remained underutilized because only 10% of those who needed decompressive surgery according to new guidelines underwent surgery. Therefore, a "adhere to guidelines" strategy is warranted for treatment of malignant brain infarction.

118 Acute stroke: emergency management, stroke units and complications

LOW HDL LEVELS BUT NOT PRIOR STATINS USE ARE PREDICTOR FOR MORTALITY AFTER THROMBOLYTIC THERAPY IN ACUTE STROKE PATIENTS

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Background: It is still unclear if lipid profile (cholesterol -, LDL -, HDL - and triglyceride levels) or prior statin use are related to post-thrombolysis intracerebral haemorrhage or affect functional outcome. This study Aims to investigate the role of those factors in acute stroke patients receiving IV thrombolysis.

Methods: From 2001 to 2010 (cut off point of the current analysis 19th November 2010) all patients admitted to our hospital and undergoing thrombolysis for acute ischemic stroke were included into an open, prospective database. Baseline variables, prior medication and lipid profiles were recorded. Outcome measures included symptomatic intracranial haemorrhage (sICH) per ECASS II criteria, mortality and favourable outcome at three months (modified Rankin scale 0-2).

Results: In total, 1066 patients were registered in our local thrombolysis database. Symptomatic ICH according to ECASS II criteria occurred in 57 patients (5.3%). Prior statin use was not associated with significantly increased odds for sICH (OR 1.05, 95%CI 0.55-2.04, P=0.864), mortality (OR 1.32, 95%CI 0.90-1.93, P=0.152) or favourable outcome (OR 0.99, 95%CI 0.73-1.35, P=0.966). Similar Results were found for triglyceride levels. In contrast, low LDL-levels and low HDL levels were associated with an increased risk for mortality at three months (LDL ≤ 100mg/dl: OR 1.68, 95%CI 1.09-2.59, P=0.019 and HDL ≤ 36mg/dl: OR 1.62, 95%CI 1.03-2.55, P=0.035).

After adjustment for baseline characteristics, only low HDL levels were associated with a significantly increased risk for mortality at three months (OR 2.34, 95%CI 1.19-4.59, P=0.014).

Conclusion: In stroke patients receiving thrombolysis therapy, low HDL levels at baseline are an independent predictor for mortality. However, the lipid profile was not associated with sICH per ECASS II definition or functional outcome.

119 Acute stroke: emergency management, stroke units and complications

TELEMEDICINE VERSUS FACE TO FACE EVALUATION IN THE DELIVERY OF THROMBOLYSIS: ARE THERE DIFFERENCES IN THE PROCESS OF STROKE CARE?

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Background: Telemedicine is now frequently adopted in the UK to deliver thrombolysis. This is in order to overcome the lack of availability of in hospital stroke expertise outside working hours. We report the process of stroke care, safety and outcome profiles comparing face to face (FTF) and telemedicine (TM) evaluation in the delivery of thrombolysis in a London Teaching Hospital.

Methods: Between July 2007 and December 2009, patients evaluated by telemedicine receiving thrombolysis with rtPA were compared with patients undergoing face to face assessment. Timings to admission, brain imaging (CT) and treatment were measured using median and interquartile (IQR) ranges. Symptomatic intracranial haemorrhage (SICH) at 24 hours, mortality and favourable outcome (Rankin 0-1) were measured at 3 months. Univariable analyses were carried out using Mann Whitney Test for process measures.

Results: Of 97 patients thrombolysed, 45 (46%) were evaluated by telemedicine. There were no significant differences in baseline NIHSS between both groups: FTF

(13) vs. TM (12) P=0.3. Onset to admission (P=0.06), admission to CT (P=0.001), CT to treatment (P<0.001) and onset to treatment (P=0.001) were all longer in the TM group. Admission to treatment time was longer in the TM group: 61 mins (IQR 43-106) compared with FTF group: 33 mins (IQR 23-47), P<0.001. SICH was 7.7% in the FTF group compared with the TM 4.4% (P=0.7). 3 month mortality was 15.5% in FTF group compared with TM group 11.1 (P=0.6). Favourable outcome was 36.5% in the FTF group compared with 42.2% in the TM group (P=0.9).

Conclusion: In this single centre experience, there were delays in achieving a number of emergency processes of stroke care with telemedicine. However the safety and outcome profiles were not adversely affected. Further evaluation of the effects of telemedicine on the quality of emergency stroke care is required.

120 Acute stroke: emergency management, stroke units and complications

PRIOR STATIN USE IN THROMBOLYZED STROKE PATIENTS IS ASSOCIATED WITH REDUCED RISK OF PNEUMONIA – BUT ONLY IN THE ELDERLY

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Background: Stroke patients are susceptible to infections. Experimental and clinical data suggest a possible protective effect of statins against pneumonia. Thus, the aim of our study was to analyze whether prior statin use was associated with reduced rate of pneumonia in patients who received thrombolytic therapy because of acute stroke.

Methods: Patients enrolled within a prospective local thrombolysis register between January 2005 and August 2010 were analyzed retrospectively. Prior statin use had to be continuous (taken at least 7 days before and 3 days after stroke onset). Pneumonia was defined according to modified criteria of the U.S. Centers for Disease Control and Prevention.

Multivariate logistic regression analyses were conducted to prove association of statin use with pneumonia and were adjusted for contributing factors identified from literature review and additional univariate analysis. Data were stratified for age ≥ 70 years.

Results: Among 350 included patients (median age 75 years, 50.3% female, median NIHSS 12, 14.3% dysphagia) 58 were on continuous statin therapy (16.6%). Patients with statin use and without did not differ in age, gender, stroke severity and incidence of dysphagia in the whole population and in patients aged ≥ 70 years (n=238). Comorbidities (hypertension, diabetes, hypercholesteremia and coronary artery disease) were more frequent in the both respective statin groups (p<0.05). Pneumonia occurred in 51 patients (14.6%) of the total population and in 44 (18.4%) patients aged ≥70 years. Factors associated with pneumonia were dysphagia [OR 6.08 (1.91-12.73)], higher stroke severity [OR 1.13 per point on NIHSS (1.06-1.19)], and diabetes [OR 2.90 (1.39-6.04)]. A protective association was found for prior statin use [OR 0.28 (0.09-0.91)] – but only in patients aged ≥70 years.

Conclusion: Prior statin use might reduce the incidence of pneumonia in elderly stroke patients who receive thrombolytic therapy.

121 Acute stroke: emergency management, stroke units and complications

RISK COMMUNICATION IN THROMBOLYSIS – REVIEW AND NARRATIVE SYNTHESIS

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Background: The risks and benefits of thrombolysis need to be communicated to the patient/carer in a time pressured emergency setting. It is unclear how thrombolysis risks are communicated. This review aimed to identify factors influencing risk communication in thrombolysis.

Methods: Web of Knowledge and PubMed databases were searched for English language articles (2000-2010), using combined terms, risk, communication, thrombolysis and stroke. Exclusions were papers not reporting risk communication or reporting conditions other than stroke. All types of articles were included. A structured matrix was used to record data and NVivo 8 was used to identify common themes.

Results: 256 articles were found; 85 duplicates were excluded;134 did not meet the inclusion criteria; 37 articles were included. Of these, 15 reported original studies; the remainder were letters, commentaries, educational articles, poster abstracts, case studies and an editorial. Of 15 original studies, 10 included stroke

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

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225

patients and of these, 2 were notes audits. Three papers used hypothetical scenarios and did not specifically include stroke patients. No study reported actual clinical practice. Factors found to influence risk communication were clinical (eg aphasia), patient emotional state, time, environmental (eg, noise in the emergency room) and medico-legal concerns. Diverse Methods were used to present risk including numbers per 100, percentage chance of risk/benefit, NNT and NNH. Risk of sICH presented included 3/100, 1/18, 6% and 8.7%. Patient/carer concerns included fear of dependency, quality of life and the balance of death versus disability.

Conclusion: A range of factors constitute barriers to risk communication in thrombolysis. Some may be minimised e.g. environmental factors. Others may require development of new Methods of management. Observational studies of clinical practice are needed to understand how barriers to communication are managed by clinicians.

122 Acute stroke: emergency management, stroke units and complications

POSTURAL EFFECT OF BLOOD PRESSURE AND OXYGENATION IN ACUTE STROKE PATIENTS

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Introduction: The effects of mobilization on blood pressure (BP) in the acute phase of ischemic stroke and the relationship with functional outcome have not been examined previously.

Method: We investigated prospectively the BP (using oscillometric method), heart rate (HR) and peripheral oxygenation in the supine, sitting and (if possible) standing position consecutively on day 1, 2 and 3 after acute stroke. A significant change of BP was defined as a reduction (fall) or increase (rise) of systolic BP of at least 20 mmHg or diastolic BP reduction (fall) of at least 10 mmHg. The functional outcome was assessed after 3 months using the modified Rankin Scale (mRS).

Results: In total 167 patients were included (mean age 68.5±15.2 years with median NIHSS of 7). Fifty percent of the patients were able to stand. Moving from the supine to sitting and sitting to standing position, the mean arterial pressure (MAP), systolic and diastolic BP increased. Changes were most pronounced on day 1; 3.9 mmHg (p<0.001) and 4.6 mmHg (p<0.001), respectively for the MAP. Also, an increase in HR was observed in all positions (for all days moving from sitting to standing, p<0.001) with stable oxygenation levels. BP decreased significantly upon standing in 13% of patients (fall) and increased significantly in 20% of the patients (rise). Only the latter was associated with good functional outcome (mRS 0-1) (p=.013).

Conclusion: We found significant increases of hemodynamic parameters during mobilization in consecutive ischemic stroke patients. A significant rise of BP was associated with good functional outcome. This effect was independent of the initial supine BP, NIHSS and age of the patients.

123 Acute stroke: emergency management, stroke units and complications

FLIGHT FOR STROKE: RESCUE HELICOPTER TO EXTEND THROMBOLYTIC IN NORTH BAVARIA

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Background and purpose: Access to thrombolytic therapy in the rural area of North Bavaria (Unterfranken) is a challenge. Helicopter transport to a stroke center is a potential way to make rtPA available to these communities in a time-window of 3 (- 4.5) hours for thrombolysis.
As part of the Stroke Angel Initiative helicopter emergency medical service (HEMS) got a special training. The rescue center and the stroke unit developed criteria for the implementation of rescue helicopters in acute stroke management in 2009-10.

Methods: Prospectively collected data of 32 consecutive helicopter transports to Bad Neustadt/Saale over a 2-year period were reviewed. Indication for rescue helicopter was a distance beyond 30 minutes for ground ambulance transport and onset of symptoms within a 3-hour time window.

Results: 1. Mean age was 64 years, 50% woman or men. 26 patients (81%) had a cerebrovascular event. 21 patients (66%) had an ischemic stroke, 5 (16%) had a transient ischemic attack, no patient had a hemorrhagic stroke. 6 patients had a stroke mimic (migraine, syncope, seizure, psychosis, somatisation disorder).

Intravenous thrombolytic therapy with rtPA was administered to 10 ischemic stroke patients (47.6%). 4 patients arrived beyond the 4.5-hour window.
2. The middle distance covered on 42.33 kilometer which would cause a time for ground based ambulance transport about 45 minutes. Therefore transport with rescue helicopter needed 13 minutes. We saved about 32 minutes for each patient.

Conclusions: A rescue helicopter-based transport can link a rural area to a stroke center and promote access to thrombolytic therapy.

124 Acute stroke: emergency management, stroke units and complications

EFFECTS OF BLOOD PRESSURE LOWERING TREATMENT IN PATIENTS WITH ACUTE ISCHEMIC STROKE AND CAROTID ARTERY STENOSIS IN THE SCANDINAVIAN CANDESARTAN ACUTE STROKE TRIAL (SCAST)

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Background: High blood pressure in acute stroke is common and associated with poor- short and long-term outcome. Under normal conditions, cerebral autoregulation maintains constant cerebral blood flow across a wide range of systemic blood pressure levels, but acute ischaemic lesions may damage the autoregulatory mechanism, and blood pressure lowering treatment may cause further ischaemic damage. SCAST has tested whether careful blood pressure lowering treatment with candesartan is beneficial in acute stroke and the main Results will be presented at the conference. In the present sub-study we have studied the effects of treatment in patients with carotid stenosis.

Methods: SCAST is a multicentre, randomised- and placebo-controlled trial of candesartan in patients with acute stroke and elevated blood pressure. Patients with stroke (ischaemic or haemorrhagic) and systolic blood pressure ≥140 mm Hg were included within 30 hours of symptom onset and randomised to candesartan or placebo for 7 days, doses increasing from 4 to 16 mg daily during the first three days. Carotid artery examination was done if clinically indicated, according to local guidelines. We assessed the effects on stroke progression, symptomatic hypotension, early stroke recurrence and functional status at 6 months (as measured by the mRS).

Results: Of 2.029 patients included, 1.733 had ischaemic stroke and data on carotid artery status was available from 993 (57%) of these patients. Baseline characteristics are presented in the table.

	Candesartan (n=491)	Placebo (n=502)
Female gender, n (%)	183 (37)	207 (41)
Age, years (SD)	68.5 (10.4)	68.6 (10.4)
Systolic blood pressure, mm Hg (SD)	170.4 (18.3)	170.0 (18.1)
Diastolic blood pressure, mm Hg (SD)	90.3 (14.1)	90.7 (13.42)
Duration of symptoms, hrs (SD)	18.1 (8.1)	18.1 (8.0)
Scandinavian Stroke Scale score (SD)	43.4 (11.5)	43.3 (11.6)
Pre-morbid modified Rankin Scale score, median (IQR)	0 (0-0)	0 (0-0)
Carotid status		
One-sided stenosis <50%	404 (82)	402 (80)
One-sided stenosis 50-69%	37 (8)	38 (8)
One-sided stenosis ≥70%	33 (7)	35 (7)
Bilateral stensosis ≥50%	17 (3)	27 (5)
Medical history		
Hypertension, n (%)	324 (68)	343 (71)
Current or previous atrial fibrillation, n (%)	78 (16)	79 (16)
Previous stroke or TIA, n (%)	109 (22)	94 (19)
Thrombolytic treatment before randomisation, n (%)	51 (11)	59 (12)

Conclusion: SCAST is to date the largest trial of blood pressure lowering treatment in acute stroke, and the first trial of effects of such treatment in patients with carotid artery stenosis. Results of this subgroup analysis will be presented at the conference. Please see abstract AID 1271 for the main Results.

125 Acute stroke: emergency management, stroke units and complications

INTRAVENOUS THROMBOLYSIS IN ANTERIOR VERSUS POSTERIOR CIRCULATION ACUTE ISCHEMIC STROKE: IS THERE ANY DIFFERENCE?

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Background: Very few studies have compared the effect of intravenous thrombolysis (IVT) in anterior and posterior circulation ischemic strokes. Our aim is to study the influence of topography in the response to IVT.
Methods: Patients treated with IVT were recorded in a multicenter prospective register from 5 stroke centres in the Madrid community. Posterior circulation (PC) and anterior circulation (AC) ischemic strokes were compared.
Results: From January 2004, to Dec 2009, 1147 patients have been included in the register. 1051 patients presented an AC stroke and 78 suffered a PC stroke. No differences in age and sex were found between the two groups. Lacunar stroke was more frequent in PC group (11% vs 3% p<0.001).Time-to-treatment (TTT) was longer in PC stroke (mean ± SD: 165 minutes ±54.4 vs 142 minutes ±42.9, p<0.001). PC strokes were less severe: mean baseline NIHSS: 11±7 vs 14±6, p<0.001. A higher proportion of better outcome (defined as modified Rankin Scale score of 0 to 2 at 3 months) was observed in the PC group (75% vs 57%, p=0.003) but logistic regression did not confirm this result: OR (adjusted by age, sex, lacunar stroke, TTT and baseline NIHSS): 0,81 (95% CI: 0,43-1,52). A lower hemorrhagic transformation rate was found in the PC group (5.19% vs 19.2%, p=0.008) adjusted OR: 3,23 (95% CI: 1,14-9,1), but symptomatic intracerebral hemorrhage rate was similar in both groups (1,4% in PC vs 3,4% in AC, p=0.4). No differences in the mortality rate were detected.
Conclusions: Stroke topography is not a determinant factor in the response to IVT. IVT in PC seems to be at least as effective and safe as in AC ischemic stroke.

126 Acute stroke: emergency management, stroke units and complications

THROMBOASPIRATION WITH THE PENUMBRA SYSTEM IN ACUTE ISCHEMIC STROKE: A SINGLE-CENTRE EXPERIENCE

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Background: The Penumbra System (PS) has been recently approved for treatment of acute ischemic stroke (AIS) secondary to large vessel occlusion. We tested safety and feasibility of PS in AIS patients.
Methods: Consecutive patients presenting within 8 hours of stroke onset with CT-angiography showing large intracranial vessels occlusion were selected. Intravenous rtPA was given within 4.5 hours, if not contraindicated. Digital subtraction angiography was used to monitor a guide catheter to the site of occlusion. Clot aspiration was done by connecting the reperfusion catheter to the aspiration pump. A 24-hour CT scan was done in all patients. 3-month outcome was assessed by the modified Rankin Scale (mRS).
Results: Over a 15-month period, 20 patients were treated. They were 12/20 (60%) males, median age (IQR) of 61 (53-70) y.o., 17/20 (85%) with middle cerebral artery infarct. Median (IQR) pre-treatment NIH Stroke Scale (NIHSS) score was 17 (15-21). 8/20 (40%) patients received IV rtPA. Median time (IQR) from last-seen normal to arterial puncture and to recanalization were 234 (173-287) and 315 (273-395) min, respectively, with median time (IQR) from arterial puncture to recanalization of 83 (72-91) min. Periprocedural stenting positioning was performed in 7/20 (35%) patients. Complete recanalization (TIMI 3) was achieved in 11/20 (55%), and partial recanalization (TIMI 2) in 6/20 (30%) patients. 24-hour major neurological improvement was observed in 11/20 (55%). Intracranial bleeding complications were observed in 9/20 (45%), with one symptomatic haemorrhage leading to death. Two patients died for malignant MCA stroke (overall mortality:15%). 3-month mRS≤2 and mRS≤3 were observed in 9/20 (45%) and 5/20 (25%) patients, respectively.

Conclusion: Thromboaspiration by the PS was safe, leading to 85% recanalization of intracranial occlusions. Despite the high mortality and disability associated with this stroke subtype, the prognosis was favourable in 70% of patients.

127 Acute stroke: emergency management, stroke units and complications

ASSOCIATION BETWEEN BLOOD PRESSURE CHANGES IN THE ACUTE PHASE OF STROKE AND OUTCOME WITH RESPECT TO STROKE ETIOLOGY

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Background and purpose: The management of blood pressure (BP) in the acute phase of stroke remains controversial. Previous research suggested that proper management of BP in the acute stroke may need to take into account the underlying etiopathogenetic mechanism.
Methods: All patients registered in the Acute STroke Registry and Analysis of Lausanne (ASTRAL) between 2003 and 2009 were analyzed. Unfavorable outcome was defined as modified Rankin Scale score >2. A local polynomial surface algorithm was used to assess the effect of baseline and 24-48 hours systolic (SBP) and mean arterial pressure (MAP) on outcome in patients with lacunar, atherosclerotic and cardioembolic stroke.
Results: 791 patients were included in the analysis. For patients with low/normal baseline BP levels, BP elevation reduced the probability of unfavorable outcome (however slightly) in atherosclerotic stroke, but on the contrary deteriorated outcome in lacunar and cardioembolic stroke. In any other case, BP elevation increased the probability of unfavorable outcome. For moderately high baseline BP levels, BP reduction seemed to be beneficial for all stroke types; on the contrary, it had only a minimal effect in extremely high baseline BP levels, with the optimal reduction being larger in lacunar strokes, modest in atherosclerotic and only mild in cardioembolic. Among patients with extremely elevated baseline BP, lacunar strokes were associated with better outcome compared to atherosclerotic or cardioembolic strokes.
Conclusions: The present study provides provide further evidence to support that BP management in the acute stroke should be tailored with respect to the underlying etiopathogenetic mechanism.

128 Acute stroke: emergency management, stroke units and complications

DUBLIN MIDLANDS STROKE NETWORK PARTNERSHIP (SNP) – IMPROVED ACCESS TO THROMBOLYSIS BY PARTNERSHIP MODEL OF TELEMEDICINE

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Introduction: Thrombolysis is a time dependent treatment. Provision of thrombolysis services is often restricted by stroke consultant numbers and large geopgraphical areas.
Method: Dublin Midlands SNP consists of 4 acute general hospitals and a regional centre covering a population of 760,000. In 2009 thromblysis available in 2 hospitals on a 24 /7 basis. In 2010 we introduced 24/7 telemedicine service, with RP-7 (InTouch Health) units at the regional centre (AMNCH Tallaght) and Naas General (NGH) and Midlands Regional Hospital Mullingar (MRHM). From four network hospitals, 5 stroke geriatricians and one neurologist participated in a unified out of hours acute stroke telemedicine rota. We present first 12 month activity data.
Results: 543 stroke patients admitted in a twelve month period across the three sites. 217 (39%) patients acutely assessed for thrombolysis, 66 (30.4%) by telemedicine. 80 (14.7%) patients received thrombolysis 31 (39%) by telemedicine. Thrombolysis rates in the three sites were 14.5% AMNCH, 11.7% NGH and 17.1% MRHM compared to 6.9%, 2% and 15% respectively in 2009.

Discussion: Introducing a telemedicine system improved thrombolysis rates in participating hospitals and provided 24/7 network cover. Working as a telemedicine partnership rather than "hub and spoke" is a successful and sustainable model of acute stroke networks.

129 Acute stroke: emergency management, stroke units and complications

CLINICALLY-CONFIRMED INFECTION LEAD TO WORSE EARLY FUNCTIONAL OUTCOME IN ISCHAEMIC STROKE, IRRESPECTIVE OF INITIAL LABORATORY FINDINGS – A PRELIMINARY HOSPITAL-BASED REPORT

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Background: Inflammation attracts increasing interest in stroke since brain-induced immunodepression has recognised as risk factor for poststroke infection (mainly of respiratory or urinary tract) with poor outcome. Otherwise, the potential role of preceding infection as stroke trigger remains unclear. The present study Aims on the relationship between inflammatory markers, clinically-confirmed infection and early functional outcome.

Methods: Extracted from a hospital-based database, 930 cases of transient or permanent ischaemic stroke were screened for inflammation at hospital admission (blood leukocyte count >11,000 or <4,000/ml). According to the occurrence of pneumonia or urinary tract infection during hospitalisation, the following groups were formed: Infection neither laboratory nor clinically (l-/c-), missing laboratory but appearance of clinical infection (l-/c+), laboratory but missing clinical infection (l+/c-) and coincidental laboratory and clinical infection (l+/c+). National Institute of Health Stroke Scale (NIHSS) was used for stroke severity at admission; prehospital impairment and outcome at discharge were assessed by modified Rankin Scale (mRS).

Results: Patients with clinical infection were – irrespective of laboratory findings – of older age, showed increased prehospital impairment (mean mRS, 0.9, 1.2 vs. 0.5, 0.6; p<0.001) and increased stroke severity at admission (mean NIHSS, 12.0, 14.6 vs. 5.6, 7.8; p<0.001). Patients devoid of inflammation (l-/c-) achieved best outcome (mean mRS, 2.1), in contrast to patients with clinical infection (l-/c+, l+/c+; 3.8, 4.0; p<0.001), confirmed by mRS distribution.

Conclusion: This study verified the previously reported adverse influence of clinical infection on stroke outcome, and revealed an association with increased neurological impairment at admission and worse prehospital condition. Further research is required to clarify the time course of infection, especially the role as risk factor preceding stroke.

130 Acute stroke: emergency management, stroke units and complications

EARLY CAROTID ARTERY STENTING AFTER SYSTEMIC TROMBOLYSIS: A SINGLE CENTER PRELIMINARY RESULTS

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Background: Safety of early carotid endarterectomy (CEA) after intravenous (IV) rtPA has been described in small single-centre case series of acute ischemic stroke (AIS) patients. Emergency carotid stent placement has safety comparable to that of emergent CEA, although is not as safe as elective carotid stent placement.

Objective: We tested safety and durability of early carotid artery stenting (CAS) after IV rtPA administration in AIS patients with residual severe internal carotid artery (ICA) stenosis.

Methods: Of consecutive IV rtPA-treated patients, those with residual stenosis ≥60% in the symptomatic ICA underwent to early CAS. The protocol included pre-treatment MRI and MR angiography and post-treatment carotid ultrasound and CT-angiography. Stroke severity was assessed by the NIH Stroke Scale (NIHSS). A filter protection device was used in all patients. Three-month and 12-month stent patency was assessed by ultrasound. 12-month functional outcome was assessed by the modified Rankin Scale (mRS).

Results: Of 145 consecutive IV rtPA treated patients, 6 (4%) underwent to early CAS. Male/female ratio was 4/2, mean age (±SD) was 72 (±8) years, median NIHSS (IQR) before CAS was 7 (1-16). Median (IQR) onset-to-CAS time was 3 (1-5) days. A single self-expandable stent was implanted to cover the entire lesion in all patients. The procedure was uneventful in all patients. There were no bleeding complications, and all patients were discharged on clopidogrel plus aspirin. At 12-month follow-up all patients had no residual stenosis and functional outcome was favourable (mRS≤2) in all but 1 patient experiencing a recurrent stroke after 4 months for new-onset atrial fibrillation.

Conclusion: This small single-centre case series suggests that early CAS may be a safe alternative to CEA after IV rtPA administration. Compared to early CEA, CAS might have the advantage of lower hemorrhagic complications post-rtPA if early reperfusion procedure of the carotid lesion is required.

131 Acute stroke: emergency management, stroke units and complications

USEFULNESS OF THE BASELINE SERUM D-DIMER LEVEL AS A PROGNOSTIC FACTOR IN PATIENTS WITH CARDIOEMBOLIC STROKE TREATED BY THROMBOLYTIC THERAPY

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Background and purpose: Compared to that of patients with other stroke subtypes, most patients with cardioembolic stroke have a higher serum D-dimer level. This is considered due to the acceleration of secondary fibrinolysis due to hypercoagulability. The elevation of D-dimer can be explained as a reflection of both the high concentration of fibrin in intracardiac thrombi, i.e. "fibrin-rich thrombi" and the strong activation of the intrinsic fibrinolytic system. We measured the baseline serum D-dimer levels in patients with cardioembolic stroke treated by thrombolytic therapy and evaluated the usefulness of the serum D-dimer value as a prognostic factor.

Subjects and Methods: Our study included 26 consecutive patients with cardioembolic stroke due to nonvalvular atrial fibrillation treated by thrombolytic therapy using alteplase in our hospital. Cases demonstrating mild neurological deficit (NIHSS < 6), known malignant disorders and death due to complication were excluded. We divided the patients into "good recovery group" (mRS = 0-1) and "poor recovery group" (mRS > 2) and evaluated the baseline D-dimer levels in each group.

Results: There were no differences between the two groups in terms of age, gender or neurological severity before thrombolytic therapy. The baseline D-dimer level in the good recovery group was significantly higher than that in the poor recovery group (1.36±0.78 microg/mL and 0.86±0.37 microg/mL respectively, p=0.037 by Fisher's PLSD test).

Conclusion: This study indicates that in patients with cardioembolic stroke due to nonvalvuar atrial fibrillation, a high serum D-dimer titer before thrombolysis may be useful as a factor predicting a good prognosis.

132 Acute stroke: emergency management, stroke units and complications

CLINICAL CHARACTERISTICS OF RECURRENT EMBOLIZATION IN ACUTE CARDIOEMBOLIC STROKE

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Background: The recurrence of embolization in acute embolic stroke might be a major factor influencing prognosis. To assess the characteristics of patients with recurrent embolization in acute cardioembolic stroke, we evaluated embolism sites, severity, risk factors and outcome in patients with and without recurrent embolization on admission.

Subjects and Methods: Among the acute stroke patients admitted to Tokai University Hospital between September 2004 and August 2010, 436 were diagnosed with cardioembolic stroke (265 men, 171 women; mean age: 73±11 years) and enrolled in this study.

Results: Of the 436 patients, 20 (4.5%) had recurrent embolization (cerebral infarction, 16; other, 4) on admission. Of these 20 patients, 10 had a recurrent event within 7 days of admission, 4 had recurrence within 8–14 days and 6 had recurrence at 15 days or later. Magnetic resonance imaging or computed tomography revealed

that the recurrent group had significantly more frequent and larger infarction, such as that of all areas of the anterior, middle and/or posterior cerebral arteries, when compared to the non-recurrent group (P<0.02), and the mortality rate was significantly greater in the recurrent group than in the non-recurrent group (40% vs 11%, respectively; P<0.005).

Conclusion: Recurrent embolization in the acute stage of cardioembolic stroke frequently occurred within 7 days after admission, and prognosis is worse in patients with recurrence than in those without.

133 Acute stroke: emergency management, stroke units and complications

EXTENDING THERAPEUTIC WINDOW FOR INTRAVENOUS THROMBOLYSIS TO 4.5 HOURS REMAINS SAFE AND EFFECTIVE IN ASIAN ACUTE ISCHEMIC STROKE PATIENTS

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Background: Intravenous tissue plasminogen activator (IV-TPA) remains the only approved therapy for acute ischemic stroke (AIS) patients within 3 hours of symptom-onset. However, the therapeutic benefit exists up to 270 minutes. Treatment rates for AIS remain low in Asian populations due to patients' late arrival and higher anticipated bleeding-risk. We evaluated safety and efficacy of IV-TPA in an extended therapeutic window among Asian patients in Singapore.

Methods: Consecutive AIS patients treated with IV-TPA from Jan2007 to March2010 were included. All patients received standard-dose of IV-TPA. Efficacy was assessed with functional outcomes at 3-months (modified Rankin Scale (mRS) score, dichotomized as good (mRS 0-1) and poor (mRS 2-6). Safety of IV-TPA was assessed by rates of symptomatic intracranial hemorrhage (SICH).

Results: Of the total of 2271 AIS patients admitted to our center, 224 (9.9%) eligible cases were treated with IV-TPA. Baseline data included mean age 63 ± 12 years; 131 (59%) males & median NIHSS 16 points. 190 patients were treated within 3 hours while 34 received IV-TPA in extended therapeutic window. Hypertension was the commonest vascular risk factor in 170 (76%) while 73 (33%) patients suffered from atrial fibrillation (AF). Strokes involved anterior circulation in 189 (84%) as compared to 35 (16%) posterior circulation. Overall, 115 (51%) patients achieved good functional outcome. Female gender, AF, pre-TPA NIHSS score were associated with poor functional outcome. Although, higher proportion of patients treated after 180 minutes had poor outcomes at 3 months (62% versus 46% in 0-180 minutes group), the difference was not statistically significant (OR 1.87;95%CI 0.88-3.96, p=0.097). SICH occurred in a total of 9 (4.01%) patients. Although, higher proportion of patients treated in an extended window developed SICH (9.7% versus 3.3%), the difference was not significant (p=0.141).

Conclusion: Intravenous thrombolysis in an extended therapeutic window is effective as well as safe in the treatment of acute ischemic stroke in our multiethnic Asian population in Singapore.

134 Acute stroke: emergency management, stroke units and complications

DELIVERING THROMBOLYSIS FOR A SCOTTISH RURAL POPULATION

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Background: Thrombolysis saves lives. It is now a licensed treatment for acute ischaemic stroke presenting within 3 hours. Evidence also suggested that reduced door to needle time improves recovery. Different models are being proposed to deliver thrombolysis, especially to the rural population in Scotland. In this financial climate in UK, it may be sometimes difficult to justify 24/7 service in a smaller hospital without clear health benefit shown against financial investment.

Method: Retrospective data was collected from June 2009 to June 2010 from the thrombolysis database. The number of patients thrombolysed locally (Monday-Friday 9am-5pm) was identified. The number of patients referred, and those actually thrombolysed in tertiary centre (24/7 service, 35 miles away from local site) were determined for comparison. The door to needle time for each group was compared, in particular the number of patients excluded due to time restraints in arriving at the tertiary centre.

Results: A total of 20 patients were thrombolysed. 10 locally and 10 were done at tertiary centre. The mean door to needle time was 1 hour and 25 minutes at local site and 3 hours 10 minutes at tertiary centre. A further 9 patients were discussed

with tertiary centre but were not considered for thrombolysis as they could not have reached even with the extended 4hrs and 30 minutes window. There were no significant adverse effects observed in local centre following thrombolysis though numbers are still small.

Presentations of patients also showed about 80% of patient's attended with stroke symptoms between 9am-10pm.

Conclusions: Centralised service has been unable to deliver thrombolysis in time to maximize benefit to rural patients. Immediate development of an extended thrombolysis service until 10pm 7 days a week, delivering treatment to at least 80% of patients, is well justified in spite of financial pressure. Other models including telemedicine needs to considered for 24/7 especially for the Scottish rural population.

135 Acute stroke: emergency management, stroke units and complications

GLYCOGENPHOSPHORYLASE ISOENZYME BB (GPBB) – AN EARLY MARKER OF ISCHEMIC LESION OF THE BRAIN

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Background: Biomarkers for ischemic stroke might be helpful for early diagnosis, evaluating therapeutic approaches and prognosis. Glycophosphorylase isoenzyme BB (GPBB) is a useful and early biomarker for acute coronary syndrome (ACS). Since it is also located in the brain, it might represent a useful biomarker in stroke. Therefore, we evaluated the clinical course and GPBB levels after ischemic stroke in this pilot-study.

Methods: Serum concentration of GPBB was analyzed in 11 patients. N=7 had the diagnosis of acute ischemic stroke (AIS), while n=4 served as control patients (other neurological conditions).

In AIS-patients, blood was drawn first within 6 hours after symptom onset and then measured daily until day 6 or discharge. Neuron-specific enolase (NSE), Troponin I, Creatinkinase (CK) and CK-MB were measured daily.

Results: GPBB was elevated in AIS-patients in comparison to control in the first 6hours after onset (mean ± S.E.M.: 9.2 ± 3.1 vs. 3.5 ± 1.6, p<0.05, Figure 1) and remained elevated until day 6 (8.2 ± 30.6, p<0.05). Cardiac origin of elevated GP BB levels was ruled out. Troponin remained below 0.5ng/ml, EKG as well as TTE showed no signs of myocardial damage. NSE-levels increased up to 35ng/ml.

Figure 1
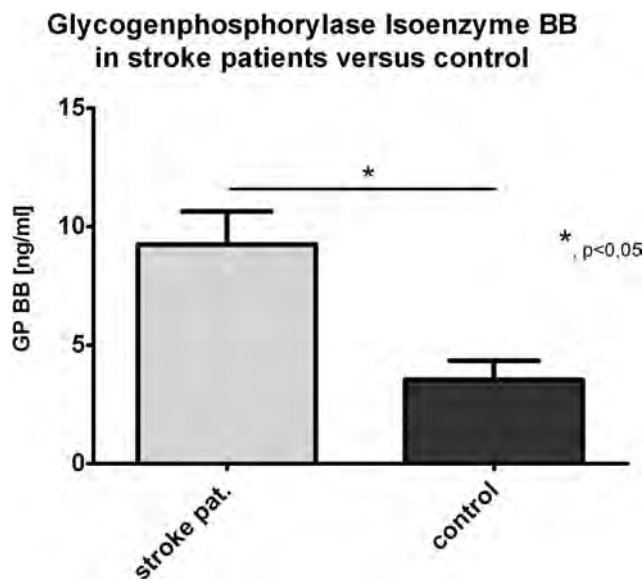
Discussion: GPBB might be useful as a biomarker for ischemic stroke and needs further evaluation in larger patient cohorts.

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

229

USEFULNESS OF CT ANGIOGRAPHY FOR THERAPEUTIC DECISION MAKING IN THROMBOLYZING DIFFICULT TO ASSESS PATIENTS WITH BASILAR ARTERY THROMBOSIS

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Background: Acute ischemic stroke (IS) due to basilar artery thrombosis (BAT) causes high mortality & severe disability. Early neurological assessment & timely thrombolysis might improve outcome. BAT is often difficult to diagnose due to wide spectrum of presentation & decreased level of consciousness. Emergency physicians often intubate such patients due to airway compromise, even before arrival of stroke neurologist. We aimed at evaluating role of CT angiography (CTA) of brain & cervical arteries in early diagnosis of acute BAT & facilitating systemic thrombolysis in intubated patients.
Methods: Consecutive acute IS patients presenting with history of sudden deterioration in level of consciousness within 6hours of symptom-onset & intubated before assessment by neurologist were included. All patients underwent limited fast-track clinical evaluation, brain CT & CTA.
Results: Thrombolytic therapy, mainly intravenous tissue plasminogen activator (IV-TPA), was administered to 161 (8.4%) of 1917 acute IS patients admitted during the study period. Acute BAT contributed 10.9% (208 cases). 5 cases (3 males, mean age 72yrs) of acute BAT & airway compromise were intubated early, sedated & paralyzed before Neurologists' assessment. CTA showed BAT in all. IV-TPA was initiated at 236±40 minutes in 4 patients and 1 received intra-arterial TPA, initiated at 13hours. There was no intracranial hemorrhage & mean length of hospital stay was 11.8 days. Despite severe strokes at presentation, good functional recovery at 3 months (modified Rankin scale- mRS 1) occurred in 2 patients; mRS 4 in one& 2 died (including the patient treated intra-arterially). 4 additional cases who met the inclusion criteria but had normal CTA were not thrombolysed. None of them showed new brain infarcts on subsequent neuroimaging.
Conclusion: In acute BAT patients, intubated before Neurologists' assessment, CT angiography is helpful in confirming the diagnosis & facilitating systemic thrombolysis.

EARLY CAROTID ENDOARTERECTOMY AFTER INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE

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Background: after intravenous thrombolysis (IVT) for acute ischemic stroke (AIS), a severe cervical internal carotid artery (ICA) stenosis may remain. Carotid endoarterectomy (CEA) has been shown to be effective in reducing the risk of recurrent stroke. However, it is still not clear what is the optimal timing to safely perform CEA after IVT. To the best of our knowledge there are two reports published of patients who safely underwent CEA respectively within 45 hours and 16 days after IVT.
Methods: We report our experience with 5 male patients who underwent CEA for residual high grade cervical ICA stenosis within 12 hours after ipsilateral ischemic stroke treated with i.v. r-TPA. All the patients underwent cerebral computed tomography (CT) scan and carotid sonography at the admission, and received IVT with full dose r-TPA within 3 hours of stroke onset. CEA was performed within 12 hours of stroke onset. Cerebral CT scan and carotid sonography were controlled within 24 hours after CEA. NIHSS score was recorded at admission, 24 hours and one week after stroke onset; mRS score was recorded at three months.
Results: patients' mean age was 63.8 years (40-77). Median NIHSS score at admission was 14 (6-23). Carotid sonography documented an ipsilateral ICA stenosis > 80% according to NASCET criteria. Median time between symptoms onset and CEA was 456 minutes (360-720). We achieved full patency of the stenotic artery in all patients and didn't observe peri or post surgical complications. None had hemorrhagic infarction or transformation of the ischemic area on control CT. Median NIHSS score was 7.6 (2-17) and 4,8 (1-14) after 24 hours and one week

respectively. Four patients had good clinical outcome (mRS 0-2) and one had moderate residual disability (mRS 3) at three months.
Conclusions: CEA for residual cervical ICA stenosis after IVT for acute ischemic stroke can be safely and successfully performed within 12 hours of stroke onset in selected patients.

INFLUENCE OF MULTIMODAL CT IMAGING ON RATE OF RECANALIZING THERAPY IN ACUTE ISCHEMIC STROKE - RETROSPECTIVE ANALYSIS OF A ONE YEAR SINGLE CENTRE EXPERIENCE

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Background: Recanalizing therapy in ischemic stroke is officially restricted to iv thrombolysis within 3 hours after symptom onset in the absence of major signs of tissue damage in native cranial CT. Multimodal imaging of vessel and parenchymal perfusion status may allow the extension of this time window.
Aim: To retrospectively analyze the rate of recanalizing off-label treatment Results in daily practice of a single stroke centre over one year dependent on multimodal CT imaging.
Methods: Patients having received recanalizing therapy comprised three groups: 1) "standard" iv thrombolysis within three hours; 2) "off-label" iv thrombolysis; 3) off-label interventional therapy. In "off-label" patients, recanalizing therapy was applied dependent on multimodal diagnostics (CT Angiography, Perfusion CT) and according to local standardized concepts of off-label intervention. Clinical data concerning short term course were analyzed in either case.
Results: Out of 543 patients with ischemic stroke or TIA referred to our department, 68 (12.5%) received any recanalizing therapy. Of those (mean age 71.3y, 37 female, mean TSO 122 min), 47 cases (mean age 73.4, 24 female, mean TSO 62 min) received standard iv thrombolysis, 10 off-label iv thrombolysis (mean age 70.8, 6 female, mean TSO 332 min), and 11 mechanical thrombectomy after "bridging" with iv rtPA (mean age 62.5, 7 female, mean TSO 186 min). Mean delta short term NIHSS (2-5 days) in these three groups were 3.7±4.7, 3.9±4.4, and 4.1±5.8, respectively.
Conclusions: Short term clinical course was similar in the three groups in this limited single centre experience. Off-label therapy is generally considered to be associated with a higher risk for complications/clinical deterioration. However, if multimodal CT imaging of acute ischemic stroke is incorporated in every-day clinical decision making, the rate of effective recanalizing procedures may be increased without apparent negative effect on short term outcome.

USE OF THE EMERGENCY MEDICAL SERVICE INCREASES THE PROBABILITY OF UNDERGOING THROMBOLYTIC THERAPY IN THE PATIENTS WITH ACUTE ISCHEMIC STROKE ADMITTED TO A KOREAN TERTIARY HOSPITAL

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Background and Purpose: Delayed hospital admission is a main limiting factor for effective thrombolytic therapy in acute ischemic stroke patients. The use of the Emergency Medical Service (EMS) allows rapid transfer of patients with acute stroke to a stroke center or community hospital. This study was designed to test the hypothesis that a direct visit to a stroke center using the EMS could increase the number of patients treated with thrombolytics and reduce prehospital time and time from stroke onset to thrombolytic therapy.
Methods: We enrolled the patients with ischemic stroke who were admitted to our stroke center within the first 6 hours after symptoms onset over a 2-year period. The patients were divided into 3 groups based on the mode of admission: 1) a direct visit to the emergency room (ER), 2) admission via the EMS and 3) transfer from community hospitals. The time intervals from symptom onset to various points

along the patient's prehospital course and the numbers of ischemic stroke patients who underwent intravenous thrombolytic therapy were analyzed.

Results: We studied a total of 213 consecutive patients with acute ischemic stroke. Nineteen percentage of acute ischemic stroke patients received rtPA therapy. The percentage of patients who received rtPA administration was higher for the patients who presented via the EMS (13.7%, 30% and 15.8%, respectively; p=0.018). The median time from onset to admission (114, 79 and 181 minutes, respectively; p<0.001) and intravenous thrombolysis (116, 105 and 156 minutes, respectively; p=0.001) was shorter for the group with access to a stroke center via the EMS. The stroke severity was milder for the patients who directly visited to ER (NIHSS: 5.6, 10.7 and 11.4, respectively; p<0.001).

Conclusions: The patients who arrived directly to the stroke center via the EMS are more frequently treated with thrombolytic therapy. Public education about the need to promptly seek help from the EMS after stroke as a medical emergency is essential so that acute stroke patients receive effective treatment.

140 Acute stroke: emergency management, stroke units and complications

TREATMENT WITH LOW-DOSE ASPIRIN PLUS DIPYRIDAMOLE IN ACUTE NON-ATRIAL FIBRILLATION STROKE REDUCES MORTALITY AFTER 3 AND 12 MONTHS IN COMPARISON WITH ONLY LOW-DOSE ASPIRIN TREATMENT

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Background: Previous studies have shown that low-dose aspirin plus dipyridamole may reduce the risk after acute stroke for the composite endpoint of vascular death, non-fatal stroke and non-fatal myocardial infarction. However, there is few data on the short-term effects (≤12 months) of aspirin plus dipyridamole on cardiovascular events and mortality after acute stroke. Therefore the aim of the present observational study was to elucidate this question.

Methods: 635 patients with acute ischaemic stroke or TIA were prospectively followed for 12 months. At discharge from the stroke unit 265 patients were treated by low-dose aspirin only and 278 were treated by low-dose aspirin plus dipyridamole.

Results: There were no differences between the groups in cardiovascular events (non-fatal stroke, non-fatal myocardial infarction), but patients on aspirin plus dipyridamole had a lower all-cause mortality at 3 months (2.2% vs.6.5% p=0.014) and at 12 months (6,2% vs. 11.8% p=0.023). In a multivariate logistic regression analysis use of aspirin plus dipyridamole was negatively related to 3 (p=0.044) and 12 (p=0.013) months mortality independent of age, initial NIHSS and history of previous ischaemic stroke.

Conclusion: In this observational study use of aspirin plus dipyridamole after acute stroke seems to be associated with lower short-term mortality compared with use of aspirin only.

141 Acute stroke: emergency management, stroke units and complications

GENERAL ANAESTHESIA ON ENDOVASCULAR PROCEDURES: NECESSARY OR NOT?

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Background: Patients undergoing endovascular acute stroke treatment may require monitoring, conscious sedation or general anaesthesia (GA) during the procedure.

Methods: We compared the type of anaesthesia performed in 37 acute stroke patients undergoing endovascular revascularization procedure: monitoring or conscious sedation (MCS group) versus GA group.

Results: 16 patients were treated under MCS (94% anterior circulation (AC) and 6% posterior circulation (PC)) and 18 patients under GA (56%AC and 45%PC), with no differences in age (53.9±14.5 vs 63±14.6), nor basal NIHSS 17[12-21]. Posterior circulation strokes required GA in 89% of cases compared to AC strokes (p 0.02). Regarding to AC strokes, left-side strokes (n 17) underwent MCS in 64.7% and GA in 35.3%; and right side (n 8) GA in 50%. Door to endovascular needle time was longer in the GA group (84[53-126]min vs 61[30-117] in MCS group, p 0.43). GA was performed in 89% of basilar artery occlusions, 55% of carotid T occlusions and 31% of MCA occlusions (p 0.049). 62.5% of patients in MCS group were independent at three months (mRS≤2) compared to 37.5% in GA group (p 0.09). No differences were found regarding the frequency of haemorrhagic transformation

between both groups. After the procedure, 100% of the patients who received MCS were referred to the Stroke Unit and 89% of GA patients to the Intensive Care Unit (p<0.05). 4 patients presented respiratory infection, 3 of them of GA group.

Conclusions: Endovascular stroke treatment is feasible under monitoring or conscious sedation and allows acute treatment of patients in a stroke unit. GA may be associated with endovascular treatment delay and worse clinical outcome.

142 Acute stroke: emergency management, stroke units and complications

DOES HISTORY OF CANCER INCREASE THE RISK OF INTRACRANIAL HEMORRHAGE IN PATIENTS WITH AIS TREATED WITH TPA?

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Background: Intravenous thrombolysis is the only approved specific therapy for acute ischemic stroke (AIS). It carries a risk of hemorrhagic complications. Cancer or history of cancer may increase the risk of hemorrhage however, this issue has not been systematically studied. Our study addresses the question: Does history of cancer increase the risk of intracranial hemorrhage in patients with AIS treated with tPA?

Methods: We conducted a case-control study, the population included all AIS patients admitted to Saint Louis University Hospital and treated with tPA during 2009. Outcome of interest was intracranial hemorrhage, exposure of interest was history of cancer. Demographic data, admission NIHSS, glucose level, and blood pressure were collected. Data were analyzed using t test, chi square, Fisher test and logistic regression as appropriate.

Results: One hundred and ten patients were included, 11 had history of cancer, mean age was 65 years and 85% were Caucasian. There were no significant differences between individuals with and without history of cancer with regards to hypertension, diabetes, race, admission glucose level, admission NIHSS, proportion of patients discharged home or deaths. A significantly greater proportion of women had history of cancer. The overall rate of all hemorrhages was 18%. The rate of symptomatic intracranial hemorrhage (parenchymal hematoma) was 6.4% and there were no significant differences between those with and without history of cancer.

Conclusion: In our population of 110 patients with AIS treated with intravenous thrombolysis, history of cancer was not associated with an increased risk of intracranial hemorrhage. Our sample is small and from a single center therefore our Results may not be generalizable. While our Results are encouraging, there is a need to confirm them in a larger prospective study.

143 Acute stroke: emergency management, stroke units and complications

ENDOVASCULAR TREATMENT OF ACUTE STROKE: A DESCRIPTIVE STUDY OF 34 PATIENTS

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Objective: We present the Results of endovascular acute stroke treatment after implementation of a Neurointerventionist Unit in a Spanish tertiary hospital.

Patients and Methods: Ischaemic stroke patients of less than 4,5 h receive iv rtPA when indicated. Endovascular treatment is performed when arterial occlusion is demonstrated and no recanalization after iv rtPA is observed after one hour, or in patients in whom it is contraindicated.

Results: 34 patients were treated (57% male, mean age 57.6±14); 73.5% were anterior circulation (AC) strokes and 30% posterior circulation (PC) strokes. Basal NIHSS was 17[13-22]. The occluded vessel was MCA in 40%, carotid T in 26.5%, extracranial internal carotid artery in 6% and basilar artery in 26.5%. 50% had received iv rtPA. Regarding to procedure, thrombus retrieving with stent and proximal aspiration was performed in 21 patients, fibrinolytic drugs were used in 4 patients, stenting in 5 and other types of mechanical procedures in 4 patients. Duration of the procedure was lower in the stent-retrieving plus aspiration group compared to the rest of procedures (p 0.070). TICI ≥ 2 was achieved in 97% of the cases and ≥ 2b in 57.7%.

Median time to endovascular treatment was 331 minutes and door to endovascular needle time was 134 minutes. Symptomatic haemorragic transformation occurred in 5.8% and mortality was 12% in AC strokes and 44% in PC strokes. Good clinical outcome at three months (mRS≤2) was 52% in AC strokes and 33% in PC strokes.

Conclusions: Implementing endovascular treatment in acute stroke patients in a tertiary hospital is safe and effective. Clot retrievement with stent plus aspiration reduces duration of the procedure compared to other techniques.

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

231

RELATION BETWEEN THERAPY IN THE ACUTE STAGE OF CARDIOEMBOLIC STROKE AND RECURRENT EMBOLISM

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Background: The recurrence of embolism in acute cardioembolic stroke can have a major influence on the prognosis. To examine the relation between stroke therapy for prior embolic stroke and recurrent embolism, we evaluated treatments for stroke in subjects with and without recurrent embolism.
Subjects and Methods: Among acute stroke patients admitted to Tokai University Hospital between September, 2004 and August, 2010, 436 subjects with cardioembolic stroke (265 men, 171 women, mean age: 73±11 years old) were enrolled in this study. We retrospectively compared the treatments for acute embolic stroke during admission between the group that developed recurrent embolism and the group that did not.
Results: Of 436 subjects, 20 subjects (4.5%) had recurrent embolism (cerebral infarction: 16, others: 4) during admission. Among initial treatments for embolic stroke, the frequencies of intravenous injection of tissue plasminogen activator (t-PA) (10% vs 15%), administration of anti-intracranial edema agents (100% vs 96%) and administration of a neuroprotective agent (edaravone, 60% vs 72%) were not significantly different between the two groups. However, the frequency of anti-coagulation therapy (warfarin or heparin) was significantly lower in the group with recurrence than in the group without (65% vs 88%, $P<.01$).
Conclusion: Recurrent embolism in patients with acute cardioembolic stroke was more frequent in patients who did not receive anticoagulant therapy during admission.

IN THE FIELD STROKE ASSESSMENT TOOL FOR PARAMEDICS: THE "HUNTER 8"

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Background: A trial is been undertaken of a Pre-hospital Acute Stroke Triage (PAST) protocol that includes pre-hospital assessment and rapid transport (road or road/air) of patients from a rural catchment to the major stroke centre, John Hunter Hospital in Newcastle, Australia. It is vital patients are assessed accurately to correctly identify patients potentially eligible for thrombolysis as the protocol increases the use of resources (particularly the helicopter). We aimed to develop and validate an assessment tool with mandatory criteria for activation and a cut-down version of the National Institutes of Health Stroke Scale (NIHSS) for use by paramedics in the pre-hospital setting.
Method:
– Workshop for senior ambulance and hospital Acute Stroke Team (AST) determined the mandatory criteria and most suitable NIHSS items;
– Paramedic training package developed and delivered;
– Data collected for all protocol activations;
– Agreement between the paramedic and AST assessment (both performed independently on hospital arrival) and activation threshold agreement (NIHSS ≥4) was measured.
Results: A tool with 7 mandatory criteria and 8 NIHSS items was developed. From April 2009 to August 2010 there were 24 activations with 15 transported by road and 9 by road/air with a median straight line distance travelled of 67km (min 39, max 134.2 km). 9 patients were thrombolysed (number needed to transport to treat= 2.7) and 4 were stroke mimics. 18 full datasets were available for analysis as 6 did not have paramedic scores done on arrival. Agreement on activation was 94.4% (Kappa= 0.82, p= 0.0002). Agreement of NIHSS scores on arrival was very good (Intraclass Correlation Coefficient = 0.80, p < 0.0001).
Conclusion: This 8 item version of the NIHSS has extremely good agreement between paramedics and AST and the assessment tool (Hunter 8) Results in accurate activation of the protocol. The trial of the Hunter 8 will be extended to the hospital metropolitan catchment to further validate.

SCREENING OF THE ISCHEMIC STROKE IN AN EMERGENCY CALL CENTRE: TESTING THE FAST SCORE

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Objectives: A key element of the alert for ischemic strokes is the recognition of symptoms by witnesses and by the initial call takers. According to current data, 52% of the strokes suspected during the initial call are later confirmed; this highlights the value of a simple and quick score adapted to call takers. We evaluated the feasibility of the FAST (Face, Arm, Speech, Time) score in a call centre caring for health emergencies.
Methods: From February to March 2010, we introduced a specific stroke card following the FAST score and had all the first responding operators trained. During this period, the FAST score was widely applied, not only for sudden onset of a neurological deficit, but for falls, headaches, vertigo and dizziness. Each and every of these calls was then sent on to a medical doctor for evaluation. Such calls were recorded for a month. The judgement of the call takers using the FAST score was then compared with the medical evaluation.
Results: In one month, 86 calls were included, 49 of these were considered strokes according to the FAST score. Among these patients, 33 were evaluated stroke suspects by the medical doctor. In the FAST non-stroke group, none were considered as suffering from stroke after the medical evaluation. This points to a high sensitivity (100%) and a specificity of 70% in our type of practice.
Conclusion: The FAST score could be a simple and reliable tool for triage in the setting of our call centres. This must be confirmed through a more comprehensive study.

QUALITY OF ISCHEMIC STROKE CARE IN SIRIRAJ HOSPITAL

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Background and purpose: Data concerning quality of acute stroke care and outcome are lacking in developing and underdeveloped world. This study aimed to access quality of acute stroke care and short term outcome in a tertiary care center in Thailand.
Methods: Relevant indicators of quality of acute stroke care including rate of stroke unit admission, intravenous rt-PA use, acute administration of aspirin, in-hospital complications and outcomes were prospectively collected in consecutive acute ischemic stroke patients admitted at Siriraj Hospital, Thailand. Disability level at discharge was measured by modified ranking scale.
Results: There were 1,393 ischemic stroke patients included between July 2007-August 2009 with a mean age (±SD) of 65.2±13.5 years. Rate of stroke unit admission, intravenous rt-PA use, acute administration of aspirin were 61%,4%,97% respectively. Ultrasound carotid was performed in 54%. Mean length of stay (±SD) was 11.8±16.1 days. Antiplatelet, anticoagulant, antihypertensive and statin medications were given prior to discharge at 85%,11%,36%,78% respectively. In hospital complications including pneumonia, UTI and seizure were found in 14%, 10%, 4% respectively. Good outcome (mRS 0-1) was 19% whereas poor outcome (mRS 5-6) was 21% at discharge.
Conclusions: Quality of acute stroke care in our study did not qualify standard in many domains. Strategic plan for acute stroke care improvement is urgently needed.

INTRAVENOUS THROMBOLYSIS APPLIED WITHIN 90 MINUTES. WHO ARE THE LUCKY ONES?

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Background: Intravenous thrombolysis using recombinant tissue plasminogen activator (IV-tPA) applied within 90 minutes of stroke onset has shown greater efficacy. However, this time is hard to achieve. Our goal is to analyze the characteristics of this group of patients.
Methods: A prospective registry was assembled using patients treated with IV-tPA at five hospitals in the Madrid Stroke Network. Patients were divided in two groups by time to thrombolytic treatment (<90 minutes and ≥90 minutes). Sex, vascular risk factors, admission glycaemia, stroke aetiology, basal National Institute Health Stroke Scale (NIHSS) score, prior stroke, ipsilateral transient ischaemic attack (TIA) and in-hospital stroke were taken into account. The primary outcome measures were the percentage of cerebral symptomatic haemorrhagic transformations, the modified Rankin scale (mRs) and the mortality at three months. We used Mann-Whitney for quantitative variables and chi-square for qualitative variables.
Results: 1,127 patients were registered. Only 80 patients were treated in the first 90 minutes (7.1%). There were no significant differences between groups in age, sex, vascular risk factors, admission glycaemia, stroke aetiology, basal NIHSS score or prior stroke. Patients treated in the first 90 minutes had more often an ipsilateral TIA (27.8% vs 5.6%, p <0.05) and they had a higher incidence of in-hospital stroke (45% vs 4.8%, p <0.05). No significant differences were found in evolution: symptomatic hemorrhagic transformation (3.8% vs2.7 p> 0.05) and mRS (mRS 0-2 61% vs58% p> 0.05).
Conclusion: The percentage of patients who benefit from very early intravenous thrombolysis is limited. A history of ipsilateral TIA or in-hopsital stroke was the only distinguishing features. The lack of difference in the evolution can be attributed to the small percentage of patients treated very early.

149 Acute stroke: emergency management, stroke units and complications

SYMPTOMATIC INTRACEREBRAL HEMORRHAGE IN WARFARIN TREATED PATIENTS RECEIVING THROMBOLYTIC THERAPY FOR ACUTE ISCHEMIC STROKE

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Background: Pre-admission warfarin use in patients receiving thrombolytic therapy for acute ischemic stroke has been reported to cause a 10-fold greater risk for symptomatic intracerebral hemorrhage even with an international normalized ratio (INR) less than 1.7. It has been recommended to not use thrombolytic therapy in these patients.
Methods: In our series of 222 consecutive patients treated with intravenous thrombolytic therapy between April 2009 and December 2010 we analyzed the rate of symptomatic intracerebral hemorrhage in patients previously treated with warfarin or antiplatelet medication. Warfarin-treated patients with an INR less than 1.7 received intravenous thrombolysis. The occurrence of intracerebral hemorrhage was determined by CT.
Results: 6.8% of all patients receiving thrombolytic therapy were taking warfarin when admitted to our hospital, with a median INR of 1.5 (range: 1.2-3.0). 43.7% of all patients were on aspirin 100 mg, 2.7% were on clopidogrel 75 mg, 1.8% were on both aspirin and clopidogrel; 43.7% were on no antithrombotic medication. The overall rate of symptomatic intracerebral hemorrhage was 5.5%. In patients taking warfarin it was 13.3%, and in patients without prior treatment was 9.2%. The only significant association for the occurrence of symptomatic intracerebral hemorrhage was a previous, but not current history of cancer.
Conclusion: Our data show an insignificantly greater rate of symptomatic intracerebral hemorrhage in patients receiving thrombolytic therapy who had pre-admission use of warfarin with an INR < 1.7 compared with patients without previous treatment. There is an option for use of thrombolysis in patients with an INR < 1.7.

150 Acute stroke: emergency management, stroke units and complications

CHALLENGES OF A LARGE CLUSTER RANDOMISED CONTROLLED TRIAL: BARRIERS AND ENABLERS TO IMPLEMENTING PROTOCOLS FOR FEVER, HYPERGLYCAEMIA AND SWALLOWING DYSFUNCTION IN THE QUALITY IN ACUTE STROKE (QASC) PROJECT

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Background: Cluster Randomised Controlled Trials (CRCT) are more complex to design, require more participants to obtain equivalent statistical power, require more complex analyses and pose unique challenges in their execution when compared to trials that randomized individuals. The Quality in Acute Stroke trial, a prospective, multicentre, single-blind, CRCT evaluated the Introduction of a complex intervention to improve management of fever, hyperglycaemia and swallowing difficulties in 19 Acute Stroke Units (ASU's) in New South Wales (NSW), Australia. The need to identify and overcome barriers before implementation of any change is well documented.
Methods: Clinical protocols were developed by panels of clinical experts; one for each clinical focus, namely, fever, hyperglycaemia and swallowing. Two multidisciplinary on-site workshops were conducted at each intervention ASU (n=10) to identify barriers and enablers to Introduction of the clinical protocols.
Results: Over one third of the attendees at both the workshops were senior nurses. The main barriers perceived to the successful Introduction of the clinical protocols were: resistance to change; increased workload; adequate skill mix to manage complex interventions; lack of equipment or lack of dedicated equipment; patient safety concerns; the impact on other research; and the blurring of professional boundaries. The main enablers were: the presence of clinical champions; support of medical staff, nursing management and allied health; easy adaption of current protocols, care plans and local policies; dedicated ASU staff.
Conclusion: Identification of barriers and enablers before implementation of an initiative to change clinician behavior is vital. The workshops allowed clinical staff the opportunity to identify barriers and make minor, local modifications to the protocols to aid successful uptake. This paper will also address some of the other challenges in managing a large, multisite CRCT.

151 Acute stroke: emergency management, stroke units and complications

IMMUNONUTRITION-ORIENTED FEEDING THROUGH A GASTRO-INTESTINAL TUBE IN SERIOUS ACUTE STROKE PATIENTS

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Background and purpose: Serious acute stroke patients are frequently led to protein-energy-malnutrition due to eating problems, secondary complications occur and result in worse clinical outcome. The purpose of our prospective study is to investigate the effectiveness of immunonutrition-oriented feeding (INOF) through a gastro-intestinal (GI) tube on management of serious acute stroke patients.
Methods: Inclusion criteria for retrospective analysis were patients, (1) who were admitted to our hospital from November 2008 to December 2010, (2) who were provided with INOF through GI tube due to serious neurological deficits within 48 hours from admission. Patients who were in comatose condition, suffered from severe aspiration pneumonia on admission, and dead within 5 days from stroke onset were excluded. Either IMPACT® or MEIN® was used as INOFs. Evaluated were 1) NIHSS score, Albumin value, and CONUT score (CONtrolling NUTritional status) on admission, 2) NIHSS score, Albumin value, and CONUT score at expiration, 3) maximum values of C-reacting protein (CRP), white blood cells (WBC), fast blood sugar (FBS) during hospitalization, 4) in-hospital death, and 5) some adverse effects.
Results: During the study period, consecutive 842 acute stroke patients were admitted to our institution, 100 patients among them were included for analysis. IMPACT® was provided in 50 patients and MEIN® in the rest. On admission and at expiration NIHSS score was 20 and 20, albumin value was 4.0 and 3.2, and CONUT score was 1.0 and 4.0. Malnutrition was prevented. Maximum value (median) of WBC, CRP and FBS were 10350, 4.91 and 140.5 during hospitalization. Among them, 10 patients were discontinued owning to some adverse effects, but discontinuation rate (10%) was low. In-hospital death was 9 (9%) due to serious stroke. There were significant differences statistically between on admission and at expiration in every evaluation items (p<0.01).
Conclusions: Immunonutrition-Oriented feeding through a GI tube is useful in management of serious acute stroke patients.

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

233

UNDERSTANDING OF THE TERM CONSCIOUS WHEN USED DURING EMERGENCY CALLS FOR SUSPECTED STROKE

S.P. Jones[1], J.J. McAdam[1], A.S.R. McLoughlin[2], J.M. Gibson[1], M.J. Leathley[1], C.L. Watkins[1], On Behalf of the Emergency Stroke Calls: Obtaining Rapid Telephone Triage Group
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Background: Stroke can result in an altered level of consciousness. When someone calls the emergency medical services regarding a suspected stroke, they are routinely asked if the patient is conscious. In general, the understanding of the term conscious by lay people is known to be poor. This study aimed to explore the understanding of the term conscious when used during emergency calls for suspected stroke.

Methods: Emergency stroke calls which resulted in the patient being admitted to one hospital over a 12 month period were identified as part of a larger study. The recordings of the emergency calls were listened to and analysed based on the caller's response to the question: "is the patient conscious?" Calls were identified where the caller was considered not to have understood the term conscious, i.e. where the call handler had to ask more than one question about the patient's level of consciousness.

Results: There were 643 calls, 44 (7%) of which demonstrated a lack of understanding of conscious. Twenty-six callers (59%) were family members and 35 (80%) of calls were made from the patient's home. The mean age of patients was 75 years and 21 (48%) were female. Three types of caller misunderstanding and interpretation were identified: 1. Difficulty in assessing conscious level; 2. Clarification needed to determine conscious level; 3. Conscious level confused with breathing.

Conclusions: The term conscious is not always understood by people who contact the emergency medical services about suspected stroke. The caller's difficulty in communicating levels of consciousness may be misleading and also leads the caller handler to use other questions in order to identify the patient's level of consciousness: this may waste valuable time. Further work is required to identify optimal Methods to elicit information about conscious level.

No conflicts of interests.

ENDOVASCULAR RECANALIZATION WITH INTRA-ARTERIAL THRMOBOLYSIS IN A PATIENT WITH ACUTE BODER-ZONE INFARCTION CAUSED BY OCCLUSION OF THE DISTAL INTERNAL CAROTID ARTERY

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Background: Recently, Intra-arterial thrombolysis with endovascular recanalization therapy is being increasingly performed in the treatment of acute symptomatic intracranial arterial occlusion, but it is limited to 6 hours post-stroke onset. We present a case of acute border-zone infarction secondary to occlusion of the distal internal carotid artery (ICA) that was successfully recanalized 2 days after symptom onset.

Case: A 61-year-old man with a history of smoking presented 24 hours after he developed anosognosia and progressive left paresis with a NIHSS score 10. Diffusion-weighted images (DWI) showed acute right cortical and subcortical border-zone infarctions between anterior, middle, and posterior cerebral artery territories. Diagnostic cerebral angiography showed total occlusion of the cavernous portion of the right ICA. We decided to treat this patient with intra-arterial thrombolysis because of progressive hemiparesis, poorly developed collaterals, and possible passing of the microcathter and microguidewire through thromboembolic filling defect. Treatment was initiated 2 days after symptom onset by mechanical clot disruption with microcathter and microguidewire and local administration of urokinase. Because only a partial recanalization was achieved, carotid artery stenting was then performed and complete recanalization was achieved. DWI performed on the next day showed subtle increased infarct volume. The patient was discharged from hospital 23 days after treatment with NIHSS 5. The follow-up cerebral angiography after 7 months showed well preserved patency of the right ICA without restenosis.

Conclusion: Combined intra-arterial thrombolysis and stenting can recanalize and improve neurologic outcome in selected patient with acute border-zone infarction caused by symptomatic intracranial arterial occlusion. This case suggests that further recanalization therapy might be considered for acute border-zone infarction associated with distal ICA occlusion.

TELESTROKE IN VOJVODINA, SERBIA – FIRST RESULTS

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Introduction: The objective of telemedicine is provision of high quality medical services that are more convenient for the patient. In addition, telemedicine reduces sick leave and medical care costs, improves the quality of service by spreading the network of available specialists and sub-specialists, and improves collaboration between primary, secondary and tertiary health care practitioners. Finally, it reduces the time of waiting for diagnostic evaluation, thereby improving health care outcomes and patient's satisfaction with medical services.

Telestroke in Vojvodina: Telestroke in Vojvodina (www.telestroke-vojvodina.com) is a project initiated with an aim to link through audio-visual communication nine regional hospitals in the province of Vojvodina, Serbia with the telestroke hub at the stroke unit at the Clinic of Neurology of the University Hospital in Novi Sad. The hub with trained vascular neurologists would thus become available to regional hospitals for teleconsultation 24 hours a day, 7 days a week. The system requirements for each participant are Windows 2000 with fast videoconference system, 22-inch monitor and video camera and DICOM interface with local CT or MRI.

Results: The first audio-visual link was established in May 2010. So far, two regional hospitals have been linked with the hub stroke unit, and seven thrombolyses have been performed under telesupervision by the hub stroke unit. The treatment outcomes of the thrombolyses are favorable and equivalent to those of patients receiving thrombolysis in a tertiary-level stroke unit.

Conclusion: Our first Results are promising and show significant benefits of the application of telemedicine in the management of stroke patients.

THE SAFETY AND EFFECTIVENESS OF TREATMENT WITH RT-PA PATIENTS WITH ACUTE ISCHEMIC STROKE AND COEXISTENCE CHRONIC KIDNEY DISEASE

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Background and purpose: Patients with chronic kidney disease (ckd) special with endstage renal disease are at high risk for cardiovascular events including ischemic stroke and TIA. The purpose of this study was evaluation of safety and effectiveness of treatment with rt-PA patients with acute ischemic stroke (ais) and ckd.

Material and Methods: Between September 2006 and January 2010 in the stroke unit in Sandomierz 1034 patients with ischemic stroke were treated, including 150 patients (aged 42-88, mean 69,11±9,78) treated with rt-PA (14,51%). We analysed status of the patients in the moment of admission, one month and 3 month after symptoms onset according to National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Score (mRS) and risk of death.

Results: 26 of patients fulfilled to criterion of ckd (21 patients -III stage GFR 30-59 ml/min/1,73m^2; 3- IV stage GFR 15-29 ml/min/1,73m^2; 2- V stage GFR <15 ml/min/1,73m^2). In the moment of admission the average neurological conditions in NIHSS 12,11±4,76 (8,00) (patients without ckd) and 12,81±5,36 (7,00) (patients with ckd), after 3 months respectively 3,22±3,98 (5,0), 3,47±4,19 (7,0) were evaluated (p=0,92). After 1 month 57,52% (without ckd) and 65,0% (with ckd) of patients were independent (mRS 0-2) (p=0,53). After 3 months were respectively 67,59% and 68,42% (p=0,94). After 1 month 8,06% of patients is 1st group and 23,08% in 2nd group died (p=0,082) and after 3 months respectively 12,1% and 26,92% (p=0,132).

Conclusion: We didn't observe difference between status of patients treated rt-PA with and without ckd evaluated after 3 months.

The renal dysfunction increase risk of late death in group of patient with acute ischemic stroke treated rt-PA (without statistical significance).

SHOULDER PAIN DURING STROKE ADMISSION: A HOSPITAL-BASED STUDY

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Background: Shoulder pain is a known complication after stroke, but data on prevalence and predictors in unselected stroke populations are limited. Our aim was to evaluate the prevalence and predictors of in-hospital shoulder pain in patients admitted with stroke in a tertiary hospital.
Methods: Retrospective analysis of prospectively collected data of patients admitted to a tertiary hospital with stroke. Clinical and demographic findings were analyzed. The presence of shoulder pain and arm motor function were obtained from medical and physical therapy reports.
Results: A total of 221 patients (mean age 71.7±15.1 yo, 55% males) were evaluated from October 2008 to October 2010 of which 04 (1.8%) had shoulder pain. There were of 204 (92.3%) patients with ischemic stroke and 17 (7.6%) with intraparenchymal hemorrhage. The median NIHSS at admission was 4[1,8]. The median length of stay (LOS) was 8 days [4,14].Most patients who had motor impairment (90.8%) were on daily physical therapy during hospital stay. All patients that had shoulder pain had an ischemic stroke. Patients who had shoulder pain and those who did not were similar in age (71.7±22.3yo vs 71.7±15.1 yo, p=0.9),stroke severity (median NIHSS 9.2 [2.2,16] vs 5.9 [1,8], p=0.53) and physical therapy prescription. Patients who had shoulder pain had longer LOS than those without (median 70 days [29,135.5] vs 8 days [4,14], p=0.03) and a higher frequency of previous motor deficit (25% vs 3,2%, p=0.02). After multivariate logistic regression analysis, only LOS was an independent predictor of shoulder pain (OR1.05, p=0.02).
Conclusion: In our series shoulder pain was infrequent during stroke admission. Only LOS was a predictor of shoulder pain. It is possible that shoulder pain occurs as a late complication, and therefore we were not able to detect it during hospital admission in some patients. Patients with prolonged LOS after a stroke should be actively screened for shoulder pain as they seem to be at higher risk.

INTRAVENOUS TISSUE – TYPE PLASMINOGEN ACTIVATOR THERAPY FOR ISCHEMIC STROKE: NIS STROKE TEAM EXPERIENCE NOVEMBER 2006 - DECEMBER 2010

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Background: To present the preliminary experience of implementing intravenous thrombolytic therapy for acute ischaemic stroke in Stroke unite, Department of neurology, Clinical center Nis, South Serbia.
Methods: This prospective and observational study included 131 consecutive patients with an ischaemic stroke treated in our Stroke unit within 3-6 hours from the onset of symptoms, between Novembar 2006. and December 2010. Patients were selected and treated in accordance with the American Heart Association guidelines. Primary safety and outcome variables were on MRI performed at 24-36 hours, mortality and independence at 90 days. Intracranial and systemic haemorrhagic complications were recorded.
Results: 131 patients (76 men and 55 women) with a median age of 69 years ±13.2 years (range 24-79) received thrombolytic treatment (approximately 3,4% of 3853 patients with ischemic stroke). The median time from stroke onset to rt-PA therapy was 110 minutes (rang 20-180) and from arrival in the emergency room to the start of thrombolysis 80 minutes. Baseline median NIHSS was 16 (range 4-44). 88 patients exhibited early clinical improvement, defined as a decrease in NIHSS score. Median NIHSS before discharge was 4,2 points. At 3 months, 80% (95% Ci, 47,9-64,1) of patients were functional independent. Six patient developed a haemorrhage. 12.9% patients died within 3 months of stroke.
Conclusions: The use of intravenous t-PA by experienced neurologists in Stroke unites, is safe and it is associated with a favourable outcome, without excess risk, similar to that observed in clinical trials. Successful experience with this therapy depends on organization of the treating team and adherence to published guidelines.

INTRA-VENOUS THROMBOLYSIS FOR ACUTE CEREBRAL ISCHAEMIA IN BELGRADE, SERBIA: COMPARISON WITH A WESTERN EUROPE STROKE CENTRE (LILLE, FRANCE)

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Background: a worse socioeconomic situation is associated with worse outcomes in stroke. Whether it influences also outcomes in patients treated by intravenous (i.v.) thrombolysis remains unknown. The aim of our study was to test the hypothesis that outcomes are less favourable in patients treated by i.v thrombolysis in Belgrade, Serbia, than in Lille, France.
Methods: we compared outcomes at day-7 and month-3, between 123 consecutive patients from Belgrade and 273 from Lille.
Results: at month-3, 49.6% patients from Belgrade had a modified Rankin scale (mRS) 0-1 or similar to the pre-stroke mRS and 11.4% were dead. There was no significant difference of outcome with patients from Lille, but patients from Belgrade were 16 years younger (p<0.0001), had a 10 mm Hg higher diastolic blood pressure (p<0.0001), were more likely to be men (odds ratio [OR]: 2.40; 95% confidence interval [CI]: 1.52-3.78), to have hypercholesterolemia (OR: 3.01; 95% CI: 1.93-4.70) or to be smokers (OR 2.24; 95% CI: 1.43-3.51), and less likely to be alcoholic (OR: 0.27; 95% CI: 0.09-0.79), or under antiplatelet agents before stroke (OR: 0.21; 0.12-0.36). They arrived 27 minutes earlier in hospital (p<0.0001), but their door-to-needle time was 37 minutes longer (p<0.0001). Compared with a subgroup of age-matched patients from Lille, they tended to have worse outcomes.
Conclusion: outcomes are good in Belgrade and did not differ from those from Lille, but these excellent Results are in part the explained by the young age of the patients.

ANALYSIS OF PATIENTS WITH ACUTE ISCHEMIC STROKE TREATED WITH THROMBOLYSIS IN OUR CENTER IN TWO YEARS. HOW TO INCREASE NUMBER OF PATIENTS ELIGIBLE FOR TREATMENT?

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Background: In Hungary people have insufficient knowledge about symptoms and importance of emergency of cerebrovascular (CV) diseases. The rate of thrombolytic treatments (TT) is still low. Regions of admission to general neurology and stroke centers are often different. Our aim was to find relationships between factors, in order to increase the number of TT-s.
Subjects and Methods: All patients receiving TT in our center in 2009-2010 were included in the analysis. Date of admissions (season, weekend, time of day), mode of referral (ambulance/family physician), location of CV event (region, location, hospital). Rates of admissions for acute stroke, thrombolysis alarms (potential TT within time-window based on on-site examination) and delivered TT were analyzed on a monthly basis.
Results: In two years, 32 of 132 potential patients received TT (21 male, 11 female, mean age: 69.3±9.51 years). This is higher than the average rate in Hungary, based on the population of the hospital region. During this period, 2521 patients were admitted for acute stroke, including a large number of elderly patients with serious medical condition. Causes of non-treatment included bleeding, undetected symptoms, delayed transfer to hospital, laboratory abnormalities, seizure and rapid improvement of symptoms. Initial symptoms were detected by the ambulance service in 78% of patients. Peak times for TT were between 12-19 hours, November and December. A similar number of patients were hospitalized at the weekends and on workdays. Most admissions were from the region for general neurology. Age, gender, NIHSS and modified Rankin scale at the time of admission influenced success of treatment, they were not useful for enrolling more patients.
Conclusion: Our Results suggest that people's more efficient education about stroke and standardization of stroke care may increase number of TT-s. Competence of the ambulance service and continuous communication with the stroke center are essential.

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

235

"STAND UP (BE)FOR(E) THROMBOLYSIS" -A COMPLEMENTARY SCALE TO EVALUATE PATIENTS WITH MILD STROKE SYMPTOMS AND/OR POSTERIOR CIRCULATION STROKE

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Patients (pts.) with posterior circulation stroke may present with symptoms not reflected on the NIH Stroke Scale, including vertigo, nausea, imbalance and disturbances of gait. Some of these symptoms are not present when evaluating patients in the supine position. Consequently, pts. with mild deficits do not receive an NIHSS score high enough in respect to severity of future loss of function. We devised an additional scale to include symptoms indicative of posterior circulation compromise in order to have such pts. more readily considered for thrombolysis.

The Stand Up (Be) for(e) Thrombolysis (SUBT) scale is conceived as a complementary scale to NIHSS. It consists of 3 basic tests to assess deficits of posterior circulation stroke, but which are not obvious when examining patients in the supine position. The scale (0-3) is meant to unmask such deficits. Normal gait absent Romberg's sign 0, Romberg's sign 1, Dependent gait 2, Unable to walk 3.

This ongoing study included so far 5 stroke pts. presenting in the time window for thrombolysis. All scored < 5 on the NIHSS (0-2-2-3-2) when evaluated in the supine position. They were subsequently scored using the SUBT scale in the standing position.

Two pts. who scored 2 and 3 respectively on the NIHSS were each given 2 additional points when evaluated with SUBT. They were administered thrombolysis and recovered completely. The other three patients either scored 0 or 1 on the SUBT. They recovered spontaneously.

Scoring neurological deficits not included in the NIHSS with an additional scale reflecting severity of compromise in the posterior circulation may provide the clinical evidence to consider thrombolysis in spite of a low NIHSS score. This is especially useful in an ER setting where patients routinely are examined by non-specialists or less experienced physicians, thus leaving a subgroup of stroke pts. at risk of not being brought to the attention of a neurologist and/or passing the time window for thrombolysis.

FACTORS INFLUENCING HEMORRHAGIC TRANSFORMATION IN ACUTE ISCHEMIC PATIENTS WITHOUT THROMBOLYIS

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Background: hemorrhagic transformation is one of the threatening complications of acute ischemic stroke. Our aim was to investigate the clinical parameters increasing the risk of transformation.

Methods: clinical and pathological data of 322 pts were analyzed. The patient had symptoms of acute ischemic stroke and all died during the hospitalization period and all pts. were autopsied after death and particular neuropathological investigations of the brain could be performed. None of the patients were treated by iv. or ia. thrombolysis and no therapeutic anticoagulation have been applied.

Results: from 322 patients 89 show ed the signs of hemorrhagic transformation at brain autopsy. The most important clinical parameters were (second number:patients with hemorrhagic trasnformation) age 72,1±11,3 vs. 75.3±10.6, hypertensives 75,1% vs 68,5, diabetes 30,9% vs 43,8%, heparin (only for DVT prevention) 18% vs. 19.1%. The blood sugar showed significant differences between the two groups: 7,8±3.9 vs 89,9±3,5.

Conclusion: the elevated admission blood sugar can increase the risk of hemorrhagic transformation in acute stroke patients.

PULMONARY COMPLICATIONS IN PATIENTS WITH STROKE

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Background: Occurance of acute bacterial lung infectuns affects the course of disease and outcome in stroke patients. Infection is the most common stroke complication. Aim of the study was to explore the frequency of hypostatic and aspiration pneumonia, their risk factor and their effect on outcome in patinets with acute stroke.

Methods: In this retrospective study, we evaluated patients with stroke who were hospitalized at the Department of Neurology in Nis, between January to December 2010. There were a total of 1231 patients with stroke. 801 (65,07%) of 1231 patients with stroke, had ischaemic stroke, and 430 (34,93%) had haemorrhagic stroke. Patients were evaluated and had the same investigations with anamnestic, clinical, neurological, biochemical analisys, physical examination by a specialist for pulmonary diseases, lung X-ray, Color-Doppler of the neck blood vessels, interictal EEG and neuroimaging (CT of lung, CT of brain, MRI of brain, MRA angiography) and variables which were compared.

Results: Of a total of 1231 patients with stroke, 56 (4,55%) of them had pulmonary complications within 10 day from the event. There were 35 male and 21 female patients, age from 43 to 85 years. Pulmonary infections in all of the patients was confirmed by x-ray immaging and biochemical analisys. 27 (48,21%) patients had lobar pneumonia, 21 (37,50%) had bileteral bronchopneumonic changes and 8 (14,29%) had pleural effusion. All of the patients were higly febrile, with increased sedimentation and leucocitosys with dominant neutrophiles. Despite the intensive antibiotic treatment, using two or more antibiotics in combination, 12 patients has died.

Conclusion: Hypostatic and aspiration pneumonia are frequent complications of stroke associated with poor outcome. Regarding to this fact, an intensive prevention of complications is necessary immediately after hospitalization.

2 CASES OF PATIENTS DIALYZED BECAUSE CHRONIC RENAL FAILURE (CRF), AND ACUTE ISCHEMIC STROKE (AIS) TREATED WITH RT-PA

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Background: During September 2006 and January 2010 we treated 150 stroke patients with rt-PA i.v. In this group were 26 patient with chronic kidney disease. 2 of them were hemodialyzed because ultimate renal failure. We present these two cases.

Material: 70-years old woman admitted to our unit with right hemiparesis, gaze paresis and aphasia, NIHSS – 15. She was hemodialyzed for many years because CRF. She had history of circulatory insufficiency. Level of creatinine was 518umol/l, level of potassium was 4,88mmol/l. Haematology and coagulation tests were normal. We decided to treat this patient with i.v. rt-PA. Just after infusion her status slightly improved – NIHHS 9. During next days standard dialysis was performed. At 3th day of hospitalization patient deteriorated, we observed massive hemorrhage from gastrointestinal tract and patient died.

The second patient was 54 – years old woman with history of CRF, coronary disease, hypertension and permanent atrial fibrillation. On admission she had mixted aphasia and right hemiparesis, NIHSS - 16. Level of creatinine and potassium were respectively: 553 umol/l and 6,69 mmol/l., other labolatory tests were normal. She received i.v. rt-PA. We observed partial diminishing of symptoms – NIHSS 10. During next days, her status gradually improved, standard hemodialisis were performed. We did not observed any side effect or complications. She was discharged independent, walking without help, with mild aphasia and paresis right hand, NIHSS – 3.

Conclusions: As thrombolytic treatment remains the only effective treatment for AIS. We should offer this treatment as many patients as possible. It requires individual approaching to all stroke patients, permanent analysis of inclusion/exclusion criteria and further large studies.

TRANSCRANIAL DOPPLER IN UNSTABLE VERTEBROBASILAR STENOSIS

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Introduction: Atherothrombosis of vertebrobasilar (VB) system has a poor prognosis with high mortality rate. The gold standard for diagnosing of VB stenosis remains digital subtraction angiography. TCD with power M-mode (PMD) can

be used with high reliability. The goal of treatment for acute VB thrombosis is recanalization of occluded vessel.

Case report: A previously healthy 64-year-old man was presented in the emergency room 6 hours after onset of vertigo, nausea, vomiting, facial and tongue numbness followed by left-sided paresis. At examination the patient had a brainstem syndrome, with dysarthria, right internuclear ophthalmoplegia, and left hemiplegia (NIHSS 14). CT showed a mild infarct in the right pons. After admission, about 90 minutes later, progressive neurologic deterioration was noted, patient became somnolent, with a new severe right-sided hemiparesis and locked in syndrome (NIHSS 25). Repeated CT showed no change. PMD-TCD showed minimal flow signal of BA, blunted flow signal in the right VA, and flow increase in the both MCAs suggestive for near-occlusion of BA and the right VA and collateral supply from anterior circulation. About three hours later, the patient regained consciousness and his right hemiparesis resolved completely (NIHSS 14). Repeated PMD-TCD showed flow velocity increase in BA, and better but still blunted flow signal in the right VA suggestive partial recanalization of BA. MRI revealed multiple subacute midbrain infarctions. MRA showed high-grade stenosis in the middle segment of BA and severe stenosis of the right VA and dominant supply of PCAs through PComAs. The patient was discharged after two weeks with mild left central facial palsy (NIHSS 1).

Discussion: The outcome of acute VB occlusive disease depends on the clinical state at presentation, the length and location of the occlusion, the degree of recanalization, and the time to treatment. The rate of spontaneous basilar recanalization is low because the etiology of VB occlusion is usually in situ thrombosis of an atheromatous vessel. This case illustrates the importance of PMD-TCD monitoring of unstable VB stenosis and detection of early recanalization.

165 Acute stroke: emergency management, stroke units and complications

FORCED-SUCTION THROMBECTOMY OF ACUTE INTRACRANIAL INTERNAL CAROTID OCCLUSION: THE ROLE OF HIGHER RECANALIZATION ON OUTCOME

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Background and purpose: Ischemic stroke from acute intracranial distal internal carotid artery (ICA) occlusion usually carries a poor prognosis. Despite the intra-arterial (IA) revascularization therapies, the Results were still unsatisfactory. The aim of this study was to compare the outcomes between two endovascular techniques, the modified Penumbra System (mPS) and mechanical clot disruption (MCD), and to confirm the influence of recanalization on the outcomes.

Methods: By retrospectively reviewing 39 consecutive cases of acute distal ICA occlusions, we were able to compare the recanalization rates and functional outcomes at 3 months of the two IA techniques during two consecutive periods (May 2006 to February 2009: MCD technique [n=19], vs. March 2009 to August 2010: mPS technique [n=20]). Univariate and multivariate analyses were performed to determine the predictors of favorable functional outcomes.

Results: The successful recanalization rates over thrombolysis in cerebral infarction (TICI) 2 were significantly higher in the mPS group than in the MCD group (85% [17/20] vs. 32% [6/20]; p=0.001). The favorable outcomes at 3 months (modified Rankin Scale score 0-2) were 9 of 20 and 3 of 19 in the MCD group and the MCD group, respectively (16% vs. 45%; p=0.048). Binary logistic regression analysis was performed, and younger age and successful recanalization were independent predictors of favorable functional outcomes.
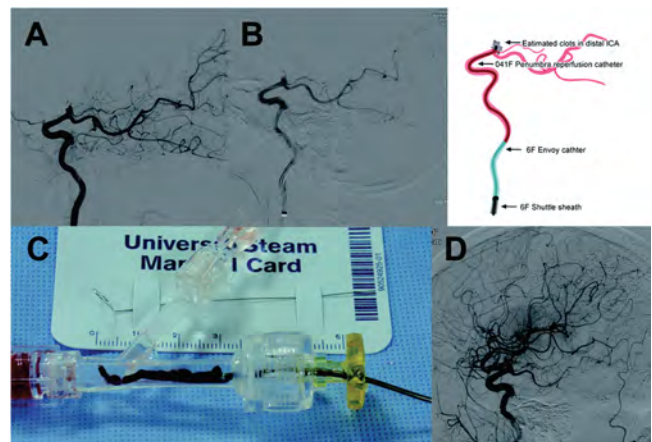
Figure 1. A. Lateral angiography showing acute occlusion of right distal internal carotid artery. B. The 041F Penumbra reperfusion catheter advancing to the occlusion and forced-suction thrombectomy. C. Retrieved 30mm-sized visible thrombi from the occlusion. D. The subsequent angiography demonstrating thrombolysis in cerebral infarction 3 recanalization.

Conclusion: Forced-suction thrombectomy using the mPS technique could be a viable option for acute distal ICA occlusion regarding the influence of recanalization on the clinical outcome.

166 Acute stroke: emergency management, stroke units and complications

SNAPSHOT OF IMPEDIMENTS IN THROMBOLYSIS IN AN ACUTE STROKE UNIT IN A LARGE GENERAL HOSPITAL IN UNITED KINGDOM (UK)

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Introduction: In recent years, there is a big push from UK government to increase the number of stroke thrombolysis backed up by resources, logistics for delivery, expertise and public awareness campaigns. However, although the number is slowly rising according to National Sentinel Stroke Audit data from 0.2% in 2006 to 1.8% in 2008, and likely to increase further when 2010 data is published, it still remains pitifully low. We set out to ascertain the main reasons for this in our unit.

Method: Medway Hospital is an associated teaching hospital in the Southeast of England serving nearly 0.5 million people. There is a hyper-acute stroke service with an acute stroke unit and arrangements for 24 hr thrombolysis. We looked at all the acute stroke patients being admitted in the unit over a three month period (April-June 2010), and collected data from their case notes, stroke register and imaging archives.

Results: There were 63 patients with new stroke, and 7 (11%) were thrombolysed. Numerically, the most common causes for not being able to thrombolyse were as follows: a. Advanced age (>80), n=23, 37%; b. Delayed presentation (> 3 hr), n=18, 29%; c. Unknown time of onset, n=15, 24%; d. Bleed, n=11, 17%; and e. Profound co-morbidity n=8, 13%. The latter was mostly associated with advanced age, and some had more than one impediment. The other causes like atypical presentation (n=5, 8%) delaying CT-head, low (<4) NIHSS or resolving symptoms (n=4, 6%), high (>25) NIHSS or severe stroke (n=3, 5%), and other pathology i.e. high BP, low platelets (<100), raised (>1.8) INR (n=1) constituted only a small percentage.

Conclusion: In this real life, unselected, current practice scenario it is obvious that a large proportion (≈40%) of stroke patients being admitted are very elderly (>80), and many are with profound co-morbidity, and so, unsuitable for thrombolysis. Despite public awareness campaign, nearly a third (29%) did not come in time and hence, this should be further enhanced.

Poster Session Blue
Acute stroke: emergency management, stroke
units and complications

Cerebrovasc Dis 2011;31(suppl 2):1–322

237

167 Acute stroke: emergency management, stroke units and complications

ANALYSIS OF CLINICAL PRACTICE IN A NOVEL STROKE UNIT. HAS STROKE CARE IMPROVED?

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Background: The Helsinborg Declaration states that Stroke Units (SU) are the best place where patients with acute stroke should be treated in order to achieve specifics goals for management of acute stroke. Our aim is to analyze how stroke care has evolved and what Results where achieved after three years of operation of a Stroke Unit (SU).

Methods: Retrospective study of patients admitted to our SU since its opening. Three groups were considered according to admission date: G1, from 6/1/07 to 5/31/08; G2, from 6/1/08 to 31/5/09 and G3, from 6/1/09 to 5/31/10. Variables analyzed were: number of admissions, patients characteristics, stroke subtypes, NIH stroke scale at admission (NIH I) and at discharge (NIH A), interval between symptoms onset and neurological assessment, fibrinolysis performed, mortality and prognosis. Chi2, Student's T and ANOVA tests were used in the statistical analysis.

Results: 779 patients were admitted (G1 226, G2 259 y G3 294). Except for age, there were no differences in patients characteristics. Clinical outcome (NIHSS) was for ischaemic strokes: NIH I 7.8, 6.8 y 6.9 and NIH A 5.1, 4.2 y 4.15 (intergroups p 0.2), for haemorragic strokes NIH I 11.7, 9.6 and 9 and NIH A 11.88, 9.11 and 7.65 (integroups p 0.2). 14, 18 and 31 thrombolysis were performed (p<0.05). Mortality was 6%, 1% and 1% (p<0.05). There were no significant differences in the interval symptoms-neurological assessment and Rankin scale at 3 months. Over 70% of patients scored less than 2 on the Rankin scale.

Conclusions: There is a trend to a higher number of admissions, an increase in the performance of fibrinolysis and a better outcome of the patients admitted in our Stroke Unit, probably related to the systematization in the implementation of clinical protocols.

Acute stroke: clinical patterns and practice

242 Acute stroke: clinical patterns and practice

THE PERSISTENCE OF CONTRAST DURING ANGIOGRAM IN ACUTE STROKE PATIENTS: A SIGN TO BE CONSIDERED?

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Background: The persistence of contrast in the artery during an angiogram is a radiological sign that may be observed in some patients with an arterial occlusion. We aimed to evaluate if the presence of persistent contrast (PC) sign in patients with acute stroke who underwent endovascular procedures may influence recanalization, clinical outcome and mortality.

Methods: Acute stroke patients (<8h) who underwent endovascular procedures were prospectively studied. Location of vascular occlusion and recanalization were confirmed by angiogram. The presence of PC was considered if after complete angiography sequence (>8seconds) the contrast remained at the location of occlusion. Patients were evaluated using NIHSS and clinical improvement was considered if decrease > 4 points from the baseline to discharge was observed.

Results: 115 consecutive patients were included, mean age was 70.8 (SD 11.8), 42.7% were female (n=50) and baseline NIHSS was 20 (IQR 17.5-21). Sixty four patients (72.1%) showed recanalization after endovascular treatment (TIMI ≥1). Distribution of occlusion location was: ICA 33.3% (n=39), MCA 48% (n=56), Basilar 12% (n=14). The PC sign was observed in 40 patients (34.2%): ICA 30 (88.2%), MCA 4 (9%), Basilar 6 (66.7%). Patients with positive PC sign had lower recanalization rate (58% vs 83.7%) (p<0.008), lower clinical improvement (23.8%vs 76.2%) (p<0.001) and a trend to high mortality rate (43.2%vs24%) (p=0.058) compared to those with negative PC sign. A logistic regression model showed that ICA occlusion (p=0.044, OR 6.08 (1.05-35.17) and PC sign (p=0.043, OR 3.60 (1.04-12.40)) were independent predictors of lower clinical improvement after endovascular treatment.

Conclusions: Pc sign was strongly associated to ICA occlusion; however it was an independent predictor of lower clinical improvement after endovascular treatment in acute stroke patients.

243 Acute stroke: clinical patterns and practice

RAPID CHANGE OF RT-PA USE IN ISCHEMIC STROKE PATIENTS AFTER PUBLICATION OF THE EUROPEAN COOPERATIVE ACUTE STROKE STUDY (ECASS) III

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Introduction: The Results of ECASS III were published in September 2008 extending the thrombolysis time window for stroke patients from 3 to 4.5 hours after symptom onset. We studied the impact of ECASS III on routine stroke care and the rapidity with that the Results of this study were implemented. We also investigated if the extension of the time window led to a delay of treatment initiation.

Methods: Data were collected prospectively within the regional Stroke Register of Northwestern Germany between January 2007 and December 2009. The time from symptom onset to hospital arrival (onset-to-door time, OTD) was categorized into <2 hours, 2 to 3 hours, 3 to 6 hours, and >6 hours. The time from hospital arrival to treatment initiation (door-to-needle time, DTN) was categorized into <30 minutes, 30 to 60 minutes, 60 to 120 minutes, 120 to 180 minutes, and >180 minutes. To compare thrombolysis rates before and after publication of ECASS III we used a logistic regression analysis.

Results: A total of 91805 ischemic stroke patients were included in the analysis. The proportion of patients treated with rt-PA significantly increased over time.

The strongest increase was observed for patients admitted between 3 and 6 hours after symptom onset between the third and the fourth quarter of 2008 (88.9% relative increase in IV 2008 compared to the first half year of 2007, P<0.05, Figure). This increase was independent from the hospital expertise with acute stroke treatment as indicated by the total number of stroke patients in a hospital per year. During the study period the proportion of patients with a DTN time <30 minutes continuously increased and the proportion of patients with DTN times of >60 minutes decreased.
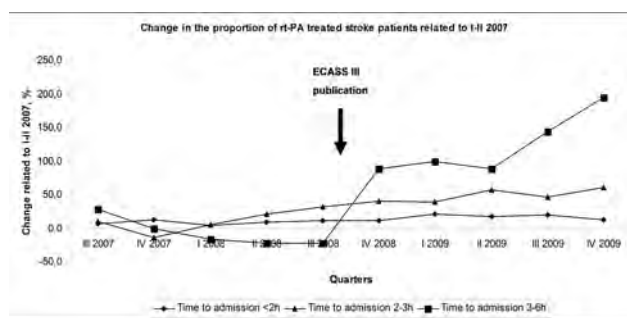
Conclusions: The Results of ECASS III were rapidly implemented in routine stroke care independently from the hospital expertise with acute stroke treatment. Previous concerns regarding an increase in DTN time were not confirmed.

244 Acute stroke: clinical patterns and practice

MOVING TOWARDS AN ELECTRONIC PATIENT RECORD FOR SPECIALIST THERAPY INTERVENTION FOLLOWING STROKE

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Background: The web-based Stroke Nav system (described at ESC 2010) now includes functionality for capturing therapy goals, measures and assessments.

Methods: The initial assessments performed by physio- and occupational therapists were converted from paper forms to electronic data entry. Fields common to both specialties can be copied between assessments. A user can add a therapy goal for a patient by choosing an area of work within their specialty (e.g. "Mobility"). The goal is described with free text and relevant categories (e.g. "Frame" and "Independent" if the aim is for independent mobility using a walking frame). The user estimates the timescale required (which may be several days or weeks). Goals are displayed until completed (or abandoned if no longer clinically relevant). Goal progress reports (behind/on/ahead of schedule) are entered before each multi-disciplinary team meeting. When behind schedule, reasons such as "clinical deterioration" can be selected. If the timescale is exceeded, the user is prompted to enter a new timescale and explanation. Reasons for deviation from the anticipated rehabilitation trajectory can subsequently be analysed. Outcome measures (e.g. Tinetti scale) can also be recorded. Community hospital therapists can view existing goals and assessments (even before a patient's arrival from the Acute Stroke Unit) and add further data, enabling continuity of goal-setting and information sharing along the treatment pathway.

Results: The system has been well received by therapy managers and used by 9 therapists to date at the Acute Stroke Unit, setting approximately 90 goals per month.

Conclusion: Therapy goals and assessments have been successfully moved from paper forms to an electronic record. The system will be extended to include

therapists' daily records. This technology is applicable to other fields. It is envisaged that this stroke-specific software can be integrated with generic Electronic Patient Records or Care Records Services.

245 Acute stroke: clinical patterns and practice

HEMODYNAMIC AND EMBOLIC CHARACTERISTICS OF CAROTID STENOSIS: CORRELATION WITH ISCHEMIC LESION PATTERN ON MRI

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Background: Two mechanisms play a role in stroke related to carotid occlusive disease. The aim of this study is to evaluate the association between hemodynamic and embolic characteristics of carotid stenosis and their correlation with MRI patterns.
Methods: Data collected prospectively from 2003 to 2010 of ischemic stroke/ TIA attributable to carotid stenosis (50-99%) were reviewed. Inclusion criteria included positive DWI, carotid US, microembolic signal (MES) detection by TCD and cerebrovascular reactivity (CVR) by breath holding index. Subjects with other potential source of emboli were excluded. Stroke patterns where categorized according to a well-established classification and assessed independently by two radiologists.
Results: 55 patients (72y) fulfilled selection criteria. 3 ischemic patterns were found: pure territorial stroke (TS, n=17), pure borderzone (BZ, n=26) and a combination of both (n=12). TS were more prevalent with moderate stenosis while BZ with severe stenosis (P=0.01). There was no difference between groups according to age, clinical presentation, stenosis side, risk factors, prior treatment. The logistic regression analysis of the pure groups showed that BZ infarcts were significantly associated with impaired CVR (P=0.04) and degree of stenosis (P=0.05), whereas TS infarcts were almost significantly related to MES (P=0.06). In the whole BZ population (BZ+TS & BZ), MES were independently associated with TS lesions (P=0.03) while CVR and degree of stenosis remained constant. In the whole TS population (BZ+TS & TS), impaired CVR was independently associated with BZ lesions (P=0.02) while MES and degree of stenosis remained non significant. In the mixed BZ+TS group, which was only associated with severe stenosis, half of the patients had positive MES in both normal and impaired CVR population.
Conclusion: This study highlights the key role of the hemodynamic component in the pathogenesis of BZ infarcts and the risk of TS lesion associated with MES.

246 Acute stroke: clinical patterns and practice

THE QUALITY OF ACUTE STROKE CARE MAY BE RELATED TO COMPLEX FACTORS THAT ARE PROXIES FOR PATIENTS' AGE

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Background: Older age has been associated with poorer quality of care provided to patients after an acute stroke. How age influences care decisions and care quality is unclear.
We explored differences in the influence of patients' age, compared to an age-proxy model, on the quality of care provided to acute stroke patients by allied health (AH) professionals.
Methods: We conducted a retrospective record audit to investigate the quality of care provided by AH professionals to 300 adults consecutively admitted to South Australian metropolitan hospitals with confirmed acute stroke in 2009. Care quality was measured by adherence to the 20 recommended process indicators (PIs), which we previously reported, as underpinning high quality AH care. Patient age was 75< or > 75years. Factors considered in the age-proxy model were gender, comorbidity, premorbid independence and abode, English proficiency, weekend admission, stroke unit care, stroke severity, length of stay (LOS).
Univariate logistic regression analysis established important associates of age (Odds Ratios, 95% Confidence Intervals). Multivariate stepwise regression analysis then determined an age-proxy model including the strongest predictors of age, based on changes to -2LogLikelihood Ratio for each new addition to the model. Associations between patients' age and PI adherence were then compared with those derived from the age-proxy model.
Results: The age-proxy model included stroke severity, premorbid independence, comorbidity, LOS, gender. Older patients were significantly less likely to receive compliant care for two PIs (p<0.05), whilst the age-proxy model was significantly

associated with poor compliance in 11 PIs (p<0.01). Severe stroke severity was a common predictor of good compliance in all 11 PIs.
Conclusion: Allied health care providers may make care decisions which appear to be related to older age. Their decisions may in fact be related to more complex factors which are proxies for age.

247 Acute stroke: clinical patterns and practice

SCOTTISH STROKE CARE AUDIT, DATA – TRENDS FROM 2005 - 2009

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Introduction: The Scottish Stroke Care Audit (SSCA) includes all hospitals managing acute stroke in Scotland and continuously monitors patients' care against NHS Quality Improvement Scotland's (NHS QIS) Clinical Standards for Stroke Care. The first report containing SSCA data was published in 2005. Since this time there have been significant improvements in stroke care across Scotland.
Method: SSCA collects data on all stroke patients admitted to 34 acute hospitals in Scotland. We have analysed all confirmed stroke patients' management from 2005 to 2009 against 2009 NHS QIS stroke standards.
Results: The trend analysis from 2005-2009 demonstrates a year on year improvement against current NHS QIS standards. The percentage of stroke patients:

- admitted to a Stroke Unit on day of admission has increased from 28% to 37% and from 49% to 61% by the day following admission;
- who had brain imaging on day of admission has increased from 27% to 49%;
- who had a swallow screen on day of admission has increased from 47% to 61%;
- who had an ischaemic event who were prescribed aspirin by one day after admission has increased from 41% to 68%; and who were seen within 7 days from referral at a neurovascular clinic has increased from 30% to 80%.

Conclusion: The quality of stroke services varies greatly across Scotland. However, an improvement has been demonstrated in the last five years. Raising standards and measuring performance against them will continue to drive improvements in the quality of stroke care in hospitals across NHS Scotland.

248 Acute stroke: clinical patterns and practice

THE FOUR SCORE: A RELIABLE TOOL TO ASSESS COMATOSE STROKE PATIENTS

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Background: One of the major concerns with the National Institutes of Health Stroke Scale (NIHSS) is that where a patient is in coma, the assessment of most of the remaining items is challenging. Moreover, the NIHSS lacks items to grade the severity of coma. The Full Outline of UnResponsiveness (FOUR) score is a new coma scale valid and reliable in severely neurologically injured patients. Aim of this study was to validate the FOUR score in stroke patients and to evaluate its adjunctive value in those with coma.
Methods: All consecutive patients with acute stroke admitted to our Department of Neurology or to the Intensive Care Unit of our hospital were prospectively enrolled. Two physicians independently examined patients by the FOUR score and a single physician by the NIHSS. The interrater agreement for the FOUR score was calculated by the weighted K (Kw). Correlation between the NIHSS and the FOUR score was evaluated by the Spearman test. Skewness and Kurtosis were used to describe distribution of NIHSS score and FOUR score in comatose patients (item 1a of the NIHSS scored 3).
Results: We enrolled 70 patients (mean age±SD 71.2±12.7; 64% men; 83% ischemic). Median FOUR score was 6 and median NIHSS score was 16. Sixteen patients were comatose. We found an excellent interrater agreement for the FOUR score in the overall cohort (Kw 0.947) and a good agreement in comatose patients (Kw 0.714). In the overall cohort the correlation between the NIHSS and the FOUR score was -0.860 indicating a good to excellent correlation between the scales. In comatose patients the value was -0.017 because the FOUR score varied while the NIHSS remained constant across few values. In comatose patients Skewness was -0.842 for the FOUR score and -1.513 for the NIHSS while Kurtosis was 0.027 for the FOUR score and 0.998 for the NIHSS indicating that the FOUR score had a more uniform distribution while the NIHSS had a peaked distribution.
Conclusions: The FOUR score is a reliable tool in patients with acute stroke including those with impaired consciousness. It can be applied in those patients in whom a full evaluation by means of the NIHSS is hindered because of impaired consciousness.

EFFECT OF EXTENDED TIME WINDOW OF THROMBOLYSIS TO 4.5 HOURS: EXPERIENCES FROM THE SWEDISH STROKE REGISTER (RIKS-STROKE)

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Background: The ECASS III trial and SITS-ISTR Results became publicly available in September 2008. Riks-Stroke, The Swedish Stroke Register, was used to explore how thrombolysis 3-4.5 h after stroke has been disseminated in different hospitals and patient groups and the concurrent development of rates for thrombolytic therapy within 3 hours after stroke onset.
Methods: All 76 hospitals in Sweden admitting acute stroke patients participate in Riks-Stroke. During the study period January 2003-June 2010, 92 150 18-80 year old patients were hospitalized for acute ischemic stroke. Joinpoint regression was used for identification of changes in thrombolytic treatment trends.
Results: The total proportion of 18-80 year old ischemic stroke patients undergoing thrombolytic treatment increased at a constant rate from 0.4% in the beginning of 2003 to 8.7% in 2010. Thrombolysis in the 3-4.5 h window increased from 0.5% before the publication ECASS III Results, to reach 2.1% in the second quarter of 2010. Small non-university hospitals reached a similar proportion of treatment with a 6-9 months delay compared to university and specialised non-university hospitals. Thrombolysis in the 3-4.5 h window was disseminated somewhat faster in men than women (P=0.04) but at a similar rate in different age groups up to 80 years. The uptake of thrombolysis within 3 h of onset of symptoms increased successively from 0.9% in 2003 to 6.6% in late 2008, where after it stabilized at the 6% level. Joinpoint regression confirmed a significant change in time trend in the last quarter of 2008. The median time from arrival to hospital to start of treatment remained unchanged before and after 2008 (65 min before and 66 minutes after, P=0.61).
Conclusions: Since the end of 2008, there has been a rapid nationwide uptake of thrombolysis in the 3-4.5 h window. However, concurrently the increased rates in the <3 h window has levelled off. Analyses of potential causes for the latter change are ongoing.

WHY MEASURING QUALITY OF STROKE CARE IS RELEVANT. ASSOCIATION BETWEEN LACK OF COMPLIANCE WITH PROCESS INDICATORS AND MORTALITY RISK

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Background: Assessing quality of stroke services is becoming widespread but whether quality is relevant to patients' outcomes has been scarcely analysed. We investigated the association between 30-day and long-term mortality risks and compliance with evidence-based process indicators among acute stroke patients included in the Second Stroke Audit of Catalonia.
Methods: The audit retrospectively explored quality of stroke care among patients admitted to all public hospitals in Catalonia in 2007, identified and selected through a pre-established sampling method. Only patients alive beyond the first 72 hours post-stroke were included in this analysis. The vital status and cause of death were obtained from the official Mortality Register of Catalonia 2007 and 2008. The magnitude of association of each quality indicator with 30-day and long-term mortality was assessed by adjusted multiple logistic regression and Cox proportional hazard regression models.
Results: We analysed 1698 patients. Median follow-up was 563 days. The cumulated 30-day, 3-, 6- and 12-month mortality rates were 10.8%, 11.9%, 18.2% and 22.5%. The adjusted 30-day mortality risk was significantly associated with non-fulfilment of screening of dysphagia (OR: 1.65; 95% CI: 1.07-2.55), antiplatelets < 48 hours (2.06; 1.23-3.45), early mobilisation (1.9; 1.24-2.93), assessment of rehabilitation needs (1.88; 1.23-2.87), management of dyslipidaemia (2.35; 1.28-4.31), and antithrombotics at discharge (3.74; 1.55-9.02). Lack of compliance with correct management of hypertension, anticoagulation if atrial fibrillation, and antithrombotic drugs upon discharge was associated with long-term mortality.
Conclusions: In view of the inverse association between quality of stroke care and mortality, healthcare systems should routinely monitor relevant indicators.

DIFFUSION WEIGHTED MRI AND PYRAMIDAL TRACT DAMAGE AS PROGNOSTIC MARKER FOR FUNCTIONAL OUTCOME AFTER SPINAL CORD INFARCTION

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Background: The pathogenesis, magnetic resonance imaging findings and the prognosis of spontaneous non-surgical spinal ischemia remain mostly unexplored. Our purpose is to phenotype spinal ischemia with clinical MR-tomographic and electrophysiological criteria to determine criteria for outcome and comparison to existing literature.
Methods: We analyzed prospectively the data from our stroke registry of patients suffering from vascular spinal cord ischemia from 2004 to 2010. Cases that were due to aortic surgery, compressive, tumoral or inflammatory pathologies were excluded. We analyzed the clinical, neurophysiological, imaging and functional outcome data for 10 patients with acute spinal cord infarction admitted to our comprehensive stroke center. Outcome was evaluated at the end of rehabilitation.
Results: Mean age was 71 (age range 50-84 years; 5 women). 7 patients showed damage of lower thoracic spinal cord (T8-L5) and 3 patients with upper thoracic/cervical damage (C4-T6). In 5 patients etiology remained cryptogenic, other etiologies were cardiac embolism, systemic atherosclerosis (myelomalacia), thrombophilia, and post-radiation. After rehabilitation 4 patients had regained full walking ability or were able to walk with aids and 6 were wheelchair bound. Spinal diffusion weighted MRI were pathological in 8/10 patients during the first week. All patients with unfavorable outcome (no walking ability) showed severe pyramidal tract lesion by performing motor evoked potentials in combination with DWI abnormalities of the spinal cord during the first week.
Conclusion: Poor outcome was associated with severe electrophysiological changes and DWI hyperintensities on the MRI. Patients with a favorable outcome had either no DWI hyperintensities or either normal/mild electrophysiological changes.

PATTERNS OF SYMPTOMS AND SIGNS OF POSTERIOR CIRCULATION ISCHEMIA IN THE NEW ENGLAND MEDICAL CENTER POSTERIOR CIRCULATION REGISTRY

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Introduction: Neurologists have desired to know which symptoms and signs (S&S) will characterize a particular lesion in the anterior and posterior circulations. We now present a study comparing and describing single or multiple focal lesions in different territories of the posterior circulation and comparing them with the resulting signs and symptoms. In this work we ask the basic questions: How can we use the S&S to predict either the location of brain ischemia or the location of the vascular lesion? If so, which signs and symptoms provide the most predictive value?
Clinical Background: The brainstem may be divided into 3 parts: (a) Proximal territory consisting of the medulla and posterior inferior cerebellum - territory supplied directly by the intracranial vertebral artery and its posterior inferior cerebellar artery branch,
(b) A middle territory that includes the pons and the anterior inferior cerebellum - territory supplied directly by the basilar artery and its anterior inferior cerebellar and penetrating artery branches, and
(c) A distal territory including the superior cerebellum, thalamus, midbrain, and occipital and temporal lobes - territory fed by the rostral basilar artery and its superior cerebellar artery, posterior cerebral artery, and their penetrating artery branches. This classification has been previously published.
Methods: We analyzed all the S&S and also the locations of the brainstem infarctions of 407 patients from New England Medical Center Posterior Circulation Registry (NEMC-PCR). We used regression analysis and other classification analysis, with regard to the patient's signs and symptoms.
Results: Analysis of 407 patients from the NEMC-PSR has proven that particular signs and symptoms of infarcts are highly specific for individual brainstem territories. The proposed clinical hypothesis of the most prominent S&S corresponding with either the proximal, middle, or distal brain stem region was proved.

THE REALITY OF JUST-IN-TIME KNOWLEDGE: BRINGING THE CANADIAN BEST PRACTICE STROKE RECOMMENDATIONS TO THE FRONT LINES OF HEALTH CARE

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Background: Dissemination and implementation of stroke guidelines continue to challenge health care systems. New developments in electronic media allow for levels of interactivity with the end-users that have not been fully exploited by evidence-based guideline developers. The Canadian Stroke Strategy (CSS) 2010 update of the Best Practice Recommendations for Stroke Care (BPR) were developed with front-line clinicians and health-care managers in mind. For the first time, the goal was to make the BPR available through an interactive website to enable real-time access to recommendations in clinical and administrative settings.
Methods: Over 200 clinical and methodological experts participated on nine writing groups, a consensus panel or as external reviewers. A specialized web-development team was engaged to develop a user-friendly interface appropriate for web and smart phones. The Contact Us button invites technical questions and feedback about the website. Google Analytics enables website-user analysis to track the most frequently accessed information and tools.
Results: The Canadian BPR span 35 domains along the continuum of stroke care. Existing topics areas were updated and new areas were added, including under-recognized issues such as access to care and transitions across care settings; technological aspects such as telestroke; and recent advances in therapeutics such as dabigatran therapy for patients with atrial fibrillation. The website allows fast access to topics and direct inks to implementation tools such as a guide to establishing stroke units, and tools for secondary prevention. Unique to the Canadian BPR is the inclusion of key performance measures to facilitate ongoing monitoring of the quality of stroke care delivery. The website is an excellent mechanism for emerging evidence to be integrated quickly.
Conclusions: On-line guidelines benefit end-users through easy access at the point of decision. For guideline makers, freedom from print media facilitates flexibility in the provision of up-to-date information.

TRENDS IN THE USE OF INTRAVENOUS RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR (IV RT-PA) FROM NORTHWEST INDIA

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Background: Intravenous rt-PA is being increasingly used in developing countries such as India. We aimed to study the trends of IV rt-PA use from a single center in northwest India.
Methods: This study was carried out at the stroke unit of Christian Medical College, Ludhiana, India between 2001-2003 (old cohort) [1] and 2008-2010 (new cohort). Demographic information, NIHSS score at admission, onset to door time, door to needle time, thrombolysis rate, rates of symptomatic and asymptomatic intracerebral hemorrhages and mortality rates of the 2 cohorts were documented. The outcome was assessed at $\geq$3 months using modified Rankin Scale (mRS $\leq$ 2: Good outcome).
Results: A total of 489 and 715 acute stroke patients were evaluated in the old and new cohorts respectively. Thrombolysis rates are as follows; [old cohort: 5/489 (1.0%) vs. New cohort: 32/715 (4.5%), p = 0.0006].The 2 cohorts did not differ in stroke severity (median NIHSS score at admission; old cohort: 15.0±2.9 vs. New cohort: 12.5±5.2, p=0.67), mean onset to door time (old cohort: 49.0±17.5 vs. New cohort: 60.0±35.7 minutes (min), p=0.50), mean door to needle time (old cohort: 108.0±11.5 vs. New cohort: 93.4±33.6 min, p=0.34), asymptomatic intracerebral hemorrhage rate [old cohort: 1/5 (20.0%) vs. New cohort: 3/32 (9.3%), p=0.45] and symptomatic intracerebral hemorrhage rate [old cohort: 0/5 (0.0%) vs. New cohort: 2/32 (6.2%), p=1.00]. Similarly, the outcome at $\geq$3 months [Good outcome; old cohort 3/5 (60.0%) vs. New cohort 19/32 (59.4%), p=1.00] and the mortality rates [old cohort 2/5 (40.0%) vs. New cohort 9/32 (28.1%), p=0.6] did not differ.
Conclusion: The thrombolysis rate has increased by four fold at this center. The possible reasons are organization of comprehensive stroke care services, reduced cost of the drug and perhaps, increasing affordability due to economic growth in India.
Reference: 1. Pandian JD, Sethi V, Dhillon R, Kaur R, Padala S, Chakrovorty R, Singh YP. Is intravenous thrombolysis feasible in a developing country? Cerebrovasc Dis 2005;20:134-136.

FREQUENCY AND TIMING OF TRANSIENT ISCHEMIC ATTACKS PRECEDING STROKE

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Background: A transient ischemic attack (TIA) is an important predictor of stroke. Up to 23% of strokes are preceded by TIA, and there is substantial interest in improving prevention during the short time-window between TIA and stroke. ABCD score (age, blood pressure on admission, speech disturbance, hemiparesis, and duration of TIA) or ABCD 2 score (diabetes with the ABCD score components) have also been used to predict early stroke after TIA.
Methods: in 120 patients with ischemic stroke (IS) we analyzed frequency and timing (0, 1, 7, 30 days) of preceding TIAs. All patients met all the clinical and radiological criteria for the diagnosis of TIA and IS. Data on past history of a TIA in patients were recorded by means of a detailed history taken by a neurologist at admission.
Results: Of 120 patients (age: median 63 years, 67 (55,8%) males) who had presented with an IS, 30 (25%) gave a history of a preceding TIA. Among these, 22 (73,3%) had one TIA, 9 (26,7%) multiple TIA. TIA preceded atherothrombotic infarct in 25% of the cases, but in only 11% and 14% of cases did it precede cardioembolic stroke and lacunar infarcts. As regards time from last TIA to IS onset, 15 (50%) of our patients had a IS on the same day, 4 (13,3%) on the previous day, 11 (36,7%) in the week previous to the stroke. Five patients (16,7%) had a stroke in the first 30 days after their first-ever TIA. The median interval from first-ever TIA to IS was 6 days.
Conclusion: Our Results show that many of patients with simptoms of TIA remain unrecognised, witch is consitent with literature data. Patients with TIA and IS are a highly heterogeneous group in terms of symptoms, risk factors and underlying pathology, and the early risk of stroke is likely to vary between different clinical and etiological subtypes. Clinical guidelines differ on how urgently patients should be assessed, but the appearance of TIAs is clearly an urgent condition and golden opportunity to prevent stroke.

DOES THE PERFORMANCE OF CT ANGIOGRAPHY PREVIOUS TO THE INTRAVENOUS THROMBOLYTIC TREATMENT IN ACUTE ISCHEMIC STROKE SUPPOSE A DELAY IN THE TREATMENT PROCEDURE?

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Background: Knowledge of the cerebral circulation status may be important when considering thrombolytic treatment. Our aim is to determinate if the performance of Computerized Tomographic Angiography (CTA) previous to the intravenous thrombolytic treatment (ITt) in acute ischemic stroke is associated with a delay in the treatment time, and if it supposes any difference in functional outcome and complications rate.
Patients and Methods: Patient with acute ischemic stroke, treated with ITt in our Stroke Unit from January 2009 to September 2010. We compare treatment delays, functional outcome at 3 month, incidence of symptomatic intracerebral hemorrhage (SICH) and mortality in patients to whom a CTA was performed before ITt (CTA+ group) and those to whom only a cranial CT was performed (CTA- group). The indication for CTA was based on expert judgments and technical availability.
Results: 92 patients were treated with ITt. 67 CTA-, 25 CTA+. Baseline NIHSS score: mean (±SD): CTA-: 13.2 (5.5), CTA+: 13 (7.1) (p=0.9). Delays (expressed in minutes): "Onset-to- Door": mean (±SD): CTA-: 87,6 (45.4), CTA+: 73.4 (40.5) (p=0.2), "Door-to-Needle": mean (±SD): CTA-: 56.7 (23.2), CTA+: 70.1 (33.8) (p=0.04),"Onset-to-Needle": mean (±SD): CTA-: 141 (41.2), CTA+: 140.5 (57.8) (p=0.95). Good functional recovery at 3 months (expressed as a score 0-2 on modified Rankin Scale): CTA-: 53%, CTA+: 63% (p=0.5), SICH rate: CTA-: 5,4%, CTA+:0 (p=0.6). Mortality: CTA-: 11%, CTA+: 8% (p=0.6).
Conclusions: Despite a significant delay in "door-to-needle" time, CTA previous to the ITt in ischemic stroke does not suppose a delay in the "onset-to-needle" time. No significant differences in efficacy or security were observed between the 2 groups. We believe that alternative approaches for vascular imaging in the acute ischemic stroke such as neurosonology should be considered.

VASCULAR TERRITORY OF ACUTE ISCHEMIC LESIONS: DISTRIBUTION AND ITS ASSOCIATION WITH STROKE SUBTYPE

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Background: The Lausanne Stroke Registry reported the overall patterns of stroke mechanisms according to the vascular territory of acute ischemic lesions in 1988. However, it was based on Brain CT, and there has no one based on MRI till now.

Methods: We studied 2702 consecutive ischemic stroke patients (age, 67.3±12.5 years; male, 59.3%) whose stroke lesions were confirmed by diffusion-weighted MRI (DWI) and who underwent MRA (98.7%) or CTA or conventional angiography within 7 days from stroke onset.

Vascular territory of ischemic lesions on DWI was classified using the maps establishing anatomic correspondence with dominant arterial territories proposed by Tatu et al. (Neurology 1996;47;1125-1135, Neurology 1998;50;1699-1708). Stroke subtype was determined using TOAST classification.

Results: Distribution of involved vascular territories was presented in Figure 1. Carotid territory only was 59.5%; vertebrobasilar territory only, 33.8%; and both, 6.7%. MCA was the most frequently involved territory (N=1618, 59.9%); MCA only in 1341 (49.6%) and MCA plus other vascular territories in 277 (10.3%). Presumed stroke subtypes according to vascular territory were summarized in Figure 2. Overall, large artery artherosclerosis (LAA) was the most common subtype, followed by small vessel occlusion (SVO), and cardioembolism (CE). Stroke of undetermined etiology was 16.1%. Compared to the carotid territory, the vertebrobasilar territory had more SVO (30.1% vs. 21.3%) and less CE (13.8% vs. 23.2%) (p<0.001, on Pearson's chi-square test). LAA was most common in ACA (65.3%) except border zone infarction; SVO in BA (58.7%); and CE in SCA territory (60%).

Fig 1. Distribution of vascular territories in acute ischemic stroke, N=2702

MCA indicates middle cerebral artery; ACA, anterior cerebral artery; ICA, internal carotid artery; PCA, posterior cerebral artery; BA, basilar artery; VA, vertebral artery; SCA, superior cerebellar artery; AICA, anterior inferior cerebellar artery; PICA, posterior inferior cerebellar artery.
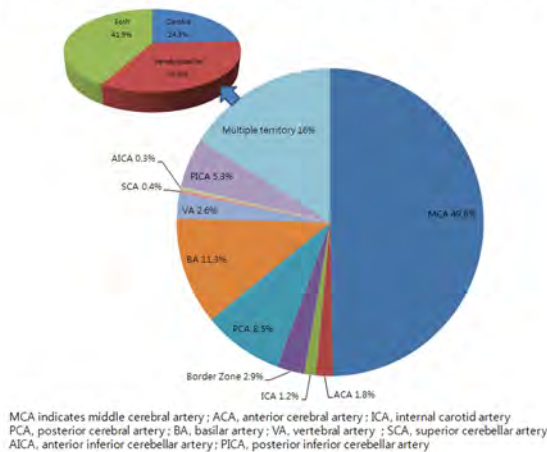
Figure 2. Subtype correlated with vascular territory of cerebral infarctions.

LAA indicates large artery sclerosis; SVO, small vessel occlusion; CE, cardioembolism; OD, other determined etiology two or more, two or more causes identified; negative, negative evaluation; incomplete, incomplete evaluation
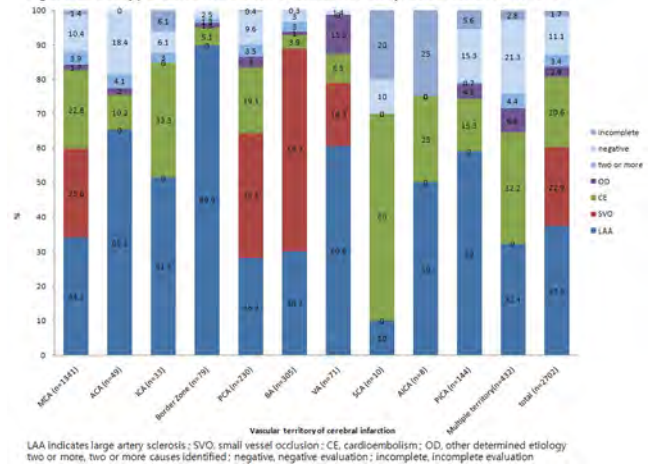
Conclusions: In the emerging era of mechanism based stroke managements, the faster and more accurate diagnosis of stroke subtype is required. We hope this study is helpful for stroke physicians who are urged to guess stroke subtype in a timely manner.

CLINICAL AND RADIOLOGIC CHARACTERISTICS OF INTRACRANIAL VERTEBRAL ARTERY DISSECTION

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Background: Little studies have paid attention to intracranial vertebral artery dissection (VAD). We evaluated the clinical and radiological characteristics of intracranial VAD by comparison with extracranial VAD.

Methods: Consecutive patients, who have been confirmed VAD by Digital Subtraction Angiography (DSA) at Ajou Stroke Center, were investigated. Clinical characteristics (initial clinical manifestations and stroke risk factors) and radiological findings (vertical nidus, laterality, and morphology) were investigated. Favorable outcome was designated as 3-month modified Rankin scale (0-2).

Results: Fifty-six patients enrolled with a mean age of 45.9±10.3 and male predominance (80.4%, p<0.001). Non-hemorrhagic type (n=48) was the most common (infarction without pain, n=31; isolated headache or neck pain, n=8; infarction with pain, n=9), whereas hemorrhagic type (n=6) and asymptomatic types (n=2) were less frequent. VAD nidus was the most prevalent in the intracranial VA segment (80.9%; p<0.001). Morphology was pearl and string sign (n=42), occlusion (n=3), double lumen (n=1), and pseudoaneurysm (n=1). Thirty-four patients (72.3%) were in non-dominant VA side (p<0.001). Intracranial VAD had a higher age (p=0.049), absence history of minor trauma (p=0.005), hypertension (p=0.046), and pearl and string sign (p<0.001). Older age (OR 1.13; 95% CI 1.00-1.27) and absence history of minor trauma (OR 11.05; 95% CI 1.18-103.59) were the independent predictors for intracranial VAD in multiple regression analysis. Most had a favorable outcome (92.9%).

Conclusion: Our Results suggest that VAD tend to occur at the intracranial and non-dominant portions of the VA. Vessel stress without direct trauma (old age and hypertension) appears to contribute to intracranial VAD.

THE EFFECT OF A PUBLIC INFORMATION MEDIA CAMPAIGN ON ACUTE STROKE PRESENTATION TO AN IRISH HOSPITAL

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Background: Sligo General Hospital is a 300 bed hospital serving a mainly rural-based catchment population of 100,000 people. On average we treat 200 acute strokes and TIAs annually. We have identified on previous audit that only 30% of patients with acute stroke present to our services within 3 hours of symptom onset, limiting our ability to deliver acute thrombolysis and early admission to the Acute Stroke Unit. In May 2010, the Irish Heart Foundation launched a media campaign

to increase public awareness of acute stroke symptoms and the need for rapid access to emergency services (the FAST Campaign).

Method: We conducted a retrospective review of charts of patients who presented with acute stroke during the 6 week period before, and again the 6 week period after, the FAST media campaign. We collected demographic data, details of timing of presentation, CT scanning, rates of thrombolysis, stroke subtype and severity, risk factors and outcomes.

Results: Seventy patients presented with acute stroke in the 6-week period prior to the FAST campaign and 64 patients in the 6-week period from the launch of the campaign in May2010. Fifty-one percent of the patients were male and 65% were over 70 years. Ten of 70 patients presented within 3 hours of symptom onset in the "pre" group compared with 20 of 64 patients in the "post" group. There was no difference in rates of acute stroke thrombolysis before and after the campaign.

Conclusions: This small study showed a two-fold increase in the numbers of patients presenting early to acute hospital services with symptoms of stroke following a public awareness media campaign. We were unable to demonstrate any difference in rates of thrombolysis or outcome in the small number studied.

260 Acute stroke: clinical patterns and practice

MONOATAXIA IN POSTERIOR CIRCULATION STROKE. A FURTHER PROOF OF THE SOMATOTOPY OF THE CEREBELLAR SYSTEM

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Background: Limb ataxia of sudden onset is due to a vascular lesion in either the cerebellum or the brainstem and it usually involves both the upper and the lower limb (hemiataxia). Monoataxia has been rarely reported in brainstem stroke, but prospective studies investigating the anatomical correlations of hemi- and monoataxia in posterior circulation (PC) strokes are lacking. Our aim was to prospectively investigate somatotopy in the cerebellar system (hemispheres and peduncles), by evaluating hemi- and monoataxia in posterior circulation stroke.

Methods: In 70 consecutive patients with acute PC stroke and limb ataxia, we used the International Cooperative Ataxia Rating Scale to quantify limb ataxia. Four topographical patterns based on magnetic resonance imaging findings were identified: picaCH pattern (posterior inferior cerebellar artery infarct); scaCH pattern (superior cerebellar artery infarct); CH/CP pattern (infarct involving both the cerebellum and the brainstem cerebellar pathways); CP pattern (infarct involving the brainstem cerebellar pathways). We compared the frequency of hemi- and monoataxia by means of chi-square test.

Results: Hemiataxia was present in 67.1% and monoataxia in 32.9% patients. Monoataxia involved the upper limb in 27.1% and the lower limb in 5.7% patients. Hemiataxia was significantly less frequent in picaCH pattern than other patterns (p < 0.0005), whereas the frequency of monoataxia was not significantly different among the patterns.

Conclusion: Although monoataxia seems of no localizing value, its occurrence suggests that the entire human cerebellar system is somatotopically organized, both the cerebellar hemisphere and the cerebellar pathways in the brainstem. Moreover, according to the higher frequency of isolated upper limb ataxia as compared to isolated lower limb ataxia, it might be hypothesized that along the cerebellar pathways the upper limb area is disproportionately represented compared with the lower limb area.

261 Acute stroke: clinical patterns and practice

MANAGEMENT OF VISUAL FIELD DEFECTS IN STROKE PATIENTS – A GENDER PERSPECTIVE

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Background: A visual field defect (VFD) is a negative indicator for post stroke outcome and causes significantly reduced quality of life. Assessing ability to drive is important in the management of stroke patients with VFDs. More male patients return to driving post stroke than female. We wanted to investigate whether this indicates that we manage women and men differently.

Methods: All patients registered in the Bergen Stroke Registry (BSR, Norway) from February 2006 to May 2009 with occipital lobe infarctions and with extra occipital infarction and a VFD were identified. Their medical records were reviewed for referral to perimetry and/or visual rehabilitation within the first year after injury.

Results: Among 1420 patients in the BSR 823 (58.0%) were male and 597 (42.0%) were female, the mean age for men was 68.0±0.49 years vs. 75.4±0.51 years for women. Among 336 patients with VFDs, 186 (55.4%) were male, 150 (44.6%) were female. Men were more often referred to perimetry than women (17.2% vs. 7.3%, p=0.004), and they were also younger (63.0 vs. 73.4 years, p=0.06) (table 3). When correcting for age and NIHSS upon admission the correlation between sex and referral to perimetry was no longer statistically significant (p=0.4). Overall 43/336 (12.8%) patients with VFDs were referred to perimetry and 11/336 (3.3%) to visual rehabilitation. The patients referred to perimetry were younger (65.6 vs. 75.1 years, p=0.001), had lower mRS (2.67 vs. 3.53, p<0.001), and lower NIHSS upon admission (6.93 vs. 14.95, p<0.001).

Conclusions: Referral rates were over all low, 1/8 was referred to perimetry and 1/30 was referred to visual rehabilitation. Men were more often referred to perimetry than women, but this difference was no longer statistically significant when correcting for age and NIHSS. Whether men are just better drivers than women we cannot say, but neurologists' apparently have an eye for women as well as men with post stroke VFDs.

262 Acute stroke: clinical patterns and practice

OPTIMIZING DRUG THERAPY IN STROKE PATIENTS AFTER HOSPITAL DISCHARGE: PROTOCOL OF A PROSPECTIVE INTERVENTIONAL STUDY

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The adherence to hospital recommendations concerning secondary prophylaxis following stroke is often less than optimal. One important reason is a lack of information transfer due to insufficient communication. In particular, discharge letters often do not contain detailed information about reasons for modifications of drug treatment.

The objective of this study is to evaluate a systematic approach to improving adherence to hospital recommendations in cooperation with a clinical pharmacist. This open prospective interventional 2-phase study is being conducted (beginning in 01/2011) in a major community hospital in Germany, involving a comprehensive stroke unit, an associated clinical pharmacist and all general practitioners (GPs) in the region of Fulda.

Patients with either a diagnosis of TIA or ischemic stroke and intake of > 2 medicines at discharge from hospital are included. Phase 1 (n=156): the neurologist of the stroke unit includes a medication list at the end of the discharge letter as previously. Phase 2 (n=156): old and new medications are listed next to each other at the end of the discharge letter; in addition, the clinical pharmacist will also include information about reasons for drug modifications, as well as key literature supporting these changes.

Three months following discharge an inquiry will be made to the GP with regard to the current medication. In particular, the adherence to recommendations regarding antithrombotic, cholesterol lowering and antihypertensive medication will be evaluated.

In Conclusion, the study will document the current state of adherence to stroke prevention medication. Moreover, it will determine the influence of adding additional Background information to treatment decisions.

263 Acute stroke: clinical patterns and practice

EPILEPSY IN PATIENTS AFTER STROKE

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Background: Seizures may appear in acute phase of the insult,or during the reconvalescence.Our goal was to analyse the frequency and correlation between epileptic seizures and the type and size of cerebrovascular lesion.

Methods: In this prospective study, we evaluated patients with stroke who were hospitalised at the Department of Neurology in Nis, between January and December 2010.Witnessed epileptic seizures occured in 112 patients. Patients

with a previous history of epilepsy and pulmonary diseases were excluded. Patients were evaluated and had the same investigations with anamnestic,clinical, neurological,EEG and neuroimaging (CT,MRI) variables which were compared. After seizure apperance patients were instantly put on an anti-epileptic drug treatment.

Results: Of the 1231 patients with stroke who were admited to the hospital, 430 (34,93%) had haemorrhagic stroke, and 801 (65,07%) had ischemic stroke. Mean age was 52±30 years.Of a total of 112 patients with witnessed epileptic seizures,71 were male and 41 female. 37 (33,04%) patients with haemorrhagic and 75 (66,96%) patients with ischemic stroke developed seizures after 14 days of the stroke. Partial motor seizures (PMS) were registered in 63 (56,25%) patients, partial seizures with secondary tonic-clonic generalisation (GTC) in 34 (30,36%) patients and primary GTC seizures in 15 (13,39%) patients. Status epilepticus (SE) was registered in 11 patients. 35 (31,25%) patients had EEG pathological changes (spike or sharp-waves) and 27 (24,11%) patients had focal or diffuse Theta-Delta waves. Normal EEG patterns were registered in 7 patients.

Conclusion: Patients with ischaemic stroke and cortical lesions are at a higer risk of developing seizures. PMS and PMS with secondary GTC are a dominant feature. Our Results differ from the ones in literature, in which patients with haemorrhagic stroke are more likely to develop seizures. It may be the consequence of the fact that the mortality in haemorrgahic stroke patiens is higher.

264 Acute stroke: clinical patterns and practice

INSULAR ISCHEMIC STROKE: CLINICAL PRESENTATION AND OUTCOME

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Background: The insula is located in the depth of the sylvian fissure, covered by the frontal, parietal and temporal operculum. Ischemic stroke limited to the insula is rare and have not been well studied.

Objective: To characterize the clinical presentation and outcome of insular ischemic strokes (IIS).

Methods: Using the keywords insula(r), infarction, and stroke, we searched the Medline database to identify published IIS cases confirmed by MRI. Minimal extension to an adjacent operculum or subinsular area was accepted. We also reviewed our institutional prospective, consecutive, stroke database to identify additional cases with IIS in 2008-2010. We distinguished the anterior (AIC) and posterior insular cortex (PIC). We collected clinical, demographic, and radiological data. Outcome was determined with the mRS.

Results: We found 16 published cases of IIS and 3 from our institution. Infarct was limited to the AIC (n=3) or the PIC (n= 10) or affected both (n=6). The five most frequent symptoms were aphasia (n=9), sensory deficit (n=8), dysarthria (n=7), unsteadiness (n=6) and motor deficit (n=4). IIS presentation simulated a lacunar infarct in 4/19 (21%) and a larger middle cerebral artery (MCA) stroke in 11/19 (58%). 11/19 (58%) cases presented findings not commonly associated with lacunar or MCA stroke. The uncommon symptoms included unsteadiness, gustatory or auditory deficits, sensory deficits restricted to specific modalities and somatoparaphrenia without neglect. No significant correlation was found between insular lesion topography and clinical presentation. At 6 months follow-up, mRS was 0 in 4/19 (21%), 1-2 in 7/19 (37%) and unknown in 8/19 (42%).

Conclusion: IIS presentation is variable. It can mimic lacunar infarct or a larger MCA stroke. Manifestations uncommonly associated with these syndromes can suggest IIS. Outcome of IIS is often favorable.

265 Acute stroke: clinical patterns and practice

DUBLIN MIDLANDS STROKE NETWORK PARTNERSHIP (SNP) – PATIENT SATISFACTION WITH ACUTE STROKE TELEMEDICINE ASSESSMENT

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Introduction: Telemedicine is a recognised means of assessing and treating acute stroke patients. Patient comfort and satisfaction is an important factor in telemedicine.

Method: Dublin Midlands SNP (population of 760,000) introduced a 24/7 "out of hours" telemedicine service (RP-7™ InTouch Health) in 2010. Patients/carers (n=47) were surveyed at time of assessment for satisfaction with telemedicine consultation. Follow up questionnaire based on the Scottish Centre for Telehealth was carried out by CNS stroke (n=12). 5 stroke geriatricians and one neurologist participated in an acute stroke telemedicine rota. We present consultant and patient survey data.

Results: In 10 months 66 patients assessed by telemedicine. 47 patients surveyed at time of assessment. 46 (98%) indicated satisfaction with telemedicine as a form of consultation and with quality of sound and vision. On follow up questionnaire 12/25 treated patients responded (44%). 42% indicated they were "very comfortable", 25% "comfortable", 25% "unsure" and 8% "uncomfortable" prior to teleconsultation. After teleconsultation 73% were "very comfortable", 18% "comfortable" and 9% "unsure". 11 (92%) happy with information provided by teleconsultation, 100% happy with image and sound quality, felt their health care was improved by teleconsultation and would use it again.

Discussion: In this small study Irish stroke patients appear happy with telemedicine as a means of assessment.

266 Acute stroke: clinical patterns and practice

FURTHER DEVELOPMENT AND USE OF STROKE NAV, A WEB-BASED INTERFACE TO FACILITATE THE DELIVERY OF EFFECTIVE MULTI-DISCIPLINARY STROKE CARE

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Background: The electronic Stroke Nav system (described at ESC 2010) includes a data collection module for multi-disciplinary team meetings (MDMs). The system has been further developed to: allow access from other hospitals; allow access through multiple devices; and, to collect and present data on therapy assessments, goals and outcome measures. The system now includes rapid data analyses and the effects of external changes on service performance can be quantified.

Methods: Patients on the Acute Stroke Unit (ASU) are often discharged to community hospitals. Stroke Nav now tracks patients between hospitals and can be fully utilised in the community hospital setting. Time-limited goals can be set and monitored electronically, and customised reports provide a broad multi-disciplinary view of progress in rehabilitation at the touch of a button. The system can also provide detailed ad hoc analyses of changes in service performance. In addition to using PCs, users can now access the system via portable devices such as the Apple iPad and iPod.

Results: During 2010, 103 MDMs were held on the ASU and 496 patients were discussed. 29 clinicians used the MDM module to enter data at various points along the patient pathway.

The system facilitated rapid investigation of an isolated decline in the performance of the service (time to documented swallow screen following stroke). Swallow screen data had been recorded for 494 patients discharged during 2010 and a step change in "time to swallow screen" was easily identified through a database query. The deterioration in performance was localised to the ASU (rather than other parts of the hospital) and coincided with the absence of key staff members.

Conclusion: The Stroke Nav electronic clinical information system continues to offer significant anticipated benefits in addition to some unanticipated benefits. Following the developments above, attention is now being directed towards how best to bring this prototype to wider use.

267 Acute stroke: clinical patterns and practice

REDUCED RELATIVE CEREBRAL BLOOD VOLUME(RCBV) RATIO ON PERFUSION MRI PREDICTS THE POOR OUTCOME AFTER USING IV T-PA IN ACUTE ISCHEMIC STROKE

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Background: It has been suggested that a rCBV map on perfusion MRI provides us the information of collateral circulation in ischemic region after acute ischemic

stroke (AIS). In this study, we demonstrated the usefulness of rCBV ratio on perfusion MRI to predict the poor outcome after using IV t-PA in AIS.

Methods: we recruited 58 patients using IV t-PA based on MRI. The poor outcome was defined as a day 90 mRS score >2. rCBV ratio was calculated by comparing the blood volume on ischemic lesion with it on contralateral region.

Result: Among the subjected patients, twenty-one patients (36.2%) showed a poor outcome (mRS 3-6) at 90 days after their ischemic events. Regarding on an occurrence of poor outcome after using t-PA, age (p=0.03), serum glucose level (p=0.01), NIHSS (p=0.05), and presence of T-occlusion (p=0.05) were related with it. In MRI findings, diffusion weighted images lesion volume (p<0.01), lower rCBV ratio on perfusion weighted imaging (p<0.01), and non-recanlization (p<0.01) had a significance for poor outcome after using it. Among them, non-recanalization (p<0.01), reduced rCBV ratio on perfusion imaging (p<0.01), age (p=0.04), and serum glucose level (p=0.01) had an independent significance for predicting it.

Conclusion: rCBV ratio on perfusion MRI might be an important tool to estimate the prognosis the fate after thrombolysis in AIS.

268 Acute stroke: clinical patterns and practice

HIGH PREVALENCE OF ABNORMAL LV GEOMETRY IN NON-CARDIOEMBOLIC STROKE PATIENTS

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Background: Echocardiography has been an integral part of the diagnostic workup in stroke patients to assess cardiac source of emboli. In non-cardioembolic patients the cardiac manifestations of high blood pressure (e.g. hypertrophy/remodeling) are of particular interest.

Objective: We sought to evaluate the prevalence of different indices of LV remodeling and hypertrophy in consecutive patients with non-cardioembolic stroke.

Methods: From 2005 to 2010 the echocardiographic findings of consecutive patients were included in a database. All patients were referred from the Department of Neurology within 48 hours after a stroke or a TIA for a clinically indicated transthoracic echocardiogram. The relative wall thickness (RWT) of the left ventricle and the left ventricular (LV) mass index were computed from 2D and M mode echocardiograms. An off-site read of randomly selected echocardiographic recordings was performed in order to assess the reproducibility of the measurements. The echocardiographic findings of consecutive patients with non-cardioembolic stroke or TIA were analyzed. Patients found clinically, by history or echo to have associated findings that may lead to an embolic stroke were excluded.

Results: Complete datasets were available in 372 out of 374 patients (male=243, female= 131, arterial hypertension at presentation 211 patients, diabetes mellitus 163 patients) Global LV function was normal in 330 patients (88.7%). Reduction of LV ejection fraction was mild in 26 patients (7%) moderate in 10 patients (2.6%) and severe in 6 patients (1.6%). LV indices are listed in Table 1.

Table 1

	Patients	%
Total	372	100
Abnormal LV mass index	118	31.7
Abnormal RWT	302	81.2
RWT 0.42-0.5	116	31.0
RWT > 0.5	186	50.0

Conclusion: In this large cohort of consecutive patients with non-cardioembolic stroke abnormal LV geometry as assessed by RWT is very frequent. Further studies are warranted to assess the usefulness of the RWT for risk stratification as compared to the more complex measurement of the LV mass index.

269 Acute stroke: clinical patterns and practice

PROCESS OF IMPLEMENTING THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE IN ESTONIA

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Background: There is about 1,34 million inhabitants in Estonia and about 6000 new strokes are diagnosed every year. Stroke patients are treated in 2 regional hospitals, in 4 central hospitals and in 11 general hospitals. The ambulance system is well developed, free of charge and stroke code is of high priority. This gives a good possibility for effective and well-organised stroke service.

Methods: The first stroke thrombolysis in Estonia was performed in 2003 in Tartu University Hospital. Information about the new treatment option together with developed local treatment protocol was spread by the Estonian neurological society to encourage every institution providing stroke care to start using thrombolysis. Stroke awareness campaigns have provided information for the general population through different media sources since 2008.

Results: The number of thrombolyses done and centres providing this treatment option has been increasing constantly since 2003. In 2004, North Estonian Medical Centre and general hospitals in Tallinn started to use alteplase for acute stroke and today all regional and central hospitals and at least 2 general hospitals provide this treatment. The proportion of thrombolysed ischemic stroke patients is up to 13% in active centres. The proportion of thrombolysed cases in view of all ischemic strokes in Estonia has grown from 0.5% in 2005 to 5.4% in 2010.

Conclusion: In Estonia, stroke patients are treated in hospitals and well developed ambulance system enables quick transportation of patients to the nearest hospital providing thrombolytic therapy. The main obstacles are certain geographical areas (especially small islands) and long in-hospital delays for patients arriving early after stroke onset. Continuous efforts will be made to address this issue and to further improve the quality of stroke care in Estonia in parallel with stroke awareness campaigns.

270 Acute stroke: clinical patterns and practice

DIAGNOSTIC SENSITIVITY OF THE DENSE ARTERY SIGN COMPARED TO TRANSCRANIAL DUPLEX SONOGRAPHY IN ACUTE MIDDLE CEREBRAL ARTERY OCCLUSIONS

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Background: Ischemic stroke due to acute mainstem occlusion of cerebral arteries is associated with poor outcome. For successful treatment an immediate diagnosis is mandatory. While diagnosis can be made by noninvasive imaging, like detection of an intravascular thrombus (dense artery sign) in computed tomography (CT), CT angiography (CTA) or magnetic resonance imaging angiography (MRA) or transcranial duplex sonography (TCDS), invasive digital substraction angiography (DSA) remains the diagnostic gold standard.

Methods: Between December 2008 and January 2011, we diagnosed 18 patients with acute mainstem occlusion of the middle cerebral artery (MCA) which was confirmed by DSA and treated with intraarterial (IA) thombolysis or mechanical thrombectomy. The prevalences of a dense artery sign in the initial CT scan and of TCDS findings indicating MCA mainstem occlusion were compared. The CT scans were reviewed by 2 (neuro-)radiologists and 2 vascular neurologists.

Results: 12 of 18 patients (67%) with MCA occlusion had a dense artery sign in the first CT. TCDS was performed in 16 patients (2 with ultrasound contrast medium) before intracranial intervention and identified 15 (94%) proximal MCA occlusions.

Conclusions: TCDS seems to be more sensitive than the presence of a dense artery sign on CT scanning in detecting acute MCA mainstem occlusions. CT sensitivity can be increased by CTA using contrast agents, but their administration is limited in patients with renal failure or hyperthyroidism. MRA is an alternative for only few patients, as it is time consuming, not available 24/7 in most hospitals, contraindicated in patients with pacemakers and not feasible in restless patients. Therefore, TCDS is a fast, noninvasive bedside technique for diagnosing acute mainstem MCA occlusion, which could even allow for continuous monitoring of recanalisation.

271 Acute stroke: clinical patterns and practice

ESTIMATION OF CORRECT DOSAGING FOR THROMBOLYSIS: A SINGLE CENTRE EXPERIENCE

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Background: Intravenous recombinant tissue plasminogen activator (rt-pa) is given to patients presenting with acute ischaemic stroke (AIS). The dose is dependent on patient weight, however, physicians estimate patient weight based on history and visual assessment. We aimed to: 1) assess how accurate physicians were in estimating patient weights and 2) assess whether errors in dosing had implications for recanalisation rate.

Methods: We prospectively followed 51 consecutive patients who were thrombolysed having presented with AIS at St Thomas' Hospital London over a 10 month period in 2010. Socio-demographic data, NIHSS on admission and at 24 hours were recorded. The optimal dose of rt-pa was defined as 0.9mg/kg ±5%. This was compared against the actual dose the patient received, hence showing whether the patient had been overdosed (OD), underdosed (UD) or had received the correct dose (CD). If NIHSS on admission had decreased by a minimum of 4 points, or returned to zero at 24 hours, this was taken as a clinically relevant surrogate for successful recanalisation.

Results: Of the 51 patients; 6 (12%) were UD, 16 (31%) OD and 29 (57%) received the CD. Patients who received the correct dose were younger than those that did not: CD 66.2 years, UD 73.3 years, OD 74.1 years [p=0.035]. The median percentage by which patients were UD was 14.2% (12.9 - 15.4) and OD was 9.8% (6.7 - 11.9). Recanalisation rates were 66% (UD), 59% (CD) and 56% (OD) (p=0.999). There were no intracranial haemorrhages (ICH) seen at 24 hours in patients who were CD, however, 1 occurred in the UD group and 1 in the OD group [p=0.135].

Conclusion: In our cohort, 43% of patients received an incorrect dose of rt-pa due to inaccurate weight estimation. No differences in: recanalisation rates or ICH were seen between the 3 groups, although there was a trend towards better recanalisation rates in UD patients. Further exploration is required in a larger study.

272 Acute stroke: clinical patterns and practice

THROMBOLYSIS IN YOUNG STROKE PATIENTS

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Introduction: Intravenous thrombolysis has been proven as an effective and safe therapy of acute ischemic stroke within the first 4.5 h after onset. Although young patients represent a substantial and important part of stroke patients, most experience regarding the use of t-PA is based on patients older than 60 years.

Methods and Results: Between January 2003 and June 2010 55 patients younger than 45 years (median age 36.4±8.5; 48.9% male) were treated with t-PA and prospectively documented in our stroke unit registry. We compared the baseline risk factors and therapy, etiology, rate of intracerebral hemorrhages and functional outcome with stroke patients treated with t-PA > 80 years from our database.

There was a significant difference in baseline characteristics regarding vascular risk factors, stroke in medical history or existing antiplatelet therapy in comparison to the group of older stroke patients. The majority of our patients had a cardioembolic stroke (19/47) or we found rare causes of stroke (11/47) like arterial dissection or coagulation abnormalities.

Mortality and functional outcome both differed significantly between our patients and the collective of older stroke patients (mRS 0-2: 67.4% vs. 43.9%, p=0.03; Mortality 2.1% vs. 34.2%, p < 0.001). We observed no symptomatic hemorrhage in our patients.

Conclusions: We demonstrated that young stroke patients benefit more than old patients from an acute t-Pa treatment, showing both a lower mortality and higher rate of good functional outcome in the young patients. This confirms the Results of good outcome described by other authors in young stroke patients treated with t-Pa. Arteriosclerosis or microangiopathy is rare among these patients and thus the diagnostic workup has to include the investigation of rare conditions like coagulopathy, arterial dissection or vasculitis.

273 Acute stroke: clinical patterns and practice

CARDIOEMBOLIC STROKE: A FOUR-YEAR HOSPITAL-BASED STUDY

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Background: About 20% of ischemic strokes (IS) are caused by cardioembolism (CE). It is considered the most preventable stroke and yet preventive measures are underutilized despite the poor prognosis. There are few studies about stroke in Lebanon and none so far addressed CE specifically.

Methods: In this retrospective four-year hospital-based study, we assessed the frequency of cardioembolic stroke (CES), risk factors, early outcome and prevention. CES was defined according to the TOAST criteria. Patients with Atrial Fibrillation (AF) were assessed using CHADS2 score and AHA/ASA guidelines.

Results: A total of 341 patients with acute IS were identified. Of these 88 (27.5%) were considered CES. Women above 75 years were at a higher risk for CE. In this age group 66% of CES occurred in women. Also CES accounted for 47% of IS in women compared to 25.8% in men. In addition, 67.3% of CES in women occurred in this age group compared to 35.7% in men. Total MCA infarct occurred in 38.3% of CES. Clinically CES were associated with aphasia (37.5%), depressed consciousness (52.3%), medical complications (53.4%), and high hospital mortality (18.2%). Good functional status at hospital discharge was achieved in only 28.4%. AF was present in 86.4% of CES and was the most common cause (71.6%) of CE. Among AF patients, newly diagnosed AF occurred in 35% and valvular heart disease in 17%. CES were considered to be preventable in 68.2% of the cases, and that was largely due to under treatment in patients with AF.

Conclusion: One quarter of IS are CE in origin in this study. Women above 75 years are particularly at more risk. AF–related IS are mostly preventable, largely under treated and associated with poor outcome.

274 Acute stroke: clinical patterns and practice

INTRAVENOUS THROMBOLYSIS IN ACUTE ISCHEMIC STROKE (AIS) PATIENTS PRESENTING WITH ISOLATED HOMONYMOUS HEMIANOPIA (IHH)

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Background: Patients with mild AIS were usually excluded from thrombolytic treatment in clinical trials and in clinical practice. Such patients may, however, end up having severe disabilities. Here, we present 3 patients with IHH due to posterior cerebral artery occlusion (PCAo) who received thrombolysis despite having NIHSS < 3 points.

Methods: Three patients presented with ischemic IHH were treated with intravenous alteplase (0.9 mg/kg of bw) within 4.5 h of onset after perfusion CT and CT angiography addressed a large perfusion deficit accompanied with a distal PCAo. This was done according to our written institutional guidelines for acute ischemic stroke patients presenting with mild neurological deficits.

Results: All 3 patients received points in NIHSS domain 3 only. Patient 1: A 42-y old woman with a history of aural migraine presented with right-sided IHH, 2 NIHSS points. Patient 2: A 60-y old male with atrial fibrillation presented with left-sided IHH, 2 NIHSS points. Patient 3: A 70-y old woman with a 4-y history of stage 4 follicular non-Hodgkin lymphoma presented with left-sided IHH, 1 NIHSS point. None of the patients had acute findings on noncontrast CT scan, however, all of them had a perfusion deficit in the symptomatic occipital cortex (parieto-occipital in Patient 3, who also had a short occlusion at the bifurcation of PCA). Symptoms of 2 female patients resolved within 2h of treatment initiation, while partial improvement was observed in the male patient at 2 h and complete improvement within 5 days. All of them achieved 3-month mRS 0. No hemorrhagic or other serious complications were observed.

Conclusion: Patients with mild AIS are usually denied thrombolysis. Although giving rise to low NIHSS points, IHH may leave to disability limiting patient's daily activities and working ability. Furthermore, PCAo can affect cognition, not assessed in NIHSS. Our case series encourage application of multimodality imaging and thrombolytic treatment in IHH patients.

275 Acute stroke: clinical patterns and practice

TWO CASES OF CERVICAL EPIDURAL HEMATOMA MIMICKING TRANSIENT ISCHEMIC ATTACKS

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Background: A spontaneous cervical epidural hematoma is a rare cause of cord compression that usually requires surgical evacuation to relieve the symptoms. Spontaneous resolution is seldom reported. In such cases, the transient neurological abnormalities resolve over several days. We present two cases of cervical epidural hematoma mimicking transient ischemic attacks, because the neurological abnormalities lasted only for short times.

Case I: A 78-year-old man had sudden-onset posterior neck pain and weakness in his left limbs. The symptoms and the weakness had disappeared by the time he arrived at our hospital, i.e., it lasted for 30 minutes. On neurological examination, there were no obvious abnormalities. Brain MRI and MRA showed no relevant

abnormalities. On the second day, he complained of severe neck pain without weakness. Cervical MRI performed that day revealed an epidural hematoma on the left side at the C2-6 level.

Case II: A 67-year-old woman came to our hospital complaining of severe posterior neck pain and right-side weakness that began 3 hours before her visit. The weakness improved while she was there. The neurological examination, brain MRI and MRA revealed no obvious abnormalities. Cervical MRI, performed because she complained of severe posterior neck continuously after admission, showed an epidural hematoma at the C3-4 level.

Discussion: The mechanism of spontaneous recovery from epidural hematoma is thought to be spread of the hematoma in the epidural space upward and downward, resulting in decompression. In such cases, the improvement usually requires several days. We experienced two cases of spontaneous epidural hematoma that improved more quickly than reported cases, so we were puzzled by the diagnosis, considering TIA. Our cases differed from typical TIAs with regard to the severe posterior neck pain. Therefore, severe posterior neck pain should be a red flag suggesting a cervical epidural hematoma, although the presentation is similar to a TIA.

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276 Acute stroke: clinical patterns and practice

CRANIOCERVICAL ARTERY DISSECTIONS: COMPARISON OF INTRACRANIAL WITH EXTRACRANIAL ARTERY DISSECTIONS. A RETROSPECTIVE, SINGLE-CENTER STUDY OF 103 KOREAN PATIENTS

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Background: We investigated the clinical findings, imaging characteristics, treatment and outcome in patients with craniocervical artery dissection (CAD) and compared the differences between intracranial (IADs) and extracranial artery dissections (EADs).

Methods: We retrospectively studied 103 consecutive patients with 118 spontaneous CADs who were admitted in department of neurology and were diagnosed by neuroradiological imaging.

Results: Among 103 patients (mean age 44.7), two-thirds of patients were men. There were total 118 CADs including 22 ICADs, 64 VADs, 15 MCADs, 9 BADs, 3 PCADs, 3 PICAs, 1 CCAD, and an ACAD, which correspond to 63 stenotic (53.4%), 30 occlusive and 25 aneurysmal forms. Nearly two-thirds (75, 63.6%) presented with IADs, 43 with EADs. VADs in the V4 segment occurred in 56.3% of all VAD. Presenting clinical symptoms were cerebral ischemic infarcts or TIAs in 94.2%. SAH was observed in only 2 patients (1.9%) with intracranial VADs with fusiform aneurysms. Territorial infarcts caused by artery to artery embolism are half of our patients with ICADs. Local branch, i.e., PICA occlusion by VAD is the essential stroke mechanism (38.2%). Antiplatelet therapy was the most frequent initial treatment in IADs (58.6%). 55.8% of patients with EADs were treated with anticoagulants. Six patients (5 IADs, 2 EADs) received thrombolytic therapy. In follow-up imaging with mean follow-up time 169.3 days, 22 patients (21.4%) had documented complete recanalization. 75 patients (86.2%) reached a favorable outcome (mRS 0-2) with a mean follow-up of 2.2 years. We found no association between clinical outcome and the location, pattern or recanalization of the dissection.

	Intracranial CAD	Extracranial CAD	P value
Baseline characteristics			
Numbers of dissected vessel	75 (63.6)	43 (36.4)	
Age (mean ± SD)	45.6±11.84	41.4±12.98	0.280
Male (%)	49 (65.3)	25 (58.1)	0.437
Head or neck pain (%)	40 (53.3)	25 (58.1)	0.613
Cerebral infarcts (%)	63 (84.0)	37 (86.0%)	0.637
Stroke pattern			
Artery to artery embolism	20 (26.7)	30 (69.8)	<0.001
Local branch occlusion	28 (37.3)	1 (2.3)	
Hemodynamic compromise	11 (14.7)	6 (14.0)	
Dissecting pattern			
Stenosis (%)	41 (54.7)	22 (51.2)	0.035
Occlusion (%)	14 (18.7)	16 (37.2)	
Dissecting aneurysm (%)	20 (26.7)	5 (11.6)	
Treatment			
Antiplatelet (%)	44 (58.6)	13 (30.2)	0.002
Anticoagulation (%)	16 (21.4)	24 (55.8)	
Thrombolysis (%)	5 (6.7)	2 (4.7)	
Follow-up			
Complete recanalization (%)	17 (22.7)	17 (39.5)	0.130
Partial recanalization (%)	9 (12.0)	8 (18.6)	
No change (%)	23 (30.7)	11 (25.6)	
mRS 0-2	45 (78.9)	27 (90.0)	0.594
mRS 3-6	9 (15.8)	3 (10.0)	

IQR = interquatile range; mRS = modified Rankin Scale.

Conclusion: Our Results about the frequency of IADs correspond that the frequency of intracranial atherosclerosis is approximately 70% in Asian countries. These Results suggest that local branch occlusion is the main mechanism of stroke of IADs and antiplatelet therapy is important in patients with IAD.

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277 Acute stroke: clinical patterns and practice

STROKE "MIMIC" REVEALING A NEUROSARCOIDOSIS: A CASE REPORT

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Introduction: It's known that sarcoidosis involves the nervous system in 5% of cases. The most common presentation of neurosarcoidosis is a cranial neuropathy, usual facial, followed in frequency by meningoencephalitis and intracranial mass lesions. Despite clear evidence of granulomatous involvement of cerebral vessels, stroke-like events in sarcoidosis are rare.

We reported the case of a young patient affected from neurosarcoidosis presenting as a sudden focal neurological deficit mimicking stroke.

Case report: 42 years-old man with known type 2 diabetes mellitus and cigarette smoking was hospitalized for sudden right upper and lower weakness and cervical pain. One month before patient presented bilateral legs paresthesias concomitant to fever and fatigue.

Neurological examination revealed right upper and lower weakness associated to tactile and proprioceptive hypoesthesia.

Magnetic resonance imaging (MRI) of the brain showed hyperintensity on the right dorsal medulla oblongata at the junction with the spinal cord on diffusion-weighted (DWI) images with reduction of the apparent diffusion coefficient (ADC). Spinal cord MRI imaging with gadolinium showed an extensive leptomeningeal enhancement.

Duplex ultrasound of cervical artery and echocardiography were normal.

Chest x-ray showed bilateral mediastinal and hilar lymphadenopathy. Cerebrospinal angiotensin converting enzyme concentration was elevated and the calcium serum concentration, ESR and C-reactive protein were normal. Autoantibody and infectious diseases screen were negatives.

We evoked a neurosarcoidosis and a corticosteroid and immunosuppressive treatment by cyclophosphamide were started. One month later patient had improvement of his symptoms and MRI showed no abnormality on enhanced T (1)-weighted images.

Discussion: Neurosarcoidosis should be considered in differential diagnosis with stroke in case of sudden focal neurological signs in a young person.

278 Acute stroke: clinical patterns and practice

INTRAVENOUS THROMBOLYSIS IN PATIENTS WITH ACUTE VERTEBRO-BASILAR STROKE: WHY DO WE TREAT SO LITTLE?

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Background: Intravenous tissue plasminogen activator (IV tPA) is an approved treatment for acute ischemic stroke (IS) within 4.5 hours of stroke onset, regardless of anterior or posterior circulation subtypes. Vertebrobasilar stroke (VBS) is frequently enigmatic in terms of diagnosis, treatment and prognosis. Our aim was to determine the characteristics of IV tPA treatment in patients with VBS.
Methods: We reviewed all IS patients treated with IV tPA at the Barzilai Medical Center (BMC) and compared patients with VBS and anterior circulation stroke for demographic data, timing (from symptom onset to emergency room (ER), ER to computed tomography, ER to IV tPA, symptom onset to IV tPA), stroke severity, hemorrhagic complications, mortality, and early outcome.
Results: Seventy- seven eligible patients with acute IS were treated with tPA between 2006-2010, comprising 4.8% of all IS patients admitted to BMC during that period. According to the BMC database we estimated that 15 patients with VBS could be treated with IV tPA. Actually, 74 (96%) were patients with anterior circulation stroke [56 males, median age 62 (37-81) years] and only 3 (4%) with VBS [2 males, median age 65 (60-70) years]. The time of symptom onset to ER was significantly longer in patients with VBS compared to patients with anterior circulation stroke (86 vs. 50 minutes, respectively, P< 0.02, ANOVA). All other parameters were similar. Despite of similar severity on admission, patients with VBS had significantly poorer early outcome. Two patients died and in the remaining one no improvement was observed after IV tPA. Significant improvement after 24 hours was observed in 57% and mortality rate was 13.5% in the anterior circulation stroke group.
Conclusions: Our data demonstrate 5-fold lower chance than would be expected of using IV tPA in patients with VBS. Potential reasons for this insufficient use include difficulties in VBS diagnosis, late referral to the ER, incompatibility of the National Institutes of Health Stroke Scale (NIHSS) for VBS and direct transfer of VBS patients to tertiary stroke centers for intra-arterial interventions.

279 Acute stroke: clinical patterns and practice

A RETROSPECTIVE REVIEW OF TELEPHONE REFERRALS: THE EXPERIENCE OF AN ACUTE STROKE CENTRE

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Background: It is recommended that all patients suspected of having a stroke should be admitted to an acute stroke unit as soon as possible. Prompt referral, diagnosis and treatment, especially thrombolysis, are the cornerstones for improving the outcome from stroke. The Acute Stroke Unit at Salford Royal Foundation Trust (SRFT) is a comprehensive stroke centre for Greater Manchester and is one of the main stroke centres in the UK. This study Aims to review the outcome of telephone referrals for patients with suspected acute stroke and its possible relation to the quality of data recorded on the referral forms.
Methods: Standardised referral forms are used for obtaining information about the date and time of the referrals, patients' demographic details and clinical history including the stroke onset time. These were analysed retrospectively for 68 consecutive patients referred to SRFT via telephone calls for consideration of thrombolysis during the period from 5th October 2010 to 1st December 2010. Two referrals were excluded, as one only had demographic details of the patient and the other was a duplicate. Descriptive statistics were used to analyse the information obtained.
Results: 66 telephone referrals from 14 hospitals were included in the study. Majority of these (74%) were received from emergency departments. 2 patients were referred by their general practitioners. Onset of symptom

time was not recorded in 26% and was documented as not known in 2 forms. Outcome from the telephone referral was recorded in 58 forms (88%). 14 patients (18%) were accepted for transfer to SRFT and consideration of thrombolysis.
Conclusion: Telephone consultations with stroke specialists identified patients suitable for thrombolysis and avoided unnecessary transfers to acute stroke unit. It is important that all information is available at this time so that informed decisions can be taken by stroke specialists and that all patients receive optimal care.

280 Acute stroke: clinical patterns and practice

CLINICAL EVALUATION OF PATIENTS WITH SPINAL CORD INFARCTION IN MASHHAD, IRAN

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Background: Spinal Cord Infarction (SCI) is a rare and disabling disease. This hospital-based study was conducted for clinical evaluation of SCI patients in a referal neurology hospital in east of Iran.
Methods: Consecutive SCI patients admitted in Ghaem hospital, Mashhad during 2006-2010 enrolled a prospective clinical study. Diagnosis of SCI was made by neurologists and radiologists. Demographic features, clinical syndrome and Magnetic Resonance Imaging (MRI) findings were recorded. All of the patients underwent a standard battery of diagnostic investigations and etiology of SCI was determined based on the Asian Stroke Criteria. All of the patients suspected to SCI had MRI of spinal cord at the symptomatic level of cord with a 0.5 Tesla generation, Philips NT Intra, Nederland equipment. An equal number of patients with Brain Infarction (BI) were randomly selected from our prospective hospital stroke rigistry data bank. Etiology and degree of disability were compared between these groups of patients.
Results: Fourteen SCI patients (9 females, 5 males) with mean age 38.8±SD: 19.9 years were evaluted. Miscellaneous causes consisted 50% of etiologies in patients with SCI. Uncertain etiology, atherosclerosis and cardioembolisms consisted 35.7%, 7.1% and 7.1% of SCI causes respectively. Distribution of etiologies was significantly different between SCI and BI patients, X2=12.94, df=3, p=0.003. Difference in mean disability score at acute phase of stroke was not significant between two studied groups, z=1.54, p=0.057. Difference in mean changes of disability score at 90 days post event was significant in two groups of patients, z=2.65, p=0.019.
Conclusion: SCI is a rare disease with poor recovery. Distribution of etiologies of SCI is quite different than BI patients.

281 Acute stroke: clinical patterns and practice

INTERRATER RELIABILITY OF THE A-S-C-O CLASSIFICATION OF ISCHEMIC STROKE

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Background: A-S-C-O is a new phenotypic system that categorizes stroke according to a combination of etiologic characteristics. The purpose of this study was to establish the interrater reliability of ischemic stroke subtyping by applying the A-S-C-O criteria to retrospectively obtained medical records.
Methods: A total of 419 patients with acute ischemic stroke were classified according to the A-S-C-O criteria by two stroke neurologists independently. Interrater reliability was assessed by means of κ statistic.
Results: The 2 raters agreed in A-S-C-O subtype diagnosis for only 190 of the 419 patients (45.3%). The κ statistics for 4 stroke phenotypes were atherothrombosis, 0.786, small vessel disease, 0.798, cardioembolic, 0.870, and other causes, 0.860; the P values were all less than 0.001.
Conclusions: Stroke can be reliably classified into one of four etiologic categories on the basis of a review of medical records, whereas the overall agreement for identifying an A-S-C-O subtype of ischemic stroke was only moderate.

MANAGEMENT OF STROKE IN ESTONIA: RESULTS OF THE NATIONAL STROKE AUDIT

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Background: Every year 6000 strokes are diagnosed among 1, 34 million inhabitants in Estonia. Stroke care is provided by 2 regional, 4 central and 11 general hospitals. The stroke audit initiated by the Estonian Health Insurance Fund aimed at analyzing the management of stroke in 2008 according to the Estonian Stroke Guidelines and comparing the Results with the previous audit (2003).
Methods: A total of 400 stroke cases of ischemic, hemorrhagic stroke and transient ischemic attack from 17 hospitals were retrospectively reviewed by 4 experts from May to June 2009 using a unified protocol.
Results: Fifty-five cases (14%) were excluded as the diagnosis was other than stroke; 345 cases (86%) were included into the audit. Only 77 of stroke patients (26%) arrived to the hospital within 3 h. Computerised tomography was done in 283 (82%) patients, in 199 (70%) of them <3 h. Intravenous thrombolysis was offered in 4 hospitals but only 3 patients (23%) of those without contraindications received it. Secondary prevention with antiplatelets was recommended/started in 89% of patients but oral anticoagulation only in 26% and statins in 14% of those having indications for this treatment. Antihypertensive therapy for secondary prevention was started according to the guidelines in 86% of patients. However, medications with unproved efficacy were used in 17% of patients. Physiotherapy was started within 48 hours in 39% of patients with indications.
Conclusion: Stroke guidelines were sufficiently followed in hospitals where the patients were treated by neurologists and in stroke units but several shortcomings were found in general hospitals. The availability of stroke imaging has improved since the last audit but thrombolytic therapy was still provided only in 4 hospitals. Although some indicators may be in part related to financial issues, patients' monitoring and basic treatment measures should be followed according to stroke guidelines. There is a need for national stroke strategy.

EMERGENCY AEROMEDICAL TRANSPORT (EAMT) OF STROKE PATIENTS FROM REMOTE ISLANDS AND RURAL AREAS

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Background: Emergency aeromedical transport (EAMT) is crucial in providing expedient and quality health care to critically ill patients while assuring high level of care during transportation. This objective of this report is to review the epidemiology and safety of EAMT of stroke patients from remote islands and rural areas.
Method: We retrospective reviewed all air medical transported patients with stroke from October 2002 to December 2010. All materials were collected from database of Taiwan National Aeromedical Approval Centre (NAAC). The charts were reviewed for patient demography and clinical characteristics.
Results: Among all 2,257 patients who were air lifted, there were 344 (15.2%) stroke patients. Male to female ratio was 2.31. Mean age of patients was 61.9 years. Intracerebral haemorrhage comprised the majority (45.9%), followed by ischaemic stroke (31.4%) and subarachnoid haemorrhage (15.1%). There was neither in-flight mortality nor air crash in all 2,257 flights. Patient management protocol was followed according to the interfacility air transport guidelines.
Conclusion: In our series, haemorrhagic and ischaemic stroke is the most common (77.3%) cause of EAMT. Flight crew education on the protocol is essential in minimising transport risks. EAMT of patients with stroke can provide safe access to tertiary centres for advanced stroke therapy.

ONE-STOP WALK-IN TIA CLINIC IN A DISTRICT GENERAL HOSPITAL – IS IT FEASIBLE?

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Background: Recent evidence as well as NICE/RCP guidelines has stressed the importance of early assessment and treatment of TIA patients in the prevention of further cerebro-vascular events. A one-stop walk in TIA clinic was set up in our DGH to model that of the EXPRESS study. We present a one-year data from our clinic.
Method: The TIA clinic was changed from a weekly appointment based clinic to a Monday-Friday ward based one-stop walk-in clinic. GPs and A&E staff were informed of the changes. Radiology provided same day slots for CT, MRI and carotid dopplers.
Results: 441 patients were referred to the clinic. 89 patients (20%) had strokes and 158 patients (36%) had TIAs. 60 (38%) were high risk. 183 (74%) of patients were referred by their GP. Referral to assessment times decreased from a mean of 4.8 days to 4 days with a median of 1 day. All high risk TIAs were seen within 24 hours of referral. Waiting times for CT scans reduced from 12 days to 1 day. Carotid dopplers from 9.7 days to 0 days. There was more access to MRI scans (38%) with a mean wait of 5 days and a median of 0 days. 100% of patients received secondary prevention medication immediately.
Conclusion: A one-stop walk-in clinic service is feasible in a district general hospital setting with a substantial reduction in the delays to investigations and treatment. Increase awareness of the walk-in policy will lead to a further reduction in assessment times.

SYSTEMIC TISSUE PLASMINOGEN ACTIVATOR IN A STROKE PATIENT WITH FACTOR VII DEFICIENCY

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Background: The use of systemic tPA for acute ischemic stroke remains constrained by extensive exclusion criteria including coagulation factor deficiency. We present a patient treated intravenous tPA with factor VII deficiency (population incidence 1 in 300,000 to 500,000).
Summary: A 75 yr old African American man with diabetes, hypertension and known factor VII deficiency (the latter was not available from history prior to tPA treatment) had no episodes of bleeding in the last ten years. Prior to an elective cardiac catheterization, he developed acute aphasia and hemiparesis (NIHSS=10). CT head showed no bleeding (ASPECTS=10). Transcranial Doppler (TCD) showed left distal M2 middle cerebral artery (MCA) occlusion (Thrombolysis in Brian Ischemia [TIBI] score 2). IV tPA bolus was given within one hour from symptom onset and the left MCA residual flow signals were monitored continuously for the next 2 hours. Nicardipine infusion was started to control BP with goal re-set to SBP<150 mmHg once family (who arrived after tPA infusion was completed) disclosed the diagnosis of factor VII deficiency established at an outside hospital over 10 years ago. Blood pressure goal was reset to reduce any bleeding complications. Follow up TCD showed complete recanalization of the left MCA (TIBI 5), patient started to show gradual neurological improvement and his 24hr NIHSS was 0. MRI at 24hrs showed a patchy acute infraction in the left MCA territory and no evidence of bleeding. Subsequent lab work up showed factor VII level at 15% (N 50-150). No adverse events were noted during his stay and mRS at 3 weeks post tPA was 0.
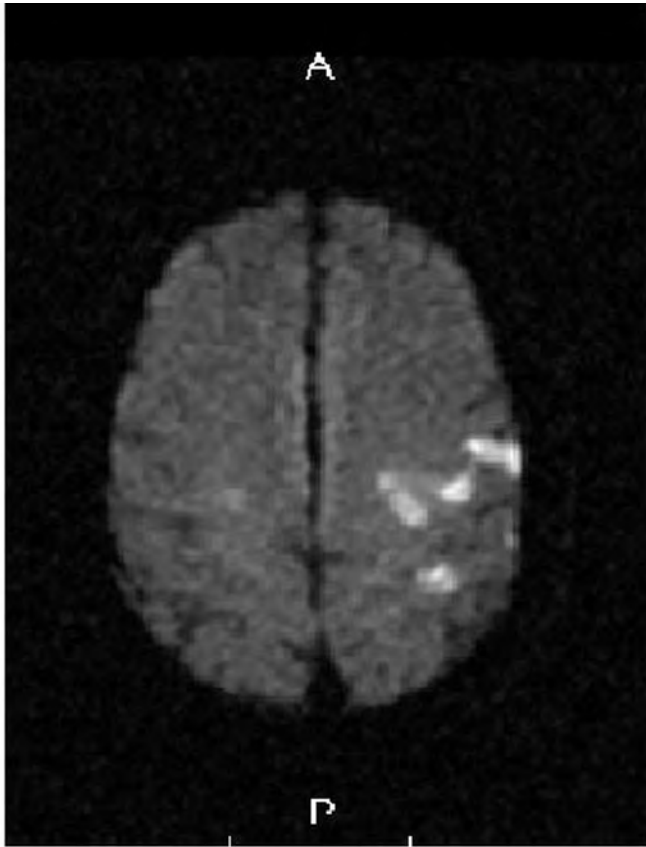
Conclusion: Inadvertent administration of tPA in patients predisposed to bleeding may be unavoidable if all medical records or pertinent history are unavailable on time. Perhaps even tighter BP control compared to currently recommended thresholds could be tested to achieve acceptable tPA safety in high risk patients.

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286 Acute stroke: clinical patterns and practice

BILATERAL SIMULTANEOUS THALAMIC HEMORRHAGES RELATED TO HYPERTENSION: CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Recurrent ICH is not uncommon in patients with hypertension but bilateral cerebral hematomas especially symmetrical ones are very rare. When present they are usually putaminal or thalamic. There are several known causes of the simultaneous multiple hemorrhages besides hypertension.
Case: A women with long standing untreated hypertension admitted to hospital because of sudden loss of consciousness. She had slurred speech and left sided weakness which followed by right sided weakness, loss of consciousness. She was obtunded and had quadriparesis, blood pressure was 200/100 mmHg. Imaging studies showed bilateral thalamic hemorrhages and vasospasm of anterior and middle cerebral arteries.
Result: She was treated medically and discharged with same clinical findings.
Discussion: Bilateral thalamic hemorrhages are very rare and usually seen in patients with hypertension as well as with other associated diseases. The abnormal changes in blood vessels may play an important part in pathogenesis. The prognosis is almost always poor.

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287 Acute stroke: clinical patterns and practice

EARLY MOBILISATION AFTER STROKE: WHAT ARE THE PROFESSIONALS' OPINIONS?

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Background: Early mobilisation after stroke may reduce complications and improve outcome. It is recommended in clinical guidelines around the world, but the evidence-base is very limited and few specific practice directives are provided with consequently large variations in clinical practise. This study sought to capture stroke care professionals' opinion about: 1) when after stroke first mobilisation should take place, 2) whether early mobilisation may affect patients' final outcome and 3) what level of evidence they would need to change their mobilisation practice.
Methods: A 9 item questionnaire was used to interview stroke care professionals during the combined Stroke Society of Australasia and Smart Strokes Australasian Nursing and Allied Health Conference 2008.
Results: We interviewed 202 professionals and 40% were in favour of mobilising both ischemic and hemorrhagic stroke patients within 24 hours of stroke onset, while 41% responded that the optimal time for at least one of the two stroke types is later than 24 hours but within 7 days. Most professionals (57-76%) thought that early mobilisation is very important for patients' final outcome. In order to change practice, only 19% required a large randomised controlled trial or a systematic review.
Conclusion: This study found that professional opinion varies. Solid evidence would help the development of specific practice guidelines; however the Results of this study suggest that high quality trials will only have some influence on professionals' opinion on the practice of early mobilisation.

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288 Acute stroke: clinical patterns and practice

ENDOVENOUS THROMBOLYSIS WITH RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR IN ACUTE ISCHEMIC STROKE – A COMPARATIVE HOSPITAL ANALYSIS

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Background: Acute ischemic stroke (IS) still the main cause of death in our country, representing 20% of the global mortality and are linked with a high level of disability. The only treatment approved to IS, that has demonstrated safety and efficacy, is intravenous recombinant tissue plasminogen activator (rt-PA). It has been approved in Europe in 2003, after NINDS study.
Methods: The authors reviewed the experience of thrombolytic therapy in a hospital, and compared them with country and international data obtained in SITS International. The data correspond to patients who were treated with rt-PA in the hospital from January 2008 to October 2010.
Results: Data will be presented in the following order: hospital/country/international data. Number of patients included: 95/1475/46134; average age: 67/68/67 years old; females: 53%/44%/43%; score 0-2 on Modified Rankin Scale before stroke onset: 98%/93%/80%; Hypertension: 73%/70%/62%; Diabetes: 36%/24%/17%; Hyperlipidemia: 53%/48%/31%; Current smoker: 22%/15%/21%; Atrial fibrillation: 21%/29%/24%; score 0-7 on baseline NIHSS scale: 21%/19%/28%; score >14 on baseline NIHSS scale: 38%/44%/37%; TACI: 43%/52%/35%; PACI: 31%/28%/41%; LACI: 24%/19%/22%; POCI: 2%/0%/1%; Average time in minutes: onset to treating hospital/door time 64/69/70; door to imaging study time 29/28/24; door to treatment/needle time 64/66/66; onset to treatment/needle time 129/147/145.
Conclusion: Our hospital started using rt-PA as treatment for acute ischemic stroke in January 2008. Since then, the Results obtained with this treatment have been gradually improving, mostly by the experience acquired. As a result, there are an increasing number of patients treated. Generally, our Results are similar to country and international Results. Considering that time spent, since symptoms onset to treatment, is still one of the main factor that contributes to a better patient outcome, one of the most positive aspects is our onset to treatment/needle time.

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289 Acute stroke: clinical patterns and practice

SAFETY AND EFFICACY OF ULTRASOUND-ENHANCED SYSTEMIC THROMBOLYSIS IN ACUTE ISCHEMIC STROKE

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Ultrasound-enhanced systemic thrombolysis has several advantages over the other Methods of increase of recanalizaion rate (intraarterial thrombolysis, mechanical thrombectomy), because it is easy-to-use and comparatively inexpensive. Our aim was to estimate safety and efficacy of ultrasound-enhanced systemic thrombolysis in ischemic stroke.

The research involved 11 patients (59,6±9,2 years old) with anterior circulation atherothrombotic or cardioembolic ischemic stroke. Systemic thrombolysis and permanent 2MHz Doppler insonation of thrombosis area during 1 hour were accomplished. NIHSS, Barthel index and modified Rakin scale examination, T1- T2- DWI MRI, MRA, TCD were performed within the first 24 hours, on 2nd-4th, 30th days after stroke onset.

Recanalization was found in 7 patients (63%), including complete recanalization in 5 patients (45%). All cases of recanalization were accompanied by clinical improvement. The symptomatic intracranial haemorrages were absent.

The ultrasound-enhanced systemic thrombolysis in ischemic stroke provides increased recanalizaion rate comparing with the Results of systemic thrombolysis in the literature. The safety profile of 2MHz ultrasound-enhanced systemic thrombolysis in involved patients was good.

Acute stroke: current treatment

336 Acute stroke: current treatment

LOW-MOLECULAR-WEIGHT-HEPARIN VERSUS ASPIRIN FOR EARLY NEUROLOGICAL DETERIORATION IN PATIENTS WITH ACUTE ISCHEMIC STROKE AND LARGE ARTERY OCCLUSIVE DISEASE: THE FRAXIPARIN IN STROKE STUDY FOR THE TREATMENT OF ISCHEMIC STROKE (FISS-TRIS)

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Background: Patients with acute ischemic stroke and large artery occlusive disease (LAOD) have an increased risk of early neurological deterioration (END) due to progressive stroke, early recurrent ischemic stroke (ERIS), or symptomatic intracranial cerebral haemorrhage. Low-molecular-weight-heparin (LMWH) has been widely advocated to prevent venous thromboembolism, but its risk and benefit in early ischemic stroke are inadequately defined.
Methods: The primary aim was to test whether, treatment with LMWH within 48h after stroke onset, is superior to aspirin for the prevention of END during the first 10 days. The events of END were defined as ERIS, progressive stroke, symptomatic intracranial cerebral haemorrhage (SICH) and increased intracranial pressure. Outcomes were assessed, by modified Rankin scale (excellent [scores 0-1], favorable [scores 0-2]) and Barthel Index (favorable [scores >85]), at 10 days and 6 months.
Results: The frequency of END during the first 10 days was 12/180 (6.7%) in LMWH-allocated patients versus 24/173 (13.9%) in aspirin-allocated patients and LMWH was significantly associated with the reduction of END (OR= 0.44, 95% CI 0.21-0.92). Compared with aspirin, LMWH was significantly associated with a lower frequency for progression of stroke during the first 10 days (7/180 [3.9%] versus 21/173 (12.1%), OR=0.29, 95% CI 0.12-0.71). Other events during the first 10 days revealed no advantage of LMWH over aspirin: ERIS 3/180 versus 1/173; SICH 1/180 versus 2/173; symptomatic and asymptomatic cerebral haemorrhage 4/180 versus 5/173. There were no significant differences in outcomes at 10 days and LMWH was significant associated with excellent outcome (mRS 0-1) at 6 months.
Conclusion: Treatment with LMWH, within 48h of ischemic stroke with LAOD improved END and progressive stroke compared with aspirin during first 10 days, which was no associated with a higher rate of symptomatic cerebral haemorrhage.

337 Acute stroke: current treatment

EARLY SYSTOLIC BLOOD PRESSURE VARIABILITY IS ASSOCIATED WITH STROKE OUTCOME AFTER INTRAVENOUS RT-PA: STROKE ACUTE MANAGEMENT WITH URGENT RISK-FACTOR ASSESSMENT AND IMPROVEMENT (SAMURAI) RT-PA REGISTRY

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Background: Early systolic blood pressure (SBP) profiles were reported to be independent predictors for long-term stroke outcome in ECASS-II trial. The aim of this study was to elucidate the association of early SBP variability with the outcomes of stroke patients treated with low-dose recombinant tissue plasminogen activator (rt-PA).
Methods: A retrospective, multicenter, observational study was conducted to identify the effects of underlying risk factors on intravenous (IV) rt-PA therapy using 0.6 mg/kg alteplase in 10 stroke centers in Japan (the SAMURAI rt-PA Registry). Consecutive stroke patients with a premorbid modified Rankin Scale (mRS) score ≤1 who received rt-PA were studied. BP was measured at 0 (just before IV rt-PA), 1, 4, 8, 12, 16, 20 and 24hours and standard deviation (SD), successive variation (SV) and difference between max and min (max-min) were used to represent SBP variability. Stroke outcomes were assessed with symptomatic intracerebral hemorrhage (sICH) within 36 hours with a ≥1-point increase from the baseline National Institutes of Health Stroke Scale (NIHSS) score, 3-month favorable outcome (mRS 0-1) and death within 3 months.
Results: Of a total of 535 patients (women 35%, 71+-12 years old), mean SD, SV and max-min were 14+-6, 17+-7 and 42+-18mmHg, respectively. High SD and max-min were associated with an increased risk of sICH [adjusted OR (/10mmHg) 2.97, 95% CI 1.61-5.63; 1.42, 1.16-1.76; respectively], although SV was not [1.61, 0.93-2.71]. High SD, SV and max-min were inversely associated with 3-month favorable outcome [0.66, 0.45-0.95; 0.68, 0.50-0.91; 0.84, 0.74-0.95; respectively] and positively associated with death within 3 months [2.57, 1.46-4.57; 1.92, 1.16-3.12; 1.35, 1.12-1.64; respectively]. Systolic BP just before IV rt-PA was not associated with any outcomes.
Conclusion: Early SBP variability was associated with sICH, 3-month favorable outcome and death in stroke patients following low-dose rt-PA therapy.

338 Acute stroke: current treatment

INTRAVENOUS THROMBOLYSIS IN ACUTE ISCHEMIC STROKE PATIENTS WITH PREVIOUS ANTICOAGULANT THERAPY: CLINICAL PROFILES AND OUTCOME

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Background: According to the current licence for intravenous (i.v.) thrombolysis, the use of oral anticoagulants (OAC) prior to the index stroke is one exclusion criteria irrespective of the INR because of the potentially increased risk of hemorrhage. Aim of this study was to evaluate clinical profiles and outcome of stroke patients with prior OAC therapy and baseline INR ≤1.7 treated with i.v. alteplase.
Methods: We analyzed the data of patients treated with i.v. rt-PA in Italy from 2003 to 2009 included in the SITS-ISTR (Safe Implementation of Treatment in Stroke-International Stroke Thrombolysis Register). Patients with OAC therapy were compared to non-OAC patients. Outcome measures were 3-month mRS 0-2, symptomatic intracerebral hemorrhage (SICH/NINDS definition) and mortality. Univariate and multivariate analyses were performed.
Results: Overall, 4194 patients were studied of whom 96 (2.3%) were on OAC therapy at stroke onset. Compared to non-OAC patients, those on OAC were older (p<0.0001), had more frequently arterial hypertension, diabetes, AF, congestive heart failure and previous stroke (p<0.0001) and less frequently hyperlipidemia

(p 0.001) in past medical history, higher times from onset-to-therapy (p0.032) and arrival-to-therapy (p0.005), and received a lower dose of rt-PA (p0.007). At univariate analysis, functional outcome (mRS 0-2) at 3 months, and the proportion of SICH were similar in OAC and non-OAC patients, while mortality rate at 3 months was significantly higher among OAC patients (p0.032). At the multivariate analysis OAC prior to the index stroke was not related to mortality while was an independent predictor of good functional outcome at 3 months (OR 2.906, 95%IC 1.99-4.24; p<0.0001).

Conclusions: Our study shows that OAC therapy with an INR ≤1.7 prior to the index stroke does not increase the risk of SICH or mortality from i.v. thrombolysis. Hence, prior OAC therapy should not be considered an absolute exclusion criteria but related to the baseline INR value.

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339 Acute stroke: current treatment

OFF-LABEL-THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE: RATE, CLINICAL OUTCOME AND SAFETY ARE INFLUENCED BY THE DEFINITION OF "MINOR STROKE"

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Background: Several contraindications for intravenous thrombolysis are not based on controlled trials. Specialized stroke centers often apply less restrictive criteria. The aim of our study was to analyze how many patients receive off-label thrombolysis. Furthermore clinical outcome and safety data were compared to patients treated on-label and the influence of different definitions for "minor stroke" were examined.
Methods: Consecutive thrombolysis patients treated between 01/2006 and 01/2010 were included. Patients treated off-label were compared to patients with on-label therapy according to the European license. Since no specified definition for "minor neurological deficit" exists in the license two distinct definitions were considered off-label: (Def.1: NIHSS<1; Def.2: NIHSS ≤ 4).
Results: 232/422 (55%) patients were treated off-label. The most prevalent off-label criteria (OLC) were: age >80a (n=113), minor stroke (Def. 1 n=3; Def. 2 n=84), elevated blood-pressure necessitating aggressive treatment (n=75), time-window >3h (n=71) and major surgery or trauma <3 months (n=20). In group comparison off-label patients had an overall worse outcome using Def 1 for minor stroke, while there was no difference when Def. 2 was applied. In multivariate analysis off-label therapy (Def. 1) in general and age >80a were independent predictors for poor outcome. None of the contraindications were associated with an increased bleeding risk.
Conclusions: Off-label therapy is frequently applied at our center and is not associated with higher complication rates. Overall outcome of off-label treatment largely depends on the definition used for minor stroke. Beside age >80 years, a known poor prognostic factor, no other specific OLC was associated with poor outcome. Our data suggest the criteria in the European licence may be too restrictive.

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340 Acute stroke: current treatment

DO INSULIN SLIDING SCALES REALLY WORK FOR ACUTE STROKE PATIENTS WITH HYPERGLYCAEMIA?

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Introduction and Aims: Early hyperglycaemia after acute stroke is associated with worse outcome. Some studies have shown controlling hyperglycaemia after acute stroke reduces mortality. Insulin sliding scales for hyperglycaemic acute stroke patients are widely recommended in numerous international guidelines. Many of these recommend tight control, with maintenance of glucose <8mmol/l. This study aimed to identify if the standard insulin sliding scale (ISS) for hyperglycaemic acute stroke patients resulted in glycaemic control in a busy Acute Stroke Unit.
Methods: All acute stroke patients requiring an ISS during acute stroke over 2 years were audited. The length of use of the ISS and blood glucose levels were recorded.
Results: The glycaemic control of 18 acute stroke patients was analysed. Patients received an ISS for an average of 48 hours although the range was wide (11 to 228 hours). Only 1 patient had a blood glucose in this physiological range (4-8mmol/l) more than 90% of the time on an ISS. 61% of patients spent more than half the time on an ISS with a glucose outside of the physiological range (4-8mmol/l). 33% of patients had a glucose > 8 mmol/l for 80% of the time on an ISS. Only half of patients avoided very poor control (blood glucose > 15 mmol/l) all of the time whilst on an ISS. 25% of patients spent 20% of their time on an ISS with a glucose above 15mmol/l. Only one patient had a hypoglycaemic event (<3 mmol/l).

Conclusion: ISS do not ensure glycaemic control within the physiological range for acute stroke patients on an Acute Stroke Unit. Hypoglycaemia was very rare on the ISS in the Acute Stroke Unit. The length of use of the ISS for acute stroke patients can be protracted. An improved, patient specific ISS is suggested in future if physiological glycaemic control is to be maintained for acute stroke patients.

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341 Acute stroke: current treatment

INTEROBSERVER VARIABILITY IN THE DETECTION OF RECANALISATION OF INTRACRANIAL ARTERY AFTER ACUTE ENDOVASCULAR TREATMENT OF STROKE PATIENTS

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Background: The occlusion of cervical or intracranial arteries is the most common cause of acute ischemic stroke. Besides the entry clinical status, timely recanalization of the occlusion is the most important independent prognostic factor of the stroke outcome. The high recanalisation rate is mostly the only one indicator of successful endovascular procedure and treatment in various studies. The aim of this study was to assess the interobserver variability of diagnosis of artery occlusion and its recanalisation after endovascular procedure.
Methods: 43 patients with acute ischemic stroke during 2009 underwent conventional digital angiography. The images were retrospectively evaluated by two experienced neuroradiologists for diagnosis of intracranial artery occlusion and for the presence or absence recanalisation in TIMI grade.
Results: 27 males, 16 females, age 70.5±14 (mean ± SD), median mRS before procedure = 0, (IQR 0-2), NIHSS before procedure 17±5 (mean ± SD). 53 arteries were assessed. Percutaneous balloon angioplasty (PTA) or intracranial stent implantation (self expandable) were done in 36 patients, local thrombolysis in 8, EKOS in 2 and IVT before procedures in 19 patients. Favorable clinical outcomes (mRS < 2) occurred in 27% and mortality was 18%. No symptomatic intracerebral hemorrhage occurred. Interobserver agreement for diagnosis of artery occlusion was good (kappa=0,635, P<0.001) with a full agreement in 73%. Interobserver agreement for recanalisation was poor (kappa =0.277, P<0.001) with full agreement in 44%.
Conclusion: Interobserver agreement in detection of recanalisation of intracranial artery after endovascular treatment in our study was poor. The only assessment of recanalisation in TIMI grade after acute endovascular treatment is not reliable for evaluation of effectiveness of endovascular Methods. The recanalisation rate evaluated by TIMI grade as a primary end point for feasibility of Methods (devices) may be irrelevant.

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342 Acute stroke: current treatment

EARLY UPPER GASTROINTESTINAL BLEEDING RISK AND HELICOBACTER PYLORI INFECTION IN PATIENTS TAKING ANTIPLATELET THERAPY FOLLOWING STROKE

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Background: Antiplatelet therapy (APT) is key to the secondary prevention of ischaemic stroke but is associated with an increased upper gastrointestinal bleeding (UGIB) risk. The long-term UGIB risk in patients taking antiplatelet therapy has been described as 0.6%. The acute risk in hospital patients and associated risk factors is less clear.
Methods: This was a prospective, inception, cohort study of consecutive patients admitted with acute ischaemic stroke and commenced on oral APT within seven days. Helicobacter pylori status was determined by stool antigen testing and gastrointestinal symptoms were assessed using the Short-form Leeds Dyspepsia Questionnaire on admission. UGIB events were determined at six weeks and major bleeding defined as fatal haemorrhage, drop in haemoglobin level of 4g/dL or more, or overt bleeding requiring a transfusion of at least two units of blood.
Results: 322 patients were recruited to the study; the six-week review was completed in 314. Seven (2.2%) patients had an UGIB event, 6 (1.9%) of which were major. Of 254 stool samples, 169 (66.5%) were H. pylori positive. Prior dyspepsia was reported by 41 (13.1%) patients. By univariate analysis, H. pylori (OR 0.75, 95% CI 0.12-4.58, p=0.76) and dyspepsia (OR 1.11, 95% CI 0.13-9.48, p=0.92) were not risk factors for UGIB. By multivariate analysis increasing age was the only significant predictor of UGIB (OR 1.13, 95% CI 1.01-1.26, p=0.001).

Conclusion: Active Helicobacter pylori infection is not associated with early UGIB events following stroke in patients taking APT. Increasing age, however, is a major risk factor. Older people warrant careful monitoring and review of therapy after the commencement of APT following stroke.

343 Acute stroke: current treatment

TRENDS IN THE MANAGEMENT AND OUTCOME OF HOSPITALIZED PATIENTS WITH ACUTE ISCHEMIC STROKE IN ISRAEL: THE NATIONAL ACUTE STROKE ISRAELI SURVEYS (NASIS) PROJECT

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Background: The management of acute ischemic stroke is undergoing major changes during the last decade. Our aim was to examine trends in the utilization of reperfusion therapy and in-hospital outcome of patients with acute ischemic stroke admitted throughout all hospitals in Israel.

Methods: Data were derived from the tri-annual two-month periods National Acute Stroke Israeli Surveys (NASIS project; Feb-March 2004, March-April 2007, April-May 2010). Admission policies did not change between periods. The NASIS project includes unselected patients admitted to all hospitals nationwide (n=28), thus avoiding institution and patient selection bias. There were in total 6,293 patients [ischemic stroke 4,452 (70.7%), intracerebral hemorrhage 486 (7.7%), undetermined stroke-98 (1.6%), TIA-1257 (20.0%)].

Results: The distribution of patients with ischemic stroke by sex and age did not differ between periods (2010 period: women 47.8%, mean age 73.0±13.8; men 52.2%, mean age 68.3±13.3 yrs.). Length of acute hospital stay did not differ significantly between periods [2010 period: median (25%-75%) 5 (3-9) days]. Utilization of CT or MR angiography increased from 2.1% in 2004 to 7.9% in 2007 and up-to 16.6% in 2010 (p<0.001). Utilization of reperfusion therapy increased from 0.5% in 2004 to 1.6% in 2007 and 5.9% in 2010 (p<0.001; 2010 period: 5.5% intravenous rt-PA, 0.9% endovascular therapy). Overall in-hospital mortality among all ischemic stroke patients has decreased from 7.2% in 2004 to 5.2% in 2007 and 4.2% in 2010 and severe disability at hospital discharge (mRS 4-5) from 33.5% in 2004 to 27.2% in 2007 and 22.9% in 2010 (p<0.001).

Conclusions: The ongoing NASIS project is designed to monitor trends in the management and outcome of patients admitted nationwide for acute stroke and supports quality improvement efforts facilitating evidence-based stroke care. Utilization of vascular imaging and reperfusion therapy for acute ischemic stroke country-wide is steadily increasing and in-hospital mortality is decreasing.

344 Acute stroke: current treatment

CT ANGIOGRAPHY CHARACTERISTICS PREDICT RECANALIZATION IN PATIENTS WITH ACUTE ANTERIOR CIRCULATION OCCLUSIONS TREATED WITH REPERFUSIONS THERAPIES

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Background: Patient selection for reperfusion therapies is critically important. We evaluated how specific thrombus imaging features by CTA could interplay to achieve recanalization in acute stroke patients treated with either IV or IA thrombolysis.

Methods: We retrospectively studied patients with anterior occlusions on CTA who underwent open label IA-procedures. We collected clinical and imaging variables: occlusion location, thrombus-length, burden-score, residual flow grade, arterial branching patterns around thrombus and leptomeningeal collateral. Recanalization was defined by TIMI-score 2-3 on initial conventional angiography for the IVtPA-group, and on final angiography post-procedure for the IA-group.

Results: Among 96 patients (42 male, mean age 62.69±15.00 years, median initial NIHSS 17) included, 11 (11.45%) received only IVtPA and 85 (88.54%) IA-treatment. In a logistic regression model examining imaging features of the thrombus, the only predictive variable was occlusion location. The odds of recanalization with thrombus location in the terminal ICA are 0.2 (0.06-0.68) compared to thrombus location in the M1-MCA, after adjustment of thrombus length, treatment type (IV only vs. endovascular therapy with/without IV tPA) and collateral score. Collateral score did not impact the probably of recanalization in this data set.

Conclusions: CT-angiogram based imaging thrombus characteristic predict imaging outcome in a cohort of patients with anterior stroke treated with reperfusion therapies. Thrombus location is the most important determinant of recanalization after IV or IV-IA treatment.

345 Acute stroke: current treatment

IS THROMBOLYTIC TREATMENT SAFE IN PATIENTS WITH STROKE DUE TO CAROTID ARTERIAL DISSECTION?

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Background: Arterial dissection is identified as etiology in up to 10-25% of ischemic strokes among young patients. There is still controversy about intravenous thrombolysis safety in patients with arterial dissection. We compare efficacy and safety of this treatment between patients with carotid arterial dissection (CAD) and patients with other stroke etiologies (non-CAD).

Methods: We prospectively evaluated 559 consecutive patients with anterior circulation ischemic stroke treated with intravenous tPA. Sixteen patients with ischemic stroke due to CAD were studied. Variables analyzed included arterial recanalization by transcraneal Doppler (DTC) using Thrombolysis In Brain Ischemia scale, symptomatic intracranial hemorrhage (SICH), early clinical evolution, and 3- month functional outcome and mortality.

Results: Mean age was 72.5±12.2 years; 273 (48.8%) were women. Median NIHSS was 17 (IQR 11-20). CAD-patients were younger (48.2±11.8 vs. 73.4±11.2 years, p<0.001) and less hypertensive (23.5% vs. 61.7%; p=0.002). No significant differences were found in time to treatment (165.4±66.7 vs. 171.3±59.16 minutes, p=0.071), basal NIHSS (14.6±6.5 vs. 15.3±5.2, p=0.61) or glucemia (124.8±40.3 vs. 133.6±49.8 mg/dL, p=0.052). Arterial recanalization (53.3% vs. 49.7%), SICH (5.9% vs. 5.3%) and 3-month-mortality (6.3% vs. 14.5%) were similar in CAD and non-CAD patients (p=ns). There was a trend towards better 3-month functional outcome (mRS<1) in CAD-patients (56.3% vs. 33.3%, p=0.059) but it did not reach statistical significance in the logistic regression model after adjusting for age and basal NIHSS (OR 1.26; CI 95% 0.38-4.15).

Conclusion: Intravenous thrombolysis in patients with ischemic stroke due to CAD is safe and almost as effective as in non-CAD-stroke patients. Therefore, carotid arterial dissection is not a contradiction for systemic thrombolysis.

346 Acute stroke: current treatment

HYPERGLYCEMIA IS AN INDEPENDENT RISK FACTOR FOR POOR OUTCOME AFTER RT-PA ONLY IN THE LARGE ARTERY STROKE SUBTYPE

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Background: Hyperglycemia is considered a risk factor for poor stroke outcome. There remains controversy whether it is an independent factor. It is also not known whether all stroke subtypes are affected. Imbalances of baseline factors that influence outcome constrain subgroup analysis, leading to the need for corrections. These corrections are imperfect because their influence is complex and non-linear. We applied a recently developed matching methodology that requires a minimum of assumptions (pPAIRS©, Mandava et al. Stroke 2010) to the NINDS rt-PA dataset to answer the question: Does hyperglycemia independently influence outcome in subjects matched for baseline NIHSS, age and stroke subtype after treatment with rt-PA?

Method: For this analysis, a threshold of 150 mg/dl of baseline glucose was applied to the rt-PA arm of the NINDS dataset. pPAIRS© finds the nearest neighbor match in multi-dimensional Euclidean space. We matched baseline NIHSS, age, and stroke subtype: small vessel (SVS), large vessel (LVS) and cardioembolic (CES) stroke for subjects </> 150mg/dl. 90 day functional outcomes and mortality were compared.

Results: Excellent matching was achieved (e.g, in LVS: Mean NIHSS 16.8 vs 17.1, p=0.9; Mean Age: 67.6 vs 68.8, p=0.6). Hyperglycemia worsened functional outcome in the rt-PA arm in the LVS subtype only (e.g. % achieving mRS 0-1: 46% normoglycemia vs 22% hyperglycemia; p=0.03; McNemars). Mortality was non-significantly increased. No consistent effects were seen in SVS and CES. Similar Results were seen with a threshold of 200 mg/dl.

Conclusions: We found that hyperglycemia worsened functional outcome in the large vessel stroke subtype after rt-PA treatment. This finding is consistent with pre-clinical literature that hyperglycemia is an independent factor, and that large arteries are vulnerable to reperfusion injury under hyperglycemic conditions (Martini and Kent, JCBF Met 2007). Treatment studies should consider such differential effects.

SYSTEMIC THROMBOLYSIS IMPROVES OUTCOME AND REDUCES SIZE OF MCA INFARCTION EVEN IF MCA RECANALISATION FAILS

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Background: Only few specific data exists concerning the effect of tPA on morphometrics and clinical fate of patients suffering from persisting middle cerebral artery occlusion (pMCAO). Increased risk of hemorrhagic transformation (HT) after tPA treatment is feared to worsen the outcome after stroke. We therefore compared stroke patients with pMCAO with and without tPA treatment.
Methods: pMCAO after acute MCA infarction was identified by transcranial colour coded duplexsonography (> 24h after symptom onset) in 55 consecutive stroke patients (22 with and 33 without acute tPA treatment). Functional outcome after two months was assessed by means of modified Rankin Scale scores. We performed a morphometric, semi-automated, voxel-based volumetry of each infarction on diffusion weighted MR imaging. Volumes were measured and size categorized as small (<50ml), middle (50-200ml) and big (>200ml). Additionally size was rated visually as up to and more than one third of MCA territory. Occurrence of secondary HT on gradient echo MRI was rated as hemorrhagic infarction (HI) and parenchymal hematoma (PH).
Results: Albeit pMCAO patients did significantly better after tPA treatment (mRS 4 points vs. 5 points; p=0.023). Mean size of infarction was 113.5ml in tPA patients and 143.6ml in non-tPA patients. Concerning infarction size there was a trend towards more small strokes in tPA patients concerning morphometric (50% vs. 30.3%; OR 2.3; 95% CI 0.77 - 6.93) and visually rating (59.1% vs. 36.4%; OR 2.53; 95% CI 0.85 - 7.53). HI was equally distributed in tPA and non-tPA patients while two tPA patients developed PH.
Conclusions: Even in pMCAO we found tPA to improve functional outcome after two months as infarction size might be smaller after tPA treatment. tPA might increase the chance of developing a small stroke even if recanalisation fails. HI was found equally often in both groups indicating that it is more associated with recanalisation instead of tPA treatment alone.

CLINICAL OUTCOMES IN PATIENTS WITH AND WITHOUT ATRIAL FIBRILLATION RECEIVING INTRAVENOUS RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

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Background: Some patients with acute stroke are less likely to respond to recombinant tissue plasminogen activator (rtPA) therapy. Atrial fibrillation (AF) is one of the most well known predictor for severe stroke. Therefore, we assessed clinical outcomes in acute stroke patients with and without AF after rtPA treatment.
Methods: We undertook a single-center, retrospective analysis of consecutive acute stroke patients treated with iv rtPA within 4.5 h of stroke onset between July 2006 and November 2010. The patients were divided into two groups (AF group and non-AF group). The NIHSS scores before, 1h, 24 h and 7 days after administration of rtPA were obtained. Modified Rankin scale (mRS) at 3 months after rtPA therapy, symptomatic intracerebral haemorrhage (SICH) and mortality were evaluated as well. SICH was based on the imaging scan changes (PH 1 and 2, PHr 1 and 2) within 36 h combined with deterioration of 4 or more point drop on the NIHSS score or death within 7 days.
Results: A total of 128 patients were registered. AF group included 39 (30.5%) patients and non-AF group 89 (69.5%) patients. The mean age of AF group patients was 71.8 years and non-AF group 63.2 years (P<0.001). The significant gender differences between the groups were observed (AF group - men 17, women 22 and non-AF group - men 58, women 31, P=0.02). The mean time from onset of stroke to drug administration did not significantly differ between the groups. Median NIHSS score was significantly higher in AF group than in non-AF group at baseline, 1h, 24h and not significant at 7 days (16 vs 12, P<0.001; 10 vs 6, P=0.005; 9 vs 4, P=0.03 and 5 vs 3, NS). Fewer patients with AF had favorable outcome (mRS 0-1) at 3 months than patients without AF (45% vs 73%, P=0.02). AF was strongly associated with SICH (AF group 5 vs non-AF group 2, P=0.045) and rate of mortality (AF group 25.6% vs 10.1%, P=0.02).
Conclusions: The presence of AF more frequently predicts unfavorable outcome in acute stroke patients treated with rtPA. The benefits of rtPA therapy in this subgroup requires further confirmation.

INTRAVENOUS CONTRA INTRA-ARTERIAL THROMBOLYSIS IN MIDDLE CEREBRAL ARTERY STROKE: A RETROSPECTIVE SINGLE CENTRE DATA ANALYSIS

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Background: Intra-arterial thrombolysis therapy for acute ischemic stroke has been widely replaced by the intravenous approach a decade ago. The Introduction of intravenous (i.v.) thrombolysis simplified the therapeutic procedures and therefore enabled a wide distribution of thrombolysis therapy for ischemic stroke. However, a comparison between these two strategies is still lacking. This study aimed at the comparison of the therapeutic Results achieved with the two approaches in a tertiary stroke centre, that switched from exclusive intra-arterial (i.a.) thrombolysis to predominant i.v.-thrombolysis in 2003.
Methods: A retrospective analysis of 142 consecutive cases of intra-arterial (n=44) and intravenous (n=98) thrombolysis in patients with ischemic stroke in the territory of the middle cerebral artery (MCA) was performed. Multiple regression analysis was applied to identify those factors that independently influence patients' outcome, defined as delta between NIHSS on admission and discharge.
Results: Patients treated with intra-arterial thrombolysis were significantly younger (60 vs. 67 years), received lower doses of rt-PA (40mg vs. 56.4mg), were treated later (184min vs. 150min after the onset of symptoms), had a higher rate of MCA occlusions at admission and showed a better risk profile with regard to heart diseases, hyperlipoproteinemia, hypertonia and previous stroke. In spite of these differences there was no difference in outcome between patients with i.a.- and i.v.-thrombolysis. Outcome was Independently influenced by gender (p=0.005), intracerebral bleeding before discharge (p=0.015) and heart disease (p=0.014). In contrast to former studies female patients showed a lower profit from thrombolysis and higher mortality compared to male patients.
Conclusion: Intravenous thrombolysis is a good therapeutic option compared to intra-arterial thrombolysis with comparable outcome even in patients with unfavorable risk profile.

DOES PREVIOUS INTRAVENOUS THROMBOLYSIS AFFECT EFFECTIVENESS OR SAFETY OF MECHANICAL THROMBECTOMY?

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Background: Endovascular treatment of acute stroke is increasingly available. Previous intravenous thrombolysis may increase the risk of haemorrhagic transformation and reduce the benefit of endovascular procedures.
Methods: We analysed the data of a prospective register of 34 patients treated with endovascular procedures in a single centre in 2009-2010. In the first group (IV-EV group), all patients underwent primary intravenous rt-PA therapy (0.9 mg/kg) and then endovascular treatment due to lack of improvement. In the second group (EV group), patients underwent directly endovascular procedures (mostly thrombus retrievement with stent plus aspiration). Haemorrhagic transformation (HT) at 24 hours and clinical outcome measured as mRS at three months were assessed.
Results: Each group included 17 patients. There were no significant differences between age (56.1±11.6 vs. 59±17.6), basal NIHSS (18 [4-26] vs. 17 [6-35]), time from stroke to endovascular treatment (364±234 vs. 479±366), and duration of the procedure (74±39 vs. 98±62). Posterior circulation stroke was more frequent in EV group (41.2%) than in IV-EV group (11.8%) (p=0.052). 50% were independent (mRS≤2) at three months in both groups. Mortality was 17.6%(n=3) in IV-EV group, and 23.5% (n=4) in EV group. HT was higher in IV-EV group (58.8%) than in EV group (31.1%), p=0.11; although HT was symptomatic in one and two patients respectively.
Conclusions: Intravenous thrombolysis prior to endovascular treatment was not associated with an increased risk of HT, and there were no differences regarding clinical outcome or mortality rate. Therefore, intravenous thrombolysis should still be the initial therapy on patients with large vessel occlusion undergoing endovascular treatment.

STROKE IN THE ANTERIOR CIRCULATION: TWO-CENTER COMPARISON OF COMBINED (INTRAVENOUS, INTRA-ARTERIAL AND/OR MECHANICAL THROMBECTOMY) WITH INTRAVENOUS THROMBOLYSIS

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Background and purpose: The aim of our study was to compare safety and potential efficacy of combined with intravenous thrombolysis in patients with acute MCA strokes with proximal occlusions.
Patients and Methods: All consecutive ischemic MCA strokes admitted within a 4h30 hour window in two different stroke centers were prospectively collected. In one center, the preferred approach was intravenous therapy (alteplase, 0.5-0.6mg/kg) during 30 minutes, and, in case of absence of recanalisation assessed by transcranial color-coded ultrasound (TCCD), intra-arterial and/or mechanical therapy. In the other center, the preferred treatment was intravenous (IV) standard thrombolysis alone. Only strokes with T, M1 and M2 occlusions confirmed by CT-angio were considered for this retrospective analysis. Endpoints were favourable outcome defined as modified Rankin scale 0-1 and mortality at 3 months.
Results: Seventy-three patients were included in the combined and 163 in the intravenous (IV) group. No significant differences regarding age and NIHSS at admission were observed. Time to IV therapy was similar: 148 min (mean) in the combined and 144 min (mean) in IV group. There were 20 (27%) and 33 (20%) T-, 44 (60%) and 94 (58%) M1- and 9 (12%) and 48 (22%) M2-occlusions respectively in the combined and in the IV group. At 3 months, 40% (n=29) of the patients treated in the combined group had a mRS of 0-1 as compared to 23% (n=38) of those treated in the IV group (p<0.01). No statistical difference was found between the 2 groups regarding mRS 0-2 at 3 months (45.2% vs 48.5% respectively in the combined and in the IV group; p=0.6). Also similar rates of mortality were observed at 3 months (13.7% vs 18.4% respectively in the combined and the IV group, p=0.45). Symptomatic hemorrhage was documented in 6.8% vs 3.7% in the combined and in the IV group respectively (p=0.32).
Conclusions: Our Results suggest that patients treated with combined therapy were more prone to have minimal or no deficit at all at 3 months as compared to the IV treated group. No difference was observed regarding symptomatic intracranial haemorrhage nor mortality.

LOW VERSUS STANDARD DOSE OF RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR IN TREATING EAST ASIAN PATIENTS WITH ACUTE ISCHEMIC STROKE

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The aim of this systemic review was to compare the data from previous studies to address the efficacy and safety of using low-dose versus standard-dose rtPA in treating patients with acute ischemic stroke.
Methods: Previous studies were searched and analyzed. The confidence interval was calculated at 95%. Baseline characteristics and outcomes of the patients were compared between 2 doses of rtPA (0.6 vs 0.9 mg/kg) using Z test for two independent proportions.
Results: Patients who received a low dose (0.6 mg/kg) of rtPA and the standard dose were compared. Patients who received standard-dose rtPA had significantly higher favorable outcome at 3 months (33.1% vs 47.2%, p<0.0001), without significant difference in the rates of symptomatic intracerebral hemorrhage (3.5% vs 4.3%, p =0.422) and mortality (13.1% vs 11.7%, p=0.559). However, patients in the low-dose group were older and had more severe stroke.
Conclusions: Patients receiving standard-dose rtPA seem to have higher rates of favorable outcome. However, there were significant differences in baseline characteristics between the 2 groups. A further, well-designed, randomized study in the same population is still needed to clarify the suspected benefit of the standard dose for East Asian patients.

OUTCOME OF MRI BASED INTRAVENOUS THROMBOLYSIS IN CAROTID-T OCCLUSION

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Introduction: Low recanalization rates and poor clinical outcome was reported after intravenous thrombolysis with tPA (IV-tPA) in carotid-T occlusion (CTO). However, there are contradictory reports. We studied clinical outcome and MRI findings of intravenous thrombolysis based on MRI criteria in CTO.
Methods: We retrospectively analyzed data of patients with acute ischemic stroke and CTO treated with IV-tPA <6 hours of symptom onset based on MRI criteria. Vessel occlusion was defined on MR-angiography (time of flight MRA and, if doubtfully by contrast-enhanced MRA). Acute diffusion and perfusion lesion volumes as well as final infarct volume after 3-7 days were delineated. Clinical outcome was assessed using the modified Ranking Scale (MRS) 90 days after symptom onset. Clinical and imaging data were compared to patients with middle cerebral artery (MCA) main stem occlusion.
Results: Data of 20 patients with CTO and 51 patients with isolated MCA occlusion were analysed. Onset to treatment time (median 170 min vs. 170 min, p=0.691), median NIHSS on admission (17 vs. 16, p=0.51), median initial DWI lesion (27 ml vs. 17 ml, p=0.415) and PI lesion volumes (141 ml vs. 118 ml, p=0.127) were similar between groups (CTO vs. MCA occlusion). Final infarct volume was larger for CTO (82 ml vs. 30 ml, p=0.006). Though not statistically significant, in CTO favourable outcome (MRS 0-1: 6% vs. 31%, p=0.053) and independent outcome (MRS 0-2: 3% vs. 20%, p=0.144) appeared to be less frequent. Mortality was comparable between groups (11% vs. 14%; p=1.0).
Discussion: There are only few patients with good outcome after intravenous thrombolysis in CTO. Moreover, final infarct volume is larger and clinical outcome appears to be worse as compared to intravenous thrombolysis in MCA main stem occlusion. Endovascular treatment options should be considered to achieve recanalization in CTO. If those are not available, there is no evidence to exclude patients with CTO from IV-tPA treatment.

INTRAVENOUS THROMBOLYSIS IN STROKE PATIENTS DUE TO ATRIAL FIBRILLATION - A SERBIAN EXPERIENCE WITH THROMBOLYSIS IN ISCHEMIC STROKE (SETIS) STUDY

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Background: The purpose of our study was to determine the efficacy and safety of systemic thrombolysis among patients with acute ischemic stroke (IS) due to atrial fibrillation (AF) comparing to stroke patients of other causes (OC).
Methods: Data were from the Serbian Experience with Intravenous Thrombolysis in Ischemic Stroke (SETIS) study, a prospective, ongoing, multicenter, open, and observational study in Serbia of all patients who have received alteplase for acute IS during four year period. We analyzed differences in the baseline characteristics, functional outcome measured by modified Rankin score, death and treatment complications between two groups of stroke patients – due to AF comparing to those without it.
Results: Among 425 patients with IS who received intravenous thrombolysis, there were 75 (17.6%) patients with stroke due to AF. Comparing two groups of patients with and without AF, we found no significant differences in excellent functional outcome (mRS 0-1) (50.6% with AF vs. 55.0% without AF; OR 1.19 [95%CI 0,73-1.94]; p=0.483), favorable functional outcome (mRS 0-2) (56.8% with AF vs. 66.5% without AF; OR 1.51 [95%CI 0.92-2.49]; p=0.101) or death (18.5% with AF vs. 14.8% without AF; OR 0.76 [95%CI 0.40-1.45]; p=0.409) at 3 months. There was a higher rate of symptomatic intracerebral hemorrhage (SITS definition) in group with AF (7.1% with AF vs. 1.8% without AF; OR 0.23 [95%CI 0.07-0.74]; p=0.017).
Conclusion: Intravenous thrombolysis in stroke patients with AF is as effective as in stroke patients without it, but with a higher rate of symptomatic hemorrhages among those with AF.

IS IT JUST A QUESTION OF TIME? COMPARISON OF NEUROVASCULAR INTERVENTION AND INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE

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Background: The use of Neurovascular Intervention (NVI) for the treatment of acute ischemic stroke is increasing. NVI provides a high recanalization rate but its clinical benefit is still unproven. There are few studies comparing clinical efficacy and security of NVI and intravenous thrombolysis (IVT).
Methods: Comparative analysis of 2 prospective registries of patients from 5 stroke centres. One registry recorded patients treated with IVT and the other one included patients treated with NVI. NVI was considered in patients with exclusion criteria for IVT, lack of improvement after IVT or basilar artery occlusion. Intra-arterial thrombolysis, thrombectomy, thrombus disruption and angioplasty+stenting were used separately or in combination. NVI was only available from Monday to Friday in working hours.
Results: Since 2004, 60 patients have been recorded in the NVI registry and 1143 in the IVT registry. Patients treated with NVI were younger (mean ± SD: 59±16 vs 67±14 years, p<0.001), presented more severe strokes (median (P25-P75) baseline NIHSS: 15 (12.5-21) vs 13 (8-18), p=0.001, and time-to-treatment (TTT) was longer (median (P25-P75): 317.5 (245-480) vs 140 (115-170) min, p<0.001). There were no significant differences in good outcome (defined as modified Rankin Scale score of 0 to 2 at 3 months) between NVI and IVT (48.9% and 58.5% p=0.2), adjusted OR for age, sex,vascular territory, baseline NIHSS and TTT: 1.2 (95% CI: 0.4-3.3). Mortality rate was similar in both groups (20% vs 12.4%, p=0,13), adjusted OR 0.4 (95% CI: 0.1-2.1). Symptomatic intracerebral hemorrhage rate was low for NVI and IVT (5% and 3.4%, p=0,5), adjusted OR 1.9 (95% CI: 0.4-9.6).
Conclusions: Both NVI and IVT are effective and safe therapeutic options for acute ischemic stroke which can be used depending on patient's characteristics.

WARFARIN PRETREATMENT IN A SUBTHERAPEUTIC RANGE IS ASSOCIATED WITH AN INCREASED RISK OF SYMPTOMATIC INTRACRANIAL AND SYSTEMIC BLEEDINGS

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Background: Stroke thrombolysis is associated with an increased risk of intracranial and systemic bleeding complications. In the US and Canada patients are eligible for thrombolysis with INR values beneath or equal to 1.7. Recently, concerns have been raised about the safety of rtPA in patients with warfarin pretreatment, however, data on this issue are sparse and controversial.
Material and Methods: A total of 548 consecutive stroke patients receiving intravenous rtPA were prospectively evaluated and warfarin pretreatment was recorded. PT-based INR values were measured before thrombolysis and consecutively thereafter. Intracranial hemorrhage was assessed in serial CT examinations (24, 72 hours and on demand) and symptomatic intracranial bleedings were defined according to the NINDS criteria.
Results: All 548 patients (mean age, 68.0; 57.7% men; median NIH Stroke Scale score, 15) had INR values ≤ 1.7. Fifteen patients were on warfarin therapy and faced an approximately 4-fold risk of intracranial hemorrhage (20.0% vs. 5.6%, OR [95%] 4.2 [1.1-15.7], P=0.033). Findings emerged as robust after adjustment for age, sex, NIH-SS, diabetes and admission glucose level (OR [95%] 4.4 [1.1-17.4], P=0.034) and additional consideration of systemic bleedings (OR [95%] 4.1 [1.2-13.9], P=0.024). Mean INR in patients with and without warfarin pretreatment was 1.21 and 1.01, respectively. In patients not receiving warfarin INR level showed no association with bleeding complications.
Conclusion: Warfarin pretreatment in a subtherapeutic range is associated with an increased risk of symptomatic intracranial and systemic bleedings.

OPTIMAL TIMING OF ANTICOAGULATION FOR SECONDARY STROKE PROPHYLAXIS IN PATIENTS WITH CARDIO-EMBOLIC ISCHEMIC STROKE - A RETROSPECTIVE ANALYSIS

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Background: The optimal timing for initiation of anticoagulation for secondary stroke prophylaxis is still unclear. According to current guidelines anticoagulation can be started 3 -5 days after the ischemic event in patients with transient ischemic attacks or minor strokes. In our department anticoagulation is usually postponed up to 2 weeks if the lesion diameter is ≥ 5 cm, while it is started on day 2 after stroke onset in patients with smaller infarcts and no progress. This study aimed to evaluate this concept.
Methods: Case records of all patients with stroke due to atrial fibrillation treated at the Department of Neurology, Hannover Medical School, Germany, from January 2001 until December 2009 were retrospectively analysed. Symptomatic cerebral bleeding was defined as a clinical deterioration of at least 4 NIHSS-points. The frequency of symptomatic cerebral hemorrhage was compared between patients with and without early anticoagulation. In addition risk factors for symptomatic cerebral hemorrhage were identified via multiple regression analysis.
Results: Four patients in the early anticoagulation group (1%) showed symptomatic cerebral hemorrhage. Bleeding occurred 24 hours after treatment initiation in 3 patients and at 10 days in one. Symptomatic hemorrhage occurred about 48 hours after ischemic stroke also in 3 patients without anticoagulation therapy (1%). These patients had shown major strokes already on admission (mean NIHSS:19), while those with symptomatic hemorrhage under anticoagulation showed minor strokes (NIHSS:4) on admission but then progressed. In 3 of them anticoagulation had been started 6 -12 hours after symptom onset, in the fourth 36 hours after symptom onset.
Conclusion: Symptomatic hemorrhage after ischemic stroke occurs predominantly in patients with ischemic lesions > 5 cm diameter. Early anticoagulation appears safe if initiated not before 24 hours after stroke onset in patients with lesion diameters of less than 5 cm.

RELATIONSHIP BETWEEN DAILY BLOOD GLUCOSE FLUCTUATION AND NEUROLOGICAL OUTCOME IN ACUTE STROKE PATIENTS

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Objective: In this study, we examined the relationships between not only mean level of but also variation of blood glucose and neurological outcome in acute stroke patients.
Methods: Subjects were a total of 651 stroke patients (mean age, 70.0±9.9 years) who were either already undergoing treatment for diabetes or had a hemoglobin A1c level of ≥5.8% at admission who were admitted within seven days of onset between April 2004 and March 2009. In addition to patient attributes, the following items were measured: NIHSS score at admission and discharge, mean morning fasting blood glucose level (mean BG), and as an indicator of variation of blood glucose levels, successive variation $(SV) = \sqrt{\Sigma(Bgi+1-Bgi)2/(n-1)}$. Mean BG and SV were calculated from the seven consecutive morning fasting measurements. Patients whose NIHSS score increased by≥4 from admission to discharge were classified into the exacerbation group, otherwise, into the non-exacerbation group.
Results: Until discharge, 39 (6%) of 651 showed neurological deterioration. The exacerbation group had higher mean BG and SV (180±51 and 44±31 mg/dl, respectively) than the non-exacerbation group (154±38 and 28±19 mg/dl, respectively), but no intergroup differences were observed for age, gender, hypertension, hyperlipidemia, type of stroke, smoking or drinking history. Using the quartile analysis, both quartiles of largest mean BG (178-336) or SV (36-162) had higher incidence of neurological exacerbation than quartiles of the smallest mean BG (69-128) or SV (5-16) (odds ratio 2.87, 95%C.I.: 1.09-7.53 or 3.95, 95%C.I.: 1.43 -10.9, respectively).
Conclusion: Larger daily blood glucose variation, was correlated with exacerbation of neurological symptoms in patients with stroke complicated by diabetes, independent on the weekly average. This finding suggests that stabilization of blood glucose variation should lead to good clinical outcome.

PREVALENCE OF LOW RESPONSIVENESS TO CLOPIDOGREL IN PATIENTS WITH STROKE OR TIA

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Background: High platelet reactivity on treatment with clopidogrel (CLP) is a well established phenomenon in patients with coronary artery disease. It has been associated with the risks of stent thrombosis and coronary syndrome recurrence. The prevalence of low responsiveness to CLP among patients with ischemic stroke (IS) or transient ischemic attack (TIA) is not well known. The relationship between this phenomenon and the risk of IS/TIA in patients treated by CLP has not been studied.
Methods: We measured CLP response using light transmittance aggregometry (LTA) in two groups of consecutive patients with acute IS/TIA. Patients in group 1 had never received CLP before IS/TIA. Patients in group 2 were already on CLP when IS/TIA occurred. LTA was performed in the first two weeks after IS/TIA. Low responsiveness was defined as maximal platelet aggregation >70%.
Results: We included 107 patients, 55 in group 1 (33 men; mean age ± SD: 72.8±12.3 years), and 52 in group 2 (36 men; mean age ± SD: 73±11.7 years). The low-responsiveness rate was 20% (11/55) in group 1, and 40.7% (21/52) in group 2 (p = 0.018 by Fisher test).Using logistic regression analysis, the odds ratio for CLP low-responsiveness in patients from group 2 was 2.7 (95% confidence interval = 1.14 - 6.42; p = 0.02).
Conclusion: This study shows a high prevalence of low-responsiveness to CLP among patients with IS/TIA already treated with CLP because of a previous cardiovascular event as compared with patients naïve to this drug. Findings suggest that low responsiveness to CLP may play a role in IS/TIA occurrence on this treatment.

EARLY NEUROLOGICAL DETERIORATION IN STROKE PATIENTS FOLLOWING INTRAVENOUS RT-PA THERAPY

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Background: Early recurrence of ischemic stroke (ERIS) as well as symptomatic intracranial hemorrhage (SICH) and progressive ischemic stroke (PS) can cause early neurological deterioration (END) after thrombolysis. This study aimed to investigate the incidence, characteristics, and mechanism of END within 24 hrs after rt-PA infusion.
Methods: We prospectively registered consecutive ischemic stroke patients who were treated with intravenous rt-PA (alteplase, 0.6mg/kg) in our center between 2005 and 2010. END was defined as an increase of ≥4 points from the initial NIHSS score within 24 hrs after rt-PA infusion. END was classified into 3 subtypes: ERIS as an additional ischemic change in a different vascular territory on subsequent DWI, SICH as associated hemorrhage on subsequent CT, and PS as others.
Results: Of 200 patients (65 women, 74±11years) who were registered, 30 (15.0%) developed END: 3 (1.5%) with ERIS, 6 (3.0%) with SICH, and 21 (8.0%) with PS. As compared to patients without END [control (C), n=170], those with ERIS were older (ERIS 87±6 years, SICH 75±5 years, PS 75±10 years, C 73±11 years; p=0.03 for ERIS vs. C), and had higher levels of D-dimer on admission (8.3±6.9 ng/ml, 1.3±0.82 ng/ml, 2.2±1.65 ng/ml, 2.65±4.09 ng/ml; p=0.02 for ERIS vs. C). Patients with SICH more frequently took oral warfarin (0%, 50%, 5%, 12%; p=0.008 for SICH vs. C) and those with PS more frequently had antiplatelets (0%, 33%, 52%, 24%; p=0.006 for PS vs. C) prior to stroke. Cardioembolic stroke (67%, 83%, 62%, 60%) was similarly identified and there were no significant differences in onset-to-needle time, ASPECTS, frequency of atrial fibrillation, and initial blood pressure among the 4 groups.
Conclusions: Early neurological deterioration after rt-PA infusion was present in 15.0%. ERIS (1.5%) was associated with advanced age and a hypercoagulable state, SICH (3.0%) with prior warfarin intake, and PS (8.0%) with prior antiplatelet intake.

CARDIOEMBOLIC STROKE AND FUNCTIONAL OUTCOME AFTER IV THROMBOLYSIS

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Background: Different functional outcomes after IV thrombolysis (IV-t) in cardioembolic stroke (CES) have been found and published over the last years. In CES a spectacular shrinking deficit with rapid recanalization and good functional outcome was ascribed to clot composition.
However, both clotcomposition and –burden also formed the explanation for an unfavourable course.
Atrial fibrillation (AF) is thought to cause large and old thrombi.
Our objective was to further investigate these discrepancies by analyzing functional outcome in CES after IV-t in a large group of patients.
Methods: We used our hospital based patient registry comprising 500 consecutive patients who received IV-t between 2001 and 2010 to study functional outcome in CES.
CES was defined as a stroke in the presence of atrial fibrillation or another potential cardiac source of embolism detected by echocardiography.
Functional outcome in ischemic stroke patients with and without cardiac embolism was compared.
Favourable outcome was defined as a modified Rankin Scale (mRS) score of 0-2 at three months.
Results: 170 patients (34%) had a CES. AF was found in 158 (32%) of them. The mean NIHSS scores were 11.3 and 10.3 in the CES and non-CES groups respectively (no significant difference). 41.4% of the patients with a CES had a favourable outcome after Iv-t versus 62.6% of the non- CES patients. 394 (78.8%) patients had a cortical infarct. In this group 39.1% of the CES had a favourable outcome versus 55.9% in the non-CES group. In patients with lacunar infarcts this was 64.7% versus 78%. 71.4% of patients with symptomatic carotid stenosis (n=60) had a favourable outcome.
Conclusion: Our Results support recent findings that functional outcome after IV-t is worse in CES compared to patients with ischemic stroke due to another etiology. Clotcomposition and -burden might be responsible for this phenomenon.

COMBINATION OF THROMBOLYTIC THERAPY WITH CITICOLINE IN TREATMENT ACUTE ISCHAEMIC STROKE

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Introduction: Neuroprictection provides increase duration of the period of a survival of neurons in the conditions of ischemic defeat of a brain.
Methods: The experimental group was made by 67 (38-male, 29-female) patients with primary hemisphere ischemic stroke, median of age made up 68,5 years old. The first group at a hospital stage received thrombolysis by alteplase in a dose of 0.9 mg on 1 kg of weight of a body; a glycocoll in a dose 1 g in day during of 3 days, sulfate of magnesium of 25%-10 ml during of 5 days. In addition to the this one therapy patients received citicoline by parenteral way to a dose of 1 time of 1000 mg a day during of the first 12 hours till 21 days. Second control group was made by 70 patients (38-male, 29-female), median of age made up 65,5 years old. Both groups were hospitalized in terms 60±30 minutes from a disease debut. Initial point of scale NIHSS was equal in both groups and according to a middle level stroke in first group–11,7; second - 11,4. Scheme of treatment was identify, but citicoline was not used. Time window of thrombolysis consist of 3,5 hours in both groups.
Results: Neurologic restoration is registered at 55% cases of first group and 30% in control group by third day. Neurological outcome by NIHS consist of 8,2 (3 day) and 7,4 (21 day) in second group and 5,7 (3 day) and 3,2 (21 day) in first group accordingly.
Hemorrhagic complications associated with rTPA was observed the same relation: 7 cases (10,4%) – control group; 8 cases (11,4%) – experimental group.
Comparing indicators of C - reactive protein (CRP) shows that against treatment citicoline was observed reliable lower indicators of the CRP by 21 day - 0,7 mg/l (p=0,003). In control group of patients was not reached normal values concentration CRP (norm – 1,0 mg/l) against only standard therapy - 0,7 mg/l (p=0,003).
Conclusions: Therapy of citicoline raises probability of a complete recovery of neurologic functions. That also reduces a total indicator of neurologic deficiency in 1,6 times by 21 day in comparison with therapy without citicoline.

ATRIAL FIBRILLATION: PREDICTOR OF RESPONSE TO RT-PA?

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Background: Atrial fibrillation (AF) is the leading cause of cardioembolic strokes and is a factor of poor prognosis for cerebral infarction. Our study focused on the outcome of AF-related thrombolysed strokes comparing to those with other etiologies.
Methods: 281 consecutive stroke patients thrombolysed with rt-PA within 4.5 hours were examined prospectively in the stroke unit of Nice. Mean age was 67±14 years, 51% were men, mean baseline NIHSS was 15.6±4. Median time for rt-PA was 54 minutes ±59. At 3 months, 144 patients (51%) were dependent (modified Rankin scale > 2) and 39 (14%) died. 12 (4.3%) patients had symptomatic hemorrhagic transformation. The outcome (death and dependency) of these patients, with and without AF, has been studied. The Results were adjusted for known predictive factors of poor prognosis: age, initial glucose level, baseline NIHSS, diastolic blood pressure at entry, plus previous stroke for dependency and heart failure and male for death.
Results: AF was documented in 111 (39%) patients. The risk of dependence (OR: 1.63 IC 95% (1.01-2.64), p = 0.048) and death (OR 2.85 95% CI (1.42-5.72) p = 0.003) was significantly higher in AF-related strokes. After univariate analysis, parameters significantly associated with presence of AF are: age, diabetes, no smoking, SBP> 160 mm Hg, high glycaemia at entry, VKA treatment, absence of internal carotid occlusion, valvular disease, LV dysfunction and left atrium dilatation. After adjustment, the functional and vital prognosis is not significantly different in the two groups. AF does not influence the risk of symptomatic hemorrhagic transformation (p = 0.45).
Conclusion: In our study, the presence of AF is associated with a worse outcome 3 months after thrombolysis. However, this is not related to an excess of symptomatic hemorrhage, but to the co existence, in this population, of several known predictors of poor outcome. The cardio embolic mechanism by AF does not modify the response to rt-PA.

SLOW PROGRESSION OF ISCHEMIA DURING BRIDGING TO ENDOVASCULAR THERAPY MIGHT HAVE AN INFLUENCE ON OUTCOME: PRELIMINARY RESULTS COMPARING TWO NEUROIMAGES PRIOR TO ENDOVENOUS AND INTRAARTERIAL THERAPIES

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Background: The use of intraarterial therapy (IAT) after refractory intravenous thrombolysis (IVT) is widely becoming available. The question of repeating a second neuroimage (NI) before performing IAT remains controversial. We sought to study the prognostic factors associated with slow progression (SP) of ischemia between both NI and whether the absence of progression had any influence on the latter outcome.
Methods: Prospective database of patients treated with IAT, who underwent CT scan previous to IVT followed by a second NI (CT or MR) prior to IAT were analyzed. ASPECTS score was retrospectively measured in NI by an investigator blinded to the clinical data. SP was defined as a difference of 0 or 1 point in the ASPECTS score between the two NI. Favourable outcome was defined as mRS 0-2 at discharge.
Results: A total of 48 patients were included. NI performed were TC + RM (54%) and TC+TC (46%). The first ASPECTS score was >7 in 98% of the patients. SP was observed in 65%; this percentage remained constant after analyzing the patients according to the time between NI (1Q (<90 min) 67%; 2Q (90-120 min) 77%, 3Q (120-193 min) 64%, 4Q (>193 min) 50%; p=0.57). Patients with SP had an increased rate of favourable outcome on discharge (46.7% vs. 11.8%, p=0.01) and a trend to a better outcome at 3 months (61% vs. 38%, p=0.19). No differences were detected regarding age, time, risk factors, etiology, hemodynamic factors or site of occlusion in patients with or without SP.
Conclusion: Patients with slow progression of ischemia in neuroimaging after intravenous thrombolysis might have a better outcome after recanalization with intraarterial therapy regardless of time. Larger studies are warranted to support this hypothesis.

INFLUENCE OF RT-PA POST-TREATMENT BLOOD PRESSURE ON CLINICAL OUTCOME, SYMPTOMATIC HEMORRHAGIC TRANSFORMATION AND MORTALITY IN ACUTE STROKE PATIENTS

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Background: We aimed to evaluate the influence of mean systolic blood pressure (sBP) and diastolic blood pressure (dBP) after IV rt-PA treatment on clinical outcomes and symptomatic hemorrhagic transformation (sHT) rate.
Methods: Consecutive acute stroke patients treated with IV rt-PA according NINDS protocol were included prospectively. sHT rates was defined according to ECASS III criteria and calculated from CT scans done 22-36 hs after IV rt-PA and also from any additional post-treatment scans. Mortality rate as well as number of patients with favorable outcome (mRs score 0-2) were also calculated. Mean sBP and dBP were calculated on basis of BP measurements after the end of rt-PA infusion and in 2, 6, 12 and 24 hs. The associations between mean sBP and dBP and clinical outcomes, sHT and mortality rates were investigated using the binary logistic regression analysis.
Results: Of the 215 patients (mean age: 64.4; 62.7% male; mean admission NIHSS score 14.2) 46.6% had mRs0-2 after 3 months, sHT rate 4.9%. Mortality rate after 3 months was 17.3%. Mean sBP was significantly associated with an increased risk of mortality (OR 1.05, 95% CI1.01-1.08, p=0.006), but not with sHT and favorable outcome. No association was found for mean dBP. Most favorable outcomes were observed in subgroup of patients with mean sBP between 100 and 140 mmHg (59.1%) or mean dBP between 81 and 90 mmHg (61.8%, p<0.05 vs other BP subgroups). Increased sHT rate was in patients with mean sBP between 161 and 170 mmHg (19.2%) or mean dBP more than 100 mmHg (11.8%).
Conclusion: In acute stroke patients the mean systolic blood pressure during the first day after rt-PA treatment is associated with an increased risk of mortality. Subgroups of patients with mean sBP between 100 and 140 mmHg or dBP between 81 and 90 mmHg had most favorable outcomes. Careful attention for blood pressure after thrombolysis and gentle management is needed.

PROGNOSTIC VALUE OF COMPUTED TOMOGRAPHIC PERFUSION SCAN IN PATIENTS WITH POSTERIOR CIRCULATION ISCHEMIC STROKE

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Background: Computed tomographic perfusion (CT-P) scans are routinely performed as a part of initial work up for all ischemic strokes including those in posterior circulation. The prognostic value of CT-P derived variables in posterior circulation ischemic stroke is controversial due to poor resolution and artifact created by surrounding cranium. This study evaluated the predictive utility of CT-P findings in posterior circulation ischemic strokes.
Methods: All posterior circulation stroke patients (based on clinical findings and occlusion documented on CT-angiogram) who had a CT-P scan as part of their initial evaluation were identified through a chart review of 685 consecutive acute ischemic stroke patients at a comprehensive stroke center over a 3 year period (2008-2010). The relationship between CT-P findings including Mean Transit Time (MTT), regional Cerebral Blood Flow (rCBF), and regional Cerebral Blood Volume (rCBV) with unfavorable outcome at discharge (defined by modified Rankin score (mRS) ≥3) were analyzed.
Results: There were 41 posterior circulation stroke patients (mean age 67.7± (SD) 13 years, 26 men and 15 women) with a mean National Institutes of Health Stroke Scale (NIHSS) score of 7.3±7. Eighteen of these patients (43.9%) had CT-P abnormalities such as increased MTT, decreased rCBF and rCBV in cerebellum, brainstem and occiput consistent with acute ischemia. There were no statistical differences between the patient groups with and without CT-P changes with regards to age, gender and risk factors such as hypertension, diabetes, dyslipidemia, smoking, atrial fibrillation, coronary artery disease, and prior cerebrovascular events. The rate of poor outcome was 8 of 18 and 6 of 23 patients with and without CT-P findings (p=0.22), respectively. Moreover there was no correlation between poor outcomes at discharge and increased MTT (p=0.09), reduced rCBF (p=0.19), and reduced rCBV (p=0.36) values among the 41 patients.
Conclusion: Standard CT-P abnormalities were infrequent and did not correlate with clinical outcomes in patients with posterior circulation ischemic stroke.

FULL DOSE IV FOLLOWED BY IA THROMBOLYSIS IS ASSOCIATED WITH HIGHER RECANALISATION RATE OF THE OCCLUDED MCA COMPARED TO IV THROMBOLYSIS ALONE IN ACUTE ISCHEMIC STROKE PATIENTS

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Background: The early recanalization of the occluded cerebral artery is substantial for clinical improvement in acute ischemic stroke (IS) patients treated with intravenous thrombolysis (IVT). Nevertheless, the rate of achieved recanalizations is low. The aim was to compare the safety and efficacy of full-dose IVT followed by intra-arterial thrombolysis (IAT) to IVT alone in acute IS patients with occluded middle cerebral artery (MCA).

Methods: In a single center retrospective study, 73 consecutive IS patients with MCA (M1-2 segment) occlusion were treated either with IVT alone (Group 1) or with full dose IVT followed by IAT (Group 2). Initial stroke severity (assessed using NIHSS), rate of achieved recanalizations, occurrence of intracerebral hemorrhages (ICH) including symptomatic (SICH) after 24 hours and 90-day clinical outcome (assessed using mRS) were compared.

Results: Group 1 consisted of 50 patients (24 males, mean age 70.8±10.2 years) and Group 2 of 23 patients (11 males, mean age 68.6±9.6 years). No difference was found in the initial NIHSS (median 16 vs. 18, p-0.121). The rate of achieved MCA recanalizations was higher in Group 2 (69.6% vs. 32.0%, p-0.003). The ICH occurrence was higher in Group 2 (47.8% versus 22.0%, p-0.025), while SICH occurrence was similar (6.0% in Group 1 vs 4.3% in Group 2, p-1.000). No difference was found in 90-day clinical outcome (median mRS 5 in both groups, p-0.154) including the number of patients with mRS 0-2 (30.0% versus 30.4%, p-970).

Conclusion: Full dose IVT followed by IAT was associated with higher rate of MCA recanalizations, with similar SICH occurrence and 90-day clinical outcome when compared to IVT alone. Acknowledgment: Supported by IGA MH CR, grants NS9920-4, NT11386-6, NT11046-6.

PREDICTORS OF OUTCOME IN SEVERE ACUTE STROKE PATIENTS TREATED WITH INTRAVENOUS THROMBOLYSIS

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Background: Severe acute stroke patients (ASP) are a cause of serious concern regarding the safety of thrombolytic therapy. Aims of this study were to define a clinical profile of severe ASP treated with i.v. rtPA and find independent predictors of outcome.

Methods: We analyzed data of ASP treated in Italy from 2003 to 2009 included in the SITS-ISTR. NIHSS ≥14 and ≥20 were considered index respectively of severe and very severe neurological deficit. Outcome measures were 3-month mRS 0-2, symptomatic intracerebral hemorrhage (SICH/NINDS definition)and mortality.

Results: Overall, 4194 patients were studied,1947/4085 (47.7%) had baseline NIHSS ≥14 and 731/4085 (17.9%) ≥20. Compared to those with NIHSS <14, patients with NIHSS ≥14 were significantly more female, older, on previous therapy with aspirin, with less pre-stroke independence, a higher proportion of AF and congestive heart failure.They have significantly lower baseline SBP and DBP,more frequent early ischemic signs on baseline CT, lower times from onset- and arrival-to-therapy. Finally, they had lower probability of 3-month mRS 0-2 and higher proportion of SICH and mortality (p<0.0001). At multivariate analysis both NIHSS ≥14 and ≥20 were independent predictors of mortality. Independent predictors of SICH in patients with NIHSS ≥14 were time from onset-to-therapy and baseline SBP, in those with NIHSS ≥20 time from onset-to-therapy, pre-stroke antiplatelets and baseline SBP. Independent predictors of mortality for the first subgroup were age, current smoke, time from arrival-to-therapy, previous diagnosis of stroke, while for the second subgroup were age and time from onset-to-therapy.

Conclusions: Our study showed that severe and very severe ASP are basically a frail category of patients with several comorbidities and at high risk of mortality. Therefore,onset to-treatment times should be kept as short as possible and these patients should be strictly monitored particularly during i.v. thrombolysis to avoid complications and improve outcome

THE SAFETY AND EFFICACY OF INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE PATIENTS AGED OLDER THAN 80 YEARS IN KOREA; PROPENSITY SCORE MATCHING ANALYSIS

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Background: Patients with acute ischemic stroke aged older than 80 years are rapidly increasing in Korea. Although intravenous tissue plasminogen activator (tPA) has been known as the most beneficial therapy for patients with hyper-acute ischemic stroke, outcomes of intravenous r-tPA administration have not been established in this age group. We investigated whether outcomes of r-tPA in patient aged older than 80 years were more beneficial than those without r-tPA in clinical practice.

Methods: We recruited 440 patients with acute ischemic stroke patients aged 80 years and older within 3 hours after symptom onset from 20 university hospitals in Korea, from Jan. 2007 to May 2010. They all were candidate to the NINDS protocols of iv tPA. One-hundred eight tPA users and sixty-nine non-users were selected. Prognostic variables in propensity score matching (PSM) model were demographics, risk factors, stroke severity on admission, subtypes of ischemic stroke, pre-stroke functional status, and laboratory findings before tPA administrations. The functional outcomes at 90 days after symptom onset, symptomatic intracranial hemorrhage (sICH), and death within 90 days were compared in PSM cohort with McNemar test.

Results: After PSM, all measured variables were well balanced in 41 matched cases. In the matched cohorts, the good outcomes (mRS 0-2) and risk of death within 90 days were similar in both group (OR 0. 944, 95% CI 0.229-3.945; 0.853 95% CI 0.118-13.240, respectively). The rate of sICH (7.3% tPA users versus 0% tPA non-users; P=0.250 in McNemar test) did not showed statistically significant difference between two groups.

Conclusion: We could not demonstrate any favorable outcomes of intravenous tPA thrombolytic therapy for acute ischemic stroke patient aged 80 years and older. However, the increased sICH frequency in TPA group did not lead to any increase in mortality or poor outcome. As the limited number of cases in our retrospective study, large-scaled randomized controlled trials should be required.

SNAPSHOT OF PREVALENCE AND MANAGEMENT OUTCOME OF AF IN AN ACUTE STROKE UNIT IN A LARGE GENERAL HOSPITAL IN UK

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Introduction: Atrial Fibrillation (AF) is common among the patients presenting with acute stroke. Although primary prevention (i.e. treatment with anticoagulant to prevent stroke in the first place) should be the aim, for a large number of stroke patients, current management and secondary prevention, become the norm. We set out to assess the prevalence and management outcome of AF in our unit.

Methods: Medway Hospital is an associated teaching hospital in the Southeast of England serving nearly 0.5 million people. There is a hyper-acute stroke service

with an acute stroke unit and arrangements for 24 hr thrombolysis. We looked at all the acute stroke patients being admitted in the unit over a three month period (April-June 2010), and collected and analysed data from their case notes, hospital data bank and imaging archives.

Results: We had a total of 60 patients with new stroke, and 16 were found to have AF (10 were known, 6 were newly diagnosed, prevalence 27%). Their median age was 84 (mean 80).Of the 10 with known AF only three were on warfarin (INR 1.8-3.4), but all presented with bleed. Most were diagnosed with initial ECGs, but a few needed 24 hr tape to establish diagnosis (Paroxysmal AF, 2/16 i.e. 13%). Of those new and old (n=13) only five (5/13 i.e. 38%) could be anticoagulated. Reasons for not being anticoagulated were: falls, frailty, dementia, bleed (not being on warfarin) and deaths. Only a few (5/16 i.e. 31%) needed rate control medication (digoxin/beta-blocker), and nearly all but one (6%) were euthyroid. None were deemed suitable for cardioversion. Mortality at three months was high (31%).

Conclusion: In this real life, unselected, current practice scenario it was obvious that a large number: (>25%) of stroke patients had atrial fibrillation, and mostly were very elderly (>80). Only a minority (≈40%) could be anticoagulated as the rest were unsuitable, and one has to be cautious about anticoagulation in the very elderly because of risk of bleed.

371 Acute stroke: current treatment

EDARAVONE USAGE IN JAPANESE STROKE PATIENTS TREATED WITH INTRAVENOUS LOW-DOSE RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR: THE SAMURAI RT-PA REGISTRY

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Background and purpose: The Japanese Ministry of Health, Labour and Welfare approved intravenous (i.v.) edaravone, a free radical scavenger for treating acute ischemic stroke in 2001. In 2005, low dose i.v. recombinant tissue plasminogen activator (rtPA) at a dose of 0.6 mg/kg was approved for use within 3 hours of stroke onset. Herein, we report on the use of edaravone and its effects on the prognosis of patients after i.v. rtPA therapy.

Methods: We enrolled 600 consecutive patients with stroke who were treated with low-dose rtPA at 10 Japanese stroke centers.

Results: Edaravone was administered to 503 (84%) of the 600 patients. Age (71.2±11.8 vs. 74.9±11.3 y, p = 0.005) and serum creatinine (0.83±0.67 vs. 1.34±1.26 mg/dl, p = 0.001) significantly differed between the groups that received edaravone (E+) and that did not (E-), whereas no differences were identified among sex, NIHSS upon admission and mRS scores before onset. Among 532 patients with premorbid mRS scores of 0 - 1, 169 of 447 patients in the E+ group (38%) and 27 of 85 in the E- group (32%) had mRS 0 – 1 at 3 months after onset (p = 0.349). The incidences of any and symptomatic intracerebral hemorrhage the difference did not reach significance. At 3 months, 105 patients in the E+ group (21%) and 32 (33%) in the E- group had mRS scores of 5 - 6 (p = 0.0014), and 28 (5.6%) and 15 (15.5%), respectively, scored mRS 6 (p = 0.001). Multivariable logistic regression analysis also showed that the E+ group was less fatal than the E- group (OR, 0.38; 95%CI, 0.16 - 0.90; p = 0.028).

Conclusions: Edaravone reduced the mortality of 503 patients who also received i.v. rtPA within 3 hours of stroke, compared with those who did not receive edaravone, presumably partly because younger patients with milder renal dysfunction were selected as eligible patients for edaravone and partly because of the therapeutic effect of edaravone.

372 Acute stroke: current treatment

PREVIOUS USE OF STATINS IS INDEPENDENTLY ASSOCIATED WITH SYMPTOMATIC HEMORRHAGIC TRANSFORMATION AFTER IV TPA

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Background: One of the major concerns regarding the use of thrombolysis for acute ischemic stroke is the potential for symptomatic intracranial hemorrhage (SIH). SIH is associated with worse outcome, and occurs in approximately 5% of treated patients. Defining accurate risk factors for tPA-related SIH would improve treatment security, and decrease unnecessary concerns about its application.

Methods: We reviewed clinical, laboratory and imaging data of 117 consecutive patients with acute ischemic stroke treated with intravenous thrombolysis in a university hospital of tertiary emergency care. Demographic data, previous medical history and medical therapy, stroke severity (NIHSS score), admission blood pressure and glycemia, onset-to-treatment time, and the presence of early ischemic changes on admission computed tomography were evaluated. SIH was defined as any intracranial hemorrhage temporally related to tPA (<48 hours after bolus) associated with clinical worsening (increase of >4 points on the NIHSS). Univariate and multiple regression analysis were performed for all variables.

Results: There were 7 SIH (6.0%) among 117 patients (mean age=62.3±13.4 years-old; male sex=52.3%). Neither demographic characteristics, previous medical history, blood pressure and glycemia at admission, onset-to-treatment time or the presence of early ischemic changes on admission CT were related to SIH. After logistic regression, the previous use of statins was the only factor independently associated with SIH related to thrombolysis (OR=9.56; CI=1.81-50.33; p=0.008). None of the 6 patients above 80 years-old suffered SIH.

Conclusions: Previous use of statins is independently associated with the occurence of symptomatic hemorrhagic transformation after IV TPA. Older age, high NIHSS scores and early ischemic changes on brain CT should not be used as isolated criteria to justify withholding therapy for eligible candidates for tPA.

373 Acute stroke: current treatment

COMBINED INTRAVENOUS AND INTRA-ARTERIAL RECANALIZATION FOR ACUTE ISCHEMIC STROKE: THE FIRST HUNGARIAN EXPERIENCE

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Background: Systemic thrombolysis is a fast and relatively simple method for treating ischemic stroke, though its efficacy is low if large arteries are occluded. Intraarterial lysis/mechanical recanalization have higher success-rate, but the acces to these technics is limited, and they are time-consuming. Combination of these two techniques might be the best solution to treat intracranial large artery occlusion.

Methods: From 2007 to 2010 in 3 different hungarian centers 32 consecutive patients underwent bridging revascularization. 20 of them were male, 12 female, their age was 62 years on average (32-84 years), mean of their stroke severity was 19 points on NIHSS (12-30 points). Time window for systemic thrombolysis was 4,5 hours according to ECASS-3. 21 individuals were treated with 0,6 mg/kg bodyweight rt-PA according to the EMS protocol, while 11 underwent intraarterial procedures after they had been treated with the total intravenous rt-PA dose (0,9 mg/kg bodyweight). The mean time of the diagnostic angiography was 4 hours 25 minutes after onset, demonstrating occlusion of the M1-M2 segments in 16, simultaneous ICA and MCA occlusion in 3, carotid "T-occlusion" in 6, basilar artery occlusion in 6 and vertebral artery occlusion in 1 patient. The intraarterial rt-PA dose was 22 mg in average (5-40 mg). Recanalization rate was determined based on the arterial patency seen on the closing angiogram. A controll CT was always done 24 hours after the lysis to reveal bleeding complications. Clinical outcome was measured by the modified Rankin-scale 3 months after the stroke onset.

Results: TICI grade 2.-3. recanalization was achieved in 19 cases (60%). Mortality within 90 days was 31%, while good clinical outcome (mRS: 0-2) was seen in 47% of the patients. The rate of symptomatic haemorrhages was 9,4% (3/32).

Conclusion: Sequential intravenous-intraarterial recanalization seemed to be relatively safe and efficacious in our series of ischemic stroke patients.

374 Acute stroke: current treatment

COMPARISON OF PLATELET AGGREGATION WITH THIENOPYRIDINES IN ACUTE CEREBRAL ISCHEMIA

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Background: Clopidogrel is the most commonly used drug for prevention of stroke recurrence. Nevertheless, clopidogrel resistance occurs in significant numbers during secondary prevention and is associated with a higher risk of recurrent cardiovascular events. Therefore, we aimed to compare the effect of platelet aggregation ability of thienopyridines, such as clopidogrel, ticlopidine, and ticlopidine plus Ginkgo biloba Extracts (EGb 761).

Methods: We randomly assigned 135 patients with acute ischemic stroke or transient ischemic attack within 3 days after symptom onset into 3 equal groups: clopidogrel, ticlopidine, and ticlopidine plus EGb 761. Dosage was maintained as 75 mg clopidogrel daily, 250 mg ticlopidine twice daily, and 250 mg ticlopidine plus 40mg EGb 761 twice daily. Platelet aggregation was measured by activators of adenosine diphosphate (ADP test, 6.4μM), arachidonic acid (ASP test, 0.5mM), thrombin (TRAP test, 32μM) at baseline (T0), 7 days (T1), and 90 days (T2) by multiple electrodes aggregometry. Side effects were analyzed in the 3 groups.

Results: There was no difference of platelet aggregation at baseline in clopidogrel, ticlopidine and ticlopidine plus EGb groups (ADP test, p=0.530; ASP test, p=0.389; TRAP test, p=0.092). A significant difference of platelet aggregation showed on ADP test in the groups at 7 days (14.9±10.8 vs. 29.5±17.3 vs. 22.2±10.1%, p<0.001), whereas there were no significant differences of platelet aggregation power on ASP and TRAP tests (p=0.139 and p=0.232). There was significant difference of platelet aggregation on ADP test in the groups at T2 (p=0.038). On ASP and TRAP tests, no significant differences of platelet aggregation were noted. Eight patients were hospitalized due to stroke recurrence (n=3), gastric hemorrhage (n=1), ureter stone (n=1), lumbar compression fracture (n=1), biliary carcinoma (n=1), severe headache (n=1) but there was no difference in the groups (p=0.993).

Conclusion: This finding suggests that ticlopidine plus EGb 761has sufficient anti-platelet ability and can be a potential combination treatment without serious side effects in acute cerebral ischemia.

375 Acute stroke: current treatment

EARLY NEUROLOGICAL DETERIORATION AND CAPILLARY GLUCOSE LEVELS IN ACUTE STROKE

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Background: Early neurological deterioration (END) and hiperglycemia are common events that occurs in acute ischemic stroke (IS) and they have been associated with poor outcome. Our objective was to analize the relationship between END and hyperglycemia, and its implication on functional outcome.

Methods: Post hoc analysis of the GLIAS (GLycemia In Acute Stroke) study, a multicenter, prospective and observational cohort study of 476 acute IS patients. We recorded capillary finger-prick glucose on admission and 3 times a day during the first two days. We considered hyperglycemia as levels ≥155 mg/dl, since it was the threshold level associated with poor outcome in the GLIAS study and END as a decrease of one or more points in the Canadian Neurological Scale (CNS). Outcome (modified Rankin Scale, mRS) was evaluated at 3 months.

Results: 476 patients studied, 93 (19,53%) have developed END. Patients with END have had higher body temperature (36,55°C ±0,65 vs 36,26°C ±0,49; p=0,001),stroke severity (CNS 6; 4,5-8 vs 4; 2-8; p=0,011) and more early computed tomography signs (75,3% vs 58,1%; p<0,001).When we have analyzed those patients with maximum capillary glucose within 48 hours ≥155 mg/dl, there were no differences in the frecuency of END development (35,2% versus 26,9%; p=0,129).END was associated with poorer outcome (mRS>2 62,5% vs 28.3%; p<0,001) than those without END.Combination of hyperglycemia and END was significantly associated with poorer outcome than those without hyperglycemia and END (mRS>2 85,7% vs 25%; p<0.001) and higher mortality (34,15% vs 5,77%; p<0,001).Cox model confirmed: the presence of END and hyperglicemia is associated with higher mortality risk at 3 months, compared with not developing any of these two characteristics (hazard ratio 7,17; p<0,001).

Conclusions: END is associated with poorer outcome and higher mortality. However, the combination of hyperglycemia and END was significantly associated with worse outcomes and higher mortality.

376 Acute stroke: current treatment

IMMEDIATE ANTICOAGULATION FOR ACUTE CARDIOEMBOLIC STROKE IS STILL POPULAR IN SELECTIVE CASES IN KOREA

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Background and purpose: There are still controversies about when and how anticoagulation (AC) is initiated in patients with acute cardioembolic stroke

(ACES). We surveyed current practice patterns of AC therapy for ACES in Korea.

Methods: Using a web-based online survey system, all staff neurologists of training hospitals in Korea surveyed about when and how they commenced AC in the following representative cases of ACES with atrial fibrillation: cases with large supratentorial or cerebellar infarction; medium-sized supratentorial infarction with or without mild hemorrhagic transformation (mHTr); small supratentorial infarction with or without mHTr; small cerebellar infarction without mHTr. We also investigated the effect of presence of multiple cerebral microbleeds (CMBs) or history of intracerebral hemorrhage (ICH) on AC therapy.

Results: 281 (78.3%) neurologists (mean age, 43.6 years) responded to the survey and 76 (27.0%) of the responders abstained from participating in the survey noting lack of interest. Although a few physicians (4.4%) performed immediate AC in all cases and some (10.7%) never did, the other most physicians made different decisions according to infarct size and presence of mHTr: immediate AC was performed more often in cases with medium or small infarct than large infarct (68.2% versus 35.9%, p<0.001), and in cases without mHTr than with mHTr (68.6% versus 34.9%, p<0.001). The most common method of AC was "intravenous heparin followed by warfarin" (68.2%), and then "warfarin alone" (16.9%) or "aspirin followed by warfarin" (15.0%). If AC therapy was not commenced immediately, it resumed most commonly between 1 and 2 weeks after the onset (44.0%). Previous ICH or CMBs did not strongly affect on the AC therapy.

Conclusion: Quite many neurologists in Korea did immediate AC in selective ACES, such as medium to small infarction without mHTr. Further trials are needed to prove the safety of AC therapy in the selective population.

377 Acute stroke: current treatment

HOW GENDER AND RACE INTERACT TO INFLUENCE OUTCOME OF ISCHEMIC STROKE AFTER TREATMENT WITH RT-PA

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Introduction: There is considerable interest in identifying subgroup effects of rt-PA. However, subgroup analyses are especially vulnerable to imbalances. We developed Methods that accommodate imbalances and applied them to assess the influence of gender and race on rt-PA outcomes.

Methods: pPREDICTS© (Mandava and Kent, Stroke 2009) generates a model based on placebo arms of randomized trials with multi-dimensional statistical intervals to assess whether a group differs from expected outcome at similar baselines (Fig 1; +/- p=0.05 intervals bound the middle surface). pPAIRS© (Mandava et al. Stroke 2010) matches subjects directly for baseline factors. We applied these to the NINDS rt-PA dataset and examined outcomes based on gender and race.

Results: pPREDICTS© : The outcome model shows percent achieving mRS 0-2 based on baseline NIHSS and age. Placebo outcomes were close to the predicted model for all groups (proximity of the control Results to the middle outcome surface). Significant improvement was seen for both Caucasian (C) genders (Fig 1a; both rt-PA outcomes are above the p=0.05 interval). AA males showed improvement that was only slightly below the p=0.05 interval. However, there was no improvement for AA females (arrow; Fig. 1b). pPAIRS© : Matching for gender, race, baseline NIHSS, age, glucose and stroke subtype indicated that outcome after rt-PA in AA females was considerably worse than C females after matching (e.g. median NIHSS was 15 for both). 37% of AA achieved mRS 0-2 vs 63% for C females; p=0.027). Mortality was higher (23% vs 7%).
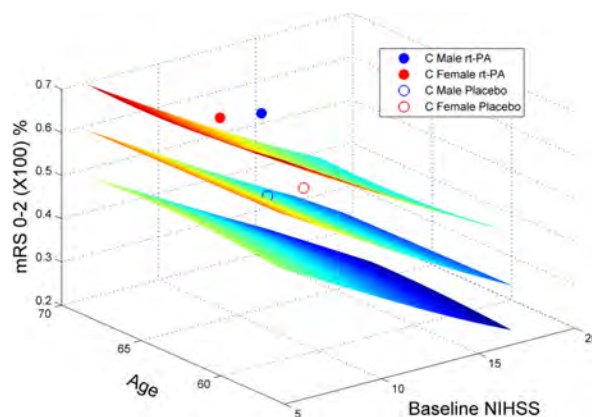
Figure 1
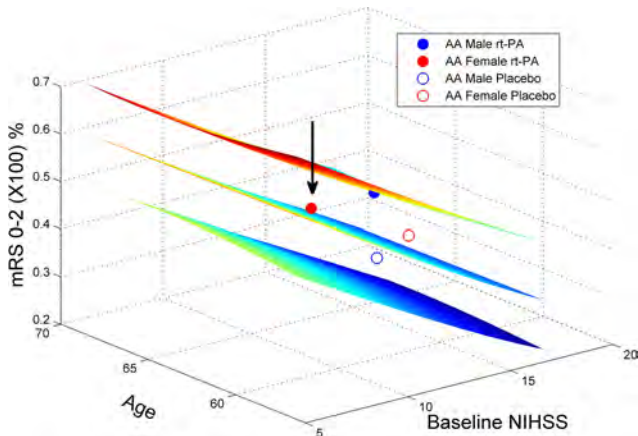
Figure 1

Discussion: These Methods were able to clarify the previously poorly understood role of gender and race in rt-PA outcome. Caucasians demonstrated good response to rt-PA regardless of gender, with marginally less in AA males, and poor outcome in AA females. A potential biochemical explanation is the finding that AA women have higher circulating levels of the endogenous t-PA inhibitor, PAI-1 (Perry, Metab Clin Exp 2008).

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378 Acute stroke: current treatment

LOW AND DECREASING LIPID LEVELS IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Background: Little is known about the validity of lipid levels measured in acute ischemic stroke. Prior work in patients with acute coronary syndrome has found that lipid levels measured within 48 hours of acute myocardial infarction can be falsely low. The purpose of this study was to compare initial lipid levels in the acute stroke setting to subsequent values.

Methods: Consecutive acute ischemic stroke patients admitted to University of Alabama Hospital at Birmingham from 10/2007 to 7/2010 were screened for repeat lipid levels obtained within 2 wks of symptom onset.

Results: Of 600 patients screened (51% men; mean age 62±15 yrs, baseline median NIHSS-11 range 0-42), 34 (6%) had a second lipid profile within 14 days (mean age 60 yrs, 59% men, median NIHSS score 3, interquartile range 1-7). The proportion of statin naïve patients prior to stroke was 83%. A decrease from the initial low density lipoprotein (LDL) levels was found in 61% patients, high density lipoprotein (HDL) showed decreased level in 64% patients, triglycerides decreased in 50% patients and total cholesterol decreased in 70% patients. In 13% of patients initially had LDL<70mg/dL and were later found to have LDL> 70 mg/dL (p<0.0001).

Conclusions: Lipid levels may be low and may continue to decrease shortly after ischemic stroke in a good proportion of patients necessitating a large prospective study. Furthermore, in 13% of patients these low levels could result in failure to initiate statin therapy.

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379 Acute stroke: current treatment

TREATMENT OF POSTERIOR CIRCULATION ACUTE ISCHEMIC STROKE. A COMPARISON BETWEEN NEUROVASCULAR INTERVENTION AND INTRAVENOUS THROMBOLYSIS

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Background: Safety and efficacy of thrombolysis in posterior circulation acute ischemic stroke has not been determined in specific randomised trials. It is not clear whether intravenous thrombolysis (IVT) is more or less beneficial than neurovascular intervention (NVI). Our aim is to compare both therapeutic modalities.

Methods: Comparative analysis of 2 prospective registries of patients from 5 stroke centres. One registry recorded patients treated with IVT and the other one included patients treated with NVI. Intra-arterial thrombolysis, thrombectomy, thrombus disruption and angioplasty+stenting were used separately or in combination in the NVI group. NVI were only available from Monday to Friday in working hours.

Results: Since 2004, 25 posterior circulation ischemic strokes have been recorded in the NVI registry and 79 patients in the IVT registry. Patients treated with NVI were younger (mean ± SD: 58±15 vs 65±12 years, p=0.02), presented more severe strokes (median (P25-P75) baseline NIHSS: 20 (13.5-26.5) vs 9 (5-13), p<0.001, and time-to-treatment (TTT) was longer (median (P25-P75): 342 (277.5-828.5) vs 156 (135-180) min, p<0.001. A higher proportion of poor outcome (defined as modified Rankin Scale score of 3 to 5 at 3 months or death) was observed in the NVI group (62% vs 23%, p=0,001) but logistic regression did not confirm this result: OR (adjusted by age, sex, TTT, and baseline NIHSS): 0.24 (95% CI: 0.02-2.7). A higher mortality rate was also found in NVI patients (38% vs 11%, p=0.007), but again multivariate anlysis did not confirm that finding (adjusted OR: 0.02 (95% CI: 0-1.1). The symptomatic intracerebral hemorrhage rate was low (1.4% for IVT, 4% for NVI, p=0,5), adjusted OR: 3.2 (95% CI: 0.07-134).

Conclusions: Both NVI and IVT seem to be effective and safe therapeutic options for posterior circulation ischemic stroke. The benefit of NVI vs IVT needs to be assessed in a specifically designed randomised trial.

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380 Acute stroke: current treatment

INTRAVENOUS THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE IN A GREEK GENERAL HOSPITAL

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Background: Intravenous thrombolysis for acute ischemic has been proved to be an established treatment for acute ischemic stroke.

Methods: All patients who received alteplase in our department were studied prospectively and retrospectively. A part of the prospective data was entered in the Safe Implementation of Treatments in Stroke and Hellas Stroke Registry databases. We examined the standard basic parameters of thrombolysis cohorts.

Results: Out of an average of 250 stroke patients per year hospitalized in our department between 2002 and 2010, 122 patients (66% men) who received rt-PA were identified. Prospective data were available for 60 patients. Median age was 57 years, median NIHSS at presentation 15, and median time from symptom onset to treatment 155 minutes. Stroke etiology was large vessel atherosclerosis (30%), cardioembolic stroke (28%), small vessel disease (10%), other identified causes (18%) and undetermined (14%). Fifteen percent of patients had posterior circulation strokes. Seventy-four percent of patients responded significantly to treatment. Large vessel atherosclerosis and cardioembolic stroke responded equally to alteplase. Symptomatic ICH occurred in 6% of patients; 7% of patients died during hospitalization. Fifty-nine percent of patients were discharged with a Rankin Score of 0 to 2. Seventy percent of patients had a 3-month-follow-up Rankin Score of 0 to 2.

Conclusion: Intravenous rt-PA is a safe and effective treatment in an urban general hospital. Despite some missing data due to partly retrospective data acquisition, our Results are comparable to published evidence, including randomized trials and observational studies.

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381 Acute stroke: current treatment

THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE IN PATIENTS WITH BETA-THALASSEMIA MAJOR

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Background: Compared to other hemoglobinopathies, e.g. sickle cell disease, stroke is an uncommon feature of beta-Thalassemia Major (BTM), probably due to the short life expectancy of such patients. Although a chronic hypercoagulable state is generally considered as cause of thromboembolic events affecting the brain,

there is certain evidence suggesting cardioembolism as cause of stroke in BTM. Whereas a longterm prophylactic treatment with antiplatelets is discussed data regarding acute stroke treatment are missing. We present the first two cases of BTM patients suffering acute stroke who were treated with systematic thrombolysis.

Case Reports: A 43y-old female and a 41y-old male BTM patient, both with a history of splenectomy, regular blood transfusions, chronic chelation therapy and with known dilative cardiomyopathy presented with acute left-side hemiplegia and right-side hemiplegia accompanied by global aphasia respectively. In both cases a dense MCA sign was demonstrated on admission CT indicating proximal MCA occlusion. The corresponding NIHSS-scores were 13 and 28 respectively. Permanent atrial fibrillation was present in the female patient whereas the male patient had episodes of ventricular tachycardia. Systemic thrombolysis following standard protocol was initiated at 90min and 270min after stroke onset respectively. Slight gingival bleeding at the end of the rtPA infusion occurred in the second case. Otherwise there were no complications. MCA recanalization was demonstrated by means of transcranial Doppler. Both patients improved significantly and regained independence leaving hospital with a mRS-score of 1 and 2 respectively.

Conclusion: These are the first reported cases of safe and effective thrombolytic treatment in BTM patients who suffered acute ischemic stroke of cardioembolic origin. This treatment option should not be preserved from these multimorbid high risk patients.

382 Acute stroke: current treatment

INITIAL 5-YEAR RESULTS OF INTRAVENOUS RT-PA USING 0.6 MG/KG ALTEPLASE IN A SINGLE JAPANESE STROKE CENTER: NCVC RT-PA REGISTRY

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Background: In Japan, IV recombinant tissue plasminogen activator (rt-PA) using 0.6 mg/kg alteplase was approved for acute stroke patients in October, 2005, and endovascular thrombectomy using the Merci Retrieval System was additionally approved in October, 2010. The goal of this study was to determine stroke outcomes after rt-PA during this five-year duration.

Methods: Consecutive stroke patients treated with IV rt-PA from October 2005 through August 2010 were registered in our single stroke center.

Results: A total of 205 Japanese stroke patients (68 women, 73 ± 11 years old) were studied. Median onset-to-needle time was 135 m and median door-to-needle time was 69 m. The leading stroke subtype was cardioembolism (62.0%). Of 182 patients receiving pretreatment MRA, 65 (35.7%) had occlusion at the MCA trunk, 29 (15.9%) at the MCA branch, and 27 (14.8%) at the ICA. IV antihypertensives were taken just before rt-PA for 31 patients (15.1%) and IV edaravone was used for 183 (89.3%). Median NIHSS score was 13 (IQR 8-18) at baseline, 8 (3-14) at 24 h after rt-PA, and 3 (1-11) at hospital discharge. Within the initial 36 h, 12 patients (5.8%) developed intracerebral hemorrhage with an increase of ≥1 point from the baseline NIHSS score. At 3 months, 70 patients (34.1%) had a modified Rankin Scale (mRS) score ≤1. Analysis of 135 patients with a premorbid mRS score ≤1 who met the criteria of the European license (≤80 years old, an initial NIHSS score ≤24, etc.) showed that 40.0% had a 3-month mRS ≤1. Four patients died within the initial week, including a patient having thoracic aortic dissection, and 9 died afterward within 3 months; thus 3-month mortality was 6.3%.

Conclusions: Chronic outcomes of patients receiving rt-PA therapy in our single center were similar to those of a nationwide post-marketing survey (J-MARS) and multicenter observational study (SAMURAI) using the same low-dose alteplase for Japanese patients. The outcomes were also similar to those of SITS-MOST.

Acute cerebrovascular events (ACE): TIA and minor strokes

426 Acute cerebrovascular events (ACE): TIA and minor strokes

EMOTIONAL AND IRRATIONAL RESPONSES BY PATIENTS TO TIA - A PERSISTING BARRIER TO SUCCESSFUL STROKE PREVENTION

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Background: Patients give multiple reasons for delay in seeking help after TIAs. Transience and variability are inherent features of TIAs from which we can gain insights into patients' thoughts and behaviour in acute illness.
Method: All patients seen in our TIA Clinic from January 2008 to June 2009 were asked what they thought, what they did, how quickly, and why. We analysed all who had definite or probable TIA (inc. possible migraine with aura), and minor stroke, excluding all with non-focal symptoms.
Results: The first 400 eligible patients were analysed, 50% male, median age 70, final diagnosis TIA 273, minor stroke 79, probable migrainous aura 48. Overall 56% delayed seeking medical advice; 35% who correctly self-diagnosed and 77% who did not (p<0.00001); 50% who were with someone and 63% alone (p=0.01); 51% with prior TIA and 58% without (p=0.24). Reasons for delay included: transience of symptoms ("I thought maybe I'd imagined it"); embarrassment ("I thought the GP would say don't be stupid"; stoicism ("I didn't want to make a fuss"); reluctance to bother others ("I waited till my friends had gone home"); concealing symptoms, even from doctors; denial ("if it had happened to anyone else I'd have sent them straight to Casualty"); failure to consider it urgent ("going to A&E seemed too panicky"); optimism ("I thought I'd be better after a rest"). Responses were often even more irrational: "I thought my leg was having a holiday"; "Me and my wife had a bit of a laugh"; "I said I'd go (to GP) when I was stronger"; "I thought it was the mouse (computer)".
Conclusions: Affective and behavioural factors are potent causes for patients' delay in responding to TIAs. Embarrassment, denial, stoicism, fear, and determination to carry on as normal are attitudes frequently encountered. Knowledge leading to correct self-diagnosis reduces delay, as does informal advice when available, but emotional and irrational responses remain siginificant barriers to preventing strokes.

427 Acute cerebrovascular events (ACE): TIA and minor strokes

NEUROLOGICAL DETERIORATION AND STROKE RECURRENCE IN THE ACUTE PHASE OF MINOR STROKE FUKUOKA STROKE REGISTRY

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Background & Purpose: A neurological deterioration in the acute phase can be associated with a bad outcome even in minor stroke. We investigated the predictive factors for an acute neurological deterioration in minor stroke.
Subjects & Methods: Among the consecutive 3062 stroke patients who were admitted to the 7 stroke centers in Fukuoka prefecture Japan within 7 days after the onset, 2113 patients with acute ischemic stroke with the initial NIH stroke scale score of 7 or less and preclinical modified Rankin scale of 0 or 1 were included in the present study. We observed a neurological deterioration (a NIHSS score worsening of ≥1-point), stroke recurrence, or any death during the first 21 hospital days.
Results: A neurological deterioration with or without stroke recurrence was observed in 338 (16%) patients. With regard to the TOAST classification, a neurological deterioration was most frequent in Large-artery atherosclerosis (18.3%). In accordance with the site of ischemic lesions, a neurological deterioration was most frequent in patients with both cortex or cerebellar lesions and deep perforating artery lesions (20.2%). A preclinical warfarin was less frequent, diabetes mellitus and a stenosis of ≥50% in the major brain artery were more frequent, and the values of

low density lipoprotein (LDL) cholesterol, blood glucose, and HbA1c were higher in patients with than without a neurological deterioration. On multivariate analysis, a stenosis of ≥50% in the major brain artery (OR, 1.40; 95%CI 1.07-1.85), ischemic lesions including deep perforating artery area (OR, 1.47; 95%CI, 1.10-1.96), LDL cholesterol (OR, 1.00; 95%CI, 1.00-1.01), and diabetes mellitus (OR 1.70, 95%CI 1.21-2.39) had a positive association, and preclinical warfarin (OR 0.61, 95%CI 0.39-0.98) had a negative association with a neurological deterioration.
Conclusions: The major brain artery stenotic lesion, the site of ischemic lesions, LDL cholesterol, and diabetes mellitus were significant predictor for a neurological deterioration in the acute phase of minor stroke. A preclinical warfarin might decrease the risk of a neurological deterioration.

428 Acute cerebrovascular events (ACE): TIA and minor strokes

LOW POOLED LIKELIHOOD RATIOS IN META-ANALYSIS OF THE ABCD2 SCORE FOR EARLY STROKE RISK FOLLOWING TRANSIENT ISCHEMIC ATTACK (TIA)

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Background: The ABCD2 score is recommended by several stroke guidelines to aid in management decisions following TIA. However there is uncertainty regarding its clinical predictive value in individual patients.
Methods: We undertook a systematic review and meta-analysis of TIA studies (January 2005-May 2010) using standard Methods. Where sufficient data was not published, authors were invited to contribute their data. We determined the pooled positive and negative likelihood ratios (post-test estimates of individual predictive value) at pre-determined cut-offs using random effects meta-analysis. Subgroup analysis was conducted to evaluate heterogeneity.
Results: ABCD2 data was available for 25 cohorts (13,097 subjects). 13/25 cohorts reported 2 day outcome (total 494 strokes) and 22/25 cohorts reported 7 day outcome (total 698 strokes). Dichotomising the score at 3 (0-3 low risk, 4-7 high risk) the positive likelihood ratio (PLR) was 1.45 (CI 1.33-1.57) and 1.46 (CI 1.36-1.56) at day 2 and 7 respectively. The negative likelihood ratio (NLR) was 0.39 (CI 0.30-0.51) and 0.41 (CI 0.33-0.50) at day 2 and 7 respectively. The heterogeneity associated with NLR was attributable to within study variance alone whilst 90% of PLR heterogeneity was due to between study variance. Heterogeneity was associated with study method on sub group analysis however the absolute differences in summary effects were small.
Conclusion: In a pooled analysis, the ABCD2 score shows low predictive value based on post-test estimates of accuracy. Depending on the score alone to guide management decisions in individual patients may not be appropriate.

429 Acute cerebrovascular events (ACE): TIA and minor strokes

MANAGEMENT AND OUTCOME OF PATIENTS ADMITTED WITH TRANSIENT ISCHAEMIC ATTACK (TIA): THE AUSTRALIAN STROKE CLINICAL REGISTRY EXPERIENCE

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Background: Limited information exists on the quality of care for patients with TIA admitted to hospitals in Australia. Care recommendations are similar for TIA and ischaemic stroke (IS). The Australian Stroke Clinical Registry (AuSCR) was established in 2009 to provide national, prospective data on clinical processes

and 90+ day outcomes for stroke/TIA. The Aims of this study were to describe in-patient care and outcomes for TIA during the first year of data collection (June 2009 – May 2010).

Methods: Online registry (www.auscr.com.au) with stroke type designated by clinical staff and confirmed by post-discharge ICD10 coding, with survivor follow-up by telephone or mail.

Results: Of 1490 patients (1524 care episodes) from 10 hospitals (mean age 71 years, 52% male, 59% Australian-born), 281 (18%) were TIA with different clinical care to IS: stroke unit management 68% vs 85% (p <0.001) and care plan at discharge 34% vs 22% (p <0.001). Most TIA patients (88%) were discharged home, 4% went to rehabilitation, 3% went to an aged care facility (n=4 to high care), approximately 1% (n=4) of TIA patients died in hospital (and none of these patients received stroke unit care), and another 1 died during the follow-up period. Median length of stay was 3 days (IQR 3.5 days). Of the ICD10 principal diagnostic codes provided, 12/170 were for stroke codes (e.g. I64). Median time to community follow-up was 223 days (IQR 134 days), with 14% reporting a subsequent stroke on follow-up.

Conclusion: As well as significant variations in the quality of hospital care for patients with TIA, there were discrepancies in the clinical definition of TIA and coding by hospital clerks. TIA outcomes may be enhanced with better access to stroke unit care.

430 Acute cerebrovascular events (ACE): TIA and minor strokes

PULSE OXIMETRY REVEALS SUBCLINICAL RESPIRATORY DISORDERS IN PATIENTS WITH FIRST-EVER MINOR STROKE OR TIA

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Background: Respiratory disorders are commonly observed in the acute phase of stroke. Aim of the present study is to evaluate respiration disorders in patients with acute minor stroke or TIA, using pulse oximetry.

Methods: A consecutive series of 71 first ever minor stroke or TIA patients with no history of apnea (Epsworth Sleepiness Scale>11), previous stroke, heart or/and respiratory failure were excluded and a group of 40 non-stroke hospitalized age and sex matched control patients with the same exclusion criteria underwent overnight pulse oximetry. The Oxygen Desaturation Index (ODI) and quantitative parameters of saturation episodes were calculated in all cases. Statistical analysis was performed using Mann-Whitney test.

Results: The average nighttime ODI differed significantly between patients and controls: 14.8 vs. 8.8 (p=0.026), while the difference between average nighttime saturation values (94 v. 94.65) did not reach significance (p=0.131). The average minimum saturation values (85.9% vs. 88.6%) also showed significant differences (p=0.002). Significant differences were found when comparing the number of <90%-desaturation episodes (19.02 vs. 4.7 p=0.004), their average cumulative duration (674.1s vs. 110.2s p<0.0001) and the average duration of the longer episode (84.2s vs. 33.5s, p=0.003). Similar differences were found when using the <95% cut-off value: desaturation episodes 227.22 vs. 68.64 (p=0.059); average cumulative duration 4643.5s vs. 2836s (p=0.010) and average duration of the longer episode 255.9s vs. 237.2s (p=0.462).

Conclusion: Patients with acute minor stroke or TIA present within the first 24 hours after symptom onset nocturnal hypoxemia of long duration. This finding needs to be further investigated and if verified it might have therapeutic implications.

431 Acute cerebrovascular events (ACE): TIA and minor strokes

PROGNOSIS OF TRANSIENT NEUROLOGICAL ATTACKS OF UNCERTAIN DIAGNOSIS IN A TRANSIENT ISCHEMIC ATTACK CLINIC

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Background: Patients with transient ischemic attack (TIA) are at high risk of stroke and vascular events. However, the prognosis of patients with transient neurological attack (TNA) of uncertain diagnosis (possible TIA) is unclear. We aimed to identify the early and long-term prognosis of possible TIA patients.

Methods: Consecutive TNA patients referred to a TIA Clinic during five years were classified as TIA, possible TIA or Mimic. Patients with transient symptoms less typical of vascular origin or with an alternative explanation were classified

as Possible TIA. We analyzed baseline data, 30th day and long-term follow-up of possible TIA patients. Primary outcome was stroke at 30th day; secondary outcomes comprised any vascular event (TIA, stroke, myocardial infarction, vascular death) at 30th day and long-term follow-up. Recurrences of transient nonvascular events were analyzed to clarify the inclusion TNA episode.

Results: From 458 TNA patients referred to the TIA Clinic, 109 were classified as Possible TIA. At 30th day, none Possible TIA patient had a stroke, and 1.9% (95% CI 0.5 to 6.6) had myocardial infarction. At long-term follow-up (median time of 679 days), 9.9% (95% CI 5.5 to 17.3) had vascular events: six patients had stroke (one fatal), three myocardial infarction (one fatal) and one TIA. During the follow-up, 25 patients (24.8%) had recurrent transient nonvascular events, and a definite diagnosis of the inclusion TNA was reached in 15 patients (15%), mainly of conversion disorder, migraine and vestibular dysfunction.

Conclusion: Long-term follow-up of Possible TIA patients was useful to clarify the TNA inclusion diagnosis in some patients. Although the early risk of vascular events was low, patients were at higher risk of having long-term vascular events. Therefore, vascular risk factors management and secondary prevention should be optimized.

432 Acute cerebrovascular events (ACE): TIA and minor strokes

INTRACRANIAL ARTERY STENOSIS OR HBA1C>7.0% IS A PREDICTIVE FACTOR FOR EARLY MOTOR WORSENING IN LACUNAR STROKE

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Intracranial artery stenosis or HbA1c>7.0% is a predictive factor for early motor worsening events patients with lacunar stroke.

Background: Early motor worsening event (EMW) is an important problem in acute lacunar stroke. However, a predictive factor for EMW has not been established. The purpose of this study is to find a clinical Background to predict EMW of lacunar stroke on hospital visit.

Methods: Seventy-two consecutive patients with acute lacunar stroke in the internal capsule, corona radiata or pons were reviewed. Motor worsening was defined as worsening by > or =1 point in the NIHSS for motor function (facial palsy, motor arm and leg, limb ataxia and dysarthria). Patients with or without EMW were compared regarding brain MRI or MRA, vital signs, biochemical markers on hospital visit.

Results: EMW appeared in 22 patients (31%) within 5 days (mean 1.7 days) from hospital visit. Patients with EMW were higher than those without EMW in HbA1c value (6.4±0.3 vs. 7.8±0.6%, p < 0.05) and in prevalence of intracranial artery stenosis (ICAS; 13/22, 59% vs. 7/50, 14%, p < 0.001). There were no significant differences regarding age, sex, site/size of the infarct, blood pressure or other biochemical markers on hospital visit between patients with EMW and without EMW.

Multivariate statistical analysis indicated that HbA1c > 7.0 (OR 1.83, 95%CI 1.07-3.17 p<0.05) or ICAS (OR 2.94, 95%CI 1.66-5.50, p<0.001) increased the risk of EMW significantly in lacunar stroke patients, and the combination of HbA1c >7.0% and ICAS increased the risk in an additive manner (OR 5.13, 95%CI 2.07-22.7, p<0.005).

Conclusion: HbA1c>7.0% or ICAD detected on hospital visit may be associated with EMW in patients with lacunar stroke.

433 Acute cerebrovascular events (ACE): TIA and minor strokes

OXYGEN SATURATION DISORDERS IN PATIENTS WITH MINOR STROKE – CAUSE OR CONSEQUENCE OF STROKE?

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Background: Sleep apnea is an established stroke risk factor. However, it remains unclear whether sleep apnea and other respiratory disturbances might also be the result of stroke.

Methods: A series of 23 patients with acute first ever minor stroke and 23 age- and sex-matched non-stroke hospitalized patients, all with no history of apnea (ESS<10), previous stroke, heart or/and respiratory failure, underwent pulse oxymetry. The Oxygen Desaturation Index (ODI) defined as the number of oxygen desaturation episodes per hour, and the number and duration of desaturation episodes were calculated.

Results: All examined differences between patients and controls were of statistical significance. The estimated average daily ODI for stroke patients and controls was

15.95 and 5.95 respectively (p<0.001). The corresponding values for the average saturation while being awake were 93.5% and 94.8% (p=0.030), while the mean minimum saturation values were 83.4% and 94.8% (p<0.0001) respectively. The average number of desaturation episodes <90% was 14.7 and 0.13 respectively (p<0.0001), with a mean cumulative duration of 837.4s and 5.21s respectively (p=0.001). When using the <95% cut-off point, the corresponding values were 58.52 and 24.21 (p=0.002), with a mean cumulative duration of 3057.3s and 880.9s (p<0.0001). Additionally, the average duration of the longest <90%-episode was 51.1s in stroke patients vs. 4.5s in controls (p=0.001) and 221.8s vs. 132.3s (p=0.009), for the <95%-episodes respectively.

Conclusion: Patients with first ever minor stroke present respiratory disorders during daytime, while being awake and alert. Statistically significant differences were found between patients and matched controls regarding saturation and duration of hypoxemia at daytime. These findings suggest that apnea and other respiratory changes might be considered as stroke consequences. This hypothesis needs to be further investigated.

434 Acute cerebrovascular events (ACE): TIA and minor strokes

DRIVING AFTER TRANSIENT ISCHEMIC ATTACK (TIA)

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Introduction: Driving is a dangerous activity associated with significant mortality and morbidity, causing 3500 deaths and 40 000 serious injuries in the UK per year. A proportion of the 3500 road traffic accident deaths in the United Kingdom each year are caused by collapse, of which stroke or transient ischemic attacks (TIA) make up 7%. The Driver and Vehicle Licensing Authority (DVLA) guidelines state that an individual should not drive a group 1 vehicle for one month after a single TIA. Patients with persistent disability or recurrent TIA must inform and seek DVLA approval to drive again. It is the duty of the doctor to make the patient aware of any restrictions which apply to them. Failure in doing this may cause prosecution for negligence. There has been relatively little research into driving issues following a TIA and stroke. This audit was set out to determine if patients referred as TIA were advised about their fitness to drive.

Methods: All patients referred to TIA clinic of Diana princess of Wales, hospital, Grimsby, UK were retrospectively studied.

1: Referal letters were checked to see whether the referring doctor had documented any driving advice or not.
2: Clinic letter and TIA Patients register was checked to see whether driving advice was given from specialist clinics.

Results: A total of 234 patients were referred as TIA to specialist TIA clinic from 01 Jan 2010 to 23 June 2010. Mean age 67 years (25 to 93 years); 118 (50.4%) were males.

35.8% patients had any documented evidence of the initial examining doctor informing them of not to drive. After assessment in specialist clinic, ninety three patients (39.7%) were diagnosed as TIA, thirty three (14.1%) as minor stroke and alternative diagnosis was made in 108 (46.1%) patients.

In specialist TIA clinic, driving advice was given to 72.2% of TIA /minor stroke patients.

Conclusion: Patients are not always informed about their fitness to drive following initial consultation and many patients do not receive driving advice after attending specialist clinic.

Further education of the doctors is needed to ensure 100% advice.

436 Acute cerebrovascular events (ACE): TIA and minor strokes

INCIDENCE AND PREDICTORS OF SUBSEQUENT STROKE DURING ACUTE HOSPITALIZATION IN PATIENTS WITH TRANSIENT ISCHEMIC ATTACK

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Background and Aims: The purpose of this study was to elucidate risk factors for early recurrent transient ischemic attack (TIA) and stroke in patients admitted with TIA.

Methods: We carried out a multicenter retrospective study to clarify the characteristics of inpatients with TIA. The subjects of this study were TIA patients admitted to 13 stroke centers in Japan within 7 days after onset between 2008 and 2009. Recurrent TIA and stroke during acute hospitalization were determined by medical record review. We investigated incidence and predictors of these events during hospitalization.

Results: 464 patients (292 men, mean age of 69 years) were registered. MRI examinations were performed in 458 patients (98.7%), and acute ischemic lesions on diffusion weighted image (DWI) were found in 96 patients (21.0%). During hospitalization, recurrent TIA occurred in 27 patients (5.8%), ischemic stroke in 8 patients (1.7%).

Multiple regression analysis showed that positive DWI lesions (OR 2.46, 95%CI 1.12-5.23, p=0.025), hemiparesis (OR 2.81,95%CI 1.19-7.76, p=0.017), and diabetes mellitus (OR 2.29, 95%CI 1.04-4.90, p=0.040) were independently significant predictors of subsequent ischemic stroke and recurrent TIA.

Conclusion: This study revealed incidence and predictors of recurrent TIA and stroke events during hospitalization in patients with TIA admitted to representative stroke centers in Japan. Subsequent ischemic stroke and recurrent TIA were associated with positive DWI lesion, hemiparesis, and diabetes mellitus.

437 Acute cerebrovascular events (ACE): TIA and minor strokes

OPTIMIZING THE RISK ESTIMATION AFTER A TRANSIENT ISCHEMIC ATTACK - THE ABCDE+ABCD2-SCORE

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Background and purpose: The risk of stroke after a transient ischemic attack (TIA) can be predicted by scores incorporating age, blood pressure, clinical features, duration (ABCD-score) and diabetes (ABCD2-score). However, some patients have strokes despite a low predicted risk according to these scores. We designed the ABCDE+ score by adding the variables "etiology" and ischemic lesion visible on diffusion-weighted-imaging (DWI) –"DWI-positivity"– to the ABCD-score. We hypothesized that this refinement increases the predictability of recurrent ischemic events.

Methods: We performed a prospective cohort study among all consecutive TIA patients in a university hospital emergency department. Area under the computed-receiver-operating curves (AUCs) were used to compare the predictive values of the scores with regard to the outcome stroke or recurrent TIA within 90 days.

Results: Among 248 patients, 33 (13.3%, 95%-CI 9.3-18.2%) had a stroke (n=13) or a recurrent TIA (n=20). Patients with recurrent ischemic events more often had large-artery-atherosclerosis as the cause for TIA (46% versus 14%, p<0.001) and positive DWI (61% versus 35%;p=0.01) compared with patients without recurrent events. Patients with and those without events did not differ with regard to age, clinical symptoms, duration, blood pressure, risk factors, and stroke preventive treatment. The comparison of AUCs [95%CI] showed superiority of the ABCDE+ score (0.67[0.55-0.75]) compared to the ABCD2-score (0.48[0.37-0.58];p=0.04), and a trend towards superiority compared to the ABCD-score (0.50[0.40-0.61];p=0.07).

Conclusion: In TIA patients, the addition of the variables "etiology" and "DWI-positivity" to the ABCD-score seems to enhance the predictability of subsequent cerebral ischemic events.

438 Acute cerebrovascular events (ACE): TIA and minor strokes

URGENT CARE TO TRANSIENT ISCHEMIC ATTACK

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Background: Incidence of ischemic stroke after suffering a transient ischemic attack (TIA) is high. Our aim is to analyze recurrence rate and related factors after 4 years of TIA rapid assessment protocol implementation in our hospital.

Methods: One hundred and ninety-seven TIA patients have been evaluated between February 2007 and November 2010. We've analysed their vascular risk factor profile and recurrence rate (stroke and other cardiovascular events) after a 3-month period, as well as related factors to these recurrences.

Results: Mean age 71.8 years old, 58.4% male. The most frequent risk factor was hypertension (69%), and 11 patients (5.6%) had a large-artery severe stenosis. During the 3-months follow-up period, 10 patients (5.1%) suffered another TIA, 8 (4.1%) an ischemic stroke and 1 (0.5%) a peripheral ischemia episode. 75% of the cerebral infarctions occurred within the first week after the TIA. Large-artery severe stenosis was associated with ischemic stroke (p<0.001). No other vascular risk factors o clinical features were related to recurrences. ABCD2 scale wasn't associated with a higher rate of vascular events nor with cerebral infarctions in particular. Among ethiologies, athetrombotic was associated with stroke recurrence (p=0.001). Crescendo TIAs were associated with TIA recurrence but not with ischemic stroke.

Conclusion: The 3-month stroke incidence after a TIA was 4.1% and the main related factor was large-artery severe stenosis. Seventy-five percent of the recurrences occurred within the first week. This supports the need for urgent attention to these patients.

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439 Acute cerebrovascular events (ACE): TIA and minor strokes

PERFORMANCE OF ABCD, ABCD2, ABCD3 AND ABCD3I SCORE IN DETECTING HIGH RISK TRANSIENT ISCHEMIC ATTACK (TIA) PATIENTS: A VALIDATION STUDY IN ASIAN POPULATION

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Background: ABCD, ABCD2, ABCD3 and ABCD3i scores were able to identify individuals at high early risk of recurrent stroke after a TIA in Caucasians. We aimed to validate these scores in Asians population.

Methods: Consecutive TIA patients were prospectively recruited from July 2007 to October 2010. The ABCD, ABCD2, ABCD3 and ABCD3i scores were used to stratify the 30-day stroke risk.

Results: The 30-day risk of stroke of 226 TIA patients was 4.6%. Patients with ABCD score of 0-3 and 4-6 had stroke 0% and 7.2% at 30 days respectively (P=0.016). The 30-day risk of stroke was 0% in patients with the ABCD2 score of 0-3, 7.2% in those with score of 4-7 (p=0.016). Patients with ABCD and ABCD2 scores ≥ 4 had a significantly higher incidence of stroke at 30 day. However, The ABCD3 score performed no better than chance for prediction of 30-day stroke (C statistic 0.392-0.701). The ABCD3i score was available for 43 (19.9%) patients in this study.

Conclusions: ABCD, ABCD2 scores were valid in identifying 30-day stroke after TIA in Asians. Further studies are needed for ABCD3 and ABCD3i scores.

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440 Acute cerebrovascular events (ACE): TIA and minor strokes

USE OF ABCD2 SCORE BY NON SPECIALISTS TO TRIAGE TIA PATIENTS

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Background: Early recognition and intervention in acute stroke and transient ischaemic attacks (TIAs) is important in reducing morbidity and mortality. The ABCD2 score has been used as a tool to risk stratify patients into high risk and low risk TIAs. It has been incorporated into many TIA clinic referral forms. There has been few studies looking at the use of ABCD2 scores by non-specialists. The aim of this study was to investigate the accuracy of non-specialists using the ABCD2 score to triage patients referred to a rapid access TIA clinic.

Method: Referral letters from primary care and emergency room physicians with ABCD2 score were collected and compared with ABCD2 score done by the specialists in the TIA clinic between the period of Sept'09 and Aug'10.

Result: A total of 469 patients were referred to the clinic. 453 patients were seen in the TIA Clinic. 16 (3.4%) patients did not attend. 271 (59.8%) patients had a diagnosis of non-stroke. 54 (11.9%) were strokes and 128 were TIAs (28.3%).

61 (47.7%) of patients with a TIA diagnosis had no ABCD2 scores from referring physicians. 49 (38.2%) had referring scores which were similar to the specialist scores. 14 (10.9%) were reclassified as high risk TIAs by the specialists in the clinic and 4 (3.1%) were reclassified as low risk TIAs by the specialists in the clinic.

Conclusion: Although the ABCD2 score was printed on the referral form, there was a poor recording of it by non specialists. There were a substantial number of patients (10%) who were reclassified as high risk and needed to be seen more urgently in the clinic. This is perhaps due to the lack of knowledge about the ABCD2 score among

non specialists. We recommend that further education regarding the ABCD2 score among non specialists would improve the use of this tool.

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441 Acute cerebrovascular events (ACE): TIA and minor strokes

PROBNP IS RELATED TO CARDIOEMBOLIC ETIOLOGY IN TRANSIENT ISCHAEMIC STROKE

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Introduction: The risk of recurrent stroke after a transient ischaemic stroke (TIA) is considered to be between 9.5-20%. Recurrence depends on the underlying pathology.

Some biologic markers have been found to be related to different etiologies in stroke. Pro-Brain Natriuretic Peptide (proBNP) and D-dimer are associated with cardioembolic etiology, whereas homocysteine and High-sensitivity C-reactive protein (hsCRP) are related to atherothrombotic events.

Hypothesis: We assessed the hypothesis that proBNP, D-dimer, hsCRP and homocysteine could be markers of recurrent stroke in TIA.

We also test the relationship between them and etiology in our cohort.

Methods: A prospective study was carried on 64 patients with a TIA attended by a neurologist in the Emergency department and followed by an specialized neurologist at 1 and 3 months.

We analysed etiology according to TOAST criteria, recurrence in 3 months and levels of biomarkers. Levels above proBNP >300 ng/L, D-dimer >250 ug/L, homocysteine >12.4 umol/L y hsCRP >0.3mg/L were considered as pathological.

Results: Etiology of TIAs was distributed as following: 20,31% large-artery occlusive disease, 18,75% cardioembolic, 17,18% small-vessel disease and 43,75% undetermined cause.

Recurrent strokes occurred in 11 patients (17'18%), 2 in large-artery occlusive disease, 1 cardioembolic, 4 in small-vessel disease and 4 undetermined cause.

Eight from 14 pathological proBNP samples were cardioembolic. Pathological ProBNP Results showed association with cardioembolic etiology (p<0.0001), with sensitivity of 66'67%, specificity of 88'46% and negative predictive value of 92%.

We failed to find any association between other biomarkers and etiology, or any biomarker and recurrent stroke.

Conclusions: Our study showed association between pathological proBNP and cardioembolic etiology. Pro-BNP could be used to priorize cardiologycal assessment in patients regarding to ist high sensitivity and specificity.

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442 Acute cerebrovascular events (ACE): TIA and minor strokes

CIRCADIAN BLOOD PRESSURE PATTERNS IN PATIENTS WITH TIA OR MINOR STROKE

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Background: Circadian blood pressure (BP) variation patterns have not been well studied in patients with Transient Ischaemic Attack (TIA) or minor stroke. We hypothesized that 24-hour diurnal BP patterns in patients with TIA/minor stroke would differ when compared to control participants.

Methods: Patients with TIA/minor stroke recruited ≤7 days after onset and age-sex group matched control participants were monitored for 24 hours using the Spacelab 90217 ambulatory BP monitor. Subjects were classified according to the percentage fall in mean systolic BP at night compared with during the day as: dippers (fall ≥ 10–20%); extreme dippers (≥ 20%); non-dipper (< 10%); and reverse dippers (< 0%). Dipper pattern was defined as the normal BP pattern. BP patterns were compared between patient and control groups.

Results: 76 patients (mean age 68 years, 59% male) and 83 controls (mean age 66 years, 54% male) were recruited. Treated hypertensives: 56 (73%) patients and

40 (48%) controls. BP pattern distributions were similar in patients with TIA/minor stroke and controls: 24 (31.6%) vs control 28 (34.2%) were dippers, 33 (43.4%) vs control 31 (37.8%) were non-dippers, 6 (7.9%) vs control 7 (8.5%) were extreme dippers, 13 (17.1%) vs control 16 (19.5%) were reverse dippers. The chance of a normal pattern was similar for patients and controls (risk difference 0.03, 95%CI -0.12 to 0.17, p=0.74).

Conclusion: Patients with TIA/minor stroke have a similar distribution of diurnal BP patterns when compared to controls. This differs from studies of acute stroke patients in whom a normal BP pattern is less likely to be present and treatment according to different circadian BP variations has been recommended. Further studies are needed to provide more information on the influence of diurnal patterns in patients with TIA and minor stroke.

443 Acute cerebrovascular events (ACE): TIA and minor strokes

INTRAVENOUS THROMBOLYSIS IN MINOR STROKE

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Background: The question whether to treat ischemic stroke patients with minor deficit at presentation may be a dilemma for stroke physicians, especially as minor symptoms have been reported to be five times more likely in patients with stroke mimics.

Methods: We describe baseline characteristics, clinical presentation, complications, and outcome in minor stroke patients treated with rtPA within 4.5 hours after onset. MRI was performed as initial brain imaging procedure in patients with very minor stroke and/or inconclusive clinical presentation.

Results: Between 2008 and 2010, 101 stroke patients (81 with initial CT, 20 with initial MRI) with minor clinical deficit (NIHSS < 5) received rtPA in our stroke centre. Patients who underwent MRI before treatment had more often inconclusive symptoms such as headache (p=0.039) or vertigo (p=0.011), and were less likely to have typical stroke symptoms such as dysarthria (p=0.005), facial palsy (p=0.003), and hemiparesis (p=0.013). Correspondingly, they had lower NIHSS scores (p<0.001). Unusual symptoms included the thalamic hand syndrome (Figure 1.1) and alien hand phenomenon (Figure 1.2). In 82/101 patients, an ischemic lesion was proven with (initial or follow-up) MRI, the remaining 19 were finally classified as stroke mimics. This was less frequent in patients who received initial MRI (p=0.078). In the MRI group, ischemic lesion size had a median volume of 2.16 cm^3, and ischemic lesions were significantly more often located in the PCA territory (p=0.020). Except for 3 cases of angioneurotic oedema, no rtPA related complications occurred. The median NIHSS at discharge was 1 (IQR 0–2). Comparing both groups, there were no differences with regard to stroke subtypes, complications, and outcome.

Figure 1. MR imaging in two patients with minor stroke before (a-c) and after (d-f) intravenous thrombolysis. Initial MR imaging shows the ischemic lesion (arrow) on DWI (a), hypoperfusion (arrows) on PWI (TTP map) (b), and vessel pathology (arrow) on MRA (c). Follow-up MR imaging shows the ischemic lesion (arrow) on DWI (d) and T2 FLAIR imaging (e), as well as recanalization or persistent vessel pathology (arrow) on MRA (f).
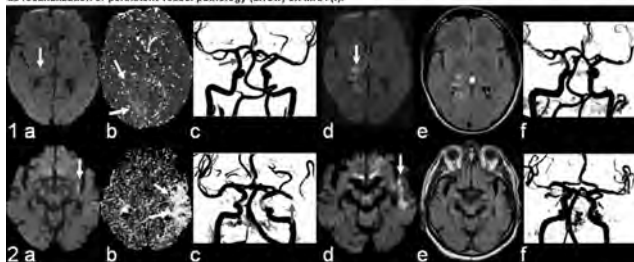
Discussion: In our collective, patients with minor stroke showed a benefit from thrombolysis without relevant complications. MRI proved to be useful especially in those patients with very minor deficit or unusual clinical presentation.

444 Acute cerebrovascular events (ACE): TIA and minor strokes

PROGNOSTIC VALUE OF S100B AND NEURON SPECIFIC ENOLASE MEASUREMENT IN PATIENTS WITH TRANSIENT ISCHEMIC ATTACKS. DATA FROM REGITELL REGISTRY

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Objective: To determine the correlation with the existence of acute ischemic lesions in diffusion-weighted imaging (DWI) and the prognostic value of S100B and serum neuron specific enolase (NSE) in a cohort of consecutive transient ischemic attack patients from the REGITELL register.

Methods: We enrolled 117 TIA patients. S100b and NSE were determined at basal time, day of DWI, 7 day and 90 day follow up. All patients underwent DWI (4.04±2.21 days after symptoms onset). The presence and pattern of acute ischaemic lesions were determined. The primary outcome measure was a composite end point (CE) consisting of stroke within 90 days or the identification of a high-risk stroke mechanism requiring specific early intervention (defined as > or =50% stenosis in a vessel referable to symptoms). The association between biomarkers, presence of DWI abnormalities and CE was analyzed by the area under the receiver operating characteristic curve (ROC) analysis.

Results: DWI was positive in 59 (50.4%) patients. The CE occurred in 26 patients (22.2%). A 50% or greater stenosis was found in 22 patients (15%) and stroke recurrence in 9 (7.7%) cases after a median follow up of 13 months. There was only a statistically significant relationship between S100bvalues measured the day of DWI and the CE (ROC 0.644, 95% CI 0.513 to 0.774, p = 0.043). There was no association between biomarkers and positive DWI, but patients with fragmented or cortical lesions had higher levels of S100b (p<0.05).

Conclusions: The measurement of S100B during the first week after symptom onset could be a prognostic and diagnostic tool in these patients.

445 Acute cerebrovascular events (ACE): TIA and minor strokes

CORRELATION OF THE ABCD2 SCORE WITH INVESTIGATION RESULTS IN TIA PATIENTS

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Introduction: The ABCD2 score is commonly used to assess the risk of stroke in TIA patients. We investigated whether there was any correlation between the ABCD2 score and investigation Results in patients attending the TIA clinic.

Methods: We investigated 114 patients from the outpatient clinic with a diagnosis of TIA, over a 6 month period. Patients with a previous history of stroke were excluded. We collected data on patients' vascular risk factors, the ABCD2 score and findings from CT/MRI brain imaging, carotid Doppler scan and ECG Results.

Results: There were 61 male (53.5%) and 53 female (46.5%) patients, with a mean age of 67.4±11.9 years. The following risk factors were present in these patients: hypertension 64.9% (n=74), Type 2 diabetes 11.4% (n=13) and smoking 37.7% (n=43). A high vascular ABCD2 score (= or > 4) was found in 68.4% (n=78). The main ECG abnormality was atrial fibrillation in 10.5% (n=12). An ICA stenosis > 50% was found in 14.9% (n=17). The presence of an infarct on cerebral imaging was found in 44.7% (n=51) and this was found to significantly correlate with ABCD2 score (= or > 4), (OR: 5.2; 95% CI: 1.4 – 18.9).

Conclusion: TIA patients with first presentation of symptoms and a high ABCD2 score (= or > 4) were more likely to have a finding of infarction on cerebral imaging. Recent studies have shown that incorporating the finding of infarction into the ABCD2 score improves the prediction of future stroke risk.

446 Acute cerebrovascular events (ACE): TIA and minor strokes

DO WE NEED 7 DAY A WEEK SPECIALIST TIA SERVICES? A COMPARISON OF RECURRENCE OF VASCULAR EVENTS AT 30 DAYS IN WEEKDAY AND WEEKEND TIA PRESENTATIONS TO A 5 DAY A WEEK SERVICE

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Introduction: The risk of having a stroke within the 10 days following a cerebrovascular event is near 10%. The EXPRESS study showed a reduction by 80% in patients receiving early treatment. Guidelines recommend specialist assessment within 24hrs of onset of symptoms for high risk TIA and 7 days for low risk TIA. Many centres have struggled to develop 7 day a week services to fulfil this need. In Swansea, the service Aims to initiate treatment at first contact followed by referral for assessment by a specialist which is available on weekdays only. This study sought to ascertain differences in rate of recurrence of cerebrovascular events during the 30 days following presentation,between patients who presented within the working week,or at the weekend.

Method: Patient information was collected as patients presented to the TIA service. This information included the day of their first contact with health services. Recurrence of vascular events was checked at 1-month follow up, and through tracking hospital attendances within this period.

Results: Data were collected from 290 patients who presented to the service between February 2009 and November 2010. There were 11 recurrent vascular events overall (recurrence rate 3.87%).98 patients presented between Friday and Sunday, in this group there were 3 recurrent vascular events within a 30 day period (3.06%).192 patients presented in the remainder of the week, in this group there were 8 recurrent events (4.17%).

Conclusion: The difference in recurrence rate between patients who presented on weekdays and those in the weekend group is not significant. The overall recurrence rate of 3.87% is higher than that achieved in phase II of the EXPRESS study. This difference may be explained by the small sample of patients used in this study. This study supports the practice of initiating treatment at first contact, with later specialist assessment. 7 day a week services may not be necessary, however a larger study is needed to confirm this.

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447 Acute cerebrovascular events (ACE): TIA and minor strokes

FACTORS AFFECTING TIA CLINIC REFERRAL EFFICIENCY

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Background: UK National Institute of Clinical Excellence guidelines recommend that patients with suspected TIA are assessed using a validated measure within one week of symptom onset. The Aims of this study were to study the referral process in our centre & explore factors that may influence it.

Methods: This was a retrospective observational study. Consecutive patients attending the TIA clinic of the Royal Victoria Hospital, Belfast were invited to participate. The study followed the tenets of the declaration of Helsinki.

Results: 41 patients (25F) participated, though recruitment is ongoing. Mean subject age was 62years (standard deviation [sd] 16y). A mean of 9 days (sd 16.5d) elapsed from the referral being sent to being received. A letter was used to make 90% of referrals, otherwise the referral was made by phone the same day. Neither grade of referrer (p=0.52) or source of referral (p=0.16) made a significant difference to the time taken. A mean of 28days (sd 10.8days) elapsed from the referral being received to the patient being seen. Those with speech disturbance (n=6) were seen significantly more quickly (p=0.048) than those without: other presenting complaints made no significant difference. The ABCD2 score was not provided in 83% of referrals. The referring diagnosis was TIA in 95% of cases, stroke in 2% & epilepsy in 2.4%. Following assessment at clinic TIA was the diagnosis in 29% of cases & migraine in 27%. There was no association of clinic diagnosis & referral source (p=0.76) or referrer grade (p=0.99).

Conclusion: The time taken for referrals even to be received was greater than that recommended for assessment of the patient with suspected TIA: letters are an inefficient means of referral. The time from receipt of referrals to clinic is also unacceptably high & suggests more resources are needed. The process could be sped up by triaging referrals: training is needed to increase the use of the ABCD2 score in rererrals. Most cases referred were not TIAs & the very low incidence of a TIA diagnosis suggests the need for education.

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448 Acute cerebrovascular events (ACE): TIA and minor strokes

PONTINE WARNING SYNDROME WITH MYOCLONUS

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Background: Pontine warning syndrome (PWS), a subset of crescendo transient ischemic attack, consists of recurrent stereotyped episodes of motor or sensory dysfunction, dysarthria, or ophthalmoplegia. It is frequently associated with pontine infarction, due to basilar artery branch disease, resulting in permanent deficit.

Methods: We report the appearance of myoclonus in a patient with PWS and review the literature for similar presentations.

Results: A 66-year-old white male with hypertension, dyslipidemia and peripheral artery disease was admitted with right-sided weakness, dysarthria and myoclonus in his right leg. A few minutes earlier, prior to the setting of this episode, he had had the same motor deficits, lasting for 10 minutes, and in the hours before, complaints of vertigo and clumsy gait, lasting for 15 minutes. Magnetic resonance imaging (MRI) showed an acute left-sided paramedian pontine infarct. Valproate was started, in order to suppress the patient's right

leg involuntary movements, without significant improvement. Small amounts of clonazepam were added, achieving myoclonus complete relief, and ceassed some days later, without myoclonus return. He was discharged one week later, clinically improved.

No reports of PWS and myoclonus were found in the literature.

Conclusion: The onset of myoclonus in our patient, shortly after neurological deficits, and the finding of a single acute ischemic lesion in the MRI establish a likely association between this manifestation and PWS.

We believe that the proximity of the ischemic lesion with the Guillain-Mollaret triangle might have contributed to functional abnormalities in the local neuronal circuitry, leading to the appeance of segmental myoclonus. Complete relief of myoclonus, even after cessation of anti-epileptic drugs, is an additional argument of its benign nature.

The presence of myoclonus associated with crescendo TIA might be a new presentation and point to a preferential location in the brainstem.

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449 Acute cerebrovascular events (ACE): TIA and minor strokes

PREDICTORS OF EARLY DETERIORATION AND 90 DAY OUTCOME IN TRANSIENT ISCHEMIC ATTACK AND MINOR ISCHEMIC STROKE

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Background and Aim: Transient ischemic attack (TIA) and minor ischemic stroke (MIS) are associated with early recurrence and deterioration respectively. The aim of the present study was to assess the rate of and predictors of early deterioration and 90 day outcome in patients with TIA and MIS.

Methods: We prospectively enrolled patients with TIA and MIS (NIH Stroke Scale [NIHSS] ≤5) presenting within first 48 hours between July 2008- 2010.Clinical and demographic factors were abstracted. They underwent standard stroke/TIA diagnostic evaluation. Early deterioration was defined as ≥ 2 points worsening in NIHSS within 7 days of symptom onset. The 90 day outcome was also assessed (excellent outcome; modified rankin scale[mRS] ≤2).

Results: Among 118 patients (mean ± SD age, 58.8±11.4 years), 82 (69.5%) had TIA and thirty six (30.5%) had MIS. Nine (7.6%) patients had early deterioration within first 7days and 8 (6.7%) had poor outcome at 90 days. The factors predicting early deterioration and poor outcome were presence of coronary artery disease (CAD), diabetes mellitus (DM), presence of limb weakness and stroke etiology being large artery atherosclerosis (LAA).

Conclusion: In patients with TIA and MIS, despite early admission there is a high rate of early clinical deterioration. Those with CAD, DM, limb weakness and LAA should be urgently evaluated and monitored closely for early deterioration.

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450 Acute cerebrovascular events (ACE): TIA and minor strokes

MRI IN THE DIAGNOSIS OF TIA – EXPERIENCES IN CLINICAL ROUTINE IN A STANDARD HOSPITAL

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Introduction: MRI reliably detects manifestation of ischemia in TIA patients. Results out of DWI data are available with the presence of cytotoxic oedema depending on the duration of the symptoms.

Methods: We evaluated the MRI/DWI investigations of patients with TIA. Acute infarctions, white matter lesions (WML) and lacunes were assessed at 1.5 Tesla.

Results: During the years 2008 to 2010 a total number of 684 TIA patients were seen. 138 of which underwent MRI. We preliminary evaluated 64 of them (30 males, 34 females). Mean age 72,3 years. The mean duration from the acute event to the MRI experiment was 6 days. Acute ischemic lesions were seen in 18,7% (12 out of 64). 35,9% showed lacunes and 87,5% were diagnosed having WML.

Discussion: The availability of MRI in standard hospitals allows only a restricted number of patients to undergo MRI. For the same reason the duration between acute symptoms and MRI is delayed. This may influence the detection rate of acute lesions which was rather low in our sample. The proportion of WML seems higher in patients with TIA than in the age related elderly. For the presence of acute ischemic lesions in TIA may influence treatment decisions exploration by MRI during the acute phase is desirable. MRI should replace CCT in the acute phase of cerebrovascular accidents also in standard hospitals.

Stroke prognosis

472 Stroke prognosis

PROGRESS OF ACUTE HEARING LOSS OF A VASCULAR CAUSE

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Background and purpose: Although several studies have been reported on the outcome and prognostic factors of idiopathic sudden sensorineural hearing loss (SSHL), there are no reports on the long-term result of SSHL of a vascular cause. We aimed to investigate the long-term outcome of SSHL as a sign of posterior circulation ischemic stroke and to identify factors predicting a poor outcome.
Methods: Over 9.5 years, 54 patients with SSHL of a vascular cause who were followed for at least 1 year (mean; 57 months; SD; 13 months) were enrolled. Quantitative audiovestibular function testing was performed during the acute (8.1 ± 6.8 days, mean ± SD) and last follow-up periods in all patients.
Results: On the last follow-up, 60% (35/58) of patients showed a recovery of hearing partially or completely. All but 2 patients had acute vertigo and approximately 92% (53/58) of patients had a unilateral canal paresis to caloric stimulation on the side of SSHL. The most commonly infarcted territory on brain MRI associated with SSHL was in the distribution of the anterior inferior cerebellar artery (52/57, 90%). Multivariate analysis showed that old age [p < 0.001, odds ratio (OR) 5.2, 95% confidence interval (CI) 2.0 to 13.7], severe impairment of canal paresis [p 0.001, OR 6.9, 95% CI 2.2 to 21.5], and profound hearing loss [p < 0.05, OR 2.9, 95% CI 1.2 to 7.2] predicted a poor outcome for recovery of hearing loss.
Conclusions: SSHL of a vascular cause has a good long-term outcome. Unlike an idiopathic SSHL, SSHL of a vascular cause is mostly accompanied by vestibular involvement with vertigo and canal paresis. Advanced age and profound hearing loss are adverse prognostic factors for recovery of hearing loss in SSHL of a vascular cause.

473 SmStroke prognosis

NATURAL HISTORY AND LONG-TERM PROGNOSIS OF CEREBRAL VENOUS THROMBOSIS (CVT) IN LARGE COHORT OF PATIENTS FROM A SINGLE HISPANIC CENTER

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Background and purpose: Data regarding the natural history and long-term prognosis of cerebral venous thrombosis (CVT) in Latino-American populations is scarce. The objective of this study was to evaluate the long-term outcome of a large cohort of Hispanic Mestizo patients with CVT.
Methods: Since 1986 patients with CVT consecutively evaluated in a tertiary-care neurological center in Mexico City were included in a stroke registry and followed-up by at least 6 months. Information was obtained on mortality rate, the rate of disability as assessed by Rankin scale (RS), and the occurrence of thrombotic recurrences and chronic neurological complications at long-term follow-up.
Results: Among 416 patients included in the registry 343 were women (during pregnancy/puerperium in 211); the median age was 28 years (IQR 22 - 37 years). Case-fatality rate during the acute phase was 11.5%. The median follow-up among 368 patients surviving the acute phase was 26 months (IQR 12 -75 months). At the end of follow-up 54.6% had no symptom or signs (RS=0), 28% had minor residual symptoms (RS=1), 9% had mild impairments (RS=2), 3% were moderately impaired (RS=3), 4.3% were severely handicapped (RS=4 or 5), and 1.1% died. Thirty patients (8.2%) had recurrent thrombotic events (CVT 2.2%, other thrombotic events 6%). Although 64 patients (17.2%) had recurrent seizures, most of them were of easy control with antiepileptic drugs (n=58). Seventy-three patients (19.8%) had chronic headache, 35 (9.5%) had anxiety or depressive persistent complaints (9.5%), and 5 (1.4%) developed a dural AV fistula.
Conclusions: Most of patients in this Hispanic cohort with CVT had a good long-term prognosis with a low risk of death, but around 15 - 20% developed mild to moderate chronic neurological/psychiatric complaints and 8% had recurrence of thrombotic events.

474 Stroke prognosis

LESIONS OF PRIMARY SENSORY AND POSTERIOR PARIETAL CORTEX IMPAIR RECOVERY FROM HAND PARESIS AFTER STROKE

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Background: Neuroanatomical determinants of motor function recovery (MFR) are incompletely understood. Since somatosensory inputs are important for re-learning motor skills, we hypothesized that in patients with stroke to primary sensorimotor (M1/S1) cortices, lesions to S1 would be associated with poorer MFR.
Methods: We recruited 29 subjects with first-ever stroke to M1/S1 and clinically significant hand paresis (24 M; 12 right hemispheric). We tracked MFR over 9 months using the modified Jebsen-Taylor-Test (mJTT). Data were standardised to z-scores based on values from age-matched controls. The mJTT subtest describing most within-subject variance was used as an index for MFR. MFR time courses were fitted with exponential models, using information-theory based criteria for model selection. Lesions were traced on DWI scans and spatially normalized using established algorithms. Lesion localization and overlap with specific anatomical areas were mapped with a probabilistic cytoarchitectonic atlas.
Results: MFR was best described by exponential models in 23/29 patients. Of those, 6 (group A) were fit by a models that did not converge to zero, indicating incomplete MFR (z-score mean ± SD: -5.3±1.3, p<0.001), whereas 17 (group B) converged to 0±0.9 (ns). The remaining 6 (group C) had no discernible pattern. Lesion overlaps showed that lesions in group A were centered on cytoarchitectonic area 2 in S1 and areas hIP1/hIP2 in the intraparietal sulcus (IPS). Group B had a pattern centered towards motor area 4a and premotor area 6. Mean lesion volumes were not different between groups.
Conclusions: Lesions to probabilistic areas within S1 and IPS are associated with poor MFR. Whereas area 2 relays shape information, IPS areas are part of frontoparietal networks for complex manual actions such as object manipulation and discrimination. Damage to both areas might thus critically disrupt sensorimotor integration processes needed to re-establish manual skill.

475 Stroke prognosis

INSULIN-LIKE GROWTH FACTOR I SERUM LEVELS INFLUENCE ISCHEMIC STROKE OUTCOME

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Background and purpose: Insulin-like growth factor I (IGF-I) is neuroprotective in animal models of stroke. We investigated whether serum IGF-I levels in acute ischemic stroke patients influence stroke severity and outcome.

Methods: Concentrations of IGF-I and IGF binding protein 3 (IGFBP3) were measured in serum samples obtained within 6 hours after stroke onset from 255 patients who took part in the placebo arm of the United States and Canadian Lubeluzole in Acute Ischaemic Stroke Study. Stroke severity was assessed with the National Institutes of Health Stroke Scale (NIHSS). Multivariate analysis was performed to assess the overall shift in modified Rankin Scale (mRS) and changes in the NIHSS score at 3 months. Survival curves were plotted using the Kaplan-Meier method, and the Cox proportional hazard model was used for multivariate analysis to investigate factors influencing survival.

Results: After controlling for statistically relevant risk factors, subjects with high IGF-I levels or IGF-I/IGFBP3 ratios had a better neurologic and functional outcome at 3 months. Baseline stroke severity was not different between high and low IGF-I groups. In contrast to the low IGF-I group, neurologic symptoms gradually improved from day 3 in the high IGF-I group.

Conclusions: Our Results suggest that high serum IGF-I levels just after ischemic stroke onset are associated with neurological recovery and a better functional outcome

476 Stroke prognosis

LACUNAR STROKE DOES NOT CONFER ADDITIONAL RISK OF POOR COGNITIVE OUTCOMES COMPARED TO OTHER STROKE SUBTYPES

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Background: White matter lesions and lacunes are frequently observed in patients with vascular dementia and patients with lacunar infarcts (LACI) often present with cognitive deficits. Therefore, it has recently been suggested that LACI patients may have a higher risk of developing cognitive impairment and dementia. To test this hypothesis, we compared the risks of developing significant cognitive impairment between patients with LACI and different stroke subtypes in a prospectively studied cohort of non-disabled stroke patients.

Methods: 362 patients recruited within 6 months after a TIA or non-disabling stroke (mRS≤3) as part of the ESPRIT trial were followed up with annual neurological assessments for up to 5 years. Stroke subtype was categorized using the Oxfordshire Community Stroke Project classification. The outcome of interest was poor cognition as defined by a diagnosis of moderate cognitive impairment not dementia or dementia Logistic regression analysis predicting for poor cognition was performed in three groups: 1) TIA versus stroke patients; 2) TIA versus LACI patients; and 3) LACI versus all other stroke subtypes.

Results: In univariate analysis, stroke patients had significantly higher risk of poor cognition (OR 3.03 CI 1.39-6.60), compared with TIA patients. LACI patients had significantly higher risk of poor cognition compared with TIA patients (OR 2.91 CI 1.32-6.41), but did not have any significantly higher risk compared with other stroke patients (OR 1.21; CI 0.65-2.23). However, in multivariate models, patients with strokes were not at increased risk of poor cognition compared to TIA patients (OR 1.07 CI 0.38-2.97) and patients with LACI were similarly not at increased risk of poor cognition when compared to TIA patients (OR 1.07 CI 0.37-3.13).

Conclusion: Patients with lacunar stroke did not have any higher risk of significant cognitive impairment compared to patients with other stroke subtypes or patients with TIAs.

477 Stroke prognosis

THE VERY LONG-TERM RISK OF VASCULAR EVENTS AFTER YOUNG STROKE. THE FUTURE STUDY

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Background: There are conflicting Results on recurrent vascular events after a young stroke. In addition interpretation is often hampered by a relatively short follow up that seldom exceeds 5 years.

Objective: To investigate the very long term risk of recurrent vascular events.

Methods: We investigated young stroke patients from the FUTURE study, a long term follow-up study on causes and consequences of young stroke, currently including 777. We here report on a subset of 50 patients who were recruited for follow-up examination 15.2 years (range 3.1-27.1) after their young stroke (mean

current age 55.6 years, SD=8.5) compared with an age, sex and education matched control group (mean age 55.7 years, SD=8.4).

Primary outcomes were recurrent ischemic stroke or TIA, myocardial infarction and cardiovascular surgery. Information on primary outcomes was retrieved from structured questionnaires and additional information was retrieved from medical records and adjudicated by two independent neurologists whenever a primary outcome event was suspected. A composite outcome was used to estimate cumulative risks. Secondary, traditional risk factors as hypertension, smoking, diabetes and hypercholesterolemia were assessed.

Results: 24.0% of patients and 16.0% of controls experienced one or more vascular events (p=0.32). Cumulative risks for composite endpoint at 5 and 15 years were 11% and 14% respectively for patients and 4% and 15% for controls (log-rank p=0.628). Diabetes Mellitus, hypercholesterolemia and hypertension were significantly more present in patients than controls (p<0.05).

Conclusion: Patients with a previous young stroke seem to remain at increased risk of vascular events and risk factors, even 15 years after their young stroke. Statistical significant differences failed to appear due to the power problem of this pilot study. Analysis of the whole cohort will allow for a more detailed analysis by different vascular outcome in our study with the longest follow up ever.

478 Stroke prognosis

THE ASSOCIATION BETWEEN BMI AND MORTALITY AFTER FIRST-EVER ISCHEMIC STROKE

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Background: The available data regarding the relationship between Body Mass Index (BMI) and mortality after stroke are still limited. We retrospectively studied the association between BMI and 1-year mortality after acute first-ever ischemic strokes.

Methods: Records of patients who entered the South London Stroke Register (an ongoing population based stroke register recording first stroke in South London) between January 2004 and December 2008 were examined. Official records were obtained of all deaths within a year after a stroke. Kaplan Meier Methods were used to estimate survival in the first year after stroke across BMI categories and survival functions were compared using log rank tests. A multivariable Cox Proportional Hazards Model was used to compare risk of mortality between different categories of BMI after adjusting for possible confounders (age, gender, ethnicity and severity of stroke).

Results: From a total of 1178 patients, 640 (54%) had a record of BMI; of these, 482 (75.3%) patients had ischemic strokes. This group was divided into 4 categories of BMI: 6.6% were underweight ($<18.5 kg/m^2$), 36.9% were normal weight (18.5-24.9 kg/m^2), 32.4% were overweight (25-29.9 kg/m^2) and 24.1% were obese ($\geq30 kg/m^2$). There was a significant difference in survival rates between the 4 BMI categories (68.8% underweight, 78.7% normal, 89.1% overweight, 81% obesity (p=0.010)). In a multivariable analysis, there was a significant difference in the risk of mortality across BMI categories (p=0.022). With the normal weight category as reference group, the risk of mortality was higher for the underweight (hazard ratio, (HR) 1.380, 95%CI, 0.794-2.399) and obese categories (HR 1.333, 95%CI, 0.870-2.043) and lower for the overweight category (HR 0.468, 95%CI, 0.288-0.760).

Conclusion: The decreased mortality rate in the overweight group is in line with previous findings (e.g. Vemmos et al. Stroke, 2011, 42, 30-36). However, this protection was not apparent in obese subjects.

479 Stroke prognosis

THE 3C SCORE: DERIVING OPTIMAL CT BASED IMAGING CHARACTERISTICS FOR PREDICTING CLINICAL OUTCOME IN ACUTE ISCHEMIC STROKES WITH PROXIMAL OCCLUSIONS

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Purpose: To derive an imaging score on CT angiography based on extent of ischemic core, leptomeningeal collaterals and clot burden and determine its ability to discriminate clinical outcomes with or without therapy.

Methods: This was a single center study of patients with acute ischemic stroke and M1 MCA+/-intracranial ICA occlusions. Clot burden score is a 10 point score assessing extent of clot in the anterior circulation and the rLMC score is a 20 point

collateral score based on scoring pial and lenticulostriate arteries in the anterior circulation. Good clinical outcome was defined as modified Rankin Score ≤2 at 90 days. The point scores for the 3C score were assigned based on prior presented multivariable-adjusted analysis. The 3C score (range 0-6) comprises 3 imaging measurements at baseline: 1.CTA-SI ASPECTS categorized as (0-4=0 points, 5-7=1, 8-10=2) 2.Collaterals (rLMC score 0-10=0, 11-16=1, 17-20=2) and 3.Clot burden (CBS 0-5=0, 6-7=1, 8-10=2). Primary measure of discrimination of clinical outcome was the c statistic.

Results: There were 133 patients (mean age 66, median NIHSS 16). Figure 1 shows the distribution of good clinical outcome based on the 3C score. The c statistic for the 3C score was 0.75, indicating moderate to good discrimination of good outcomes. By comparison, the c statistic for NCCT ASPECTS was 0.62 and for CTA-SI ASPECTS was 0.66, and for a multivariable model containing age and NIHSS was 0.67. Figure 2 shows the probability of good clinical outcome according to 3C score in subjects receiving any IA therapy. The relationship between 3C score and the probability of good outcome was similar across all treatment categories.
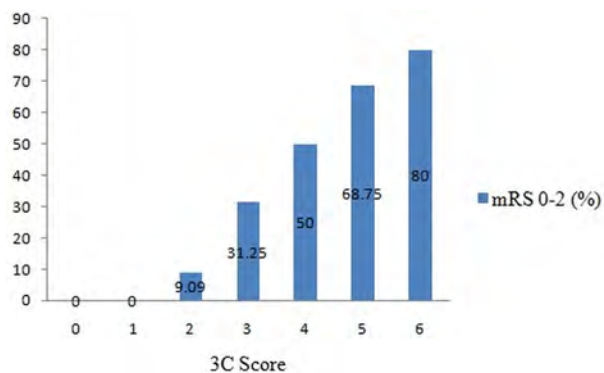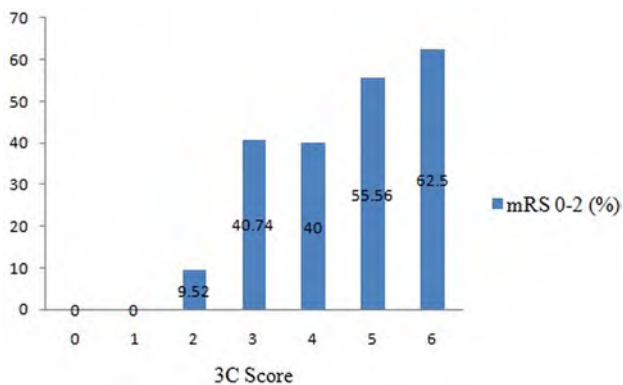
Conclusion: The 3C score combines information on extent of core, leptomeningeal collaterals and thrombus burden using CTA in patients with acute ischemic strokes caused by MCA occlusion. It is better at discriminating the chance of a good clinical outcome than either NCCT, CTA-SI ASPECTS or the combination of age and NIHSS. Based on these preliminary analyses, the 3C score warrants further validation studies in independent patient cohorts.

480 Stroke prognosis

DETECTION OF VCAM-1 BY MRI IN CEREBRAL ISCHEMIA

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Background: The detection of inflammatory processes would therefore be of great interest, particularly in order to design individual therapeutic strategies after stroke. In this purpose, we have developed a specific contrast agent, an USPIO that targets a component of the neuroinflammatory response, VCAM-1. The aim of this study was to determine the relevance of this USPIO to visualise VCAM-1 in MRI in a model of cerebral ischemia in mouse.

Methods: Ischemia was carried out in male Swiss mice by transient (1h) intraluminal occlusion of the left middle cerebral artery. At first, VCAM-1 expression was detected by immunofluorescence at 6, 24 and 72h post-ischemia (n=4-5). Secondly, ischemic mice were intravenously injected with 100 μmol/kg of VCAM-1-USPIO or non-targeted USPIO 5h after the ischemia. MRI (7T) was performed 6h (n=2-6) or 24h (n=2-5) after ischemia onset. Control ischemic animals without injection of USPIO were also included in our study (n=4-6). Just after MRI, mice were euthanized and their brains removed for ex vivo MRI (2.35T). Immunohistochemistry was performed on 20 μm-thick cryostat-cut brain sections in order to search the presence of USPIO by Perls technique (revealing iron particles) and the expression of VCAM-1.

Results: Time course of VCAM-1 showed positive vessels 6h after ischemia and a significant up-regulation 24h after ischemia both hemispheres (P<0.05). Injection of VCAM-1-USPIO created hypointense foci in MRI at 6h and 24h, which could correspond to iron particles. Post-mortem analysis of these brains showed a co-localisation of the iron particles and VCAM-1. MRI of ischemic animals without USPIO or with the non-targeted USPIO did not show hypointense foci. While histological examination revealed the presence of VCAM-1.

Conclusions: Our USPIO seems able to detect VCAM-1 in our model of cerebral ischemia. However, the signal observed in MRI needs to be confirmed histologically by a more specific method than the Perls technique. This kind of contrast agent could be an interesting clinical tool for the follow-up of specific therapeutic strategies targeting the inflammatory phenomenon.

481 Stroke prognosis

LONG-TERM OUTCOME IN PATIENTS WITH ACUTE BASILAR ARTERY OCCLUSION

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Background: Acute basilar artery occlusion has the highest case fatality rate in ischemic stroke. Patients who undergo successful recanalization have a consistent survival benefit. Some of the survivors regain functional independence. However, long-term outcome in these patients has rarely been systematically analyzed.

Methods: In this monocentric retrospective study we analyzed mortality, long-term functional outcome and quality of life in all consecutive patients that had been treated for acute occlusion of the basilar artery in our institution between 12/2002 and 12/2009.

Results: We identified 98 patients (59 male; median age 62.3±14.5 years, 20-89 years). Therapy included systemic intravenous thrombolysis (n=37; time to treatment 3.0±1.3 h), partially in combination with intra-arterial therapy (intra-arterial thrombolysis and/or mechanical recanalization; n=23; time to treatment 5.5±1.7 h) or intra-arterial therapy alone (n=61, time to treatment 6.6±5.8 h). The overall recanalization rate was 89.8% (88 of 98 patients). During the acute hospital phase 36 patients (36.7%) died, among them all 10 patients with failed recanalization. After a median observation time of 3.9 years (0.8-7.5 years) 15 more patients had died; 6 patients were lost to follow up. Among the remaining 41 long time survivors (44.6%), 30 patients (73.2%) had a good or moderate long-term outcome (modified Rankin Scale (mRS) ≤ 3) (see Figure 1). Motor (n=17, 41.5%) and visual (n=13, 31.7%) deficits were the most relevant residual symptoms. Health-related quality of life was slightly better compared to a historical population of unselected stroke patients (see Figure 2).
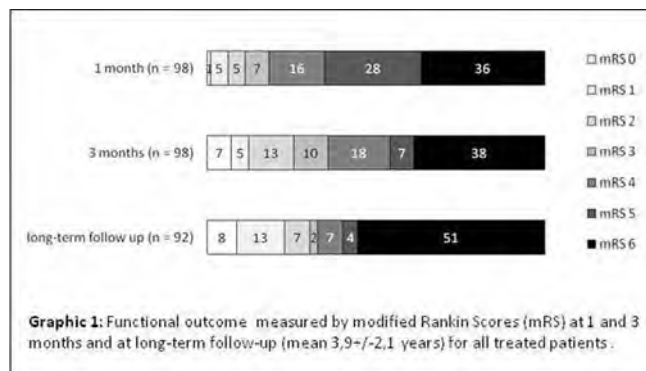
Graphic 1: Functional outcome measured by modified Rankin Scores (mRS) at 1 and 3 months and at long-term follow-up (mean 3,9+/-2,1 years) for all treated patients.

Graphs A) SF-36 scores of patients (BAO, breathe arditised compared to a healthy Bernese population (A) after correction for age and sex and compared to a non-selected stroke population of the International Stroke Trial 1997 (B). The following 8 domains of quality of life were assessed: ph: physical functioning; rolph: physical role functioning; pain: bodily pain; ghe: general health; vital: vitality; social: social functioning; roleem: emotional role functioning; mhl: mental health. For all domains, higher values represent better quality of life.

Conclusions: With multi-modal recanalization therapy, long-term survival is reached in almost half of the patients with acute basilar artery occlusion. More than two thirds of the survivors have a good to moderate functional long-term outcome. Quality of life seems to better than in unselected stroke patients.

482 Stroke prognosis

ACUTE ISCHAEMIC STROKE IN CHILDREN AND YOUNG ADULTS

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Background: The aim of this study was to compare children and young adults with acute ischaemic stroke (AIS) in two large registries.
Methods: We compared clinical characteristics, stroke aetiology, work-up and outcome (mRS at 3-6 months) in children (1 month-16 years) and young adults (16.1-45 years) with AIS. Data of children were collected prospectively in the nationwide Swiss NeuroPaediatric Stroke registry, young adults in the Bernese stroke database.
Results: From 01/2000 to 12/2008 128 children and 199 young adults suffered an AIS. Children were more likely to be male than young adults (62%/49%, p=0.023) and had less frequently hypertension (p=0.001), hypercholesterolemia (p=0.003) and a family history of stroke (p=0.048). Stroke severity was similar in children and young adults (median PedNIHSS/NIHSS 5/6; p=0.102). Stroke aetiology (original TOAST classification) was more likely to be "other determined cause" in children than in young adults (51%/29%; p<0.001). Cervicocerebral artery dissections were less frequent in children than in young adults (10%/23%; p=0.005). Outcome at 3-6 months did not differ between children and young adults (p=0.907): 59% of children and 60% of young adults had a favourable outcome (mRS 0-1). Mortality was similar among children and young adults (4%/6%; p=0.436). In multivariate analysis, low PedNIHSS/NIHSS was the most important predictor of favourable outcome (p<0.001).
Conclusion: Even though stroke aetiology and risk factors in children and young adults are different, stroke severity and clinical outcome at 3-6 months were similar in both groups. A new version of the mRS for children with age-specific modification is proposed (Table 1).

Panel 1 Modified Rankin scale (mRS) for children and adults

Score	Children	Young adults
0	No symptoms at all	No symptoms at all
1	No significant disabilities despite symptoms; behaviour appropriate to age and normal further development	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but same independent as other age- and sex-matched children (no reduction of levels on the gross motor function scale)	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance; in younger patients adequate motor development despite mild functional impairment (reduction of one level on the gross motor function scale)	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance; in younger patients reduction of at least 2 levels on the gross motor function scale	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, requiring constant nursing care and attention	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead	Dead

[a]Palisano R, Rosenbaum P, Walter S, Russel D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol. 1997;39:214e23.

483 Stroke prognosis

C-REACTIVE PROTEIN DOES NOT PREDICT OUTCOMES IN NON-DISABLED STROKE PATIENTS

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Background: Although there is growing evidence of C-reactive protein (CRP) being associated with outcomes after stroke, since both CRP and stroke severity independently predict for outcomes, the prognostic value of CRP in patients with less severe stroke has not been established. We therefore determined the associations between CRP and risk of death, recurrent vascular events, dependency, incident dementia and significant decline in cognitive status in a prospectively studied cohort of non-disabled stroke patients.
Methods: 311 patients within 6 months after a TIA or non-disabling stroke (mRS≤3) were followed up for up to 5 years. Sera were taken at a median of 47 days after the index stroke. Cox proportional-hazards regression analyses were performed to determine associations between CRP and death, recurrent vascular events, dependency and incident dementia, while logistic regression was performed to determine association between CRP and significant decline in cognitive status. All analyses were performed for tertiles of CRP.
Results: The highest tertile of CRP (>3.3 mg/L) had no significant association with death (hazard ratio, 0.88; 95% CI, 0.32-2.43), recurrent vascular events (HR, 0.56; 95% CI, 0.24-1.29), dependency (HR, 1.10; 95% CI, 0.45-2.65), incident dementia (HR, 0.39; 95% CI, 0.08-2.02), or significant decline in cognitive status (odds ratio, 0.51; 95% CI, 0.18-1.43), compared with the lowest tertile (<1.8 mg/L).
Conclusion: CRP did not predict for death, recurrent vascular events, dependency, incident dementia or significant decline in cognitive status in a cohort of non-disabled stroke patients. Hence previous studies on the prognostic value of CRP may not be applicable to less severe stroke patients.

484 Stroke prognosis

VENOUS HYPERTENSION AS A POTENTIAL CAUSE OF FATAL HEMORRHAGIC COMPLICATION DURING ENDOVASCULAR THERAPY FOR STROKE

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Purpose: Endovascular procedures have been widely used to rescue those stroke victims. However, unusual or unexpected complications often result in severe deficits or fatal complications. The goal of this investigation is to evaluate the potential etiology of severe hemorrhagic complications.
Materials: We have reviewed 5 cases with carotid stenting and 2 cases with thrombolysis/thrombectomy in those severe complications from 299 stroke patients from January 2008 to December of 2009. Those 7 patients were 5 males and 2 females, with age from 64 to 77 yeas (mean age 69.3 years). Stents used for carotid endovascular procedures were bare stents. Thrombolytic procedures were performed with either Perfusion catheter or Merci device.
Results: 3 of 5 hyperperfusion cases ended with extensive hemorrhage had either hypoplasia of ipsilateral transverse sinuses. Two cases who had hyperperfusion without hemorrhage had symmetry transverse sinuses. Those two fatal hemorrhagic complications treated with thrombectomy had hypoplasic transverse sinuses too. Bilateral anterior cerebral arteries were from the same side of endovascular thrombectomy. Susceptibility-weighted MR also showed extensive deoxygenated vessels at the same side of endovascular procedures. As our experience, excessive deoxygenated vessels in infarct area had worse result and with more infarct volume.
Conclusion: The cerebral venous drainage may be compensated by contralateral venous drainage even with ipsilateral hypoplasia of transverse sinus. The reopening of carotid artery, either by stenting or thrombolysis/thrombectomy, may suddenly increase cerebral blood flow to the disease side and hypertperfusion. If there is normal venous system to drain venous outflow, it may not be to severe. However, impairment of venous drainage which Results from hypoplasia may induce venous hypertension. We postulated that sudden venous hypertension may be the etiology of hemorrhagic complication.

485 Stroke prognosis

NEUROLOGICAL DETERIORATION AND STROKE RECURRENCE IN THE ACUTE PHASE OF STROKE WITH ATRIAL FIBRILLATION -FUKUOKA STROKE REGISTRY

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Background and purpose: The risk for stroke occurrence in patients with atrial fibrillation (Af) can be predicted by using CHADS2 score. However predictive factors for an early neurological deterioration in stroke patients with Af remain to be uncertain. We examined predictive factors for an early neurological deterioration or stroke recurrence in the acute stroke with Af.
Methods: Six hundred consecutive acute stroke with Af patients within 7 days of symptom onset were included from the Fukuoka Stroke Registry. All patients were treated with anticoagulant agents. We investigated the relationships between clinical factors and an early neurological deterioration or stroke recurrence. A neurological deterioration was defined as a NIH stroke scale score worsening of ≥1-point within the first 21 hospital days. CHADS2 score was evaluated after admission, thus the score of all patients were 2 or more.
Results: One hundred patients (16.7%) had a neurological deterioration with or without stroke recurrences. In the univariate analysis, female (59.0% vs 43.4%, p=0.0043), blood glucose level (148.8±74.3 vs 132.6±44.9mg/dl, p=0.0041) and d-dimer level (4.6±12.1 vs 2.9±4.4μg/dl, p=0.0449) on admission were associated with a neurological deterioration. Also preclinical modified Rankin Scale was associated with a neurological deterioration (p=0.0098). According to CHADS2 score, a neurological deterioration was most frequent in patients with score 6 (23.1%), followed by score 5 (18.8%), score 4 (17.7%), score 3 (11.0%), and score 2 (0%), in order. After multivariate logistic regression analysis, female (OR 2.14, 95% CI, 1.184-3.861) and blood glucose level (OR 1.01, 95% CI, 1.001-1.011) were significantly associated with a neurological deterioration.
Conclusions: Our Results suggested that female and blood glucose level were independently associated with an early neurological deterioration or stroke recurrence in the acute stroke with Af. Furthermore, CHADS2 score might be useful for predicting an early neurological deterioration or stroke recurrence even after the stroke onset.

486 Stroke prognosis

DEVELOPMENT OF A SIMPLE CLINICAL SCORE FOR OUTCOME PREDICTION AFTER STROKE

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Background: Several outcome prediction models have been developed following stroke. Commonly clinical variables such as age and stroke severity are utilized in multiple regression analyses to produce predictive models requiring complex calculations. Four simple clinical variables, age, a normal verbal component of GCS, ability to walk and lift both arms are consistent predictors of independent survival (mRS<3). We hypothesised that a simple score using these variables could assist in outcome prediction.
Methods: Patients admitted with a diagnosis of ischemic or hemorrhagic stroke in 2001-02 to the Halifax Infirmary, Nova Scotia, Canada, were enrolled in the Stroke Outcomes Study. Patients previously dependent pre-stroke were excluded. Clinical variables from the first neurological assessment and outcome at six months (mRS) were collected. Different scores were attributed to each of the four variables dependent on their predictive power in multivariate analysis. External comparison was made using the Oxfordshire community stroke project dataset.
Results: 437 patients were analysed and 59% were independent at six months after stroke. Mean age was 68.9 years old, 45% female and 26% had a severe stroke. After multivariate analysis using the four variables the odds ratios for independent survival were 0.95 per year for age, 3.0 for a normal verbal GCS, 5.7 for ability to lift both arms and 2.6 if able to walk independently. A score was developed with one point for inability to perform any of the three tasks and trichotomizing age (<50 years, 50-64, 65-79 and >79; scoring 0, 1, 2 and 3 points). This produced outcome scores plotted in Figure 1. With scores 0-1 the likelihood of independent survival was 91% whereas with scores of 5 or 6 the likelihood was 5%. This model

performed well (area under the receiver operating curve=0.831). Similar outcomes were seen testing the score on an external dataset (Fig.1).
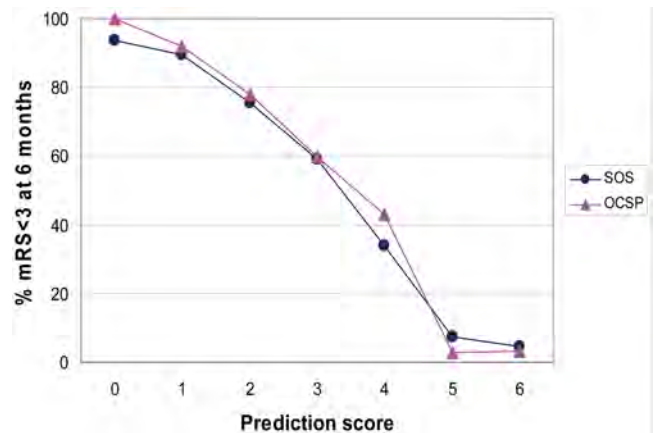
Figure 1. % independent (mRS <3) 6 months post-stroke.

Discussion: This simple clinical score predicts probability of independent survival in both the development and external datasets. Clinical utility would require demonstration of equal or superior predictive value compared to experienced stroke physicians.

487 Stroke prognosis

PRIOR USE OF ANTI-PLATELET OR ANTICOAGULANT THERAPY AND STROKE OUTCOME: STROKE REGISTER DATA BASE STUDY

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Background: We previously studied the impact of prior use of antiplatelet (AP) and anticoagulation (AC) on survival up to 90 days for stroke patients. Beyond 90 days, there is limited follow up data and long term mortality outcomes are uncertain.
Methods: We analysed Norfolk and Norwich Stroke Register (January 2004-November 2008) to examine the relationship between prior AP or AC use and 1 year mortality (1226 deaths) by specific stroke type, adjusting for age, sex, premorbid RANKIN and Oxfordshire Community Stroke Project classification.
Results: A total of 3,308 stroke patients (mean age=78, range=19-101 years, 53% female, 86% ischaemic stroke, 14% haemorrhagic stroke) were included. The distribution of the prior AP/AC use was 1077 aspirin only, 80 aspirin & dipyridamole, 56 clopidogrel, 206 warfarin & 1620 none. The adjusted OR from logistic regression 1 year mortality for ischaemic stroke were 0.90 (0.73-1.10) for aspirin, 0.66 (0.37-1.17) for aspirin & dipyridamole, 1.45 (0.75-2.78) for clopidogrel, 1.06 (0.71-1.59) for warfarin compared to none. The corresponding values for haemorrhagic stroke were 1.67 (0.89-3.12) for aspirin and 2.44 (1.06-5.62) for warfarin compared to none.
Conclusions: Evidence suggests that prior warfarin use is associated with poorer one year survival for patients with haemorrhagic stroke. AP therapy was not associated with reduced survival. Compared to no prior medication, prior AP and AC use did not affect one year mortality for patients with ischemic stroke. This suggests that AP and AC therapy does not confer any advantage or disadvantage for ischemic stroke patients but there is increased mortality in haemorrhagic stroke patients on warfarin.

488 Stroke prognosis

NATURAL HISTORY OF UNTREATED STROKES DUE TO PROXIMAL ANTERIOR CIRCULATION OCCLUSIONS: A SUBSET ANALYSIS OF THE SENTIS TRIAL

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Background: Detailed knowledge about the natural history of strokes due to proximal arterial occlusion (PAO) is essential for the proper design of revascularization trials yet little is known about their long-term outcomes.

Methods: SENTIS trial was a prospective randomized single-blind multicenter study of NeuroFlo™ treatment plus standard medical management vs. standard medical management alone within 14 hours of stroke onset. The subjects of the current analysis include untreated patients with complete occlusion of the intracranial ICA, MCA-M1, and MCA-M2 segments as detected on initial CTA or MRA evaluation.

Results: A total of 515 patients were enrolled in the SENTIS trial over a 52-month period; 257 were randomized to non-treatment (control group). Out of these 126 (49%) presented with isolated occlusion involving the intracranial ICA (n=28), MCA-M1 (n=48), or MCA-M2 (n=50). Out of the 28 identified cases of untreated ICA occlusion (mean age, 63.5; mean baseline NIHSS, 12.6; 53.6% male) 5/28 (17.9%) achieved a good outcome and 8/28 (28.6%) were dead at 3 months. Out of the 48 cases of untreated MCA-M1 occlusion (mean age, 68.8; mean baseline NIHSS, 12.2; 43.7% male) 15/48 (31.2%) achieved a good outcome and 8/48 (16.7%) were dead at 3 months. Out of the 50 cases of untreated MCA-M2 occlusion (mean age, 70.8; mean baseline NIHSS, 10.3; 62% male) 26/50 (52%) achieved a good outcome and 9/50 (18%) were dead at 3 months. Considerably worse outcomes were seen in patients with baseline NIHSS >10 with good outcome rates of 9.5%, 18.7%, 36% and mortality rates of 28.6%, 21.9%, 28% in ICA (mean NIHSS, 14.8), MCA-M1 (mean NIHSS, 14.8), and MCA-M2 (mean NIHSS 13.8) occlusions, respectively.

Conclusion: This prospectively collected cohort confirms that untreated patients with PAO involving the anterior circulation have overall poor prognosis with low likelihood of achieving functional independency and high mortality rates, in particular if their baseline NIHSS is >10.

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489 Stroke prognosis

DELIRIUM IN ACUTE STROKE IS AN INDEPENDENT PREDICTOR FOR POOR COGNITIVE FUNCTIONING 2 YEARS LATER: PRELIMINARY FINDINGS

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Background: Delirium has been established as an independent risk factor for cognitive impairment in several clinical populations. While this link between delirium and cognitive decline has also been suggested in the stroke population, it has never been thoroughly studied in this patient group. Our aim was to evaluate the effect of delirium experienced in the acute phase after stroke on subsequent cognitive functioning assessed two years later.

Methods: 50 stroke patients (22 with and 28 without delirium in the acute phase) were evaluated 2 years after stroke (see Table 1). A cognitive profile was determined using a neuropsychological examination covering multiple cognitive domains (see Figure 1). Raw scores were converted into standardised z-scores based on the means and standard deviations from a healthy control group. A z-score<-1.65 was considered as a cut-off to indicate severe impairment. Chi-square tests were used to compare the 2 patient groups on the presence of a domain-specific disorder. Furthermore, the predictive value of delirium on cognitive functioning was explored using multivariate regression models.

Results: More patients with than without delirium in acute stroke were classified as having severe impairments on 5 of the 8 domains at follow-up (see Figure 1). In multivariate regression models, delirium was a significant independent predictor of poor performance 2 years later on verbal memory (standardised beta (B) -0.46, p<0.01), visual memory (B -0.34, p=0.04), visual construction (B -0.49, p=0.01), language (B -0.36, p=0.03), and executive function (β -0.35, p=0.02).
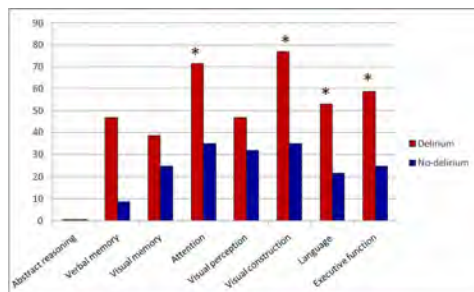
Figure 1. Percentages of patients with and without delirium post-stroke having a domain-specific cognitive disorder at 2 year follow-up.

Table 1. Characteristics of the 2 patient groups

	Delirium (N=22)	No-delirium (N=28)	*p*-value
Demographics			
Age (years), mean±SD	75.8±8.9	74.6±12.1	0.70
Sex, male, number (%)	11 (50.0)	18 (64.3)	0.36
Education, median [range][†]	4 [1-7]	5 [2-7]	0.31
Stroke characteristics			
NIHSS score, median [range]	5 [1-23]	7 [1-21]	0.52
Stroke subtype, number of patients (%):			
LACI	4 (18.2)	8 (28.6)	0.39
PACI	8 (36.4)	11 (39.3)	0.83
POCI	4 (18.2)	1 (3.6)	0.16
TACI	4 (18.2)	1 (3.6)	0.16
ICH	2 (9.1)	7 (25.0)	0.27
Post-stroke complications, number of patients (%):			
Infection	9 (40.9)	3 (10.7)	0.01*
Metabolic disturbances	17 (77.2)	11 (39.3)	0.01*
Rating of ACH medication, number>0 (%)	4 (18.2)	4 (14.3)	0.72
Degree of white matter changes, mean±SD	8.0±5.4	6.6±4.9	0.32
Degree of cerebral atrophy, mean±SD	15.5±6.5	12.6±6.1	0.23
IQCODE, mean±SD	51.5±6.6	49.5±5.9	0.11

*Significant at p<0.05; [†]Education was rated according to a Dutch classification system ranging from 1: did not finish primary school to 7: university degree. SD=standard deviation; NIHSS=National Institutes of Health Stroke Scale; LACI=lacunar infarct; PACI=partial anterior circulation infarct; POCI=posterior circulation infarct; TACI=total anterior circulation infarct; ICH=intracerebral haemorrhage; ACH=acetylcholine medication; IQCODE=Information Questionnaire on Cognitive Decline in the Elderly.

Conclusion: These data are preliminary given the relatively small sample size. The results do however suggest that delirium in acute stroke increases the risk of subsequent cognitive impairment. We conclude that it is crucial that delirium is detected quickly after stroke and that these vulnerable people are monitored cognitively on a regular basis.

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490 Stroke prognosis

INFLAMMATORY MARKERS AS PREDICTORS OF MORTALITY IN LONG-TERM STROKE SURVIVORS

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Background: Inflammatory markers are independent risk predictors for cardiovascular events and death in population-based studies, but uncertainty remains of their predictive role in secondary prevention, particularly among long-term stroke survivors.

Methods: In 1997, 187 ischemic stroke survivors (median 7.0 years after index stroke) and 243 stroke-free subjects were recruited from a population-based study. Beside clinical examination and assessment of common risk factors, serum inflammatory markers were analysed. In Cox proportional hazards regression models we examined the relationship between inflammatory markers and risk of death during a 13 year follow-up.

Results: During follow-up, 107 (57.2%) stroke subjects and 85 (35.0%) stroke free subjects died with an increased age and sex adjusted risk of mortality (HR=1.89; 95% CI, 1.42-2.58). Stroke survivors had significantly elevated levels of white blood

cell counts (WBC), fibrinogen, interleukin-6 (IL-6) and C-reactive protein (CRP) at baseline. In models adjusted for age, sex, smoking and previous myocardial infarction or diabetes mellitus, fibrinogen and IL-6 were significant predictors of all cause mortality (p-value 0.002 for fibrinogen and 0.02 for IL-6) among stroke subjects. None of the markers were associated with mortality among stroke free subjects.

Conclusions: Long-term ischemic stroke-survivors had elevated levels of inflammatory markers at baseline as compared to stroke free subjects. Fibrinogen and IL-6 were independent predictors of all cause mortality among stroke subjects, whereas WBC and CRP only reached borderline significance. To establish the inflammatory markers' relevance in secondary prevention strategies and mortality prediction, further studies are required.

491 Stroke prognosis

PREDICTORS OF EARLY NEUROLOGICAL IMPROVEMENT AFTER UNCLEAR-ONSET STROKE

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Background: More than 25% of patients with ischemic stroke have unclear-onset stroke (UOS). Data on optimal management and early outcome in this patient group are sparse. Our aim was to identify predictors of early neurological improvement in a clearly defined subset of patients with UOS.

Methods: In our local prospective stroke registry we identified 250 patients admitted to our stroke unit during the period 2004-2010 who fulfilled the following criteria: 1) acute ischemic stroke confirmed by clinical and imaging definitions; 2) unclear onset of stroke; and 3) baseline National Institute of Health Stroke Scale Score (NIHSSS) of at least 5 points. Early neurological improvement was defined as complete normalization or improvement of 4 or more points on the NIHSSS during the patients' stay in our stroke unit.

Results: 121 (48%) patients were men. Compared to patients without early improvement (n=186, 74%), patients with early improvement (n=64, 26%) were younger [mean age (SD) 70 (16.3) vs. 73.9 (11.2) years, p=0.016] and less likely to be diabetics (14.1% vs. 31.2%, p=0.008), while baseline NIHSSS did not differ significantly between groups (mean NIHSSS (SD) 12 (6.8) vs. 14 (8.4), p=0.562). Patients with intravenous or intraarterial thrombolysis had significantly more often early improvement than patients without recanalization treatment (11/21, 52.4% vs. 52/226, 23%, p=0.003). However, multivariable logistic regression analyses identified only younger age (OR 0.98, 95%CI 0.96-0.99, p=0.044) and lack of diabetes (OR 0.41, 95%CI 0.18-0.94, p=0.036) to be independent predictors of early improvement, while thrombolysis treatment just failed significance.

Conclusion: Our data suggest that younger age and lack of diabetes are independent predictors of early improvement following UOS. A subset of patients with UOS may benefit from thrombolysis treatments.

492 Stroke prognosis

SUSCEPTIBILITY-WEIGHTED IMAGING IN ACUTE ISCHEMIC STROKE: COMBINED STUDY WITH MR PERFUSION-WEIGHTED IMAGING FOR PREDICTION OF STROKE PROGRESSION

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Purpose: Susceptibility-weighted imaging (SWI) has a potential ability to reflect increased oxygen extraction faction as metabolic information of the ischemic brain area by presence of prominent hypointense vessels (HV). The aim of this study was to verify whether SWI was able to replace PWI to predict ischemic penumbra and subsequent infarct progression.

Methods: We retrospectively reviewed consecutive cases with acute stroke admitted from January 2009 and September 2010. Inclusion criteria were cases with ischemic stroke, concurrent MR sequences of PWI, DWI, and SWI within 24 hours of symptom onset, and follow-up MR or CT more than 5 days after symptom onset. We had 16 cases fulfilling the criteria for analysis. Two neuroradiologists qualitatively compared the areas of prolonged mean transit time (MTT) on PWI and restricted diffusion areas on DWI to determine whether the ischemic penumbra (MTT/DWI mismatch) was present. Extents of HV on SWI were compared with DWI (SWI/DWI mismatch) and MTT map (SWI/MTT mismatch). We also documented mismatches among SWI, CBF map and DWI. Follow-up CT or MR fluid attenuation inversion recovery (FLAIR) images or CT were compared with initial DWI to assess progression of ischemic stroke.

Results: Both MTT/DWI and SWI/DWI mismatches were significantly related with infarct progression (P = 0.01 and 0.001 respectively). The ability of the SWI and PWI to predict infarct progression is similar by using SWI/DWI and MTT/DWI mismatches (p = 1.0). The CBF/DWI mismatch was not associated with infarct progression (P = 0.4). The accuracies in prediction of infarct progression were 87.5% for SWI/DWI mismatch, 75% for MTT/DWI mismatch, and 62.5% for CBF/DWI mismatch.

Conclusion: SWI has a potential to be an alternative or even replacing of PWI to assess metabolic condition and intrinsic collaterals as penumbra. Further prospective studies are needed to evaluate its role in guiding thrombolytic therapies for patients with acute ischemic stroke.

493 Stroke prognosis

OVERWEIGHT AND OBESITY PREDICT IMPROVED SURVIVAL AND MORBIDITY AFTER STROKE

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Background: Obesity is an established risk factor for cardiovascular disease including stroke. The impact of obesity on outcome after stroke is less well established and increasing evidence suggests an obesity paradox in secondary cardiovascular prevention.

Methods: We analysed data from 1521 acute stroke or TIA patients who were studied in the Telemedical Project for Integrative Stroke Care (TEMPiS). Patients were grouped for body mass index (BMI) as underweight (BMI ≤18.5), normal (BMI >18.5-25) overweight (BMI >25-30), mild obesity (BMI >30-35) and advanced obesity (BMI >35 all kg/m²). Outcome after 30 months was recorded for mortality, recurrent stroke, institutional care, and dependency (institutionalisation, Barthel index <60 or modified Rankin score >3).

Results: During 30 months, 401 patients (27%) died. Mortality rates in BMI subgroups (BMI≤18.5, >18.5-25, >25-30, >30-35, and >35 kg/m²) were 61%, 33%, 24%, 18%, and 13% respectively, P<0.01) and rates for death or re-stroke were 64%, 40%, 31%, 22%, 18%, respectively (p<0.01). Institutional care and dependency showed the same pattern with lowest rates in obese subjects (all p<0.01). Analyses for stroke and TIA separately showed the similar Results (both p<0.01). BMI was a significant inverse predictor for poor outcome after multivariable adjustment for age, sex, comorbidity, living in partnership, and stroke severity: Compared to normal BMI (HR 1.0, reference) risk for death or re-stroke was higher in underweight patients (HR 2.74, 95%CI 1.23-6.03) but lower in overweight (HR 0.79; 95%CI 0.60-1.03, p=0.08), mild obesity (HR 0.56, 95%CI 0.37-0.86; p<0.01) and advanced obesity (HR 0.51, 95%CI 0.27-0.97; p<0.05). Also the risk of death or institutional care and dependency was highest in underweight patients and decreased stepwise with increasing BMI being lowest in obese and very obese patients.

Conclusion: Obese patients with stroke or TIA have better outcome for mortality, recurrent stroke, need for institutional care, and dependency than patients with normal BMI. This finding may be in contrast to primary prevention data but concurs with evidence of an obesity paradox in other cardiovascular diseases.

494 Stroke prognosis

DOES ETIOLOGY HELP PREDICT LONG-TERM STROKE RECURRENCE AND MORTALITY IN YOUNG ADULTS WITH ISCHEMIC STROKE?

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Background: There is limited data concerning recurrence of ischemic stroke (IS) and mortality in young adults. Furthermore, it remains unclear whether the outcome differs between etiological subgroups, including IS of undetermined etiology.

Methods: Since 2001-02, consecutive individuals hospitalised for IS have been prospectively registered in a single-center database and followed-up clinically. Clinical data, investigation Results, stroke etiology, treatments and outcomes are prospectively recorded. Cases of IS aged 18-50 were included and recurrent IS and all-cause mortality outcomes were compared between etiological subgroups. The TOAST classification was used but we considered arterial dissection and isolated patent foramen ovale (iPFO) as separate subgroups.

Results: We identified 450 individuals with IS aged 18-50. Etiology was determined in 360/450 (80%) and remained undetermined in 90/450 (20%) despite investigation by brain imaging (90/90, 100%), echocardiography (85/90, 94%), Holter (64/90, 71%), large artery imaging (83/90, 92%), and prothrombotic work-up (85/90, 94%).

Median follow-up duration was 41 months. Recurrence rate by subgroup was: large-artery atherosclerosis (10/38, 26%), cardioembolism (13/83, 16%), small-vessel occlusion (5/35, 14%), arterial dissection (8/61, 13%), iPFO (7/53, 13%), other determined causes (26/90, 29%) and undetermined etiology (15/90, 17%). IS recurrence rate did not differ between etiological categories (p=0.08). Mortality rate was 9/360 (2.5%) for determined etiologies and 3/90 (3.3%) for undetermined etiology (p=0.71). Survival analysis showed no significant difference between determined and undetermined etiologies for recurrent IS (HR = 0.88; 95%CI = 0.51-1.51) or mortality (HR = 1.46; 95%CI = 0.34-6.26).

Conclusions: Recurrent IS and death affect a substantial proportion of young adults with IS, but are not predicted by the main IS etiological categories.

495 Stroke prognosis

CHOLESTEROL, STATINS AND STROKE OUTCOMES IN ACUTE ISCHEMIC STROKE PATIENTS

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Background: Hyperlipidemia and pre-stroke statin treatment have been associated with better stroke outcome; however, their relative contribution to outcomes is not clear. We aimed to assess the association between cholesterol levels on admission and clinical and functional outcomes, independently of pre-stroke use of statins in patients with ischemic stroke (IS) participating in the National Acute Stroke Israeli Surveys-NASIS).
Methods: Consecutive IS patients admitted in all hospitals nationwide during February-March 2004 and March-April 2007 were included. Data on patients' demographics, risk factors, stroke characteristics, in-hospital management and outcome were systematically assessed. Associations between cholesterol level and stroke severity (by NIHSS), etiology, arterial territory, disability (by mRS), and in-hospital death were assessed using multiple logistic regression. Death at 3 years was assessed in the NASIS 2004 participants by Cox-survival analysis, adjusting for pre-and post-stroke statin treatment, age, gender and vascular risk factors.
Results: All 2333 IS patients assessed for cholesterol on admission (77% of all IS) were included (mean age 70.1±12.7 yrs; 57% males). Mean (sd) cholesterol was 196.2 (49.3) mg/dl. Adjusted ORs (95% CI) for 1 sd increase in cholesterol were 0.89, 0.80-1.00 for severe stroke; 0.64 (0.56-0.73) for cardioembolic stroke; 0.75, 0.62-0.90 for total anterior circulation infarction; 0.93, 0.85-1.03 for disability and 0.75, 0.60-0.95 for in-hospital mortality. HR (95% CI) for death at 3 years was 0.81, 0.72-0.92. In the analysis of stroke severity, a significant interaction between cholesterol levels and pre-stroke statin treatment was observed.
Conclusion: Higher levels of total cholesterol were associated with improved outcomes after IS in patients with and without pre-stroke statin treatment. Severe stroke was negatively associated with total cholesterol in patients with no pre-stroke statins, but not in those reporting statin use on admission.

496 Stroke prognosis

ELEVATED PLASMA CONCENTRATIONS OF OPIOID PEPTIDE PRECURSOR PROENKEPHALIN (PENK A) AS PREDICTOR OF MORTALITY AND NON-FATAL CARDIOVASCULAR OUTCOME AFTER CEREBRAL STROKE

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Background: Proenkephalin A (PENK A) is a stable fragment of the precursor opioid peptid of enkephalin and is expressed throughout the nervous system. The concentration of PENK A is about 100 times higher in cerebrospinal fluid than in serum representing a high concentration gradient with intact blood brain barrier (BBB). Impairment of BBB contributes to the pathology of stroke and reperfusion injury. We investigated the role PENK A in plasma of patients with acute cerebrovascular events as potential biomarker of stroke.
Methods: We evaluated 189 consecutive patients who were admitted to a stroke unit with acute symptoms of stroke. Patients were grouped for stroke, transient ischemic attack (TIA) and non-ischemic cerebral event (NI) based on cranial computed tomography and clinical evaluation. Plasma concentrations of PENK A were determined by a newly developed chemiluminescence sandwich luminescence immunoassay (LIA). Clinical outcome for recurrent stroke, non-fatal and fatal cardiovascular events were assessed at three months follow-up.
Results: Plasma concentrations of PENK A were significantly elevated in stroke patients (n=123; 65%, mean ± SEM: 154.6±16.6 pmol/L) but not in patients with TIA (9%; 115.4±7.9 pmol/L) and patients with non-ischemic events (26%; 119.3±8.8pmol/L; both vs. stroke P<0.05). PENK A predicted severity of stroke as assessed by NIHSS (r=0.225; P=0.002). The cut-off value of 108 pmol/L was identified by receiver operating characteristic analysis (AUC 0.604; 95%CI 0.52-0.69). Patients with PENK A concentration ≥108pmol/L showed a poorer clinical outcome for event-free survival (HR 2.6; 95%CI: 1.1-6.6; Log rank; P=0.032) and for composite endpoint of recurrent stroke, myocardial infarction, and death at three-month follow-up (HR 2.1; 95%CI: 1.1-4.4; Log rank; P=0.042).
Conclusions: Elevated plasma PENK A differentiates patients with acute stroke from TIA and non-ischemic events. PENK A is associated with clinical severity of cerebral injury and predicts impaired outcome for recurrent stroke, and fatal and non-fatal cardiovascular event. PENK A may be a suitable biomarker to assess 3 months outcome in patients with stroke.

497 Stroke prognosis

PULSE WAVE VELOCITY IS A PREDICTOR OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE

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Objective: The reliable prediction of stroke outcome might support treatment decisions. Increased aortic pulse wave velocity (PWV) has been shown to be an independent predictor of stroke in the general population and of fatal stroke in patients with hypertension. The augmentation index (AIx), derived from pulse wave analysis, independently predicted all-cause mortality and cardiovascular events in patients with coronary artery disease. Whether PWV and AIx may predict a functional outcome after ischemic stroke is unknown.
Methods: We studied 99 patients with acute ischemic stroke (15 patients with a history of previous non-disabling ischemic stroke, mean ± SD age 63.7±12.4 years, admission NIHSS score 6.6±6.6). Carotid-femoral (CF) PWV, augmentation index (AIx) and aortic systolic pressure were measured non-invasively with applanation tonometry (Sphygmocor®) within seven days after stroke onset. Functional outcome was evaluated with modified Rankin Scale (mRS). The end point was a 90–day favorable functional outcome (defined as mRS 0 or 1). Data were analysed with multivariate logistic regression.
Results: At 90 days, there were 53 (53,5%) patients with favorable outcomes. CF-PWV (P=0.000001) and AIx (P= 0.028) were significantly associated with favorable stroke outcome. Moreover, in univariate analysis, age, severity of stroke, infarct size, presence of previous stroke, diabetes, heart rate and peripheral pressures, had also predicted stroke functional outcome, whereas central pressures had not. The predictive value of CF-PWV, remained significant (OR=0.21 [95% CI, 0.06 to 0.74]; P=0.03) after adjustment for clinical predictors, and cardiovascular risk factors, including age, admission NIHSS score, infarct size, presence of previous stroke, mean blood pressure, and pulse pressure. AIx did not remain a significant predictor for functional stroke outcome.
Conclusions: This study indicates that aortic stiffness (CF-PWV) is an independent predictor of functional outcome in patients with acute ischemic stroke.
Keywords: ischemic stroke, arterial stiffness, pulse wave velocity, augmentation index, stroke outcome

499 Stroke prognosis

SELF REPORTED PHYSICAL FUNCTION IS INDEPENDENTLY ASSOCIATED WITH SURVIVAL AFTER STROKE

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Background: There is no information about the effect of health-related quality of life (HRQoL) on long term survival after stroke. In this study we investigated the predictive value of self reported HRQoL in a cohort of stroke patients.

Methods: From 1994 to 1995 a consecutive series of 315 prospective and eligible acute stroke patients were recruited from who 234 responded. HRQoL was assessed with the Short Form 36 (SF-36) health status questionnaire.

Results: In a multivariate model 12 years survival was independently associated with the following variables: female sex (hazard ratio, 2.12; 95% confidence interval, 1.53-2.94), self reported physical function (1.02, 1.01-1.03), lower age (1.09, 1.06-1.12), previous stroke (0.69, 0.49-0.97), diabetes (0.52, 0.35-0.76), and stroke severity (0.97, 0.96-0.99).

Conclusion: The physical functioning summary score (PSC) of the Short Form-36, female sex and lower age were all statistical associated with increased 12-years survival. HRQoL may add prognostic information to established risk factors in stroke.

500 Stroke prognosis

NATURAL HISTORY OF MIDDLE CEREBRAL ARTERY OCCLUSION IN 112 PATIENTS: A CLINICAL SERIES

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Background: Natural history of acute ischemic stroke due to middle cerebral artery occlusion (MCAO) not treated with reperfusion therapy is not well established. With the advent of new reperfusion therapies, this knowledge becomes essential to guarantee an appropriate selection of patients that would benefit from these techniques.

Methods: From a prospective stroke databases we selected patients with transcranial duplex confirmed MCAO not treated with reperfusion therapies, admitted to our Stroke Unit from January 2005 to September 2010. Proximal occlusion was defined as a TIBI 0-1 and distal occlusion as TIBI 2-3 at 45mm depth. Clinical and radiological findings at baseline and follow-up were studied. Good outcome was considered as a mRS 0-2 at three months.

Results: A total of 112 patients were studied (age 68±12; 57.1% men; NIHSS on admission 16 [8-20]). The main reasons not to treat these patients were: signs of early ischemic changes in neuroimaging (50%), presentation beyond 3 hours prior to ECASS III publication (28%), anticoagulation (11%) and minor stroke (3.6%). Time from onset to admission was <3 hours in 25% and <6 hours in 50% of the patients. Site of occlusion was proximal MCA in 70 (62.5%) and distal MCA in 42 (37.5%). Overall, good outcome was achieved in 29.5% of patients. According to the site of occlusion, good outcome was achieved in 12.9% of proximal MCA and 57.1% of distal MCA occlusions (p<0.001). There were differences between proximal and distal occlusion regarding malignant edema (30% vs 4.8%, p<0.001), intrahospital medical complications (40% vs 12%, p<0.001) and mortality at three months (12.5% vs 2.9%, p=0.003).

Conclusions: According to our series, outcome of acute stroke patients seems to be extremely poor in patients with proximal MCAO and relatively good in distal MCAO. These findings are relevant considering the increasing number of reperfusion therapies series without a control group.

501 Stroke prognosis

CLINICAL SIGNIFICANCE OF THE PRESENCE OF ENDOTHELIN-1 GENE RS1800541 AND RS5370 SNPS IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Background: Cerebral edema is associated with poor outcome in patients with acute stroke. Endothelin-1 (ET-1) is a powerful vasoactive peptide leading to vasoconstrictor actions. In this study we analyze the association of ET-1 gen SNPs (rs1800541, rs5370, rs2071942) with serum levels of ET-1, development of severe cerebral edema, infarct volume and functional outcome.

Methods: 302 patients with non-lacunar acute ischemic stroke (mean age, 74.2±12.3 y; males, 51.3%) were prospectively included within 12h of sympons onset. Stroke severity was evaluated by NIHSS. Severe brain edema was diagnosed if extensive swelling causing any shifting of the structures of the midline was detected on CT at 24-36 hours (h). Infarct volume was measured by CT betwween 4th-7th day. Functional outcome at 3 months was evaluated by the modified Rankin scale (MRS), considering poor outcome mRS ≥3. Serum levels of ET-1 were measured in blood samples obtained on admission.

Results: The presence of rs1800541 (β, 1.6) and rs5370 (β, 1.5) SNPs were independently associated with higher serum levels of ET-1 (all p<0.0001). However,

there was no relationship between serum levels of ET-1 and the presence of rs2071942 SNP (Spearman coef: 0.052, p=0.365). On the other hand, higher ET-1 levels at baseline were also associated with development of severe cerebral edema (OR, 2.4; CI95%, 1.4-4.0). Likewise, serum levels of ET-1 were also associated with infarct volume (OR, 19.8; CI95%, 16.2 - 23.4) and poor outcome (OR, 1.3; CI95%,1.1 - 1.7).

Conclusions: These findings suggest that the presence of rs1800541 and rs5370 SNPs may increase teh synthesis of ET-1. By the other hand, increased serum levels of ET-1 predict severe cerebral edema, greater infarct volume and poor functional outcome.

502 Stroke prognosis

TOLL LIKE RECEPTORS 2 AND 4 IN ISCHEMIC STROKE: OUTCOME AND THERAPEUTIC VALUES

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Background: Stroke triggers an intense inflammatory response that could be a consequence of Toll-like receptors (TLR) activation. However the clinical significance and the therapeutic possibilities of TLR in stroke is not so clear. Our objective was to analyze the association between the expression of TLR2 and 4 and clinical outcome of ischemic stroke patients, together with the expression of inflammatory molecules and endogenous ligands and to test in vitro the blockage of TLR2 and 4 and their endogenous ligands as anti-inflammatory strategy.

Methods: 110 patients with a first-ever ischemic stroke were included within 12h of symptoms onset. Functional outcome was assessed at 3 months by the modified Rankin Scale (mRS). Infarct volumes were measured on CT images. TLR2 and 4 expression on monocytes were analyzed on admission, 24h, 72h and 7 days by flow cytometry. Inflammatory markers and potential endogenous ligands were analyzed by ELISA. Monocytes and HUVEC cells were cultured and treated with serum from patients, and with antibodies for TLR2 and 4 and their endogenous ligands. Inflammatory response of cells was analyzed measuring inflammatory molecules in culture supernatant.

Results: TLR2 and TLR4 expression was independently associated to poor outcome. TLR4 expression was independently associated to lesion volumes. TLR2 and TLR4 mean expression on monocytes at baseline was correlated to higher levels of IL1β, IL6, TNFα and VCAM1 at 24h, 72h and 7 days. Monocytes and HUVEC cells showed a strong inflammatory response when cells were treated with serum from ischemic stroke patients. This inflammatory response was decreased when TLR2/4 or cFN or HSP60 were blocked.

Conclusions: TLR2 and TLR4 expression is associated with poor outcome and higher inflammatory response in acute ischemic stroke. Besides, TLRs and/or endogenous ligands could be therapeutic anti-inflammatory targets.

503 Stroke prognosis

PROGNOSIS OF STROKE IN MALAWI, A COUNTRY WITH HIGH PREVALENCE OF HIV

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Background: are the sixth commonest cause of mortality in Malawi a country in Central-Southern Africa.

Objectives: Describe outcome of first ever stroke in patients admitted in Queen Elizabeth Central Hospital (QECH) the city of Blantyre, Malawi.

Setting: Medical wards in QECH.

Materials and Methods: A prospective cohort study of 150 adult stroke patients with first ever stroke recruited in QECH. Patients were followed up for one year. Modified Rankin scale (mRs) for functional outcome and modified National Institute of Health Stroke Scale (mNIHSS) for stroke severity were used.

Results: 72 (48%) patients were women. The mean age was 53 years. 73 were young (≤ 55 years). 92 (62%) had ischemic, 32 (21%) had hemorrhagic stroke. Two were found subsequently not to have had strokes, 21 (14%) were not imaged. 50 (33%) were HIV seropositive, 43 of them were young.

62 (41%) patients died (mRs=6) during the follow up, 33 (53%) of them died during the first 30 days from stroke. 37 (60%) were old and 26 young. Stroke severity (p< 0.0001) was a risk factor for mortality. Mortality was higher in women (71% p< 0.05). HIV did not affect mortality.

50 (33%) recovered well (mRs ≤ 2 after one year). 28 (56%) of them were young, 13 (59%) of the young had HIV-infection. 9 (6%) were bed ridden after one year

(mRs = 4 -5). 11 (7%) were known to have another nonfatal stroke during the year. 2 patients developed epilepsy.

15 (10%) patients were lost to follow up.

Conclusions and Recommendations: A third recovered well from their first ever acute stroke. Mortality for stroke in Malawi is 41% during first year; most patients die during the acute phase. Women have higher risk of dying even if stroke severity does not differ from men. Severity is a risk factor for poor outcome. HIV does not affect the mortality.

More effort is needed for primary and secondary prevention of stroke to prevent the attack, improve the outcome and reduce the risk of another stroke.

504 Stroke prognosis

ASSOCIATION OF STROKE RECURRENCE WITH METABOLIC SYNDROME IN PATIENTS WITH NONCARDIOEMBOLIC STROKE

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Background: Metabolic syndrome defines a cluster of metabolic risk factors (abdominal obesity, insulin resistance, dyslipidemia, hyperglycemia and hypertension) that come together in a single individual. Metabolic syndrome is associated with an increased risk of cardiovascular diseases, but there is limited data about the association between metabolic syndrome and stroke. In this study, we aimed to determine the association between stroke recurrence and metabolic syndrome in patients with first ever stroke who had non cardioembolic etiology.

Methods: Patients with first ever stroke who had noncardioembolic etiology were enrolled prospectively in this study. Patients were divided into two groups; patients with and without metabolic syndrome. Clinical outcomes and survival analysis was performed for stroke recurrence at sixth month.

Results: Of 132 patients, 90 patients (%68.2) had metabolic syndrome. Recurrence of ischemic stroke was higher in patients with metabolic syndrome (8/88, 9,09%) when compared with the patients who had no metabolic syndrome (1/40, 2.5.0%) but the association was not statistically significant. However, recurrence of ischemic stroke was higher in patients with insulin resistence (4/21, 19%) when compared with the patients who had no insulin resistance (4/102, %3,9 p<0.05).

Conclusion: Presence of insulin resistance was found as a predictor for stroke recurrence in patients with noncardioembolic stroke.

505 Stroke prognosis

CHA2DS2-VASC SCORE AND PROGNOSIS IN ISCHEMIC STROKES WITH ATRIAL FIBRILLATION

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Background: We sought to analyze the distribution and prognostic value of the CHA2DS2-VASc score in a cohort of ischemic stroke (IS) patients with AF.

Methods: A total of 502 consecutive stroke patients with isolated AF and no previous thromboembolic events were studied. Vascular risk factors, initial stroke severity and previous antithrombotic therapy were also recorded. Poor outcome was defined as a mRs of 3-6 at 3 months.

Results: CHA2DS2-VASc >1 was found in the 96.6% of patients. Poor outcome was found in 50% of the patients. CHA2DS2-VASc score, age, female gender, current smoking, hyperlipidemia, congestive heart failure, stroke severity and therapeutic (INR>2) anticoagulation were associated with the outcome in univariate analysis. In multivariable analysis, CHA2DS2-VASc score was independently associated with poor outcome [OR 1.26 (95% CI: 1.05-1.52), p=0.015] as well as stroke severity [OR 15.55 (95% CI: 9.92-24.42), p<0.001]. After removing stroke severity from the analysis therapeutic anticoagulation was also associated with stroke prognosis [OR 0.42 (95% CI: 0.20-0.89), p=0.024].

Conclusions: CHA2DS2-VASc punctuation is associated with 3 months outcome independently from stroke severity.

506 Stroke prognosis

FUNCTIONAL OUTCOME OF HAEMORRHAGIC AND ISCHEMIC STROKE IN A REHABILITATION SETTING: A MATCHED COMPARISON

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Background: Intracerebral haemorrhage (ICH) is associated with a higher risk of mortality compared with ischemic stroke (IS) but, it is believed that ICH survivors have better neurological and functional prognoses. Availability of data related to outcome difference in two groups is limited. Hence, the objective of this study is to assess the influence of stroke aetiology in rehabilitation outcome.

Method: This was a case-control study of 96 patients admitted to stroke unit at National Hospital of Sri Lanka from 2008 to 2010 with sequelae of first stroke. A Total of 48 consecutive patients with ICH were compared with 48 IS patients matched for age (within 3 year), sex, dexterity, stroke severity, basal disability, and onset admission interval (within 5days) who were different only in terms of stroke aetiology, infarction versus haemorrhage. On discharge functional outcome of the ICH and IS subgroups was analyzed and the improvement of disability according to Modified Barthel index (BI) and Modified Rankin's scale (RS) were compared.

Results: Mean age of ICH and IS groups were 58.3 (SD 12.6) and 58.7 (SD 12.1) years respectively. In both groups sex ratio (M: F 1:2.3) and hemispheric involvement (dominant 60%, non dominant 40%) were common. Neuro imaging revealed that 61.2% of patients in the ICH group had deep haemorrhages while 50.3% in IS group had lacunar infarctions. In both subgroups, on admission mean BI and RS were 5.1 and 4.0. Length of rehabilitation unit stay in ICH and IS groups were 34 and 39 days respectively (p = 0.43).

At discharge, according to the BI and RS, the mean functional outcome improvement in ICH group (BI 8.3, RS 2.3) was statistically significant than in IS group (BI 5.1, RS 1.6) (p <0.001).

Conclusion: The Results of this study provide further evidence of better functional prognosis in survivors of hemorrhagic stroke comparative to ischemic stroke. A repeat study matched for location of pathology would further strengthen this statement.

507 Stroke prognosis

ROLE OF SERUM S100B PROTEIN IN PREDICTION AND OUTCOME OF MALIGNANT MIDDLE CEREBRAL ARTERY INFARCTION: CLINICAL AND LABORATORY STUDY

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Background and Objectives: Early prediction of the outcome of the malignant middle cerebral artery infarction may help the proper choice for the therapeutic decision for this stroke subtype. This study investigated the possible role for serum S100 B protein, beside other clinical and radiological determinants in prediction of the outcome of malignant cerebral infarction.

Subjects andMethods: This study was conducted on 42 stroke patients with clinical and CT evidence of malignant cerebral infarction (group I), and 20 patient with non malignant cerebral infarction (group II), and 20 healthy individual as a control (group III). All the groups were subjected to general medical and neurological examination including assessment of the disability by modified Rankien Scale (mRS) after one week, one month and after three months of admission. CT brain was done for all patients on admission and repeated after one week for (group I). Measurement of serum S100 B protein was done initially for the studied groups and after one week for group I patients.

Results: S100B protein level was significantly higher among patients with malignant cerebral infarction (group I) compared with patients with non malignant infarctions and healthy controls (group II and group III). Follow up of S100 B protein level in group (I) patients was increased but with no significant difference from the initial level on admission. Also in our study the relation of S100B value to the mortality showed significant results.

Conclusion: Estimation of serum S100 B protein on admission beside other clinical and radiological findings can predict the outcome of the malignant middle cerebral artery infarction.

508 Stroke prognosis

DIFFERENCE IN PLATELET FUNCTION TEST COULD PREDICT PROGNOSIS IN THE ACUTE STAGE OF ISCHEMIC STROKE

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Background: The relative risk reduction of prevention of recurrent ischemic stroke by antiplatelet agents is 20-30%. Clinically, it's difficult to identify non-responders until the next vascular events. This study is aimed to test if the point-of-care measurement of platelet function would be associated with favorable clinical outcome in the acute stage of ischemic stroke.

Methods: In this cohort study, we prospectively recruited the patients with acute ischemic stroke admitted to Landseed Hospital in Taiwan from Jun. 2009 to Nov. 2010. The platelet function tests of each patient were scheduled at arrival, one week and one month after admission, determined by the closure time of CEPI and CADP cartridges of Platelet Function Analyzer (PFA)-100®. The outcome of interest is the independence state of modified Rankin Scale (mRS) 0 and 1 at one month.

Results: We recruited 346 patients in the study period, the values of the 1st measurement by CEPI and CADP cartridges were not associated with independent mRS state (P=0.83 and 0.18, respectively). Twenty-four patients (6.9%) with prior antiplatelet agents had longer CEPI closure time than those without (215.7±78.6 vs. 183.0±82.5 seconds, P=0.06). The platelet function of 246 patients had been measured twice. After excluding 57 without antiplatelet agents between 2 measurements, the difference between the 1st and 2nd CEPI measurement in 189 patients was 47.0±104.5 seconds in the group of mRS of 0,1 and 17.9±36.0 in the group of mRS 2-6 (P=0.04). The patients with uppermost quartile of CEPI difference >91 seconds between measurement had an adjusted odds ratio of 3.59 (95% CI 1.33-9.74) to have mRS 0,1 after adjustment for age, initial scores of National Institute of Health Stroke Scale, and the interval of measurements.

Conclusion: The Results supported the difference of sequential PFA-100 measurements in antiplatelet naïve patients with ischemic stroke could be served as an indicator for the favorable outcome in acute stage.

509 Stroke prognosis

MANAGEMENT AND OUTCOMES OF ISCHEMIC STROKE – COMPARISON OF PATIENTS WITH HISTORY OF STROKE AND TRANSIENT ISCHAEMIC ATTACK IN POLAND

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Background and Aims: Previous stroke and TIA are associated with increased cardiovascular risk and both need careful medical attention. We aimed to compare the management and long- and short-term outcomes in ischemic stroke patients with a history of stroke and history of TIA.

Methods: POLKARD Stroke Hospital Registry collected data via internet based questionnaire on patients hospitalized with acute stroke in 84 stroke centres in Poland between March 2007 and February 2008. The follow-up was completed at end of February 2009 by checking the Death Records National Database of The Ministry of Interior and Administration. The management prior to stroke, comorbidities, risk factors, acute stroke severity and outcomes were compared for two ischemic stroke patients groups: those with a history of previous stroke and those with a history of TIA. The Cox regression model was developed to compared long-term outcomes in both groups.

Results: The total numbers of 6489 and 939 ischemic stroke patients with history of stroke or TIA were reported, respectively. Patients with previous TIA were less likely to have AF or coronary artery disease and disability prior to stroke, but smoked much more often than patients with secondary stroke. Antihypertensives, aspirin and statins were used only for 66.3, 42.7 and 21.1% patients with TIA history compared to 71.1, 53.8 and 24.1% patients with previous stroke. On admission TIA history patients presented consciousness disturbances less often. In-hospital, 3,6 and 12 month mortality rates were 12.5, 20.3, 23.9, 28.5% and 16.1, 26.9, 31.8, 37.2% for TIA and stroke history patients, respectively. After adjusting for case mix both history of TIA and stroke were associated with similar long-term survival prognosis (OR for death 0.97, 95%CI: 0.85-1,10).

Conclusions: Secondary prevention of stroke is poorer in the ischemic stroke patients who experienced only TIA then those who had previous stroke, although death prognosis for both groups are similar.

510 Stroke prognosis

COMPARISON OF OUTCOMES FOLLOWING INTRAVENOUS RT-PA TREATMENT AMONGST PATIENTS WITH OR WITHOUT ATRIAL FIBRILLATION

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Background and purpose: Ischemic stroke patients with atrial fibrillation (AF) were reported to more likely have poor outcome after intravenous recombinant tissue plasminogen activator (rt-PA) therapy compared to those without AF. It might be caused by a lower rate of recanalization after rt-PA infusion in patients with AF. However, other reports demonstrated higher frequency of early recanalization in patients with cardioembolic stroke after rt-PA therapy. We aimed to investigate the impact of AF on the 3-month functional outcome following rt-PA treatment.

Methods: Consecutive ischemic stroke patients treated with intravenous rt-PA in two study hospitals were studied prospectively via a systematic registry. The association between AF and favorable outcome at 3 months (modified Rankin Scale score ≤1) was explored in univariate and multivariate logistic regression analysis.

Results: Of 90 patients (59 men, 67±12 years old) enrolled, 36 (40%) patients had AF. The median NIHSS score at baseline for patients with AF was 17.5 (interquartile range 10.5. to 22), and for patients without AF, 13 (9 to 18). The median time from onset to treatment for patients with AF was 125 minutes (100 to 153), and for patients without AF, 139 (110 to 163). Two patients (without AF) were dead at the time of discharge. At 3 months, favorable outcome was 42% in patients with AF and 31% in those without AF (P=0.323). On multivariable logistic regression analysis, AF was independently associated with 3-month favorable outcome (OR 2.99, 95% CI 1.03 to 8.65, P=0.043), after adjusted for baseline NIHSS and onset to treatment time.

Conclusions: In our study cohort, acute ischemic stroke patients with AF more frequently had favorable outcome after rt-PA therapy compared with those without AF.

511 Stroke prognosis

ADMISSION LEUKOCYTOSIS IN ACUTE CEREBRAL ISCHEMIA: INFLUENCE ON EARLY OUTCOME

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Background: Leukocytes are the first cells that arrive in the stroke region(s) and they increase in peripheral blood. Leukocytes contribution in the early acute phase of cerebral ischemia has not yet been investigated.

Purpose and Methods: We aimed at establishing in consecutive first-ever ischemic acute stroke patients whose symptoms had started less than 12 hours earlier whether the admission leukocyte count affects the short-term neurological outcome, and whether there are differences between the various clinical syndromes of stroke. National Institute Health Stroke Scale (NIHSS) was assessed at admission (NIHSS0) and after 72-hour (NIHSS72). Modified Rankin Scale (mRS) was evaluated at discharge. Sperman's rank correlation was used for the correlation between leukocytes and outcome measures.

Results: Eight hundred and eleven patients were included [median age 77 (68-82) years; 418 (53%) male; median NIHSS0 7 (4-12), median NIHSS72 6 (3-12), median mRS 2 (2-4)]. Median leukocyte count at admission was 8100/mm³ (6500-10300). Higher leukocyte levels predicted a worst clinical presentation and a poor functional outcome (NIHSS0: p<0.001, NIHSS72: p<0.001, mRS: p<0.001). The correlation between leukocyte count and outcome measures remained significant after multivariate analysis (NIHSS0: p<0.001, NIHSS72: p<0.001, mRS: 0.008). Focusing on clinical syndromes, higher leukocyte count predicted a severe NIHSS0 and NIHSS72 in TACS (p=0.001), PACS (p=0.004) and POCS (p=0.026) patients.

Conclusions: Elevated leukocyte count in the acute phase of cerebral ischemia is a significant independent predictor of poor initial stroke severity, poor clinical outcome after 72 hours, and discharge disability. The involved underlying mechanism is still to determined.

512 Stroke prognosis

THE STROKE OUTCOME PREDICTIVE INSTRUMENT

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Background: We aimed to develop predictive instrument that could provide clinicians with probabilities of stroke outcome. The predictions concerned the two stages of stroke severity, i.e. the lower and the higher degree.

Methods: The study included consecutive 604 ischemic stroke patients not treated with tissue plasminogen activator. For the Barthel's Index (BI), a higher disability due to stroke was assumed at the cut-point of score 70 or below. For the mRankin score good outcome was defined as a score 0-2 (or 0-3), while the higher stroke severity was classified within the ranges 3-6 (or 4-6 – for details see table 1). In the statistical analysis a regression method was used. The number of clinical, laboratory and demographic variables were assessed at admission to hospital.To model mRankin score or BI in 30, 90, 180 and 360 days after stroke (dependent variables) a multiple ordinal logistic regression was implemented for assessed factors (independent variables). The best subset of predictors was established following the Akaike's information criterion and the estimated p-values (<0.05). Simple predictive instrument based on the estimated regression coefficients were created in the final step of the statistical analysis. The computation was performed in the R software.

Results: The best subset of 6 variables: NIHSS, Sex, Age, Diabetes, C-Reactive Protein, and Red (cell) Distribution Width was found to reliably predict the stroke outcome. The fraction of total matched 30, 90, 180 and 360 days outcome predictions reached for mRankin (0-2 vs. 3-6) were 78%, 80%, 81%, and 81%, respectively, and for BI 78%, 84%, 85%, and 83%, respectively. The predictions were less precise for mRankin score 0-3 vs. 4-6.

Conclusions: Our outcome predictive instrument showed reliable prediction of good or unfavorable outcome in stroke patients. The instrument is more precise in patients outcome assessed with the use of BI than mRankin score.

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513 Stroke prognosis

ISOLATED CEREBELLAR INFARCT: IMAGING FINDINGS, AETIOPATHOGENESIS AND CLINICAL OUTCOME

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Purpose: To describe computed tomography (CT) and/or magnetic resonance imaging (MRI) findings in patients with isolated cerebellar infarct (ICI) correlated to aetiopathogenetic mechanisms and clinical outcome.

Materials and Methods: From a consecutive series of 568 patients with posterior circulation infarction that evaluated prospectively we identified by imaging studies 140 (24.6%) patients with cerebellum involvement. After extensive study, cases were a) classified according to the aetiopathogenetic mechanisms: atherosclerosis, cardioembolism, infarcts unknown cause (IUC) and other etiologies b) categorized based on vessel cerebellum territories and c) followed up to 5 years regarding mortality and stroke recurrence.

Results: We identified 74/140 (53%) cases with ICI. Infarcts distribution was: posterior inferior cerebellar artery (PICA) 23 (31%), anterior inferior cerebellar artery (AICA) 8 (11%), superior cerebellar artery (SCA) 37 (50%) and multiple territories in 6 (8%) cases. Hemorrhagic transformation was more common in SCA infarcts (40.5%) compared to PICA (8.7%) and AICA (11.1%), (p=0.012), while brain edema with mass effect was similar among vascular territories (11.9%, 8.7%, and 11.1% respectively, p=0.923). The most common causes were deferent (p=0.004) among vascular territories: cardioembolism in SCA (60%), atherosclerosis in AICA (67%) and in PICA equal cardioembolism and atherosclerosis (34% and 31%). After a median follow-up of 30 months (interquartile range 20-60), mortality was 47%, 16%, 11% for SCA, PICA and AICA respectively, while for the same period recurrence rate was 65%, 29% and 62% respectively.

Conclusions: Cerebellar infarct vascular distribution is related to different stroke mechanism and radiological features and is associated with different long-term stroke outcome.

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514 Stroke prognosis

BOTH HIGH AND LOW BODY MASS INDEX ARE ASSOCIATED WITH WORSE FUNCTIONAL OUTCOME AFTER ISCHEMIC STROKE

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Background and purpose: Excess weight is an independent risk factor for stroke, and stroke mortality. Little is known about the contribution of body mass index (BMI) to functional recovery after stroke. We aimed to assess the association between BMI and functional outcome at discharge in patients with acute ischemic stroke.

Methods: We analyzed the relationship between BMI and discharge outcomes in 341 patients with acute ischemic stroke with multivariable logistic and linear regression. Outcome measures were unfavorable functional outcome defined as modified Rankin Scale score >2, length of hospital stay, and incidence of infections. Given the observed nonlinear relationship between BMI and functional outcome, patients were classified, according to their BMI, as low weight (<20 kg/m^2), normal weight (20-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obese (≥30 kg/m^2). We adjusted for age, sex, NIHSS score, HDL levels, and diabetes, and tested for interaction between age and BMI.

Results: A BMI of 25 or higher was present in 216 patients (63%). Mean age was 60 (SD 13). We found a J-shaped relationship between BMI and unfavorable outcome, and those with normal weight had the lowest risk. After adjustment for potential confounders, the odds ratios for unfavorable functional outcome (relative to BMI 20-24.9) were 5.1 (95% CI, 0.6-45.4) for BMI <20, 3.5 (95% CI, 0.7-15.4) for BMI 25-29.9, and 7.9 (95% CI, 1.5-40.7) for BMI ≥30. No interaction with age was found (p=0.40). Patients in the highest BMI categories had a longer duration of hospital stay than those with normal weight (1.9 days, 95% CI 1.3-2.4, respectively, 4.0 days, 95% CI 3.7-4.3). No significant differences in incidence of infections were found across BMI categories.

Conclusion: Both high and low BMI are associated with unfavorable functional outcome in acute ischemic stroke as shown by a J-shaped relationship.

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515 Stroke prognosis

CLINICAL FEATURES AND OUTCOME OF APHASIA AFTER INTRAVENOUS RT-PA THROMBOLYSED ISCHEMIC STROKE

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Introduction: Whereas the rt-PA thrombolysis at the acute stage of an ischemic stroke significantly decreases dependency at 3 months, no data about the outcome of the thrombolysed aphasia is available.
Our aim was to describe the features of aphasia (severity and aphasic syndromes) after a thrombolysed stroke.

Methods: This retrospective cohort study has included the aphasic patients hospitalised at the Stroke Unit of the University hospital of Dijon, France, between 2006 and 2009, for a first-ever left sylvian ischemic stroke which was thrombolysed by intravenous rt-PA. Non thrombolysed patients hospitalised in 2004 and 2005 were compared thanks to a logistic regression.
Aphasic syndromes and severity (French version of the Boston Diagnostic Aphasia Examination) were evaluated during the first week and at 3 months after stroke.

Results: In multivariate analyses, the severity of the aphasia after the 37 thrombolysed strokes was weaker than in the 38 non thrombolysed patients, during the first week (aOR=5.2 CI95% 1.33-20.16 p=0.017) and at 3 months (aOR=5.45 CI95% 1.85-16.01 p=0.002). The frequency of non severe aphasia (conduction or nonclassified aphasia) was increased during the first week after the thrombolysed strokes (OR=5.79 CI95% 1.16-28.94 p=0.025), only in bivariate analyses.

Discussion: The weaker severity of the aphasia at 3 months after a thrombolysed cerebral ischemic infarct agrees with the improvement of the dependency. A selective reperfusion of the cerebral ischemic area is the most probable hypothesis which can explain the increase of the frequency of conduction aphasia after the thrombolysis. However, the small number of patients in our retrospective study does not allow us to obtain other significant results.

Conclusion: The severity of the aphasia during the first week and at 3 months after thrombolysed stroke is weaker than in non thrombolysed patients, probably because of a greater frequency of conduction and nonsevere nonclassified aphasia.

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516 Stroke prognosis

PREDICTORS OF FUNCTIONAL OUTCOME AFTER LARGE HEMISPHERIC INFARCTIONS TREATED WITH HYPEROSMOLAR HYPOTHERMIC NORMOGLYCEMIA (H2N)

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Introduction: Large hemispheric infarctions carry a mortality rate up to 80% and lead to moderate-severe disability in 60-80% of the surviving patients. Potential prognostic factors to determine outcome in these patients are poorly defined.

Methods: Patients with large hemispheric infarctions between August 2006 and March 2009 were treated with the combination of insulin infusion (target glucose 4.6-6.1 mmol/L), mild hypothermia (33-35°C), and hypertonic saline (goal sodium

150-155 mmol/L) within 72 hours of symptom onset and were prospectively enrolled in the Large Hemispheric Infarction Outcome Project. We analyzed impact of demographic, clinical, radiological variables and hospital complications on outcome using forward stepwise multiple logistic regression analysis. Poor functional outcome, assessed at 3 and 12 months, was defined as modified Rankin Scale (mRS) of 4 to 6.

Results: Of the 50 patients enrolled 22 had right-sided infarctions and median age was 64 (range 36-83) years. Baseline NIHSS was 18.3±5.7. At 3 months, 28 patients had died (56%); 17 had a mRS of 4 and 5 (34%). In the univariate analysis, advanced age (63.9±1.9 vs 46.0±3.6 years), infarction caused by atrial fibrillation (51 vs 0%), and uncal herniation (55 vs 13%) were more common among the patients with poor outcome, whereas rebound fever (43 vs 88%), tracheobronchitis (53 vs 100%), and hemicraniectomy (31 vs 80%) occurred less often (p<0.05). Older age was the only significant predictor of poor functional outcome at 90 days (1.14 (1.02-1.27), P=0.019) and 12 months (1.12 (1.03-1.21), P=0.006).

Conclusions: Advanced age is independently associated with poor functional outcome at 3 and 12 months after large hemispheric infarction. Complications did not affect long term outcome, and hemicraniectomy did not have a protective effect in our patient population. Prognostication and management decisions should include the age of the patient.

517 Stroke prognosis

IDENTIFYING SIGNIFICANT ASYMPTOMATIC CORONARY DISEASE FOLLOWING FIRST ISCHAEMIC STROKE OR TIA USING CT CORONARY CALCIUM SCORE AS A SCREENING TOOL

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Background: Coronary calcium has been proven as an independent predictor of cardiovascular mortality. A score of >160 gives a ten fold increase to the calculated Framingham 10 year risk of cardiac death. Identifying and treating undiagnosed cardiovascular disease in patients after ischaemic stroke therefore improve prognosis. As risk factors are similar in ischaemic stroke and cardiovascular disease, CT Coronary Calcium score can be used as a screening tool to select patients for more invasive investigations.

Method: 75 patients under the age of 65 with proven ischaemic stroke or clinical diagnosis of TIA made by a stroke physician were risk assessed using a CT based Coronary Calcium score. Patients with a score over 100 or localised disease were referred to cardiology for further management.

Results: 30 patients were referred on, 24 were males. Average age was 60 for both sexes. Calcium scores ranged from 0 to 2406 with an average of 496. 26.7%, 96.7% and 83.3% had Diabetes, Hypertension and Hypercholesterolemia. 24 (80%) had follow up investigations and 8 (27%) had coronary angiograms. 6 (20%) needed revascularisation and 5 (17%) more are followed up in cardiology clinic for possible revascularisation. 5 of the revascularised patients had a score of over 200 the other 69 but localised disease and all six had at least two risk factors.

Conclusion: CT Coronary Calcium score is a useful tool to identify patients at risk of coronary disease following ischaemic stroke. 37% of patients referred were identified as high risk and 20% had revascularisation. The 5 year risk of MI or vascular death is estimated at 17.4% following first ischaemic stroke. In our cohort no deaths were recorded though the longest follow up was 31 months. This is probably related to timely intervention. A calcium score of >200 and having two risk factors seem to predict higher risk patients in this study but need a bigger sample to prove statistical significance.

518 Stroke prognosis

PROGNOSTIC FACTORS OF THE RECURRENCE CEREBRAL EVENTS AFTER ISCHEMIC STROKE: A PROSPECTIVE STUDY

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Aim: to study the prognostic factors of the recurrence cerebral events after ischemic stroke.

Methods: We consequently included 100 patients (76 male, mean ages 60±8 years) at 21 day after ischemic stroke and having sinus rhythm. All of them were examined with brain MRI, echocardiography, 24-hour Holter monitoring. Arterial hypertension was diagnosed in 87 patients, coronary artery disease – 34, congestive heart failure (CHF) - 60, rheumatic or degenerative valve defects - 13 ones. At baseline mean score of Scadinavian stroke scale was 51±11 points and mRS≤3. Primary outcome: recurrent stroke, transient ischemic attack (TIA), fatal stroke.

Results: Mean follow-up period was 39 month (ranged 3-72). Primary outcome was recorded in 16 patients (1 group): fatal stroke – in 5, nonfatal recurrent stroke – in 7, TIA – in 4 ones. Remainder 84 patients consisted 2 group. At baseline in 1 group patients compared 2 group there were more frequent diagnosed CHF (75% vs 57%, p=0,06), double ventricular extrasystoles (13% vs 2%, p<0,05) and paroxysmal ventricular tachycardia (13% vs 5%, p=0,06). But then diuretics were used more rare in patients of 1 group compared 2 group (6% vs 30%, p<0,04). Other sighs (neurological, cardiac) were similar in both groups.

Conclusions: CHF, double ventricular extrasystoles and paroxysmal ventricular tachycardia may consider adverse prognostic factor of recurrence cerebral events. Contrariwise diuretics treatment benefits prognosis after ischemic stroke.

519 Stroke prognosis

THE FUNCTIONAL INDEPENDENCE MEASURE (FIM) AND 30 DAY OUTCOME IN STROKE: LOCAL EXPERIENCE

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Background: The modified Rankin Scale (mRS) immediately following stroke is one of several measures of disability that has been shown to be associated with subsequent outcome. The Functional Independence Measure (FIM) is an alternative scale which has recently been adopted in rehabilitative settings throughout our institution. Very limited evidence exists that baseline FIM score can predict outcome amongst stroke patients. We examined the relationship between first recorded FIM after stroke and 30-day outcome in 116 consecutive stroke patients admitted to our unit, making use of a stroke-specific clinical information system in use locally (Stroke Nav).

Methods: We reviewed the records of 116 consecutive stroke patients admitted to the John Radcliffe Hospital, Oxford, UK, in the three months April 2010 to June 2010. Admission and 30-day outcome data, including mRS and FIM, was collected. Recorded FIM and mRS were compared between admission and at day 30.

Results: FIM and mRS on admission for those patients alive at 30 days (n=103) were 82 and 3 respectively, while those for patients who had died (n=13) were 43 and 4. FIM and mRS at day 30 for those patients alive were 97 and 2 (n=103).

Conclusions: A low FIM on admission was associated with increased likelihood of mortality at 30 days. The FIM appears to be a good predictor of stroke outcome. Baseline FIM is a reasonable candidate for inclusion in outcome prediction algorithms that we are developing. FIM has several advantages over other disability scales in the setting of stroke rehabilitation including clear delineation between physical and cognitive deficits.

520 Stroke prognosis

IS HYPOALBUMINEMIA CAN CONSIDER AS A VALUABLE FACTOR IN THE ESTIMATION OF HOSPITAL MORTALITY IN ACUTE PHASE OF STROKE?

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Background and Aim: In spite of growing stages of treatment of acute stroke, the hospitalized mortality rate is high and unthinkable. This study aimed to investigate the effect of these risk factors on the increase the hospitalized mortality rate during the acute phase, as well as point out the role hypoalbuminemia, especially in Iranian stroke patients.

Subjects and Methods: The information of total 183 (107 males and 76 females, mean age of 66.7±12.25 years) consecutively admitted patients with acute stroke in Neurology ward of Golestan Hospital, Ahvaz, Iran from 2009 to 2010 were recorded.

Results: Out of 183 cases, 112 cases with arterial ischemic stroke and parenchymal hemorrhage have been selected and studied. There were 29 cases of deaths among 112 patients. With regard to normal range albumin (5/3-5/5 g/dl), 43% of the patients were show hypoalbuminemia. The mean difference in presence of hypoalbuminemia between female and male patients was not statistically significant (44% vs. 42% respectively). Between the hypoalbuminemia and mortality rate significant correlation has been observed (P <0.001), while the mean albumin levels in patients who had died was less than the others.

Conclusion: The role of hypoalbuminemia in stroke's mortality is independent of age and gender. The present study showed that hypoalbuminemia is a strong risk factor for ischemic stroke patients, probably in context of the hospitalized mortality rate. Consequently, an intervening plan to determine the role of confounding albumin therapy in patients with ischemic stroke is more tangible and concrete.

CHADS2VASC2-SCORE AS PREDICTOR FOR STROKE OUTCOME IN PATIENTS WITH ATRIAL FIBRILLATION?

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Background: Atrial fibrillation (AF) is a major source of cardioembolic stroke. Several scores try to improve the ability to predict the stroke risk in individual patients with AF. The CHADS2VASC2-Score is an advancement of the CHADS2-Score and is based on two groups of risk factors: definitive risk factors like previous stroke or transient ischemic attack (TIA) and/or age >65/75 years and female gender as well as vascular risk factors. According to a numeral score it is possible to characterize patients as low, intermediate and high risk. We evaluated the predictive value of this score with view to clinical outcome after acute stroke.

Methods: In 2009 we prospectively collected in our stroke data registry 174 consecutive patients with AF and acute stroke admitted to our stroke center. All patients were classified as C1 with the ASCO-Score, none was scored as A1, S1 or O1. All patients were also scored for their individual stroke risk using the CHADS2VASC2-Score. Outcome was documented from the NIHSS, modified Rankin Scale (mRS) and the Barthel-Index on admission and discharge.

Results: Out of 174 patients with AF and acute ischemic stroke 157 patients had a CHADS2VASC2-Score >2 points. Only 17 patients showed a CHADS2VASC2-Score ≤2 points, no patient had a score with 0 points. 28 patients were on an existing oral anticoagulation therapy (15 efficient anticoagulated) at onset of symptoms. The 17 patients with the CHADS2VASC2-Score ≤2 points had a significant lower NIHSS (p=0,007) and a significant higher Barthel-Index (p=0,001) on admission and a lower mRS on discharge (p=0,003).

Conclusion: The CHADS2VASC2-Score may not only identify patients with AF and a high risk for thrombembolic events but may also predict outcome of acute stroke. A higher CHADS2VASC2-Score was correlated with a higher NIHSS, a lower Barthel-Index and a higher mRS. This may be due to a higher grade of atherosclerosis which promotes the attachment of the thrombus.

PREDICTIVE VALUES OF EARLY IMPROVEMENT AFTER IV RT-PA

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Introduction: Thrombolytic therapy with intravenous rt-PA (IV-tPA) within 4.5 hours of stroke onset has demonstrated its effectiveness. Clinical improvement at 24 hours of IV-tPA is a marker of favourable outcome, but little data exists assessing early recovery and its prognosis value.

We studied the clinical course with the help of the National Institute of Health Stroke Scale (NIHSS) in the early hours after IV-tPA to identify predictive values for a good recovery.

Methodology: Retrospective study of IV-tPA procedures at University Hospital of Limoges between January 2005 and December 2008. The outcome is determined using the modified Rankin Score (mRS) and early clinical improvement by the NIHSS at 15, 30, 60, 120 and 180 minutes.

Results: During the study period, 103 patients underwent treatment with tPA-IV with a median NIHSS of 12 (SD 5.9). Among these patients, the rate of bleeding complications was 7.8% and mortality rate of 13%. 39 patients had a good prognosis (mRS 0-1). Over time, improvement in NIHSS became statistically different between the two groups from the first hour after IV tPA (NIHSS 2.51 - SD 3.38 - vs 0.95 - SD 2.52- points). A decrease of 4 points or more from the NIHSS at the first hour after IV tPA was correlated with percentages of good evolution from 75% to 93.3%.

Conclusion: Clinical recovery appears quite early after tPA-IV. Since the first hour after tPA-IV, a group of unfavourable outcomes can be identified, of which we will discuss other of revascularization techniques.

APPROBATION OF NATIONAL INSTITUTE OF HEALTH STROKE SCALE LATVIAN VERSION, GENDER AND AGE IMPACT ON THE TEST RELIABILITY

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Background: The National Institutes of Health Stroke Scale (NIHSS) is widely used in clinical trials and practice to assess stroke-related neurological deficit, outcome, the evolution and degree of recovery. At the year 2009 was started a development of NIHSS Latvian version (NIHSS LV). The original English NIHSS version was translated into Latvian according Latvian grammar, phonetic and semantic principles. During NIHSS LV approbation was assessed an inter-rater agreement of NIHSS LV points' ratings between two independent examiners and also was analyzed age and gender impact on inter-rater agreement of the test.

Methods: In the research 160 Latvian speaking stroke patients (mean age 72,2±11,2, 56% female, 82% anterior circulation CI), were scored by each examiner independently. Both patients' examiners verified their knowledge by on-line certification test of the original NIHSS and received the Certificate.

Data was analyzed using Wilcoxon Signed Rank test and Kappa statistics for whole group and subgroups (age, gender) as well. All data was estimated at the level of significance p=0,05.

Results: Whole group: 1.a: κ=0,95, Z=0,57, p=0,56; 1.b: κ=0,89, Z=1,66, p=0,09; 1.c: κ=0,94, Z=0,57, p=0,56; 2.: κ=0,96, Z=1,41, p=0,15; 3.: κ=0,97, Z=1,34, p=0,17; 4.: κ=0,94, Z=1,63, p=0,10; 5.a: κ=0,98, Z=1,00, p=0,31; 5.b: κ=0,95, Z=1,70, p=0,08; 6.a: κ=1, Z=0, p=1; 6.b: κ=0,96, Z=0,57, p=0,56; 7.: κ=0,94, Z=0,57, p=0,56; 8.: κ=0,92, Z=1,26, p=0,20; 9.: κ=0,97, Z=0,82, p=0,41; 10.: κ=0,95, Z=2,00, p=0,05; 11.: κ=0,97, Z=1,41, p=0,15. For total test Z=1,42, p=0,16.

Age subgroup: >65 years: κ ranking from 0,70 to 1, Z=0, p=1; ≤65 years: κ ranking from 0,92 to 1, Z=0,56, p=0,58.

Gender subgroup: male: κ ranking from 0,86 to 1, Z=0,97, p=0,33; female: κ ranking from 0,92 to 1, Z=1,06, p=0,29.

Conclusions: NIHSS LV inter-rater agreement for the whole group as well as for age and gender subgroups is significantly high. Neither patients' age nor gender influenced reliability of NIHSS LV and the test can be used for assessment of Latvian speaking stroke patients.

CLAF CIRCUMFERENCE AND PROGNOSIS OF ACUTE ISCHEMIC STROKE: WINDOW OF SARCOPENIA AND STROKE

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Background & Methods: The body composition and fat distribution are of major importance in determining vascular risk factors. Cerebrovascular events are known to be strongly associated with abdominal obesity, which is commonly represented by anthropometric markers such as waist circumference and waist-to-hip ratio. Furthermore, it has currently been suggested that peripheral fat mass may exhibit antiatherogenic effect, probably due to different metabolic process and due to its attribution to lean mass. However, studies relating this notion to ischemic stroke is scarce at the present. The aim of this study was to examine the association of ischemic stroke with calf circumference (C.C.), which is an uncommonly used anthropometric marker representing peripheral adiposity.

Results: 390 acute ischemic stroke patients were admitted during above period. 75 patients were excluded due to past stroke history. 8 patients with complicated disease affecting calf circumference and 2 patients under 20 years old were excluded. Finally a total of 304 patients (mean age 65.62±12.37, male 175, 57.6%) aging from 32 to 94 years old were enrolled in the study. The average calf circumference was 33.49±3.60 centimeters. Older patients had smaller C.C (p<0.001). C.C showed significant positive correlation with A.C (p<0.001). Patients showed smaller C.C presented more severe stroke (p=0.001). The average C.C showed statistical difference between the good and poor outcome groups classified by 3-month mRS; smaller measurement in the poor-outcome group (p=0.004).

Conclusion: Through the current study, it can be suggested that a positive correlation exists between the C.C. and functional outcome of ischemic stroke. Measurement of C.C. should be promoted, because it is helpful in predicting the functional outcome after first ischemic stroke attack, and it can be easily and noninvasively measured in clinical fields.

Stroke prevention

583 Stroke prevention

HOW DO THE VERY ELDERLY WITH ATRIAL FIBRILLATION FARE IN AN OUTPATIENT WARFARIN CLINIC?

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Introduction: Warfarin is effective in reducing the risk of stroke in atrial fibrillation in the very elderly. This survey aimed to define characteristics and problems of patients aged ≥80 attending an outpatient anticoagulant monitoring service (AMS) in a university hospital.

Methods: All patients aged ≥80 with atrial fibrillation attending the AMS from October 2007 to March 2008 were included. Data were collected from AMS written and computer records.

Results: 226/1410 (16%) patients were aged ≥80. 168/226 (74%), average age 85.8±3.1 years, had atrial fibrillation. Average age of commencement was 81.3±4.5 years. Average length of time on warfarin was 57±39 months. 53% of patients managed their own warfarin and took instructions for dosing. The rest relied on relatives or carers for dosing instructions.

In the entire period on warfarin, 61% of patients had problems including bleeding, bruising, falls, difficulty with transport, medication interactions and erratic International Normalized Ratio (INR) readings. 11/168 (7%) patients had INR readings of >8.0, necessitating emergency department assessment for reversal with vitamin K. The AMS staff had concerns with difficulty contacting 21/168 (13%) patients with elevated INRs and missed appointments in 19/168 (11%).

In the 6 months, only 45% remained within target INR range of 2.5 (±0.75) in 90-100% of 10 consecutive readings. 16% of patients were within target INR in ≤60% of readings. 14/168 (7%) patients died, one from a subdural haemorrhage post fall. 23/168 (15%) were admitted to hospital.

Discussion: The findings illustrate significant difficulties encountered by this elderly, vulnerable age group in proven effective treatment for patients with atrial fibrillation. Changes need to be made to increase resources for monitoring in the community, including home visits, portable INR monitors and point-of-contact dose adjustment. Patients should be assessed carefully for risk to benefit ratio.

584 Stroke prevention

DIFFERENT EFFECT OF CAROTID ANGIOPLASTY AND STENTING ON CHANGES IN BAROREFLEX SENSITIVITY: A ONE-YEAR LONGITUDINAL STUDY

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Background and purpose: The long-term cardiac autonomic activities after carotid angioplasty and stenting (CAS) remain unclear. Therefore, we investigate the cardiac autonomic activities longitudinally in patients undergoing CAS.

Methods: A total of sixty-three patients (all male, mean age: 77.3±6.3 years, range: 51-86) were studied prospectively. Cardiac autonomic activities were represented by the measurement of baroreflex sensitivity (BRS). Instantaneous systolic blood pressure (SBP) and heart rate of all participants were assessed noninvasively using servo-controlled infrared finger plethysmography. The fluctuation in SBP as well as interpulse interval (IPI) was divided into three components at specific frequency ranges by fast Fourier transform as high-frequency (HF) (0.15 to 0.4 Hz); low-frequency (LF) (0.04 to 0.15 Hz); and very-low-frequency (VLF) (0.004-0.04 Hz).

The BRS was expressed as (1) Transfer function with its magnitude in the HF and LF ranges, (2) BRS index alpha, and (3) regression coefficient by sequence analysis. All parameters were followed at baseline, 1, 3, 6 and 12 months after CAS.

Results: Of the 63 patients, 28 had left ICA stenosis and 35, right ICA stenosis. Post-operatively, All the BRS indices, including the magnitude of SBP-IPI transfer function at LF and HF ranges, the computed BRS index alpha, and the linear regression analysis of beat-to-beat fluctuation in SBP and IPI signals, revealed the identical Results: the values of BRS decreased significantly 1 month after stenting and returned to baseline levels six months after CAS. There was no significant difference in BRS changes between right and left sided stenting.

Conclusions: CAS Results significant BRS indices decrease, but they are likely to return to baseline values 6 months after stenting.

585 Stroke prevention

ORAL ANTI-COAGULATION IN THE PREVENTION OF STROKE IN ATRIAL FIBRILLATION: A SURVEY OF PRIMARY CARE PHYSICIANS

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Background: Atrial Fibrillation (AF) is the commonest cardiac arrhythmia; it increases the risk of Stroke six fold, while also leading to strokes with worse prognosis. Although clear guidance exists to recommend Oral Anti-Coagulation (OAC) which reduces the risk of stroke by up to 70%, there is evidence it is not prescribed in up to 40% of those patients. We have found the incidence of AF in our stroke patients over 12 months to be significantly higher than the national average (25.9% Vs 15%) and that very few patients were prescribed OAC despite a diagnosis of AF. We aimed to study the low prescribing of OAC amongst local primary care physicians, and what patient and/or physician factors were involved.

Methods: A postal tick box survey was sent to all local General Practitioners (GPs), giving 16 common reasons for not prescribing OAC in AF, including Terminal Illness, Dementia, Recurrent Falls, Recent G-I Bleed, old Age, Patients' Refusal and non-compliance. We asked what GPs considered to be their top 3 reasons. 62 GPs responded to questionnaire.

Results: around 75% of GPs did not consider OAC in patients with any of the following conditions: Terminal Illness, Dementia, Recurrent Falls, Recent GI Bleed, or if the patient refused OAC. Further analysis showed that patient related factors (Refusal, non-compliance and logistics of monitoring) only accounted for 32% of cases where OAC would not have been prescribed. Overall, recent GI bleed was the commonest reason that GPs did not prescribe OAC.

Conclusions: Our survey showed that the low uptake of OAC in primary care is primarily due to physician preference rather than patient choice. Some of the risks associated with OAC were overestimated by GPs without using a risk assessment tool, while some patients may have refused OAC due to lack of accurate information.

586 Stroke prevention

CONTROL OF MAIN RISK FACTORS AFTER FIRST EVER ISCHEMIC STROKE ACROSS FOUR EUROPEAN COUNTRIES: DATA FROM THE STROKE SPECIFIC MODULE OF EUROASPIRE II

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Background: Previous cross-sectional surveys in different European countries (EUROASPIRE) demonstrated a high prevalence of modifiable risk factors, unhealthy lifestyle and inadequate drug treatment in coronary heart disease patients. Comparable data for ischemic stroke are lacking.

Methods: A stroke specific module was introduced to the core EUROASPIRE III survey in four European countries between 2006 and 2008. This multicentre cross-sectional study included consecutive ischemic stroke patients between 6 and 36 months after the first event. Data were obtained from medical records and from patient interviews and examinations including measurements of blood pressure, weight and height, carbon monoxide in breath and venous blood samples using standardised Methods from EUROASPIRE surveys.

Results: A total of 895 patients were recruited in Croatia, Czech Republic, Germany and Poland. Median age was 68 years, 38% were female; average time from stroke event to interview was 547 days. At interview, 17% of stroke patients smoked cigarettes, 35% had a body mass index ≥30 kg/m², 63% had blood pressure ≥140/90 mmHg (≥130/80 in people with diabetes), and 49% had a total cholesterol ≥5.0 mmol/l (≥ 4.5mmol/l in patients with diabetes). There were statistically significant differences between the countries in the prevalence of smoking (p=0.04) and raised cholesterol (p<0.03). Antiplatelet drugs or oral anticoagulants were used by 87%, antihypertensive medication by 85%, and statins by 54% of patients. In 34% of patients on antihypertensive and 63% on lipid-lowering medication, blood pressure and cholesterol target values were achieved, respectively; 46% of patients who had smoked prior to the stroke event quitted smoking.

Conclusion: The EUROASPIRE III stroke specific module shows that secondary prevention and risk factor control in patients after ischemic stroke need to be improved with about half of patients not achieving targets defined in current guidelines.

587 Stroke prevention

IS F.A.S.T EFFECTIVE ENOUGH? – NORTHAMPTON DISTRICT GENERAL HOSPITAL EXPERIENCE

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Introduction: The FAST (Face Arm Speech Test) campaign is one of the major approaches by Stroke association UK in the recent years in order to improve the public awareness of the signs of stroke and get help swiftly and thereby receive the early treatment it warrants.

This study Aims to look at the impact of FAST campaign by means of a questionnaire survey among post stroke patients and carers /family members in inpatient stroke unit and outpatient setting at Northampton General Hospital.

Method: Patients with diagnosis of acute stroke/transient ischemic attack and their carers/family members at Stroke unit and daily TIA clinic were chosen randomly for the study between Sep'2010 -Nov'2010. Eligible participants were given a questionnaire form and a sealed envelope for completed questionnaires.

Results: Among 100 respondents, 88% were patients and 12% carers and 60% were in the above 70 years age group and females.Only half of the respondents (53%) were aware of the FAST campaign and mode of awareness was through TV adverts. FAST awareness was not related to their educational Background. Only 40%(n=21) of those who were FAST aware found it was useful in diagnosing signs of stroke and yet a significant proportion of them called their GP as apposed to calling 999. Nearly 40% of the GP receptionists contacted by respondents did not think stroke was a medical emergency.

Conclusion: In our study we found nearly half of the respondents were unaware of FAST campaign, hence there is room for new innovative ways of educating those at risk of stroke and primary care allied health staff. We plan to hold regular educational sessions for primary care staff and general public and re audit in 6 months time.

588 Stroke prevention

MODIFIABLE LIFESTYLE BEHAVIOURS INCLUDING DIET ACCOUNT FOR MOST CASES OF SUBARACHNOID HAEMORRHAGE: A POPULATION-BASED CASE-CONTROL STUDY

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Background: We aimed to confirm smoking, hypertension and alcohol as the main causal risk factors, and explore the hypothesis that other modifiable lifestyle factors (including diet) may underpin a substantial proportion of the population attributable risk (PAR) of subarachnoid hemorrhage (SAH).

Method: In a prospective, multi-centre, population-based, case-control study, information on smoking, hypertension, physical activity, diet, alcohol, body mass index, and family history, were obtained from 432 incident SAH cases and 473 frequency-matched community-based SAH-free controls. Multivariate analysis was used to identify PARs for SAH.

Result: Smoking and history of hypertension accounted for 30% (95%CI 23-37%) and 21% (10-30%) of SAH, respectively. Additionally, 25% (11-37%) and 15% (5-24%) of SAH were attributed to drinking skim or reduced fat milk, or eating fruit, <1 weekly, respectively, while the PAR was 13% (5-21%) for eating either the fat on meat or skin on chicken >4 times weekly. Among people with a history of hypertension, frequently adding salt to food was associated with an increased risk of SAH, irrespective of whether they were (OR 2.58, 95%CI 1.29 to 5.13) or weren't (OR 2.88, 95%CI 1.46 to 5.70) currently taking antihypertensive treatment.

Discussion: Smoking cessation and blood pressure control are the most important strategies to prevent SAH. However, modest additional benefits are likely to be appreciated from the adoption of healthy lifestyles that include drinking skimmed/ reduced fat milk, eating fruits regularly, and removing the fat from meats before consumption.

589 Stroke prevention

EARLY SLEEP APNEA MONITORING IN PATIENTS WITH ACUTE CEREBRAL ISCHEMIA

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Background: Sleep apnea (SA) in acute cerebral ischemia is associated with an increased risk of stroke recurrence. An early screening for SA is rarely considered in acute ischemic stroke (AIS) patients. The first goal of this study was to evaluate prevalence and clinical presentation of SA in this patient population, as well as the feasibility of a sleep apnea monitoring in the acute setting of stroke.

Methods: We studied consecutive patients with acute cerebral ischemia. Clinical and sleep-related data (Epworth Sleepiness Scale [ESS]) were recorded at baseline. All patients underwent overnight cardiorespiratory monitoring within 3±2 days of symptom-onset. Feasibility was defined as an analyzable study assessed by a sleep neurologist or a stroke fellow.

Results: Of 48 patients (88% AIS, 12% TIA), 46% were male, median age was 67 (range 44-75), mean BMI 27.3±4.0, median NIHSS 1 (range 0-15), median ESS 5 (2-13), median apnea-hypopnea-index (AHI) 23 (2-71). Ninety percent (43/48) of the sleep studies performed were analyzable, (100% in TIA, 90% minor stroke, 83% major stroke). Nearly 91% (39/43) had AHI≥5; 21% (9/43) mild, 40% (17/43) moderate, and 30% (13/43) severe SA. Of the 5/48 that did not have analyzable studies, 20% (1/5) was due to flow missing, 40% (2/5) to SO2 missing, and 20% (1/5) to patient compliance. In the entire study population, no significant correlation was found between BMI (r= –0.184, p=0.238) or daytime sleepiness r= –0.101, p=0.519) and AHI≥5. In addition, there was no significant difference in the prevalence of SA in TIAs, minor strokes, major strokes (100%, 100%, and 88%, respectively).

Conclusion: Early SA monitoring was feasible in nearly all patients with acute cerebral ischemia. Given the high prevalence and atypical presentation of SA in this patient population, early monitoring for SA should be considered in all ischemic stroke patients. Further studies are required to determine its impact on stroke outcome and recurrence rate.

591 Stroke prevention

IMPACT OF IMPLANTABLE HOLTER ECG MONITORING ON DETECTION OF PAROXISMAL ATRIAL FIBRILLATION IN PATIENTS WITH CRYPTOGENIC STROKE

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Background: Although atrial fibrillation (AF) is the most common cause of cardioembolic stroke, the 24-hour (24h) Holter electrocardiogram (ECG) only detects AF in less than 5% of strokes of undetermined etiology. The detection of AF in the general population has been increased with prolonged monitoring with an implantable Holter (IH) ECG when compared to 24h Holter ECG. However, its diagnostic value in patients with stroke remains unknown. The aim of this study was to determine the performance of IH in the detection of AF in patients with ischemic stroke of undetermined etiology.

Methods: We prospectively studied 20 patients with ischemic stroke of undetermined etiology. After complete diagnostic workup including lab tests, carotid and transcranial Doppler, basal ECG, two 24h Holter ECG, TT and TE echocardiography, all patients underwent subcutaneous Holter implantation (Reviel TX). We collected demographic and clinical data as well as neuroimaging, ECG and echocardiography variables at baseline that may potentially predict further AF during follow-up. All patients were followed-up for a minimum of 6 months to determine the incidence of paroxysmal AF and clinical outcome.

Results: Mean age was 63.4±20 years, and 11 (55%) patients were male., 14 (70%) of infarcts were located in the anterior (40% superficial), 3 (15%) posterior circulation and 1 (5%) in both vascular territories. After Holter implantation, the mean time of follow-up was 10.6±3.7 months. AF was detected by IH in 4 (20%) patients and mean time AF diagnosis was 4 months. In 3 (75%) patients AF was detected in the first 3 months after implantation. Two patients referred palpitations at the time of the AF episode. Anticoagulant therapy was started in all patients diagnosed of AF by HI.

Conclusion: The use of IH increases up to 20% the diagnosis of paroxysmal AF during the first 6 months after acute cryptogenic stroke, allowing an appropriate treatment in these patients.

592 Stroke prevention

BARCELONA-ASYMPTOMATIC INTRACRANIAL ATHEROSCLEROSIS STUDY (ASIA STUDY): METABOLIC SYNDROME AND BIOLOGICAL MARKERS

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Objectives: Association between metabolic syndrome (MS) and symptomatic intracranial atherosclerosis is well established. We aimed to determine if this association is already present at the asymptomatic stage of intracranial atherosclerosis (ASIA).

Methods: Crossover, population-based study of a representative sample of 1503 individuals (randomly selected from a reference population of 600.000 inhabitants) aged older than 50 with a moderate-high vascular risk and prior history of neither stroke nor ischemic heart disease. Anthropometric, clinical data and blood samples were collected at baseline. Intracranial atherosclerosis was assessed by transcranial Color-Coded Duplex (TCCDx) according to systolic peak-spectrum criteria. Echo-contrast was used in cases with a deficient bone window. The following inflammatory, endothelial, haemostatic and metabolic markers were determined: C reactive protein (CRP), asymmetric dimethylarginine (ADMA), plasminogen activator inhibitor-1 (PAI-1), resistin.

Results: A total of 933 subjects (64% men, mean age 66.3 years) were included in the study. Diagnosis criteria of MS were fulfilled in sixty-nine per cent of subjects, and 8.4% had asymptomatic intracranial stenoses. MS was independently associated with the presence of ASIA after adjusting by age and sex (OR 2.75; CI 1,42-5,34; p=0.003).Although PAI-1 levels were significantly higher in MS (p<0.001), they were not associated with ASIA. CRP, resistin and ADMA levels were associated with neither MS nor ASIA.

Conclusion: Metabolic syndrome was found to be an independent risk factor for asymptomatic intracranial atherosclerosis. New biological markers must be studied to better understand this association.

593 Stroke prevention

MAKING SENSE OF TIA: HOW PATIENT AND PARTNER PERCEPTIONS INFLUENCE PATIENT HEALTH BEHAVIOUR

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Background: This qualitative study explores patient and partner perceptions of transient ischaemic attack (TIA). TIA patients can reduce their risk of stroke but adherence to recommended medication and lifestyle change is suboptimal. Using Leventhal's Common-Sense Model two questions are addressed: (a) How do patients and partners make sense of a diagnosis of TIA? (b) How do these perceptions influence patients' health behaviours?

Methods: A purposive sample of 6 patients and partners was recruited from a larger study. Three patients with higher mean age and ABCD2 score refused. Participants were White British/Irish with no history of stroke. Patients had a first diagnosis of TIA and were not admitted as inpatients. Participants' mean age was 56.6 yrs,

mean ABCD2 risk was 3.16. Participants were interviewed 12 -16 weeks after diagnosis using semi-structured interviews. Interviews were transcribed verbatim and analysed separately by two researchers using Interpretative Phenomenological Analysis.

Results: Three main patient themes emerged: Symptom Experiences varied and did not match prior knowledge of stroke resulting in delay in seeking treatment; Ambivalence about Diagnosis was apparent either through challenging the medical examination, recall bias for clear brain scan Results or minimising the diagnosis; Self-concept as "ill" or "well" separated adherent from non-adherent patients. Two partner themes, Patterns of Support and Uncertain Future influenced behaviour and emotions in patients.

Conclusion: Patient health behaviours after TIA are influenced by their illness perceptions and are also explained in terms of self-rated health, cognitive bias, purposiveness, optimism and partner support. Clinical implications were evident in poor knowledge of stroke related symptoms, bias in favour of brain scans and neglect of blood Results, and ambivalence in the context of transient symptoms and absence of feedback to motivate adherence to behaviour change.

594 Stroke prevention

RISK OF VERY EARLY RECURRENT CEREBROVASCULAR EVENTS IN SYMPTOMATIC CAROTID STENOSIS – IS THERE A NEED FOR CAROTID INTERVENTION WITHIN THE FIRST HOURS AFTER SYMPTOM ONSET?

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Background: The very early risk of recurrent cerebrovascular events in hospitalised patients with symptomatic carotid stenosis (SCS) is largely unknown. Therefore, the benefit from emergency carotid intervention (CI) within the first hours after symptom onset in patients with SCS is undetermined.

Methods: Ninety-four patients with a non-disabling stroke, transient ischemic attack (TIA) or amaurosis fugax (AF) and SCS ≥ 50% underwent CI (90% carotid endarterectomy, 10% carotid artery stenting) within 14 days of symptom onset at our stroke unit. The recurrence rate of stroke, TIA or AF was determined at 48h, 7 and 14 days. In case of CI, procedure-related cerebrovascuar events were assessed.

Results: Mean time from admission to CI was 7.1d (SD ±6.86). 21 patients (11.9%) were treated within 48h of symptom onset. Overall 15 recurrent cerebrovascular events occured in 12 patients (12.1%) between admission and CI: Two strokes-in-progression (2%), 5 TIAs (5.1%) and 1 AF (1%) within the first 48h (total 8.1%); 1 stroke (1%) and 1 TIA (1%) be-tween 48h-7d (total 2%) and 5 TIAs between 7-14d (5.1%). The overall risk of procedure-related cerebrovascular events was 4.3% (3 strokes and 1 TIA). Patients with CI < 48h were not at increased peri-procedural risk (4.8% vs. 4.1%, P=0.896).

Conclusions: The risk of early stroke recurrence in hospitalised patients with symptomatic carotid stenosis was quite low. Further studies are needed to determine whether very early CI may further decrease the rate of recurrent stroke without increasing peri-procedural complications.

595 Stroke prevention

POOR CONTROL OF RISK FACTORS IN RECURRENT STROKES AND EFFECT OF AWARENESS CAMPAIGNS

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Background: The still high rate of recurrent stroke is challenging. The stroke risk factors should be better controlled and notably patients' adherence to treatment should be improved. We assessed the rates of non controlled risk factors and the use of antithrombotic therapy at the time of the recurrent stroke and compared 2 periods of time to estimate the effect of regional stroke awareness campaigns.

Methods: The risk factors and cardiovascular treatment at the time of recurrence were prospectively recorded. A total of 241 patients (men, 56.0%; mean age, 72.8±12.9 years) with a recurrent stroke or TIA were evaluated between Jun. 2005 and Feb. 2008 (n=168) and between Jan. 2009 and Nov. 2010 (n=73). The rates of uncontrolled risk factors, the proportion of antithrombotic therapy taken before the recurrence, and the rate of patients on anticoagulant therapy with a INR value < 2.0 were calculated in the total population and compared between the 2 inclusion periods.

Results: The risk factors already known before the recurrence were hypertension in 82% of patients, hypercholesterolemia in 48%, and diabetes in 22%. In the total population, blood pressure was not satisfactorily controlled in 29% of patients and LDL-cholesterol was higher than 100 mg/dl in 45%. Diabetes (GlycHb > 6.5%) was not controlled in 52% of diabetics. A significant minority of patients (12%) were not taking any antithrombotic agent despite a history of stroke or TIA. In 23 patients on coumarin therapy the INR was <2.0 in 61% of them. The rates of uncontrolled hypercholesterolemia, diabetes, and non use of antithrombotic therapy significantly decreased in the 2nd study period compared to the 1st period.

Conclusions: This study shows that the risk factors remain poorly controlled despite a history of stroke or TIA, but awareness campaigns and the use of well-designed discharge forms documenting the individual cardiovascular risk and therapy may improve prevention.

596 Stroke prevention

CAN WE IMPROVE CEREBROVASCULAR RISK REDUCTION IN REAL-LIFE? A SINGLE CENTRE'S EXPERIENCE

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Background: The study presents the effects of a standardized, cerebrovascular disease prevention program to improve adherence and reduce stroke recurrence rates. Influence on functional outcome of cardiovascular risk factors and patient characteristics for nonadherence were identified.

Methods: A 1-year cohort of patients with an ischemic cerebrovascular accident was prospectively followed. A standardized follow-up program (at 3, 6, 12 and 24 months) was performed. Self-reported persistence and the factors associated with nonpersistence were examined at each visit.

Results: A total of 132 patients were eligible for analysis. On admission, the majority of the patients had a minor stroke (NIHSS<10 =79%). At discharge, antiplatelet or anticoagulating drugs were given in 98%, antihypertensive drugs in 97%, antilipidemic in 84% and antihyperglycemic drugs in 15%.

At 24 months, 71% of the patients persisted all the secondary prevention medications prescribed at discharge. This adherence was greatest for antiglycemic drugs (97%), antiplatelet drugs (95%) and less for antihypertensive (76%) and antilipidemic drugs (71%). Due to these therapeutic interventions systolic blood pressure was normotensive in 69% of the patients, mean total cholesterol lowered from 199mg/dl at onset to 154mg/dl and 73% patients on anticoagulants had a therapeutic INR. Other, non-pharmacological measures as smoking cessation, weight control and regular exercise (>1h/week) were achieved in at least 38%.

A 2-year all-case-fatality was 25% and with a stroke recurrence rate of 14%. Mortality and stroke recurrence were significantly associated with a higher NIHSS, age <75y and elevated systolic blood pressure (>160mmHg) at 6 and 12 months (p<0.01).

Conclusions: Persistence was high with both pharmacological and non-pharmacological strategies during 24 months post discharge. These first data of adherence to secondary prevention in Belgian clinical practice illustrates the importance and feasibility of an intense, vascular risk management. Knowledge of the complexity of patient and caregiver characteristics is essential in the promotion of adherence to secondary prevention measures.

597 Stroke prevention

KNOWLEDGE OF STROKE RISK FACTORS AND WARNING SIGNS IN IRELAND: DEVELOPMENT AND APPLICATION OF THE STROKE AWARENESS QUESTIONNAIRE (SAQ)

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Background: Lack of awareness of stroke warning signs is a significant cause of delay in seeking medical attention, thus contributing to treatment delay and limiting potential for emergency intervention, and negatively impacting on stroke outcome.

Aim: This study aimed to assess knowledge of stroke risk factors and warning signs, and likely response to stroke in the adult population in Ireland.

Methods: A nationally representative sample comprising 1000 members of the general public were interviewed by telephone in June 2009 using quota-based population sampling of adults aged 18+ years. A questionnaire was developed for purposes of this survey (the Stroke Awareness Questionnaire) using questions derived from existing national and international surveys, and questions developed de novo for purposes of the survey.

Results: Two or more risk factors for stroke were correctly identified by 70% of participants. Risk factors identified tended to be generic lifestyle risk factors. Over two-thirds of participants were unable to identify two warning signs for stroke. For the one-third of participants who could identify two or more stroke warning signs, there was no consistency in warning signs identified. If they thought they were having a stroke, less than 50% of participants stated they would contact emergency services. Overall, there were significant gaps in knowledge, particularly of stroke warning signs, with poorest levels evident in those aged 65+ years.

Conclusions: Awareness of stroke warning signs in adults in the Republic of Ireland was poor, as was awareness of the need to call emergency services. This lack of awareness in the general public is a major contributor to delay in seeking medical attention following stroke, with resulting implications for stroke outcome.

598 Stroke prevention

CHRONIC, MULTIDISCIPLINARY POST-STROKE CARE AND AEROBIC EXERCISE AFTER TRANSIENT ISCHEMIC ATTACK OR MINOR STROKE – BASELINE CHARACTERISTICS OF A PILOT STUDY (MOTIVES & MOVEIT)

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Background: Patients with a transient ischemic attack (TIA) or minor stroke have an increased risk of recurrent stroke, myocardial infarction and vascular death. Physical inactivity is an independent modifiable risk factor for stroke. The majority of patients with stroke are physical inactive and have reduced cardiorespiratory fitness. Cardiac rehabilitation, including an exercise program, reduces mortality in patients after myocardial infarction. This has not been investigated in patients after TIA or stroke.

Objectives: We performed a pilot study to determine the feasibility and safety of a randomized controlled trial consisting of a post-stroke care program and an exercise program in patients with a TIA or minor stroke. The baseline data of the pilot study are presented.

Baseline data	N=20
TIA/minor stroke	40% TIA
	60% minor stroke
Sex	70% male
Age, median (IQR)	64 (56-70) years
NIHSS, median (IQR)	0 (0-1)
VO2max, median (IQR)	22 (16-24) ml/kg/min
Maximal heartrate, median (IQR)	136 (119-149) /min
	85% age-predicted heartrate
Reason for exercise termination	35% leg fatigue
	25% hypertensive response
	5% ECG-abnormalities

IQR = interquartile range.

Methods: Twenty patients with a TIA or minor stroke without known cardiac contra-indications for physical activity were randomized to either an outpatient post-stroke care program during 1 year or this program in combination with an 8-week aerobic exercise program. Data were collected at baseline and will be collected 6 and 12 months after the event, and include measures of secondary prevention, maximal exercise capacity, and cognition.

Results: All patients completed the maximal exercise test and achieved a heart rate indicating maximal exercise. The median exercise capacity (VO2max) was 22 ml/kg/min, lower than the 10th percentile of age- and sex related normative values. Exercise termination was often due to abnormal blood pressure response or leg fatigue. No adverse events occurred during or after the test.

20 adult patients
- TIA or minor stroke
- No known cardiac contra-indications

↓

Randomised
- Stroke care program
- Stroke care program and aerobic exercise intervention

↓

Referral to cardiologist, if
- Positive cardiac screening questionnaire
- Randomisation in aerobic exercise group

yes → / no →

17 patients seen by cardiologist
Ancillary tests
- 94% cardiac stress test
  - no abnormalities
- 18% echocardiography
  - 1 patient moderate left ventricular dysfunction

3 patients

↓

Conclusion cardiologist
No contra-indications for exercise intervention in all patients

↓

20 patients continuing in trial

Conclusions: Participation in an aerobic exercise program was possible for all included patients. An exercise program will thus be investigated in a future randomized controlled trial. Cardiorespiratory fitness was markedly impaired after TIA and minor stroke.

599 Stroke prevention

NORTH SHORE HOSPITAL STROKE AUDIT: 12 MONTH POST RAPID IMPROVEMENT EVENT

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Aim: To assess the long term effect of a Rapid Improvement Event (RIE) on improving delivery of care to stroke patients at North Shore Hospital (NSH) and identify if further actions needed to improvement from RIE.
Methods: Stroke patients admitted in the two months from 17.11.2009 were audited using the UK National-Sentinel-Stroke-Audit-Tool-2008. Key-performance-indicator outcomes were measured and compared against data with the NSH stroke register from 2007, previous two month NSH-audit immediately post RIE (audit-2008/2009).
Results: 70 patients from current audit was compared with 2007 stroke registry of 486 patients and 73 patients from 2008/2009 audit. Mean age for current audit was 76.4 years and 60% female. There was significant improvement in CT-scan within 24 hours of admission (93%vs.81%,P-Value=0.0379). No significant differences were found in Aspirin commenced within 48hrs of admission, Physiotherapy within 72 hours, Swallow test within 24hrs, Weighed at least once during admission, Rehabilitation goals agreed by multidisciplinary-team and Occupational therapy within 4 days when compared to previous audit immediately post RIE.
Conclusion: Developing organised stroke services has sustained improvements of process indicators of patients care. RIE appears to be a helpful tool to implement swift change. Periodic audit is needed monitor deficiency and develop future strategies of improving stroke care.

600 Stroke prevention

REASONS FOR FAILURE OF CONTROL TO HYPERTENSION IN PATIENTS WITH CEREBROVASCULAR DISEASE

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Background: Intensive blood pressure control has been shown to reduce risk of recurrent stroke and current international guidelines mandate lowering of blood pressure to what would be regarded as "normotensive" systolic levels for the general population. We have developed a system whereby tight blood pressure control may be achieved by regular monitoring and supervision of blood pressure in a nurse led clinic however a proportion of subjects still fail to meet guideline targets. We reviewed our data to determine the cause of these treatment failures.
Methods: Results on 150 consecutive patients attending a secondary prevention clinic for cerebrovascular disease were reviewed. This clinic is run by a clinical nurse specialist and all patients are subsequently discussed with a senior physician in stroke medicine and have their medication titrated. Patients are seen and undergo ambulatory blood pressure monitoring on a regular basis in order to record and maintain the mean 24 hour blood pressure within range.
Results: The data from consecutive 150 patients was analysed of whom 119 (79%) were hypertensive at baseline. We failed to lower mean 24 hour systolic Blood pressure below 140mmHg in 19 (16%) cases. The reason for the failure was as follows: 9 (47%) suffered symptomatic hypotensive episodes recorded on the monitor preventing further therapy. A further 3 (16%) had hypotensive episodes at other times. Three subjects (16%) were non-compliant with therapy, Two subjects (11%) had severe but asymptomatic carotid stenosis and two (12%) were of advanced age where very tight control was felt inappropriate. No patients were inadequately controlled through lack of therapeutic response. Median number of anti-hypertensive medications used was 2 (range 0-4).
Conclusion: The predominant reason for failure to reach guideline blood pressure levels in this population is blood pressure variability and symptomatic hypotension rather than failure of therapy.

601 Stroke prevention

A CALL FOR REORGANISATION OF SECONDARY PREVENTION

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Background: Literature on real life secondary prevention in stroke survivors is scarce and the Results are discouraging.
Methods: We conducted a follow up study of patients admitted with acute stroke in two Copenhagen Hospitals. Patients were interviewed during hospital stay and we collected data from medical files. One and 2 years after inclusion a study nurse visited patients in their homes. She measured blood pressure and filled in a questionnaire on patients' present medical history. Here we report the Results concerning hypertension (HT), diabetes (DM) and hypercholesterolemia (HC).
Results: Of 303 patients, 148 (49%) were women; mean age was 69.3 (12.9). At discharge 173 (57%) were hypertensive and of those 56 (32%) were without antihypertensive treatment. At 1-year follow up 37 of those (66%) remained untreated. Forty-four of 110 patients (38%) discharged without treatment were hypertensive at follow up and altogether 62% were hypertensive 1 year after stroke. At discharge 193 patients (64%) received a mean of 1.7 antihypertensive drugs. At follow up 216 patients (71%) were treated with a mean of 1.7 drugs. At baseline 31 patients (10%) had a history of DM, and 33 (11%) had the diagnosis at discharge. At follow up 37 (12%) reported having diabetes. Of 210 patients with HC 76 (36%) were untreated at discharge, and 56 (74%) remained untreated. After 1 year 29 untreated patients (39%) had had a check up of their blood cholesterol versus 85 (66%) of treated patients (p=0.001). A 2-year follow up of 274 of the patients revealed little change in HT, DM, and HC.
Conclusion: More than half the patients were hypertensive 1 year after stroke, and of those who left the hospital without treatment of HT or HC the majority remained untreated and received less attention in the primary care setting. DM was probably under-diagnosed. Secondary prevention clinics in the hospital setting might be the solution to these problems

602 Stroke prevention

EVALUATION OF STANDARDISED INTENSIVE CHRONIC CARE AFTER TIA AND STROKE

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Introduction: Patients with stroke or transient ischemic attack (TIA) have a high risk of recurrent stroke, myocardial infarction and death from vascular causes. It is thought that this risk can be decreased up to 80% by treatment with antithrombotics, antihypertensiva and statins, and by addressing life style factors. However, neurovascular care in the Netherlands is dominated by acute stroke care. Improving adherence to guidelines and lifestyle changes by standardised chronic post-TIA and stroke care might be a powerful way to increase efficiency of secondary stroke prevention. Therefore in our clinic all patients with TIA or stroke are invited to visit our outpatient clinic on a regular basis during the period of one year for a standardised intensive chronic care program.

Methods: To evaluate the effect of standardised intensive chronic care after TIA and stroke on secondary prevention, we retrospectively evaluated the medical charts of 52 consecutive patients with TIA or stroke. The primary outcome measure was the percentage of patients who achieved the combined targets for the use of antithrombotics, blood pressure (<140/90 mm Hg), and LDL-cholesterol (<2.5 mmol/L) after one year. Secondary endpoints were the individual components of the primary endpoint.

Results: Baseline characteristics of all patients are shown in table 1. Only 13 patients (25%) completed the follow up period of one year. As shown in figure 1, of the 13 patients who completed the follow up 31% reached the primary endpoint, all used antithrombotics, 38% reached the endpoint of a blood pressure <140/90 mm Hg and 69% reached the endpoint of a LDL cholesterol <2,5 mmol/L.
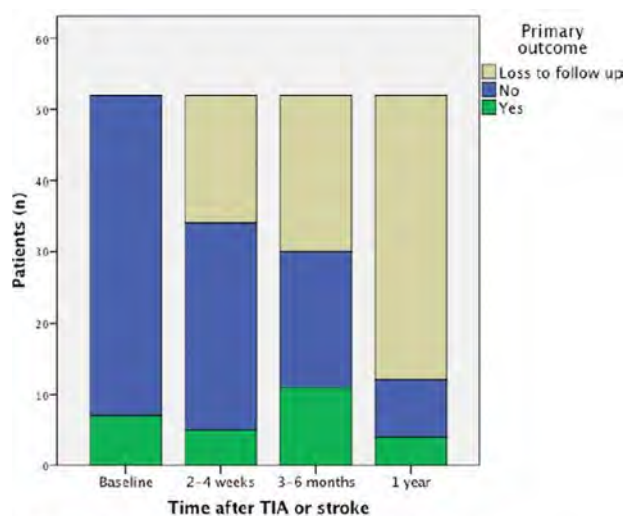
Figure 1. Primary outcome: patients who achieved the combined targets for use of antithrombotics, blood pressure <140/90 mm Hg, and LDL-cholesterol <2.5 mmol/L.

Table 1. Characteristics of study subjects

	n	%
Patients	52	100
Stroke	40	77
TIA	12	23
Mean age (y)	70	
Risk factors		
Hypertension	26	50
Diabetes	11	21
Smoking	15	29
Atrial fibrillation	8	15
History of cardiovascular disease	26	50

Conclusion: Despite the effort put into standardised intensive chronic care for our patients with TIA or stroke, secondary prevention is far from optimal. This is particularly due to the unexpected loss to follow up. It remains unclear if the loss of follow up is caused by patient or doctor related factors.

603 Stroke prevention

DETECTION OF CLOPIDOGREL RESISTANCE IN ISCHEMIC STROKE PATIENTS - COMPARISON OF LABORATORY METHODS

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Background: Clopidogrel, an irreversible inhibitor of platelet P2Y12 ADP receptor, is widely used as monotherapy or in combination with aspirin to reduce the risk of recurrent ischemic stroke. Although clopidogrel has potent antiplatelet effect, clinical studies suggest that approximately 10-30% of patients are resistant to the therapy. Although the identification of patients resistant to clopidogrel is of primary importance, comparison of Methods used for testing clopidogrel resistance in ischemic stroke patients has not been carried out.

Methods: The study population included 110 patients with non-cardiogenic ischemic cerebrovascular disease on clopidogrel monotherapy and 120 age and sex-matched controls. The effect of clopidogrel was tested by ADP induced platelet aggregation and secretion, VerifyNow P2Y12 assay, flow cytometric analysis of vasodilator stimulated phosphoprotein (VASP) phosphorylation and a newly developed P2Y12 receptor specific, modified platelet aggregation test. For each method, diagnostic cut-offs were determined according to the guidelines of Clinical and Laboratory Standards Institute.

Results: The ratio of clopidogrel non-responders varied between 10-54% depending on the method used. Approximately 50% of patients were found to be resistant by the traditional ADP aggregation and the VerifyNow tests. The newly developed method identified 25.9% of patients as non-responders, 32.6% as weak responders and 41.3% as strong responders. The best correlation was observed between this method and VASP phosphorylation (r=0.81, p<0.0001). No correlation was found between clopidogrel non-responsiveness and the use of statins or proton pump inhibitors.

Conclusion: We have developed a new, reliable test for monitoring P2Y12 receptor inhibition by platelet aggregation. Monitoring clopidogrel response by adequate Methods is essential as a subset of patients are unprotected by clopidogrel monotherapy.

604 Stroke prevention

HOW CLOSE ARE WE FROM ACHIEVING TARGET GOALS OF STROKE SECONDARY PREVENTION

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Background: Current guidelines recommend a set of target goals for effective secondary prevention after ischemic stroke. However, little is known about the rate of achievement of these target goals outside clinical trials. This study Aims to estimate the proportion of patients who achieved target goals.

Methods: We conducted a retrospective cohort study by identifying patients admitted to King Abdul-Aziz medical city in Riyadh from 2007 to 2009 due to ischemic stroke. Clinical, radiological and laboratory characteristics were reviewed. Electronic, follow up, records beyond six weeks after discharge were reviewed for blood pressure, LDL and HbA1c levels. Statins and antiplatelets therapy was assessed via pharmacy records. The target goals were blood pressure (BP) ≤130/85, LDL <1.7, HbA1c <0.07, and antiplatelets and statins therapy. Study was approved by local IRB.

Results: 215 patients were identified. Among 190 survivors, the mean age was 67±12 SD, 66% were males. At baseline, 81% had hypertension, 64% diabetes, 27% dyslipidemia, 8% atrial fibrillation and 34% old stroke. Also, 43.6% were on aspirin and 7% on clopidogrel. Mean follow up was 18 months. At least single BP measurement was found in 75% of our cohort, LDL 83% and HbA1c 67%. Considering those with no follow up data as if they did not achieve the target goals, 77% achieved BP, 68% HbA1c, 59% LDL target goals. Also, 98% and 68% were prescribed antiplatelets and statin therapy, respectively.

Conclusion: Secondary prevention of ischemic stroke is suboptimal. Significant portion of our cohort did not achieve the target goals as per guidelines. This might be due to failure of implementation, utilization and adherence of both patients and physicians. Strategies to overcome this issue should be implemented.

605 Stroke prevention

AN AUDIT OF ADHERENCE TO SECONDARY ISCHAEMIC STROKE PREVENTION IN A NIGERIAN GENERAL HOSPITAL SETTING

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Background: Health personnel, often without the involvement of a neurologist, care for approximately two-thirds of stroke patients. The goals of this survey were to evaluate the adherence to secondary preventive strategies with 1 year after ischaemic stroke and to identify possible causes of poor compliance with strategies.
Methods: We carried out a descriptive audit at a district general hospital in northeast Nigeria among 90 discharged ischaemic stroke patients at 1-year follow up. Patients who had suffered either acute ischemic stroke or transient ischemic attacks (TIA) were recruited at the medical outpatient clinic. The survey included whether the patient was prescribed antithrombotic treatment (aspirin and/or clopidogrel) and statins at discharge and reasons for non-compliance with these prescriptions both immediately after discharge and 1 year after discharge.
Results: None of the patients was reviewed by a neurologist. Of the 90 patients; only 67 (74%) were treated with aspirin alone. None had clopidogrel alone or combined with clopidogrel. During a mean follow-up of 3.5 months, 24 patients (36%) prematurely stopped treatment, 8 (11.9%) did so without a clear medical reason. Age > 60 years, no formal education, lack of care givers was independently associated with non-adherence. Of 10 (15%) patients on statins, 8 patients discontinued after a mean follow-up of 2 months.
Conclusion: Adherence to stroke prevention strategies was poor. Increased priority needs to be given to stroke prevention in developing countries, as this would lead to a reduction in the risk of dying as a result of stroke.

606 Stroke prevention

INTENSIVE CONTROL OF HYPERTENSION THROUGH A NURSE-LED SECONDARY PREVENTION CLINIC FOR CEREBROVASCULAR DISEASE

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Introduction: Blood pressure lowering is an effective intervention in reducing risk of future stokes in patients wit cerebrovascular disease. Guidelines now recommend control to levels that would historically have been considered "normotensive". To achieve these levels in a typical stroke population is challenging and requires frequent review and close supervision. To achieve this we established a nurse-led secondary prevention clinic including facilities to perform frequent measures of 24 hour blood pressure and provide both pharmacological and non-pharmacological interventions to lower blood pressure.
Methods: Results for 150 consecutive subjects attending the clinic were reviewed. Clinics were supervised by trained stroke physicians and blood pressure measurements were performed using British Hypertension Society approved ambulatory monitors using standard protocols. The patients' medications and any reasons for poor blood pressure control were also recorded.
Results: The data from 150 subjects was analysed, (M:F 81:69). 31 patients were normotensive (mean 24 hour blood pressure ≤135/85mmHg) at baseline. Of the remaining, 119 hypertensive subjects, 82 (69%) achieved blood pressure control as per ESO Guidelines, i.e.≤135/85mmHg and 97 (82%) patients (80%) achieved a blood pressure <140/90mmHg (ESC parameter of normal). The median number of anti-hypertensive medications needed to control blood pressure was 2 (range 1-5). Angiotensin converting enzyme (ACE) inhibitors were the most commonly prescribed medication (39%).
Conclusion: This study demonstrates that a supervised nurse led clinic is an effective means of achieving blood pressure control in subjects with cerebrovascular disease

607 Stroke prevention

AN EVALUATION OF THE FIRST NATIONAL MEDIA CAMPAIGN TO INCREASE STROKE AWARENESS IN IRELAND

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Background: Pre-hospital delay has been identified as a significant barrier to stroke care, with The Irish National Audit of Stroke Care reporting that only 5% of stroke patients present to an Emergency Department within three hours of symptom onset.

Aim: The first national campaign in Ireland to increase stroke symptom awareness (FAST - Irish Heart Foundation) was launched in May 2010. This study is an evaluation of the effect of this campaign on presentations with stroke-like symptoms to the Accident and Emergency (A&E) Departments of two Dublin hospitals - Beaumont Hospital and Connolly Hospital.
Method: An audit of all presentations to the two hospital A&E Departments with possible stroke or TIA related symptoms was conducted using a screening tool developed for this purpose. Evaluation of Wave 1 of the FAST campaign took place from March 1st 2010 to July 31st 2010, the FAST campaign taking place throughout three weeks of the month of May 2010. All case presentations to the two A&E Departments were reviewed. Cases pertaining to stroke and ambiguous cases were examined in detail.
Results: There were 417 presentations with "stroke-like" symptoms in the 5-month period. There was an observable trend of increased frequency of FAST related presentations, decreased time from symptom onset to A&E attendance and increased admissions during the campaign wave. However these differences were not statistically significant ($1\chi^2 = 5.54$, p<0.47, $2\chi^2 = 1.21$, p<0.54, $3\chi^2 = 5.83$, p<0.21).
Outcomes: There is evidence of initial campaign impact. However these observations subsequently decline, indicating that the desired campaign effect is not sustained following withdrawal of advertising. Evaluation of Waves 2 and 3 of the campaign is ongoing.

608 Stroke prevention

BLOOD PRESSURE LOWERING LESS SIGNIFICANTINT IN HYPERTENSIVE POSTSTROKE PATIENTS COMPARING TO HYPERTONICS WITH THE SAME DOSIS. NOT APPROPRIATE DOSIS OR ADEQUATE COMPENSATORY HEMODYNAMIC RESPONSE? LONG-TERM FELLOW UP

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Introduction: Despite EBM documented good effect of antihypertensive therapy, real life medicine (RLM) demonstrated low AH control in secondary CI prevention.
Aim: To compare effect of BP lowering drugs in isolated AH and hypertensive poststroke pts.
Material: 3554 out-ward patients with moderate AH (BP: 150.4/94.2 mmHg), BM: 28.9 were included in the prospective, multicenter, multidisciplinary open-labeled STAIRS study. Whole group divided into two subgroups: 1. hypertonics (AH) without complications (n=3292), mean age 59,2 yrs, male 49.6%, 2. hypertensive poststroke patients (CI+AH, n=262), mean age 69.3 yrs (p<0.001), male 50.4% (NS).
Methods: sBP/dBP monitored every 4-6 weeks, tChol, LDL, HDL, TGI, urea, uric acid, smoking, DM, BMI, GF were analysed before study and at the end of the 3rd and 6th months. All pts treated by monotherapy (Amlodipin/Lizinoprinol) and their combination.
Results: The group of CI+AH pts were 10 yrs older comparing to AH (p<0.001). DM in 13.7% vs 5.5% (p< 0.001), smoking 4.6% vs 7.5% (p<0.02). After 3 months signif. decrease in sBP, dBP, significantly less marked in Cl+AH (p=0.00001). LDL-chol increased, HDL-chol. decreased.
Interpretation: 1. Is it due to not appropriate therapeutic efficacy in poststroke pts? or 2. is it due to the compensatory mechanisms, guided by biological brain computer to prevent brain functions from BP lowering, consequently PP lowering and CBF lowering. Brain "rejected" significant BP lowering and prefers "gently" BP lowering, and "gently" BP keeping. Compensatory circulatory mechanisms prevent brain from PP lowering and CBF. lowering. Hypotensive reaction was associated with decreased glomerular filtration (p<0.00001).
Conclusion: Different blood pressure lowering less significant in hypertensive poststroke patients comparing to hypertonics with the same dosis is interpreted as compensatory response to prevent brain from CBF lowering. Unexpected decreased glomerular filtration should be explain.

609 Stroke prevention

THE OBSTACLES TO CONTROL OF HYPERTENSION THROUGH A NURSE-LED SECONDARY PREVENTION CLINIC FOR CEREBROVASCULAR DISEASE

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Background: Elevated blood pressure is considered the most important determinant of the risk of stroke due to cerebral infarction or haemorrhage, and thus warrants prompt detection and treatment.

Resistant hypertension is a recurrent problem in secondary prevention for many patients.

Methods: This audit was carried out on patients attending a secondary prevention clinic for cerebrovascular disease. This clinic is run by a clinical nurse specialist and all patients are subsequently discussed with a stroke consultant or Specialist Registrar (SpR) in geriatric medicine. Patients are seen on a regular basis in order to record and maintain the mean 24 hour blood pressure within range, i.e.≤135/85.

Results: The data from 150 patients was analysed.

31 patients were normotensive, i.e. had a mean 24 hour blood pressure ≤135/85mmHg.

119 hypertensive patients remained.

82 of these (69%) achieved blood pressure control as per Irish Heart Foundation Guidelines, i.e.≤135/85mmHg.

96 patients (81%) achieved a blood pressure≤140/85mmHg.

19 patients (16%) had a mean 24hour systolic blood pressure>140mmHg.

Of these 47% (9/19) had symptomatic blood pressure drops: 3 patients were day-time dippers and 6 patients were night time dippers.

16% (3/19) patients were symptomatic for hypotension with no recorded blood pressure drops.

10.5% (2/19) had concomitant critical carotid stenosis and thus were deemed unsafe for further anti-hypertensive medication.

16% (3/19) had poor compliance with medications and 10.5% (2/19) were deemed unsuitable for further medication secondary to age.

Conclusion: This study highlights the many reasons for persistent hypertension in this high risk group in spite of considerable medical intervention.

610 Stroke prevention

PREDICTIVE VALUE OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL TO HIGH-DENSITY LIPOPROTEIN CHOLESTEROL RATIO FOR THE PREVENTION OF STROKE RECURRENCE

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We investigated whether the on-treatment low-density lipoprotein-cholesterol/high-density lipoprotein cholesterol ratio (LDL-C/HDL-C) is a predictive marker of stroke recurrence in patients with acute ischemic stroke.

A total of 137 dyslipidemia patients who had suffered acute ischemic stroke were enrolled and were treated with rosuvastatin 2.5 mg. During a mean follow-up of 34.9±0.8 months, there were 10 cases of stroke recurrence. Age, CKD at baseline, and an on-treatment LDL-C/HDL-C ratio > 2 after one month of rosuvastatin treatment were predictors of stroke recurrence by univariate analysis. Stepwise regression analysis showed that CKD (standardized adjusted OR 6.55 [1.12-36.43]; P = 0.030) and on-treatment LDL-C/HDL-C > 2 (standardized adjusted OR 9.70 [1.70-55.33]; P = 0.011) were independent risk factors associated with stroke recurrence. These results suggest that the use of statin therapy to achieve an on-treatment LDL-C/HDL-C ratio ≤ 2 is a suitable treatment strategy in patients with acute ischemic stroke. In addition, post-hoc analysis indicated that more intensive lipid control, to LDL-C/HDL-C ≤ 1.5, may offer additional clinical benefits; further study will be required to substantiate this point.

611 Stroke prevention

PREVALENCE AND PREDICTORS OF PERSISTENT IMPAIRED GLUCOSE TOLERANCE AFTER ACUTE ISCHEMIC STROKE OR TIA

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Background: Impaired glucose tolerance (IGT) is highly prevalent in patients with acute ischemic stroke or TIA, and nearly doubles the risk of stroke in these patients. This IGT can be transient and due to the acute stress response or persistent, representing undiagnosed impaired glucose metabolism. We aimed to assess the prevalence and predictors of persistent IGT in non-diabetic patients with acute ischemic stroke or TIA.

Methods: We prospectively evaluated 46 patients with acute ischemic stroke or TIA and IGT (defined as 2-hour post-load glucose levels of ≥7.8 and <11.1 mmol/L on admission). Detailed clinical information, fasting blood glucose, and HbA1c were recorded during hospital stay and at the outpatient clinic. A standard oral glucose tolerance test was performed on admission, and 3 months later. Patients

were classified as transient IGT (2-hour post-load glucose levels of <7.8mmol/L at 3 months) or persistent IGT (2-hour post-load glucose levels of ≥7.8 and <11.1 mmol/L at 3 months). We performed univariable logistic regression to identify predictors of persistent IGT compared with transient IGT.

Results: Nineteen patients (41%) remained with IGT 3 months after the event. Five of them (26%) even developed diabetes (2-hour post-load glucose levels of ≥11.1 mmol/L). Patients with high 2-hour post-load glucose levels or hypercholesterolemia on admission had an increased risk of persistent IGT (OR 2.6, 95% CI 1.2-5.9, respectively, OR 4.7, 95%-CI 1.0-21.3; p<0.05). Notably, admission HbA1c and fasting glucose levels were not associated with persistent IGT.

Conclusion: Our study shows that only 41% of patients with newly identified IGT in the acute phase of ischemic stroke or TIA still had IGT after 3 months, with high baseline 2-hour post-load glucose and hypercholesterolemia as potential predictors.

612 Stroke prevention

PERCEPTIONS OF STROKE AMONGST THE YOUNG BRITISH BANGLADESHI COMMUNITY: WHERE SHOULD WE BE TARGETING STROKE EDUCATION IN THE FUTURE?

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Background: Tower Hamlets, is a borough of London, consisting of a population of 200,000 people.It has one of youngest populations of all London boroughs with 45% aged 20-39 compared to 36% in London. Previous research has found that members of the South Asian community are at a higher risk of stroke than the general population.Objectives-Research has shown shortening the time onset to arriving at hospital and controlling of stroke risks depend on public knowledge of stroke signs and risk factors. We evaluated the understanding of the risk factors and common presentations of stroke within a group of 16-25 year old British Bangladeshi men living Tower Hamlets.We aimed to understand where this community were accessing information so we can effectively target stroke prevention information.

Methods: Questionnaire study of 42 British Bangladeshi men (aged 14-22) asked if they could recognise key symptoms and risk factors of stroke.

Results: Less than half (42.86%) of those that participated in our study were able to recognise common presenting features of a stroke and most recognised a stroke as a medical emergency (88.10%). The majority of participants understood that leading an active lifestyle (69.05% of responses), smoking increases risk (76.19%) being obese increases risk (76.19%). Participants identified hypertension (88.10%), diabetes (54.76%), excessive drinking (69.05%) and a high salt diet (64.29%) as increasing the chance of stroke. Less than a quarter (21.43%) of participants recognised that being from an Ethnic Minority as a risk factor for stroke.When asked where they would commonly access information, participants rated General Practitioner (GP) as their main source (76.19%).

Conclusion: Recognition of major stroke symptoms needs to be improved amongst the British Bangladeshis in Tower Hamlets. A community based educational campaigns to increase awareness of the symptoms of stroke and targeted messages may help to reduce time to treatment for adults suffering acute strokes and therefore improve outcomes.

613 Stroke prevention

ANKLE BRACHIAL INDEX: CORRELATION WITH RISK FACTORS IN A NON-VASCULAR HOSPITAL POPULATION

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Background: Cardiovascular disease (CVD) are the leading cause of death worldwide. Risk stratification is essential to define the aggressiveness of therapeutic and preventive measures. The search for markers for increased accuracy and its correlation with the classic risk factors have been explored. The measurement of ankle brachial (ABI) is a bedside examination, rapid, noninvasive, and inexpensive, used to diagnose peripheral arterial disease (PAD). Patients with abnormal ABI, even without symptomatic PAD are at higher risk of cardiovascular fatal and nonfatal as an independent risk factor. The authors determined the prevalence of ABI change and its correlation with cardiovascular risk factors in clinical and surgical wards of a university hospital.

Method: The measurement of ABI and a questionnaire about the presence on risk factors in 210 patients aged 40-80 years were obtained. We excluded anyone who had a history of vascular disease or whose technique was inadequate. We used the Doppler Vascular MedPedia with methodology previously established. The measurement was bilateral and was considered the lowest value for the analysis.

Results: The prevalence of abnormal ABI (less than 0.9) in asymptomatic patients was 21% and was significantly higher among patients in medical beds (27.3%) than

in surgical (13.8%). Only four patients had no vascular risk factors. There was a correlation between abnormal ABI and presence of hypertension (OR 2.96, 95% CI = 1.39 to 6.35, p = 0.01), overweight or BMI> 25 (OR 2.54, 95% CI 1, 1 to 5.84, p = 0.015), dyslipidemia (OR 18.95, 95% CI 6.94 to 54.55), alcoholism (OR 2.74, 95% CI 1.1 to 5.84, p = 0.006) and diabetes (OR 2.85, 95% CI 1.34 to 6.11, p <0.01). There was a trend in correlation with central obesity (p = 0.08) and current smoking (p = 0.09). There was no correlation with sex, glucose intolerance and physical inactivity.

Conclusion: The ABI is easily applied and the presence of change is significant in asymptomatic patients, correlated directly to main vascular risk factors. The routine use can improve the preventive treatment of stroke.

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614 Stroke prevention

ANTICOAGULATION FOR STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION. SEX AND AGE DIFFERENCES IN A STROKE-POPULATION IN SWEDEN

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Background: Atrial fibrillation (AF) is an important independent risk factor for stroke. Its prevalence increases with age and some studies have shown that the risk of stroke is greater among women with AF than men and that warfarin is as effective in women as in men with AF. Despite the efficacy associated with warfarin, the rate of warfarin prescribing in the elderly population remains low.

Subjects and Methods: The objects were a random, non-selected stroke-population that was admitted to the stroke-unit in Sahlgrenska University Hospital between February 2005 and December 2009 (N=961). ECGs obtained on admission to the hospital were analyzed by one blinded observer, by using the Minnesota modified score.

Results: The analysis included 961 patients (466 men, 495 women) and 456 patients were 80 years or older (60% women, 40% men). A significantly higher proportion of the elderly had atrial fibrillation (104 vs 54), slightly more frequent among women (48 vs 56). Among all patients with AF on admission only 63 patients were on warfarin compared to 137 at discharge from hospital, no gender difference (reasons for not treating with warfarin will be examined). Significantly more patients older than 80 were on warfarin at discharge. 81 patients died in the acute phase, among these 21 patients with AF and 8 patients of these were on warfarin.

Conclusions: In this population the prevalence rate of atrial fibrillation was found to be 14.2% and AF was more common in the elderly, no gender difference. Only 63 patients were on warfarin on admission compared to 137 at discharge from hospital. The Results showed that anticoagulation was underused in this population and the rate of warfarin prescribing could improve.

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615 Stroke prevention

SOCIAL MARKETING TO SAVE LIVES FROM STROKE: A PROCESS EVALUATION OF NATIONAL STROKE WEEK CAMPAIGNS IN AUSTRALIA, 2006-2010

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Background: This paper will provide a process evaluation of the National Stroke Week campaigns led by the Australian National Stroke Foundation from 2006 to 2010, highlighting key issues in the design and delivery of a successful health promotion program with a limited financial budget. Key practical considerations in the planning and execution of campaigns will be highlighted.

Methods: Lefebvre and Flora's (1988) model of social marketing will be used to describe the development of the National Stroke Week program in terms of: consumer orientation; social exchange; audience segmentation; formative research; communication channels; marketing mix; process tracking, and management process.

Results: The promotion of National Stroke Week has encompassed a wide variety of activities, including mass-media advertising, media releases, internet-based and community-based work. Messages have been adapted for multiple formats and distributed through diverse communication channels to maximise the population reach of each annual campaign. Partner organisations, health professionals and community members have been actively engaged in dissemination, increasing the impact of a limited financial spend on promotion materials and advertising.

Conclusion: Intangible assets such as public and professional interest in stroke have been central to the promotion of National Stroke Week campaigns, with community-based and other activities simultaneous to mass-media pushes. Annual review has enabled revision of program objectives and processes to progressively increase the effectiveness and reach of each campaign. The development of this program can be understood in the light of Lefebvre and Flora's (1988) eight principals of effective social marketing.

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616 Stroke prevention

GENERIC SUBSTITUTION OF CLOPIDOGREL FOR CARDIOVASCULAR PREVENTION FOLLOWED BY STROKE

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Background & Purpose: The European Medicines Agency has recently approved numerous generic versions of clopidogrel for the prevention of cardiovascular diseases. However, some aspects of clopidogrel pharmacokinetics/pharmacodynamics are associated with adverse cardiovascular events. We sought to evaluate whether generic substitution of clopidogrel (GSOC) for cardiovascular protection can be complicated by stroke.

Subjects & Methods: We established a population-based registry in Evros province located in North-Eastern Greece (149.354 inhabitants). We attempted to identify all subjects with stroke during a two year period (2/2010-1/2012) using standard WHO definitions and overlapping case-finding Methods. The use of antiplatelet agents (brand and generic compounds) or anticoagulants prior to stroke was documented. We also recorded the sales of generic and brand clopidogrel in Evros province during the study period using the IMS Sales Analyzer Data.

Results: During the first 10-month period we documented 306 cases (mean age 74±13 years; 51% men) of stroke (83% ischemic, 17% hemorrhagic). Prior antiplatelet medications use included aspirin (17%), brand clopidogrel (12%) and generic clopidogrel (5%). A total of 16 patients (5%) experienced a stroke (13 ischemic and 3 hemorrhagic) within a median of 3 months (range 1-7 months) of GSOC. During the same period the sales of generic and brand clopidogrel in Evros province were 8105 and 36475 boxes respectively. The rate of stroke/1000 sold boxes of clopidogrel was two-fold higher for the generic (1.97‰) compared to the brand compound (1.01‰; p=0.023).

Conclusions: Our findings indicate that cerebrovascular events may followg GSOC. Although the design of the present study cannot establish an association between GSOC and stroke incidence, the creation of an international registry where similar cases can be gathered may provide more reliable information regarding GSOC.

Heart and brain

649 Heart and brain

COGNITIVE DECLINE AND ISCHEMIC MICRO-LESIONS AFTER CORONARY CATHETERIZATION. A COMPARISON TO CORONARY ARTERY BYPASS GRAFTING AND HEALTHY VOLUNTEERS

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Background: Neuropsychological impairment is a known complication of coronary artery bypass grafting (CABG). However, it is largely unknown, whether cognitive dysfunction occurs after coronary catheterization.
Methods: Neuropsychological data were obtained from 38 patients who received coronary catheterization at baseline and 3 months after the intervention. The Results were contrasted to 47 patients who underwent elective CABG and 33 healthy volunteers who were tested at the same intervals. Cerebral magnetic resonance imaging (MRI) with diffusion-weighted sequences (DWI) was performed in 30 cardiac catheter patients and 39 CABG 2-4 days after the procedures.
Results: The rate of acute ischemic lesions, as detected on DWI, amounted to 3.3% in the cardiac catheter group and to 17.9% in the CABG group. Post-interventional cognitive dysfunction (PICD) was detected in 2 (of 8) tests in the cardiac catheter group as compared to the healthy volunteers (verbal memory, t=-2.62 (p=.005) and nonverbal memory, t=-2.65 (p=.005)). The CABG group showed a decline in 7 (of 8) tests in comparison to the healthy volunteers (statistics ranging from t=-1.97 (p=.026) to t=-5.18 (p<.001)). Psychiatric scores and health-related quality of life were not associated with PICD (p>.05).
Conclusions: PICD and cerebral lesions are verifiable after coronary catheter intervention. These side-effects appear to be substantially milder, as compared to CABG, but not negligible.

650 Heart and brain

CONGESTIVE HEART FAILURE AND STROKE OUTCOME

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Background: Chronic heart failure (CHF) is associated with increased mortality in stroke, but there is limited knowledge about the impact of heart failure on stroke severity. The aim of this study was to further investigate this question.
Methods: A prospective study of 1036 patients with an acute (<7days) stroke/TIA, who were admitted to the Stroke Unit at The Department of Medicine. Patients had a follow up visit after 3 and 12 months. Stroke severity was evaluated with the National Institutes of Health Stroke Scale (NIHSS). Modified ranking scale (MRS) was registered at 3 and 12 months. CHF was determined as a previous history of heart failure in medical records. CHF and known risk factors for poor stroke outcome were analyzed in a logistic regression model.
Results: There were 103 (10%) patients with CHF. It was only in ischemic stroke patients and TIA (n= 931) that CHF was a significant predictor of acute mortality; OR 3,7 (CI 1,99-6,96, p<0,001). Those with CHF had higher mean NIHSS score (8,25 vs. 5,00 p<0,001). We found a linear correlation between NIHSS and HF (p=0,007) but an even stronger correlation between atrial fibrillation and NIHSS (p<0,0001). At followup CHF patients had a significantly higher mean MRS at 3 months (0,53 vs 0,34 p<0,001) and 12 months (0,58 vs 0,33 p<0,001). CHF patients had a significant higher mortality rate at 3 and 12 months but this was no longer significant when adjusting for NIHSS and previous history of stroke.
Conclusions: As in previous reports we have found that heart failure is a predictor of mortality in acute stroke. We have also found that heart failure is predictor of stroke severity in the acute phase. In the long run it seems to affect morbidity but not mortality. Further research is needed to validate our findings.

651 Heart and brain

CONTINUOUS BEDSIDE ECG MONITORING: AN INTERESTING METHOD TO INCREASE ATRIAL FIBRILLATION DIAGNOSING RATE IN STROKE PATIENTS

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Background: Detecting paroxysmal atrial fibrillation (pAF) after ischemic stroke is challenging. The difficulty of diagnosing leads to the underestimation of pAF prevalence and the underutilisation of anticoagulants in secondary prevention of stroke. Routine diagnostic techniques such as 24-hour Holter ECG have a low sensitivity. We hypothesized that continuous bedside ECG monitoring increases the probability of diagnosing pAF.
Methods: 1185 consecutive ischemic stroke patients were included. In routine clinical practice for AF diagnosis, patients had baseline ECG, 24-hours Holter ECG, supplemental ECG if clinical symptoms. Patients initially admitted in intensive care unit had continuous monitoring ECG during hospitalization. At three months, AF was retrospectively documented by review of each patient's data. We used multivariate logistic regression to evaluate the adjusted OR of diagnosing pAF with continuous ECG monitoring compared with routine strategy.
Results: 342 (29%) patients were diagnosed in AF. AF was the leading cause of stroke in our cohort. Patients with AF on baseline ECG (66%) and patients with AF adjudicated only on medical history (6%) were excluded. 584/937 (60%) patients had ECG telemetry during hospitalization in ICU (average 134 hours). This patient's group was significantly different by initial clinical severity of stroke (NIHSS: 9.5 vs 3.5). After adjustment for demographics data and baseline NIHSS, the use ECG monitoring during hospitalization has 5.5-fold greater odds of having pAF compared to routine strategy (95% CI, 2.5 to 12). AF detection sensibility with telemetry is 97% for 7 days and 72% for 3 days monitoring.
Conclusion: Continuous bedside ECG monitoring is significantly associated with increased odds of diagnosing pAF. Our data are consistent with existing evidence that duration of ECG monitoring improves the rate of paroxysmal AF detection. This study suggests that this accessible and simple method could be used in stroke units.

652 Heart and brain

POTENTIAL OF BRAIN NATRIURETIC PEPTIDE (BNP) LEVEL TO IDENTIFY TIA AND STROKE DUE TO OCCULT ATRIAL FIBRILLATION: POPULATION-BASED STUDY

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Background: Brain Natriuretic Peptide (BNP) may be a biomarker for occult paroxysmal atrial fibrillation (AF) in patients with ischaemic stroke of undetermined aetiology. We related baseline BNP levels at the time of a first TIA or ischaemic stroke to aetiology in patients who had a recurrent ischaemic stroke during follow-up.
Methods: We studied all patients in the Oxford Vascular Study (2002-2009) with TIA or ischaemic stroke who had a recurrent stroke more than 90-days after the initial event. Blood was drawn at the first event and stored. Aetiology was classified according to TOAST criteria. Undetermined etiology implied a normal investigation. Recurrences classified as undetermined aetiology by TOAST were also classified (blind to BNP Results) as probably cardioembolic versus probably non-cardioembolic based on clinical and imaging criteria. Non-parametric tests were used to compare BNP levels.

Results: Among 99 patients with a recurrent stroke during follow-up (mean age 77.3 years), those with known AF (n=32) had a higher (p<0.001) median (IQR) BNP (1988; 788-3542 pg/mL) than those without AF (248; 97-1259). Among patients with initially undetermined stroke aetiology, those in whom AF was discovered at the time of the recurrent stroke (n=19) had had higher (p=0.05) baseline BNP (584;294-1467 pg/mL) than those (n=10) with a recurrent stroke of other definite aetiology (173;95.4-337). The same was true in patients with initially undetermined stroke aetiology with later AF or probable cardioembolic recurrence (n=27) versus those (n=24) with probable or definite non-cardioembolic aetiology: 437 (154-1410) vs 159 (64-380); p=0.026.

Conclusion: Patients with TIA or stroke of initially undetermined etiology in whom AF was detected at the time of subsequent recurrent stroke had had high BNP levels at the time of the first event. BNP may be useful in identification of patients with paroxysmal AF and in the etiological classification of TIA and stroke.

653 Heart and brain

ENHANCED DETECTION OF OCCULT ATRIAL FIBRILLATION BY 24 HOUR HOLTER MONITORING IN SELECTED PATIENTS WITH ACUTE ISCHEMIC STROKE

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Background: Identifying unknown atrial fibrillation (AF) is difficult but highly relevant in patients with ischemic stroke or TIA. Previous studies have reported low rates of detection using Holter monitoring.
The present study was undertaken to determine the rate of detection of AF with Holter monitoring in patients with suspected stroke of cardiac origin.

Methods: 309 consecutive patients admitted to the neurology ward with ischemic stroke or TIA were prospectively included. Experienced vascular neurologists diagnosed all patients through a routine diagnostic workup and were classified according to TOAST criteria. Epidemiological and clinical data, OCSP and NIHSS were collected. All patients received serial daily ECGs during 7 days after admission. Patients with no prior history of AF, negative serial ECGs, normal angioMRI or colour-coded Duplex and evidence of embolic stroke received Holter monitoring.

Results: Holter monitoring was performed on 120 patients detecting 17 (16%) cases of previously unknown AF. Factors such as old age, high NIHSS at admission and anterior stroke syndromes were more frequent in patients with AF (p < 0.001; 0,007; < 0.001).

Conclusion: 24 hour Holter monitoring performed on selected patients improves the rate of detection of AF.
A stepwise sequential cardiac workup might improve the detection of occult AF. More studies with specific Methods and a better selection of patients for the detection of AF are warranted.

654 Heart and brain

CRYPTOGENIC ISCHEMIC EVENTS AND PATENT FORAMEN OVALE: ENDOVASCULAR TREATMENT RESULTS IN THE TURIN SAN GIOVANNI BATTISTA HOSPITAL REGISTRY

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Background: In pts with cryptogenic cerebral ischemic events (CCIE) and Patent Foramen Ovale (PFO) a higher rate of recurrencies is known to occur if an interatrial septal aneurysm (ISA), or a hypercogulable state are associated, or the ischemic events are multiple, or the shunt is large.

Methods: 90 such pts performed clinical and lab examinations, neuroimaging, duplex scanner, transthoracic (TTE) and transesophageal echocardiography (TEE). Antiplatelet agents were employed before closure. The procedure had a 45' mean duration time. An Amplatzer PFO-occluder was employed in 95% of cases. The follow up included a cardiological and neurological re-evaluation at 1 and 6 months and subsequently every 6 months, a TTE at 1 month, a TEE at 6 months. Subsequently TEE was repeated every year only if shunt persistence. The postprocedural treatment was ASA + Clopidogrel for 3 months, then ASA for 3 months. Afterward ASA was continued if a residual shunt was present.

Results: In the periprocedural time a transient paroxistic atrial arrythmia was observed in 4 pts and 1 TIA occurred; no residual large shunts or hemorrhagic events were identified. During the follow up (mean duration 27,2 months) 9 small and 8 severe residual shunts were identified (2 treated with a second procedure), 1 stroke, 3 transient arrhythmias and an interatrial sept erosion occurred, 2 pts underwent surgery. No major cardiac events were observed.

Conclusions: Mas (2001) reported a 4 year recurrence rate (RR) of 19,2% for pts with CCIE +PFO+ ISA; Nedeltchev (2002) and Anzola (2003) showed respectively an annual RR of 9,9% in pts with multiple ischemic events and of 8,2% in pts with a large shunt; finally Almekhlafi's metaanalysis indicates a 4% CCIE annual RR. In our group percutaneous closure of PFO proved safe and effective in the short and middle time. Also if the sample is still narrow it seems promising the annual recurrence rate is considerably lower (0,6%) than reported in literature.

655 Heart and brain

ATRIAL FIBRILLATION AND INTERNAL CAROTID ARTERY OCCLUSION

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Background: Ischemic strokes resulting from ipsilateral internal carotid artery (ICA) occlusion are associated with very different clinical and outcome patterns. Atrial fibrillation (AF) is considered as a predictor of bad prognosis. The aim of this study was to compare three month outcome in two groups of ICA occlusion, with and without AF and to determine the clinico radiological pattern of AF patients.

Methods: We analysed data of 114 ischemic strokes with ICA occlusion. The average age was 61.2±13.8 years, 66% were male and mean initial NIHSS was 12.7±8.3. Twenty-three (20%) patients had AF. Death and dependency (defined by modified Rankin scale score > 2) were evaluated at three month follow-up. Univariate then multivariate analysis by logistic regression was conducted in order to determine the clinico radiological pattern of AF group.

Results: Three month outcome is significantly worse in AF group: 30% of death versus 10% in non AF group (p=0.019) and 67% dependency rate versus 51% (p=0.002). After univariate analysis, patients with AF were more frequently females (p=0.042), older (p=0.001), non smokers (p=0.037), with high blood pressure (p=0.015), cardiac insufficiency (p=0.005), severe strokes evaluated with baseline NIHSS (p=0.0001) and had more likely proximal middle cerebral artery (MCA) occlusion (p=0.0023). After multivariate analysis, two parameters are significantly associated with AF: age (p=0.0009) and tandem ICA/proximal MCA occlusion (OR, 5.3; 95% CI 1.8 to 16).

Conclusion: The presence of AF in ICA occlusion strokes increased in 5 fold the probability of having tandem ICA/proximal MCA occlusion. Therefore, these high risk patients must be rapidly identified and more aggressive therapeutic reperfusion strategies might be proposed, since this pattern may represent the worse case-scenario for intravenous thrombolytic therapy in terms of recanalization and outcome.

656 Heart and brain

A RATIONAL APPROACH TO RAISED TROPONINS ON A HYPERACUTE STROKE UNIT

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Background: Troponin is commonly measured on admission to hyperacute stroke units (HASUs). Modest elevations in stroke are common and create diagnostic dilemmas in absence of chest pain or electrocardiograph changes.

Methods: 412 consecutive HASU admissions over 6 months were assessed for measurement of troponin and any action taken. Clinical factors guided investigations rather than research protocol.

Results: 245 patients had 435 troponin-I levels measured without chest pain or ischaemic ECG changes. 70 patients had positive levels (>0.032ng/L): 53 (22%) were "low" (0.032-0.3ng/L), 17 (7%) were "high" (>0.3ng/L). Stroke increased the likelihood of troponin rise compared to non-stroke, OR 4.3 (2.0-9.7 p=0.0001).
Cardiology review made no change in management in 91% of cases. Five patients with "high" troponins had cardiac stress testing (1 perfusion scan; 4 stress echo): all were negative. Six patients had invasive coronary angiography (3 high and 3 low troponins). Two required percutaneous coronary intervention (PCI); both had troponin >0.3 and multiple cardiac risk factors. Three patients with troponin <0.3 had normal coronary arteries.

Conclusions: Medical management was appropriate in the majority of acute strokes with troponin rise. We propose a pragmatic pathway for when troponin is performed routinely (Figure 1). "High" troponins >0.3ng/L with chest pain or ECG changes suggest true myocardial infarction. Without these, non-invasive assessment and optimal medical therapy is appropriate.

"Low" troponins (0.032-0.3ng/L) represent patchy myocytolysis triggered by sympathoadrenal activation. Without chest pain or ECG changes, optimal medical management without investigation is appropriate. This is not a true acute coronary syndrome, and an early invasive strategy confers no additional benefit over medical therapy. Aspirin and statin therapy will benefit both stroke and any latent coronary disease present.

657 Heart and brain

CLINICAL PROFILE AND OUTCOME OF PATIENTS IN SINUS RHYTHM AND NO UNDERLYING CARDIAC DISEASE WITH A FIRST-EVER ISCHEMIC STROKE DUE TO LEFT ATRIAL THROMBUS: A SINGLE CENTER EXPERIENCE

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Background: Patients (pt) with left atrial thrombus (LAT) are at high risk for cerebral ischemic events. LAT are often associated with atrial fibrillation or serious cardiac conditions. LAT in pt with sinus rhythm (SR) and no underlying cardiac disease is described as a rare cause of cardioembolic stroke. The aim of our study was to evaluate the clinical profile, management and outcome of pt with a stroke attributable to LAT.
Methods: From 2007 to 2010, 872 consecutive pt with ischemic stroke were admitted in our Unit. 193 pt were in SR, without any significant cardiac disease (clinical history and transthoracic echocardiogram)and suffered a possible cardioembolic or cryptogenic stroke. These pt were submitted to a transesophageal echocardiogram (TEE) and we evaluated 14pt (mean age 64.5±13; 50% male) where we found LAT in TEE. Pt with LAT under 55 years old and few or unknown risk factors were submitted to a hypercoagulable state study. Follow-up (mean16±15.3 months) included functional status (NIHSS scale).
Results: LAT is the cause of 14/193 (7.2%) of the ischemic strokes in SR pt without any significant cardiac disease. Eight pt (57%) had parcial anterior circulation infarcts (PACI-Oxfordshire Community Stroke Project Classification). In 3 pt we found a history of neoplasic disease and 3 other pt were heterozygote to PAI-1 and MTHFR 1298 A>C genes. Doppler ultrasound revealed carotid artery occlusion in 4 pt and vertebral in one. Treatment was anticoagulation in 13 pt (93%) and antiplatelet in one (unsuitable to dicumarinics). At the end of the follow-up we verified an improved functional outcome (NIHSS in admission 10.4±7.4 compared with 5.4±4.2 in the end of follow-up; p=0.03) and there were no stroke recurrence or mortality.
Conclusion: LAT is a rare cause of ischemic stroke but not so uncommon in SR pt without any significant cardiac disease. The diagnosis of LAT modified the treatment strategy, preventing stroke recurrence and improving functional status.

658 Heart and brain

DETECTION OF CLINICALLY UNSUSPECTED ATRIAL FIBRILLATION WITH LONG TERM OUTPATIENT MONITORING IN PATIENTS WITH NON-CARDIOEMBOLIC ISCHEMIC STROKE: PROSPECTIVE STUDY

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Background: Patients with ischemic stroke undergo cardiac telemetry to detect paroxysmal atrial fibrillation (PAF). Longer periods of outpatient telemetry have been shown to increase the yield of this test in patients with stroke of unknown cause (cryptogenic stroke). However, detection of PAF in patients with stroke of known cause has the same treatment implications as it does in patients with cryptogenic stroke. This study describes the Results to date in a prospective series of patients with non-cardioembolic stroke of known cause who underwent 3 weeks of continuous outpatient telemetry with the goal of detecting clinically unsuspected PAF.
Methods: To date 17 patients out of a planned 100 with ischemic stroke due to either lacunar infarction, large vessel cervical atherosclerosis, or large vessel intracranial atherosclerosis, all of whom underwent at least 24 hours of inpatient telemetry and had vascular and cardiac imaging, have been enrolled. Patients wore a mobile telemetry unit with automatic AF detection (Lifewatch, Inc) for 3 weeks. The primary endpoint is the detection of any episode of atrial fibrillation; the main secondary endpoints are initiation of anticoagulation; and recurrent ischemic stroke.
Results: As of this date, paroxysmal atrial fibrillation has been detected in one patient out of 16 who have completed the monitoring. This patient had ischemic stroke attributed to large vessel intracranial atherosclerosis; therapy was changed to dabigatran from clopidogrel. Results will be updated closer to time of presentation.

Conclusion: Continuous outpatient telemetry for three weeks has the potential to detect clinically unsuspected atrial fibrillation in patients with ischemic stroke not due to cardiac embolism. The yield of this test is unknown, as is the optimal duration of monitoring. This study may shed light on the usefulness of this test as well as ist clinical impact.

659 Heart and brain

PATENT FORAMEN OVALE IN PATIENTS WITH CRYPTOGENIC AND NONCRYPTOGENIC STROKE: COMPARATIVE STUDY

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Background and purpose: Paradoxical embolism (PE) is one of mechanisms of cerebral lesion. Patent foramen ovale (PFO) is considered to be the main way of PE realization. The frequency of PFO detection is approximately 35% in population, but it is increased in young patients with cryptogenic stroke (66%). At the moment, there is no single opinion about PFO's role in stroke pathogenesis. Thus, there are some harsh questions about PFO characteristic in cryptogenic and noncryptogenic stroke. The aim of study was to investigate anatomic and functional PFO characteristic in cryptogenic and noncryptogenic stroke patients in order to clear it's pathogenic role in ischemic stroke.
Methods: there were examined 56 ischemic stroke patients (male – 35, female – 21, age 46,7±16,5 years) with PFO. Diagnostic, anatomic and functional analysis of PFO were made by transesophageal echocardiography (TEE), contrast transcranial Doppler monitoring (C-TCD), contrast transthoracic echocardiography (C-TTE). Group 1 was made up of patients with definite stroke cause (cardioembolic, lacunar, atherothrombotic) (n=40), and group 2 – of patients with cryptogenic stroke (n=16).
Results: patients in group 2 were younger, than those in group 1 (38,7±13,4 and 50,4±16,5 years, p<0,05) and had slight neurological sympthoms. These patients more frequently had "valvular" or "window-like" anatomic types of PFO (2[13%] and 4 [27%] patients, respectively), combination of large anatomic (3 mm and larger) and functional (3 degree of the right-to-left shunt by C-TCD) size of PFO (p<0,05).
Conclusion: pathogenic role of PFO can be determined by combination of it's characteristics, such as certain structure type ("window-like", "valvular"), large anathomic (>3 mm) and functional (3 degree of right-to-left shunt) size.

660 Heart and brain

IMPROVED DETECTION OF UNKNOWN ATRIAL FIBRILLATION IN ACUTE STROKE PATIENTS THROUGH PROLONGED SERIAL DAILY ECG ASSESSMENTS

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Background: Atrial fibrillation (AF) is the most common cause of cardioembolic stroke. Identification of unknown AF is crucial but is often underdetected in general practice. Basal ECG and continuous monitoring during the first 24-48 hours is a general recommendation but previous studies suggest low detection rates.
The present study was undertaken to determine the rate of detection of AF through repeated serial Daily ECG (SD-ECG) assessments during the first 7 days after admission in acute stroke patients.
Methods: 309 consecutive patients admitted to the neurology ward with acute ischemic stroke or TIA were prospectively evaluated. Epidemiological and clinical data, OCSP and NIHSS were collected. All patients underwent routine diagnostic workup and were classified according to the TOAST criteria by experienced vascular neurologists. All of them received SD-ECG during the first 7 days after admission.
Results: AF was detected on SD-ECG in 74 (23.94%) patients. After excluding known cases of AF, SD-ECG detected 31 (10%) new cases of AF. Baseline ECG detected 13 new cases (41.9%), while 18 (58.1%) new cases were detected over the next 7 days, 4 of them (12.9%) being detected on day 7.
Conclusion: SD-ECG is a simple method to diagnose AF and prolonging assessments to 7 days enhances the rate of detection of unknown AF.
Prolonged monitoring and more specific Methods to diagnose occult AF are warranted.

661 Heart and brain

INCREASED LIPOPROTEIN(A) IS ASSOCIATED WITH POLYVASCULAR DISEASE IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFT

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Objective: Polyvascular disease is the term used to describe atherosclerosis involving multiple vascular territories. The purpose of our study was to identify the clinical and biochemical predictors of polyvascular disease in patients with established coronary heart disease.

Methods: A total of 470 patients (329 men, 141 female) who had undergone coronary artery bypass grafting (CABG) were enrolled in this prospective study. Polyvascular disease was defined on the presence of existing symptomatic or asymptomatic carotid artery stenosis and/or peripheral artery disease, which is present in 32.1% of patients (n=151).

Results: Clinical and laboratory features independently associated with the presence of polyvascular disease included age ≥65 years, male gender, hypertension, former or current smoker, low BMI, and high Lp(a). Lp(a) was the only biochemical marker that had an independent association with polyvascular disease (OR=1.01 per 1 mg/dl increase; 95% CI, 1.00 to 1.01). The fourth quartile of Lp(a) has significant associations with the risk of two or more vascular territories involvement (OR=1.866; 95% CI 1.056 to 3.297), and three vascular territories involvement (OR=4.240; 95% CI 1.405 to 12.798). There were a significant trend towards patients with the highest quartile of Lp(a) has association with more advanced polyvascular disease (Test for trend: P = 0.008 for involvement of three vascular territories).

Conclusion: High Lp(a) was independently associated with polyvascular disease in patients who undergo CABG, which is suggestive of an indirect evidence of the pathophysiologic function of Lp(a) in polyvascular disease.

662 Heart and brain

PATENT FORAMEN OVALE AS A RISK FACTOR FOR CRYPTOGENIC BRAIN ABSCESS: CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Brain abscess is clinically uncommon but potentially devastating disease. We present this report to draw attention to the importance of patent foramen ovale (PFO) with Eustachian valve as a risk factor for cryptogenic brain abscess.

Clinical Presentation: We encountered a patient with brain abscess presumably caused by dental infection. The patient displayed PFO and giant Eustachian valve, through which spontaneous right-to-left shunt was revealed by transesophageal echocardiography. Reviewing the literature, we find additional cases where brain abscess originated from an increased amount of flora commonly found in the oral cavity that bypassed the pulmonary vascular bed and the lymphatic system through PFO.

Intervention: In the present case, surgical drainage effectively reduced the mass lesion, and study of the aspirated pus revealed normal flora commonly found in the oral cavity.

Conclusions: If a brain abscess is identified without an identifiable proximal cause (adjacent infection, recent head trauma, or neurosurgical procedure), PFO may be revealed by transesophageal echocardiography. If PFO is found, then hematogenous spread of flora normally found in the oral cavity should be suspected through a right-to-left shunt. Additionally, Eustachian valve should be considered an adjunctive risk factor for initiating a spontaneous right-to-left shunt and predisposing cryptogenic brain abscess in patients with PFO.

663 Heart and brain

CARDIOGENIC EMBOLISM AS CAUSE OF STROKE IN PATIENTS WITH BETA THALASSEMIA MAJOR

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Background: Beta-Thalassemia Major (BTM) is an inherited hemoglobinopathy leading to hemolytic anemia. Heart disease is the main cause of death due to heart failure and arrhythmia. A co-existing chronic hypercoagulable state is another major cause of morbidity and mortality due to thrombotic complications that affect several organs including the brain. We present four BTM patients with hemispheric infarcts with characteristics that strongly suggest cardioembolism as cause of stroke instead of thrombosis, as generally assumed.

Case Reports: A 32y-old woman with dilative cardiomyopathy, permanent AF and previous TIAs presented with hemiplegia due to a right MCA infarction. Under warfarin, she remains free of any cerebrovascular events for 2 years.

A 34y-old man with dilative cardiomyopathy and paroxysmal AF suffered acute stroke with right-sided hemiparesis and aphasia due to partial MCA infarction. Under clopidogrel he presented 8 months later transient homonymous hemianopsia, indicative of ischemia in the PCA territory. Under oral anticoagulation the patient remains free of cerebrovascular events for 1 year.

A 43y-old woman with permanent AF presented acute left-side hemiplegia due to a proximal MCA occlusion. Under oral anticoagulation, she now remains free of any further cerebral symptoms for 6 months.

A 41y-old man with dilative cardiomyopathy and episodes of ventricular tachycardia presented right-side hemiplegia and aphasia due to MCA occlusion. Under oral anticoagulation he presented no further cerebral symptoms over 3 months.

Conclusion: The presentation of several vascular events in different vascular territories at various time points in patients with dilative cardiomyopathy and/or AF on the grounds of cardiac siderosis strongly suggest cardiac embolism as cause of stroke in BTM patients. Extensive cardiological evaluation is warranted and oral anticoagulation is indicated for secondary and eventually primary stroke prevention in this high-risk patients' group.

Behavioral disorders and post-stroke dementia

679 Behavioral disorders and post-stroke dementia

EARLY DEMENTIA AFTER FIRST-EVER STROKE IN DIJON, FRANCE, FROM 1985 TO 2008

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Background: This study aimed to evaluate trends in the prevalence of early post-stroke dementia and factors that contribute to it.
Methods: Thanks to multiple overlapping sources of information, overall first-ever hospitalized and non-hospitalized, fatal and non-fatal strokes occurring within the population of the city of Dijon, France (150,000 inhabitants) were recorded from 1985 to 2008. Dementia was diagnosed during the first month following stroke, according to DSM-III and DSM-IV criteria. Vascular risk factors and prestroke treatments were also noted, as were clinical features at onset. Time trends were analyzed according to four periods: 1985-1990, 1991-1996, 1997-2002 and 2003-2008.
Results: A total of 3948 first-ever strokes occurred in Dijon over the 24 years of the study. Among stroke patients, 3201 (81%) were testable of whom 653 (20.4%) had post-stroke dementia (337 women and 316 men). In multivariate analysis, the prevalence of post-stroke dementia in the second and fourth periods was respectively almost half and twice that in the first period. The prevalence of post-stroke dementia associated with lacunar stroke was seven times higher than that in intracerebral hemorrhage, but declined over time as did prestroke antihypertensive medication. Age, several vascular risk factors, hemiplegia, and prestroke antiplatelet agents were associated with an increased prevalence of post-stroke dementia.
Conclusion: This is the first population-based study that demonstrates temporal changes in the prevalence of early dementia after first-ever stroke, over 24 years. The observed changes may be explained by concomitant determinants of survival and incidence such as stroke care management or prestroke medication.

680 Behavioral disorders and post-stroke dementia

PAIN ASSESSMENT IN A STROKE REHABILITATION UNIT

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Introduction: UK national guidelines recommend that all stroke survivors are assessed for pain. Several tools exist, with no instrument specific for stroke pain. Post-stroke impairments may complicate administration of certain tools. We explored the feasibility of pain assessment using various scales and compared this pain assessment against the multidisciplinary team's (MDT) informal assessment.
Methods: Over a four-month period, we assessed all consenting stroke survivors, inpatient in a stroke rehabilitation unit. A variety of validated scales were utilised:"Abbey Pain Behaviours"; simple (dichotomous) question; "Faces Pain Scale"; visual analogue scale (vertical); ordinal numerical scale. Clinical and demographic data were collected including:analgesia prescriptions; disability (Barthel Index [BI]); cognitive impairment (abbreviated mental test [AMT]). For each patient, an independent, blinded researcher questioned the relevant multidisciplinary team. Proportions were compared using Fisher's exact test.
Results: Forty patients were included. Median age:79 years (range:44-98); median BI:8 (0-19); median AMT:6 (0-10). Overall, 18 patients (45%) were unable to complete at least one scale. Greatest difficulty was for numerical scale, 13 (33%) unable to complete. Twenty patients (50%) were classified as in pain according to at least one scale, MDT classified 5 patients (13%) as in pain. There was no significant relationship between MDT and scales pain assessment (p=0.34) or between analgesia prescription and scale assessment (p=0.20). Presence of visual, cognitive, speech or motor impairment predicted difficulty with scales (p=0.0001).
Conclusions: Standard pain assessment tools are not appropriate for all stroke survivors and potential difficulties can be predicted. However, pain assessment remains important as informal team assessment may underestimate pain.

681 Behavioral disorders and post-stroke dementia

RELATIONSHIP BETWEEN COGNITIVE IMPAIRMENT AFTER STROKE AND BASELINE FACTORS AND FUNCTIONAL OUTCOME: ASSESSMENT USING DATA FROM THE VIRTUAL INTERNATIONAL STROKE TRIALS ARCHIVE (VISTA)

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Background: 30% of stroke patients develop dementia over 5 years. Determining the relationship between cognition and baseline prognostic factors, and other functional outcomes, may help in developing preventive strategies.
Methods: The analyses included 11,648 patients with acute stroke from the VISTA dataset. A subset of the National Institute of Health Stroke Scale (NIHSS), Cog-4 (Cumming et al. Cerebrovasc Dis 2010;30:7-14), corresponding to orientation, executive function, language and inattention, was used to assess cognition. The relationship between cognitive impairment at day 90 with baseline demographic and clinical factors (ordinal logistic regression) and other functional outcome measures at day 90 (Spearman's correlation coefficient) was assessed.
Results: Patient characteristics were mean age 70 (12.4) years, female 45%, previous stroke 26.9%, atrial fibrillation (AF) 24.8%, left hemispheric stroke 49%, and mean NIHSS score 13.5 (5.9). Age, female sex, stroke severity, atrial fibrillation, ischaemic and left hemispheric strokes were significantly correlated with cognitive impairment on univariate analysis (p<0.001). Age, stroke severity and left hemispheric strokes continued to be significant on multivariate analyses (p value <0.05). Cognition was significantly correlated with dependency (modified Rankin Scale, rS=0.536, p<0.001) and disability (Barthel Index, rS=-0.544, p<0.001).
Conclusions: Post stroke cognitive impairment at 3 months is associated with increasing age, stroke severity and left hemispheric involvement at baseline. Since cognition is closely related to dependency and disability, treatment directed towards reducing dependency may also reduce cognitive decline.

682 Behavioral disorders and post-stroke dementia

MRI CORRELATES OF VASCULAR COGNITIVE IMPAIRMENT: CONTRIBUTION OF CEREBRAL MICROBLEEDS AND OTHER MARKERS OF CEREBROVASCULAR DISEASE IN A LARGE, CROSS-SECTIONAL HOSPITAL-BASED STROKE SERVICE COHORT

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Background: Vascular cognitive impairment (VCI) is a major cause of disability in the elderly. Magnetic resonance imaging (MRI) correlates of cerebrovascular disease can be used to investigate the complex and heterogeneous underlying mechanisms. Cerebral microbleeds (CMBs) are a marker of small vessel pathology, including hypertensive arteriopathy and cerebral amyloid angiopathy (CAA), but only a few studies have explored how they relate to cognitive function; some data suggest an association of CMBs with frontal-executive impairment. We hypothesised that CMBs would contribute to specific cognitive domain impairments in a stroke service population.
Methods: All patients referred to our stroke service without contraindications underwent detailed neuropsychological testing and a standardized vascular MRI protocol including FLAIR, T1, T2 and T2* gradient-echo sequences. CMBs,

white matter changes (WMC), lacunes and territorial cortical infarcts (defined by standardized criteria) were identified by 2 trained observers and their association with cognition was assessed.

Results: 445 patients were included, of which 84 had at least one CMB. Frontal-executive impairment was more prevalent in patients with CMBs than without (36% vs 22%; p=0.012). In univariate analysis, the presence of strictly lobar CMBs predicted frontal-executive impairment (odds ratio [OR] 2.32, p=0.019), as did mean WMC score (OR 1.04, p=0.05). In multivariate analysis, the presence of strictly lobar CMBs (OR 2.19, p=0.029) remained an independent predictor of frontal-executive impairment. The presence of territorial cortical infarction, and WMC score, predicted impairment in multiple (≥2) cognitive domains.

Conclusion: In stroke service patients, strictly lobar CMBs are independently associated with frontal-executive impairment. As strictly lobar CMBs may reflect underlying CAA, our findings suggest that previously unexpected CAA pathology may contribute to cognitive dysfunction after stroke.

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683 Behavioral disorders and post-stroke dementia

CLINICAL EVALUATION OF VASCULAR PARKINSONISM IN PATIENTS WITH VASCULAR DEMENTIA: THE JAPANESE MULTI-CENTER STUDY OF VASCULAR DEMENTIA

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Background: In the post-stroke state, vascular dementia (VaD) and vascular parkinsonism (VaP) are known as the critical neurological conditions deteriorating activity of daily life and quality of life. These troublesome conditions can be co-morbid and result in life-limiting events induced by these conditions, such as falling, bone fractures and a possible bed-ridden state, in a clinical practice. However, there is no clinical evidence in the relationship between VaD and VaP. Therefore, we investigated clinical features of VaP in patients with VaD retrospectively in this study.

Methods: Clinical records of patients with VaD, who visited from 2000 to 2005, were retrospectively corrected in 12 Japanese medical centers. Their clinical features were registered in all medical centers as original and unified format made by database software and were analyzed statistically. Parkinsonism-related items were prepared in the same registration format.

Results: In 12 medical centers, 224 patients with VaD could be registered. Sixty-nine patients (30.8%) were co-morbid with VaP (male 75.4%, mean onset age 71.5 y). Gait disturbance like "Marche à petit pas" was the most important symptom (62.3%, p<0.0001) in the diagnosis of VaP. In patients with the gait disturbance, frozen gait was the most frequent coexisting symptom (p=0.0004). In addition, postural impairment and no abnormal involuntary movement were also emphasized in the diagnosis. In patients with VaP, onset of stroke was significantly younger (p=0.016), whereas a recurrence and subtypes of stroke were not contributed. Brain MRI showed severe leukoaraiosis, including para-ventricular or deep white matter ischemic lesions, and Binswanger-type or multiple-lacunar-type ischemic patterns in 91.2% of patients with VaP.

Conclusion: VaD is frequently co-morbid with VaP, which is characterized by gait disturbance, postural instability, no abnormal involuntary movement, younger-onset stroke and severe leukoaraiosis.

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684 Behavioral disorders and post-stroke dementia

LESIONS IN THE LEFT PRECENTRAL GYRUS WAS ASSOCIATED WITH ANARTHIRIA IN PATIENTS WITH ACUTE ISCHEMIC STROKE IN THE MCA TERRITORY

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Background: Accumulated reports of anecdotal cases of pure anarthria or aphemia suggested that the left precentral gyrus is the responsible lesion, while the anterior insula or posterior part of the inferior frontal gyrus in the left hemisphere has been demonstrated to be a responsible site for speech articulation in analyses of stroke patients with or without speech deficits. The aim of this study is to address this issue in consecutive patients with acute stroke.

Methods: We retrospectively studied consecutive 1311 ischemic stroke patients who were admitted to our department within 7days after onset from April 2007 through March 2010. According to the inclusion criteria of first-ever stroke onset, right-handed, not complicated with dementia, isolated non-lacunar infarct in the left middle cerebral artery (MCA)territory, and evaluated for spontaneous speech

by speech pathologists, consecutive 58 patients (69.7±13.3years old, 31 male) were enrolled in this study. The location of lesions in the territory of the left MCA, including the anterior insula, posterior frontal gyrus, and precentral gyrus, were evaluated with T2 weighted or Fluid Attenuated Inversion Recovery images, and compared between patients with and without anarthiria.

Results: Neuropsychological evaluation was carried out in 9.0±4.0 days after onset. Of the 58 patients, 11 patients (19%) showed anarthiria. MRI was performed in 10.1±6.1 days after onset. In 11 patients with anarthiria, 8 patients (72%), including 4 patients with pure anarthiria, had a lesion in the precentral gyrus, as compared with 13 (28%) in 47 without anarthiria (p=0.012). None of the sites were significantly correlated with anarthiria.

Conclusion: In Japanese patients with acute stroke, lesions in the left precentral gyrus is the most likely site causing anarthiria.

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685 Behavioral disorders and post-stroke dementia

POST-STROKE DEPRESSION AND ANXIETY: A LONGITUDINAL COHORT STUDY

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Background: Few longitudinal studies explore the patterns of psychological morbidity and factors contributing to their change over time post-stroke. The study Aims is to explore the predictors of Post-Stroke Depression (PSD) and anxiety and factors contributing to change in symptoms in stroke survivors over a 12 month period.

Method: A prospective cohort study of 130 stroke survivors participating in face-to-face interviews at baseline (stroke onset), 3, 6, 9, and 12 months. Outcome measures were depression and anxiety (HADS). Independent variables included MRS, BI, AQOL social support and community participation.

Results: Natural history of anxiety is positively associated with PSD (<0.0001), anxiety at baseline (<0.0001), greater community participation (0.028) and a past history of depression (0.049). Natural history of PSD is associated with anxiety (<0.0001), depression at baseline (0.006), high MRS (0.0289), low social support (0.004) and low community participation (0.002). No baseline factors predicted the resolution of PSD (if depressed at baseline). Baseline factors that predicted the onset of depression (if not depressed at baseline) where low community participation (0.026) and past history of depression (0.047).

Discussion: Anxiety tends to resolves over time. Depression remains problematic and is associated with higher disability and low social support. Predicting recovery from or development of depression post-stroke is difficult. Clinical implications are a need for long-term psychological monitoring of post-stroke with early intervention strategies (counseling and low threshold Introduction of anti-depressants). Ongoing rehabilitation should address disability and social support.

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686 Behavioral disorders and post-stroke dementia

QUALITY OF LIFE AND DEPRESSION AFTER TIA COMPARED TO MINOR STROKE - THE AARHUS TIA-STUDY

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Background: TIA has the same pathophysiology and carries a similar risk of future disease as stroke and may possibly affect mood and life quality, even if it does not lead to disability. While reduced quality of life and depression after stroke is reported to be common, no data on TIA are available. We compared quality of life and depression in TIA and stroke in a one-year follow-up study.

Methods: Patients with first ever TIA (N=167) and minor stroke without disability after one year, estimated with Barthel Index and Scandinavian Stroke Scale (N=114) were included. Data on Stroke Specific Quality of Life (SSQoL) and Major Depression Inventory were obtained at baseline and after three and twelve months. Depression was defined as fulfillment of the criteria for minor, moderate or major depression in the MDI, or use of antidepressants.

Results: TIA patients reported some decline in self-rated change of SSQoL after one year compared to pre-illness state. Compared to TIA, more stroke patients reported changes in personality (48.3 vs. 23.3% p≤0.0001), decrease in energy (58.5 vs. 40.9%, p<0.01), family role (17.5% vs. 8.5% p<0.05) and quality of life after one year (33.3 vs. 21.5%, p<0.05). The combined rate of depression and

antidepressant treatment was 8.3% and 26.1% among TIA and stroke patients, respectively (p≤0.0001).

Table 1. One year comparison of self-perceived changes and depression, TIA vs. stroke without disability at one year

Domains	TIA (N=167)	Stroke without disability‡ (N=114)	Minor vs. TIA
At least some deterioration in stroke specific quality of life scale, %			
Thinking	19.1	28.3	n.s.
Personality	23.3	48.3	p≤0.0001
Energy	40.9	58.8	p<0.01
Mood	21.0	29.0	n.s.
Family role	8.5	17.5	p<0.05.
Social roles	10.4	17.5	n.s.
Overall quality of life	21.5	33.3	p<0.05
Depression or treatment with antidepressants, %			
Antidepressants	7.1	25.2	p≤0.0001
Depressive symptoms*	1.3	1.7	n.s
All depression†	8.3	26.1	p≤0.0001

*Patients fulfilling the MDI-criteria for depression.
†Patients fulfilling the MDI-criteria for depression and/or patients treated with antidepressants.
‡Barthel index=100 and Scandinavian stroke scale=58 after one year.

Conclusion: After one year, quality of life in patients with TIA is less affected, and depression is much less frequent compared to patients with minor stroke without persistent disability. This difference may at least partly be related to the biological effect of the brain lesion causing increased vulnerability to distress.

687 Behavioral disorders and post-stroke dementia

COGNITIVE IMPAIRMENT IS EQUALLY FREQUENT AFTER TIA AND ISCHEMIC STROKE

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Background: Cognitive impairment is estimated to be present in about half of patients who experienced ischemic stroke. Although transient ischemic attacks (TIAs) are considered benign, it is uncertain whether these attacks may also affect cognitive function. The Montreal Cognitive Assessment (MoCA) is a sensitive neuropsychological screening instrument for mild vascular cognitive impairment, especially after stroke. Our study aimed to assess, and compare, cognitive performance after TIA and ischemic stroke.
Methods: We evaluated consecutive patients who experienced a TIA or ischemic stroke during a follow up visit 3-4 months after the qualifying event from October 2009 to September 2010. Cognitive function was assessed by means of the Mini-Mental State Examination (MMSE) and MoCA. Patients filled out the Center for Epidemiological Studies Depression Scale (CES-D) to adjust for depressive feelings, which may interact with cognitive performance. Cognitive impairment was defined as MoCA <26 or MMSE <27.
Results: We screened 59 TIA and 84 ischemic stroke patients, 52 patients were not tested due to aphasia, language barrier, blindness or other causes. Mean (SD) scores on both tests were similar in TIA and ischemic stroke patients (23.7 (4.7) and 23.4 (4.0) respectively on MoCA, p=0.66; and 27.3 (2.6) and 27.4 (2.4) on MMSE, p=0.92). Cognitive impairment was present in 34 TIA patients (58%) and 52 ischemic stroke patients (62%, p=0.55), after adjustment for CES-D scores both groups still had equal rates of cognitive impairment. Scores on all subtests were similar between TIA and ischemic stroke patients. In 17 (40%) TIA and 26 (46%) ischemic stroke patients with normal MMSE scores, MoCA indicated cognitive impairment.
Conclusions: Cognitive impairment is not only common after ischemic stroke, but also after TIA, indicating that TIAs are not as benign as often assumed.

688 Behavioral disorders and post-stroke dementia

COMPARING STROKE CARE IN SOUTH LONDON AND BERLIN USING THE EROS QUALITY ASSESSMENT TOOL (EQAT)

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Background: Many studies of the quality of stroke care have concentrated on acute hospital care and information on key structures, processes and access to rehabilitation facilities after discharge and beyond is limited. The EROS Quality Assessment Tool (EQAT) was developed to assess care related to the available evidence base and European Stroke Guidelines including structures and processes across all phases of stroke care. As part of a quantitative comparison of outcomes between centres in London and Berlin we aimed to:1. compare quality of stroke care provision in 2 populations in European urban multiethnic centres;2. examine the utility of the EQAT in a German setting where it has not previously been used.
Methods: The EQUAT was used to assess quality of care in stroke services in Berlin and London. The full length (251 items) version was completed based on information gathered at face –to face interviews with 3 – 6 key stroke service providers (medical, nursing and allied health professional) from each site. Interviews were conducted in English with a formal written translation and translator available in Berlin, Data were compared to the evidence based guidelines and existing quality indicators.
Results: Broadly similar evidence-based acute stroke care was provided in both centres with hyper acute and comprehensive stroke unit models used. Access to co-ordinated multi-disciplinary care was similar but rehabilitation services, whilst generally less stroke-specific, may provide more intensive intervention in the German setting, particularly for outpatients. Long term follow up for patients is variable and, in general, limited in both centres.
Conclusion: Organisation and process of community rehabilitation elements of stroke care appear to vary even more widely than hospital care provision across different geographical areas and healthcare systems in Europe. The EQAT was successfully used in a novel setting but requires further validation.

689 Behavioral disorders and post-stroke dementia

VASCULAR MCI: NEUROPSYCHOLOGICAL AND NEUROIMAGING CHARACTERIZATION

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Background: Mild cognitive impairment (MCI) is a transitional state of cognitive decline that does not fit all the criteria for dementia. Different MCI subtypes can be recognised based on clinical, neuropsychological and neuroimaging aspects. Vascular MCI (V-MCI) is thought to be characterized by a specific cognitive profile with impairment in attention and executive functioning and partially preserved memory function. We aimed at characterizing some V-MCI features.
Methods: We reviewed the neuroimaging and neuropsychological data of 35 V-MCI patients followed-up in our dedicated clinic.
Results: The underlying vascular lesions were strategic (mostly lacunar) in 20 patients (57.2%), multiple lacunar infarcts with leukoaraiosis in 11, and large lesions in 4. Extensive neuropsychological evaluation was performed in a subgroup of patients (n=23). The number of impaired ADL and IADL items was 0.3±0.72 and 1.37±1.79 respectively, the mean Clinical Dementa Rating score was 0.10±0.21. The MMSE was normal in 92.6%, memory tests were normal in 100% (immediate recall) and 68.2% (delayed recall); language assessment was normal in 93.8% (phonemic) and 89.5% (semantic), psychomotor speed in 56.5%, attention in 52.9% (divided), 38.1% (sustained visuospatial), 55.6% (selective), and 78.6% (focused).
Conclusions: With the limitation of the small sample, our study suggests that small vessel disease (SVD) represents the main substrate of V-MCI and reinforces the hypothesis that SVD-related forms of V-MCI are the main ones that may progress to dementia through lesions load accumulation. Strategic lesions are a more frequent cause of MCI than hitherto thought. In this setting, V-MCI is characterized by an overall preservation of mnemonic performance, language skills, basic attention capacity (such as focusing and maintaining attention), and an initial impairment of attention capacity of the higher level (such as divided attention and sustained visuospatial attention).

POST-STROKE DEPRESSION AND ETHOLOGICAL EVALUATION

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Introduction: Despite the high prevalence and impact of post-stroke depression (PSD), questions persist concerning the nature and stability of PSD over time. The current study examines the evolution of depression levels in stroke patients over a three month period, and uses ambulatory monitoring techniques to assess daily life symptoms most associated with elevated scores on standard clinical assessments.
Methods: 48 individuals with ischemic or hemorrhagic stroke completed a clinician-administered measure of depression prior to hospital discharge and then participated in computerized ambulatory monitoring for a one-week period concerning the experience of depression symptoms. Clinician-administered measures of depression were obtained again three months later.
Results: The percentage of the sample with elevated depression scores was the same at both time periods, but consistency in depression profiles was low. Ambulatory monitoring revealed that elevated depression levels at hospital discharge were most strongly associated with anhedonia (t ratio=4.840, p<.001) and fatigue (t ratio=4.00, p<.001), whereas individuals with elevated scores three months later demonstrated a more classic depression profile associated with negative thoughts (t ratio=4.051, p<.001), anxious mood (t ratio=3.489, p<.01), sad mood (t ratio=2.621, p<.05) and stress reactivity (t ratio=2.466, p<.05).
Conclusions: The prevalence of depression may appear stable during the immediate weeks and months following stoke, but is likely to be composed of very different symptom profiles. The immediate physical and psychological impact of stroke may induce somatic symptoms that explain elevated depression levels and which may not indicate a risk factor for later depression.

COGNITIVE EVALUATION IN THE ACUTE PHASE OF STROKE: PROPOSAL OF A CLINICAL PROTOCOL

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Background: Stroke patients are at high risk of developing dementia, but no instrument, to be used in the acute stroke phase, has yet been identified as capable of detecting patients at higher risk of cognitive decline. Our Aims were to investigate: 1) the feasibility and applicability of the Montreal Cognitive Assessment (MoCA) test in the acute phase of stroke; 2) the predictive value of MoCA on the diagnosis of cognitive impairment.
Methods: Consecutive stroke patients (ischemic or hemorrhagic) admitted to our Stroke Unit were evaluated between 5-9 days after stroke with MoCA. Pre-morbid functional and cognitive status were evaluated by a structured interview to caregivers. Clinical and neuroimaging information were collected. Clinical and neuropsychological follow-up was scheduled after 6 months.
Results: From December 2009 to December 2010, out of 208 patients with stroke, 138 (66%) were enrolled [mean age 69.1±15.0; males 62%; mean NIH Stroke Scale (NIHSS) score 5.7±7.7]. Non-enrollment was mainly due to unfitting of the time window inclusion criteria. MoCA was applicable to 114/138 (83%) of enrolled patients (mean score 17.9±7.2). Multivariate analyses showed that non-applicability was mainly associated with NIHSS [OR (95% CI)=1.4 (1.2-1.7) for each point] and left sided lesions [OR (95% CI)=13.3 (1.8-97.9)]. After 6 months, out of the 58 patients so far re-contacted, 33 (57%) have been assessed: of these 18 had cognitive impairment (4 dementia, 14 MCI). MoCA was the only predictor of cognitive decline [OR (95% CI)=1.2 (1.1-1.5) for each test point], independently of age, gender, years of school, NIHSS, and pre-morbid cognitive status.
Conclusions: MoCA showed a good feasibility and applicability in the acute phase of stroke, with lesion location and stroke severity as major determinants. MoCA seems to reveal some degree of cognitive deficit even in patients with mild stroke, and to have a predictive effect on the diagnosis of cognitive decline at follow-up.

ASSOCIATION BETWEEN CIRCULATING HAEMOSTATIC MEASURES AND COGNITIVE FUNCTION OR DEMENTIA – A SYSTEMATIC REVIEW AND META-ANALYSES

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Background: Haemostasis and thrombosis may contribute to cognitive decline. We aimed to collate evidence for association of circulating haemostatic variables with cognitive function and dementia.
Methods: Systematic review of studies describing blood markers of haemostatic function and cognitive function or dementia in adult humans. Manuscript titles and abstracts were reviewed by two independent assessors and studies selected for inclusion based on pre-specified criteria. We described methodological quality of studies and performed meta-analyses where data allowed.
Results: From 7103 titles, 488 abstracts were assessed and 21 studies included in the review (n=32,773 participants). There was substantial heterogeneity in methodology and presentation of data. In 3 longitudinal studies risk of incident dementia was increased for D-dimer (hazard ratio:1.50, 95%CI:1.15-1.96). For case-control data, we calculated standardised mean differences (SMD) and associated standard errors (SE). For vascular dementia, significant associations were: Factor VII (SMD: 0.93; SE: 0.17); prothrombin fragments 1 and 2 (SMD: 0.64; SE: 0.16); plasminogen activator inhibitor (SMD: 0.68; SE: 0.21) and D-dimer (SMD: 2.36; SE: 0.91). For studies describing patients with any dementia diagnosis, associations were: D-dimer (SMD: 0.36; SE: 0.10) and von Willebrand factor (SMD: 0.31; SE: 0.10). For haemostatic measures and specific cognitive domains, significant (p<0.001) correlations were fibrinogen and speed of processing (0.76, SE: 0.045); verbal memory (0.69, SE: 0.07); non-verbal reasoning (0.57, SE: 0.04) (table).

Table 1. Summary of all analyses of haemostatic variables and dementia diagnoses or specific cognitive test

Haemostatic variable	Analysis	Number of studies	Standardised mean difference (95%CI)	I^2	p
F VII	Vasc. dementia	2	0.93 (0.60 - 1.26)	96	<0.001
F1+2	Vasc. dementia	2	0.64 (0.32 - 0.96)	88	0.001
PAI	Vasc. dementia	2	0.68 (0.26 - 1.10)	99	<0.001
D-dimer	Vasc. dementia	3	2.36 (0.57 - 4.14)	56	0.010
D-dimer	All dementia	2	0.36 (0.15 - 0.56)	00	0.001
vWF	Vasc. dementia	3	1.57 (-0.22 - 3.35)	38	0.086
vWF	All dementia	2	0.31 (0.11 - 0.51)	78	0.003
Fibrinogen	Vasc. dementia	3	1.11 (-0.26 - 2.49)	08	0.116
Fibrinogen	All dementia	3	0.10 (-0.03 - 0.22)	00	0.121

95%CI = 95% confidence interval. Vasc. dementia = Vascular dementia phenotype; F VII = Factor VII; F1+2=prothrombin fragment 1+2; PAI = Plasminogen activator inhibitor; vWF = von Willebrand factor; g = General measure of cognitive function; DST = Digit symbol test; VFT = Verbal fluency test.

Conclusion: Our Results suggest a moderately strong association between activation of haemostasis and thrombosis and vascular dementia including increased levels of markers of thrombin generation (D-dimer and prothrombin fragment 1+2) and endothelial dysfunction (von Willebrand factor and plasminogen activator inhibitor). Associations are weaker when all dementias are combined.

CATASTROPHIC REACTIONS AFTER FIRST-EVER STROKE

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Background: Although the catastrophic reaction (CR) is relative frequent complication of stroke (Starkstein et al., 1993), the studies of its features are relatively sparse. We aimed to study clinical features and clinico-pathological correlates of poststroke CR.

Method: 231 patients hospitalized with first-ever ischemic or hemorrhagic stroke (55% of males, mean age 66+- 12 years) were observed in fixed time-points during 6 month. Depression was diagnosed using criteria DSM-IV. For diagnosis of CR the criteria of Starkstein et al.(1993) were applied. For statistical assessment nonparametric Methods were used.

Results: The frequency of CR was 7,4% (17 patients, 53% males, mean age 67+-3). There were found to variants of CR: 1) with predominance of anguish and crying, and 2) with predominance of irritability, negativism and aggression. The first type of CR (6 of 7 cases) occurs in acute period of stroke. The second type was observed lately, usually in early recovery period. CR manifested in patients with left-hemisphere strokes (13 of 17 CR patient had lesion in left hemisphere compared with 99 of 214 non-CR patient, p=0,05). The frequency of CR increased to 3. month after stroke (from 3 to 9%, p=0,020), but than decreased to 6. month (from 9 to 5,8%, p=0,046). CR had equal rate in patients with or without depression (p=0,375). Most frequently CR manifested in patients with severer disability: Rankin score on 3. month after stroke was 2,9 in patients with CR and 1,4 in non-CR patients (p<0,001).

Conclusion: CR is obviously the heterogeneous syndrome that is associated with the damage of the left hemisphere and the severer disability.

694 Behavioral disorders and post-stroke dementia

ELEVATED PLASMA B-TYPE NATRIURETIC PEPTIDE LEVELS IN PATIENTS WITH SUBCORTICAL VASCULAR DEMENTIA
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Background: B-type natriuretic peptide (BNP), a serum marker for congestive heart failure, is secreted by the cardiac ventricles in response to excessive stretching. Recent reports suggest that high BNP levels may predict cognitive dysfunction in older patients with cardiovascular disease. Also, BNP study for different type of dementia is very rare. The aim of the study was to compare the plasma BNP levels between Alzheimer's disease (AD) and subcortical vascular dementia (SVaD) and to estimate the clinical significance of BNP for dementia.

Methods: We selected two groups of elderly with neurocognitive and functional impairment described as AD and SVaD. Obtained data were analyzed with respect to neuropsychological tests (Korean version of Mini-mental State Examination, Clinical Dementia Rating, and Global Deterioration Scale) and clinical parameters. We measured the plasma BNP levels in 73 patients with AD and 40 patients with SVaD. Plasma BNP concentration were measured by the Triage BNP test.

Results: Clinical parameters and neuropsychological tests did not differ significantly between patients with AD and SVaD. BNP was elevated in patients with SVaD (101.4±225.7 pg/ml, P=0.037) than Alzheimer patients (56.5±45.7 pg/ml). But no significant association was found between K-MMSE and BNP.

Conclusion: SVaD is associated with elevated BNP levels than AD. Elevated BNP probably reflects the larger cardiovascular burden in patients with SVaD. The result probably reflects the large amount of cardiovascular comorbidity in patients with subcortical vascular dementia.

695 Behavioral disorders and post-stroke dementia

MONTREAL COGNITIVE EXAM (MOCA) VERSUS THE MINI MENTAL STATE EXAMINATION (MMSE) IN THE ACUTE STROKE SETTING
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Current literature suggests that 2/3 of patients will have cognitive impairment at 3 months post stroke and 20-30% of patients will have dementia 6 months post stroke. Post stroke cognitive impairment Results in impaired function and is associated with increased mortality. Current UK guidelines recommend all patients with stroke have a cognitive assessment as soon as they are medically stable. There are no gold standards for a suitable cognitive screening tool. The pattern of cognitive impairment is different from that seen in degenerative dementias, with greater numbers having impairment in executive dysfunction. The Montreal Cognitive Assessment (MoCA) is a 30-point global cognitive screening tool that is more sensitive than MMSE in mild cognitive impairment and for cognitive impairment in the post-stroke rehabilitation setting.

Methods: All patients aged >18 admitted with a Stroke or TIA within the last 14 days and medically stable for 24 hours were eligible to screening with the MoCA and MMSE. We excluded patients with major physical disability mRS>4, significant aphasia or dysarthia that impeded cognitive assessment or had a major active psychiatric disorder.

Results: We have screened 19 patients with acute stroke within 14 days.
The MMSE detected 6 out of 19 with cognitive impairment (MMSE <24). The MoCA detected 14 out of 19 with cognitive impairment (MoCA <26). Both were abnormal in 5. 1 patient had an abnormal MMSE a normal MoCA. 9 patients had an MMSE score within the normal range whilst the MoCA was abnormal.

Discussion: The MoCA is easy and quick to use in the acute stroke setting and shows greater sensitivity than the MMSE. This is consistent with the literature. Further work is required to see whether a low score on MoCA in the acute stroke setting will predict cognitive and functional status.

696 Behavioral disorders and post-stroke dementia

DEPRESSION AFTER STROKE
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Background: Depression after stroke (PSD), is one of the more frequent complications of stroke, and has negative consequences on the recovery of motor and cognitive deficits.
In clinical practice, only a minority of patients with depression: are diagnosed and even fewer are treated.

Methods: Diagnosis of depression was based on clinical consensus and supported by the nurse and family impression.
Patients were treated with tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs). Treatment efficacy was evaluated at 1, 3, and 6-month visit by the Hamilton Depression (HAM-D) scale and the Beck Depression Inventoty (BDI).

Results: There were selected 278 patients with depression (35%) out of 796 patients hospitalized in our clinic during January-July 2010 aged 52-78 years, comprising 169 women and 109 men. 27% (75 patients) suffered from major depression. 127 patients with stroke in the territory of the middle cerebral artery and 151 with stroke in other vascular territories.
Duration of PSD symptoms dependent on the vascular territory of the stroke, 78% (99) of patients with middle cerebral artery stroke continued to be symptomatic at six month, versus 22%(33) of those with strokes in other vascular territories.

Conclusion: PSD is frequent neurological complication after stroke it is associated with less neurological recovery after stroke. Regular monitoring and supervision is important for patients with depression after stroke to improve the quality of life.

697 Behavioral disorders and post-stroke dementia

TYPES OF COMORBIDITY BETWEEN POSTSTROKE DEPRESSION AND OTHER POSTSTROKE PSYCHIATRIC DISORDERS
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Background: Poststroke depressions (PSD) is the frequent consequence of stroke. It was hypothesized that high comorbidity rates between PSD and other psychiatric syndromes were caused by pathogenetic role of depression (Kontzevoj et al., 2009). Although in some cases high comorbidity can be explained also by co-ocurrence of symptoms in severer stroke. We aimed to study the relation between PSD, other psychiatric symptoms and the severity of the stroke.

Method: 160 patients hospitalized with first-ever ischemic or hemorrhagic stroke without severe aphasia (56% of males, mean age 65+- 12 years) were observed in fixed time-points during 6 month. Binary regression analysis was applied, with the presence of a psychiatric syndrome other than PSD as dependent variable, presence of PSD and stroke severity (initial Orgogoso score) as covariates. Psychiatric syndromes were diagnosed using criteria DSM-IV.

Results: Apathy, generalized anxiety disorder (GAD), agoraphobia, fear of falling, fatigue, emotionalism, catastrophic reaction, dementia were more frequently observed in patients with PSD than in those without depression. In regression analysis the presence of GAD, agoraphobia and fatigue was depended on presence of depression; the presence of fear of falling, emotionalism and dementia was depended only on the severity of stroke. The presence of apathy and catastrophic reaction was influenced both by the stoke severity and the presence of PSD.

Conclusion: Our study could differentiate three possible types of comorbidity between PSD and other psychiatric disorders: 1) pathogenetic comorbidity 2) comorbidity mediated by initial severity of stroke 3) mixed type of comorbidity.

698 Behavioral disorders and post-stroke dementia

PREVENTING COGNITIVE DECLINE FOLLOWING STROKE – A NEGLECTED AREA OF RESEARCH

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Background: The incidence of new-onset dementia is up to 29% within the first year post-stroke. Furthermore, 17-76% of stroke patients were found to have mild cognitive impairment at 3 months post-stroke. In spite of this high prevalence, therapeutic possibilities are extremely limited. Vascular diseases such as stroke and dementia share the same cluster of modifiable risk factors. Thus, life style modification and adherence to medication prescribed at hospital discharge may not only decrease the risk of recurrent stroke, but also the risk of post stroke cognitive decline.

Methods: We performed a systematic literature search for published or registered randomized clinical trials (RCTs) targeting modifiable risk factors for the prevention of cognitive decline following stroke.

Results: Evidence for a positive effect of lipid or blood pressure lowering drugs on post stroke cognitive decline is limited (overall eight trials; of which only two were restricted to stroke patients). Similarly, only few RCTs investigated life style interventions. Two small published, and four ongoing RCTs tested the effect of exercise. Additionally, one ongoing study exploring the effect of B-vitamins for the prevention of recurrent stroke and dementia was identified. Despite, six RCTs testing the effect of multiple risk factor intervention for secondary prevention of stroke, none investigated the effect on cognition. However, 6 ongoing RCTs were identified (two of these test drug interventions only, whereas four include also life style intervention).

Conclusion: Overall, evidence for risk factor modification for the prevention of cognitive decline is low and comes mainly from observational studies. There is need for more RCTs targeting the prevention of post stroke dementia - especially for life style interventions.

699 Behavioral disorders and post-stroke dementia

COGNITIVE FUNCTION IN STROKE PATIENTS WITH CONTRALATERAL ARTERIAL STENOSIS

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The association between vascular risk factors and cognitive impairment is well documented. However, new risk factors have been questioned. The purpose of the present study is to understand if patients with stroke and contralateral arterial stenosis to stroke location have worst cognitive performance when compared to stroke patients without stenosis.

During a 12 months period, 35 subjects were selected fulfilling our inclusion and exclusion criteria: 15 with stroke and contralateral arterial stenosis (intra and extra-cranial), 10 with stroke without stenosis and 10 healthy controls, with a mean age of 57.7 (±6.6). All subjects were submitted to clinical complementary exams and to neuropsychological evaluation.

A significant statistical relation was verified between stroke patients and healthy controls, in cognitive domains such as attention, executive function and memory. When considering stroke patients with and without contralateral arterial stenosis, a significant statistical relation was verified for executive function domain. For stroke patients with contralateral intracranial and contralateral extracranial stenosis, a significant statistical relation was verified considering attention.

Associations between having a stroke and cognitive impairment were verified. Intracranial or extracranial stenosis, contralateral to stroke location, were associated to cognitive impairment not justified by the vascular lesion.

Cognitive impairment is associated to stroke, however this impairment was not verified in all of the cognitive domains studied. Contralateral arterial stenosis contributed for the difference on the cognitive performance. The short dimension and characteristics of our sample might contribute to the study bias. Nevertheless, arterial stenosis are a risk factor for vascular cognitive impairment and may create the need to include in clinical check-ups, a standard neuropsychological evaluation and an eco-doppler More research is needed to define a cognitive profile for arterial stenosis and to better understand the mechanisms that might lead to this process.

Cerebrovascular Diseases

Etiology of stroke and risk factors

719 Etiology of stroke and risk factors

SOD3 AND IL10 GENES ARE HYPOMETHYLATED IN THE BLOOD OF ISCHAEMIC STROKE PATIENTS

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Background: The genome sequence determines the composition of expressed proteins but epigenetic regulation determines where, when and how the genetic information is used. Altered epigenetic regulation (DNA methylation in particular) is thought to play a role in diseases such as cancer and atherosclerosis. Animal data points to links between methylation status and stroke risk factors and stroke occurrence but this has yet to be evaluated in humans.

Methods: We tested for associations between methylation status and ischemic stroke in184 patients; 46 with large vessel disease (LVD); 46 with small vessel disease (SVD); 46 with cardioembolic stroke (CE) and 46 controls. We measured methylation status of genes whose activity is regulated by methylation and are implicated in aging (LINE1 and ER alpha) or atherosclerotic processes (SOD3, ALOX15, IL10, TNF-alpha; PITX2 which is involved in synoatrial node development and may predispose to arrhythmia). Methylation was determined by pyrosequencing (PyroMark MD Qiagen, Crawley, UK) after bisulphite conversion of lymphocyte DNA using Epitect Bisulfite kits (Qiagen, Crawley, UK). Differences between cases and controls were determined by ANOVA with adjustment for age.

Results: IL10 was significantly hypomethylated (p value<0.0001) in all stroke cases and in each subgroup compared to controls. There were no differences between stroke subgroups. IL10 appears to lose methylation with age (p< 0.001), but the difference between controls and strokes remained significant after correction for age. SOD3 was significantly hypomethylated in LVD patients compared to controls and SVD group (p=0.046 and 0.002 respectively). There were no significant differences for the other genes.

Conclusion: Hypomethylation of IL10 and SOD3 is associated with ischaemic stroke in this population. We plan to extend this preliminary work on the role of epigenetics in the aetiology of stroke to larger samples sizes.

720 Etiology of stroke and risk factors

ISCHEMIC STROKE SUBTYPES ACCORDING TO TOAST CRITERIA – FINDINGS FROM NATIONAL HOSPITAL STROKE REGISTRY IN POLAND

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Background and Aims: The major categories of the TOAST classification comprise: large-artery atherosclerosis (LAA), including large-artery thrombosis and artery-to-artery embolism; cardioembolism (CE); small-artery occlusion (SAO); stroke of other determined cause (OC); and stroke of undetermined cause (UND).To compare the patients characteristic and short and long-term outcomes in ischemic stroke subtypes according to TOAST criteria.

Methods: POLKARD Stroke Hospital Registry collected data via internet based questionnaire on patients hospitalized with acute stroke in 84 stroke centers in Poland between March 2007 and February 2008. The follow-up was completed at end of February 2009 by checking the Death Records National Database of The Ministry of Interior and Administration. The management prior to stroke, comorbidities, risk factors, acute stroke severity and outcomes were compared for stroke subtypes according to TOAST criteria. The survival analysis and Cox regression models were developed to evaluate long-term outcomes.

Results: The total numbers of 8780 (33.6%), 3727 (14.3%), 4872 (18.7%), 2761 (10.6%) and 5954 (22.8%) ischemic stroke patients classified as LAA, CE, SAO, OC and UND were reported, respectively. Stroke subtypes varied substantially for age, gender, risk factor distribution, disability prior to stroke, stroke severity, length of hospital stay and stroke outcomes. In hospital and 12 month mortality rates were 14.6 and 31.3, 18.9 and 39.2, 5.1 and 17.0, 10.4 and 28.1, 16.1 and 33.7% for LAA, CE, SAO, OC and UND strokes, respectively. After adjusting for case mix lacunar stroke was still associated with best prognosis, while differences between other TOAST stroke subtypes decreased.

Conclusions: TOAST criteria used as a mechanism-based subtype classification of ischemic stroke subtypes provide also understanding of the distribution of underlying risk factors, stroke severity and outcomes.

721 Etiology of stroke and risk factors

DIFFERENCE IN INFARCT PATTERN AND CLINICAL STATUS BETWEEN PATENT FORAMEN OVALE AND ATRIAL FIBRILLATION

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Background and purpose: Atrial fibrillation (AF) and patent foramen ovale (PFO) are established sources of cardioembolism. Compared to cardioembolic infarction related to AF, infarct prognosis and pattern of PFO remain unclear. We investigated differences in stroke prognosis and patterns between PFO and AF.

Methods: We performed a retrospective review of the medical records and brain MR image of patients with AF or PFO from the prospective acute stroke and transient ischemic attack (TIA) registry. Infarct patterns on MR were classified on basis of diffusion weighted images. Infarct volume, symptomatic stenosis or occlusion (SSO) of the relevant artery, and existence of PFO were assessed in all patients. Territorial infarction without SSO or multiple vascular territorial infarction was regarded as probable systemic embolism (PSE) pattern.

Results: From June 2004 to July 2008, a total of 289 subjects were identified among 1559 acute stroke patients (AF group, n=156; PFO group, n=133). Analysis of MR images revealed more PSE pattern in AF compared to PFO (71.8 vs. 41.4%, p<0.01). The patients with PFO had the smaller infarct than those with AF (5.7±8.7 vs. 51.9±85.1 ml, P<0.01). Compared to AF, the existence of PFO was the independent predictor for the better clinical status (NIHSS≤3) after adjusting old age, sex, and previous stroke history.

Conclusions: Compared to AF, cerebral infarction related to PFO might be smaller and lead to better prognosis. These Results suggested that different sources of cardioembolism would result in different infarct patterns as well as different stroke risk.

722 Etiology of stroke and risk factors

DETECTING PAROXYSMAL ATRIAL FIBRILLATION IN THE STROKE UNIT. PREVALENCE AND PREDICTORS ON ECG MONITORING

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Background: Detecting paroxysmal atrial fibrillation (AF) is a key part of the etiological workup of patients with unexplained cerebral ischemic events. Holter monitoring identifies new AF in only about 5% of patients poststroke. Stroke Unit (SU) cardiac monitoring is an useful technique to identify paroxysmal AF. Our study aimed to evaluate the yield of SU cardiac monitoring for detecting paroxysmal AF and to determine potential predictors of paroxysmal AF.

Methods: Consecutive acute ischemic stroke patients admitted to the SU between January 2005 and September 2010. Cardiac monitoring was completed for 48-96 hours. Clinical, echocardiographic and neuroimaging data were registered. Statistical analysis was performed using logistic regression models.
Results: Of 1136 consecutive ischemic stroke patients admitted to SU, 12.3% had a history of AF, and an additional 7.6% had new AF detected on admission ECG. In the group of patients with < 50% carotid artery stenosis (n=790) paroxysmal AF was detected in 48 (6.1%). Multivariate logistic regression analysis demonstrated that a NIH >15 (OR=3.6;95% CI 1.7-7.3); history of hypertension (2.4, 95%CI 1.1-5.0); hemorrhagic infarction (OR= 3.7, 95%CI 1.2-11.4); territorial infarction (OR=3.0, 95%CI 1.3-6.7); left atrial size (OR=4.7, 95% CI 2.4-9.4) and aortic valvulopathy (OR=5.1, 95%CI 22.1-12.1) were independent factors associated with paroxysmal AF.
Conclusions: Paroxysmal AF is present in 6.1% of patients with acute stroke of undetermined etiology. A NIH score >15, hypertension, hemorrhagic infarction, territorial infarction, atrial enlargement and aortic valvulopathy can be considered markers for paroxysmal AF. Ischemic stroke patients with these findings may warrant further long-term cardiac monitoring.

723 Etiology of stroke and risk factors

ANTIPHOSPHOLIPID SYNDROME IN STROKE PATIENTS UNDER 55 YEARS OLD: COMORBIDITY AND PROGNOSIS

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Background: The antiphospholipid syndrome (APS) is one of the most frequent acquired thrombofilias, sometimes presenting with vascular thrombosis, particularly in the young. Brain strokes represent the most common arterial thrombosis – and the only one accepted as diagnostic criterion. Our purpose was to study the presence of APS in patients under 55 years old with cerebral ischemia, as well as the stroke outcome and the associated comorbid conditions.
Methods: Consecutive patients under 55 years old with brain infarction or transient ischemic attack (TIA) were included in a specific database during a three years period (2007-2009). Variables analysed: demographic data, vascular risk factors (VRF), type of stroke and 3-months outcome by the modified Rankin Scale (mRS). Two groups were compared, regarding presence or absence of APS.
Results: 159 patients were included, 62.3% men. Mean age 44.3 (SD 8.3) years old. 9 patients (5.7%) fulfilled diagnostic criteria for APS. Demographic data, previous treatment and VRF were similar in both groups, although APS was associated with a higher load of classic VRF (>1 VRF) (66.7% vs. 31.3%, P= 0.029). Stroke severity was similar in both groups. However, APS patients tended to a worse 3-months outcome (mRS >1) (25% vs. 5.7%, P= 0.098).
Conclusions: APS in stroke patients under 55 years old is associated to higher burden of VRF and would be related to worse clinical outcome.

724 Etiology of stroke and risk factors

GENES ASSOCIATED WITH ADULT CEREBRAL VENOUS THROMBOSIS

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Background: Quantitative predictions of risk of cerebral venous thrombosis (CVT) conferred by certain genotypes have yet to be reliably established. We conducted a comprehensive meta-analysis of all candidate genes studied to assess their genetic contribution to its aetiology. We compared our findings against equivalent analyses for paediatric CVT and adult ischaemic stroke.
Methods: Databases were searched to August 2010 for all genes investigated in adult CVT and Odds Ratios (OR) for each gene-disease association calculated. A mendelian randomisztion strategy was also undertaken to determine whether a causal relationship to one gene could be ascertained.
Results: We identified 26 case-control studies, investigating 6 polymorphisms in 6 genes and included 1183 CVT cases and 5189 controls. Statistically significant associations with CVT were found for Factor V/G1691A (OR 2.40, 95% CI: 1.75-3.30, p<0.00001) and prothrombin/G20210A (5.37, 95% CI: 3.78–7.63, p<0.00001). After iterative analysis controlling for inter-study heterogeneity, MTHFR/C677T was also found to be significantly associated (OR 2.30, 95% CI: 1.20–4.42, p=0.02). Variants in the remaining 3 genes (JAK2, PAI-1 and Protein Z) were not significantly associated. Pooled odds ratios for CVT risk in adults for Factor V Leiden and Prothrombin were significantly greater when compared against childhood CVT and adult arterial ischaemic stroke. A causal relationship with MTHFR may exist.

Conclusions: CVT has a genetic basis. Genes involved in the clotting cascade provide a greater level of thrombosis risk in the cerebral venous circulation compared to ist arterial circulation, and; a greater level of risk for adults compared to children.

725 Etiology of stroke and risk factors

TOTAL AND DIFFERENTIAL LEUKOCYTE COUNT IN RELATION TO INCIDENCE OF STROKE SUBTYPES

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Background: Atherosclerosis is an important cause of cerebral infarction, whereas the significance in intracerebral hemorrhage (ICH) is less clear. Inflammation plays an important role in the pathogenesis of atherosclerosis. Elevated leukocytes and leukocyte subtypes are markers of inflammation, and the aim of this study is to evaluate the association of leukocyte count and the incidence of stroke subtypes.
Method: In a prospective cohort study design, 26 927 stroke-free participants out of 28 448 participants in the Malmö Diet and Cancer Study were included.
Results: During the follow-up period (11±3 years), 1515 suffered a stroke (cerebral infarction n =1314, and ICH n=201). At baseline, as compared to stroke-free subjects, those with cerebral infarction had significantly higher levels of total leukocyte count (TLC) (6.7÷/-1.7 vs 6.4±1.7, p<0.001), neutrophils (4.1±1.4 vs 3.9±1.3, p<0.001), lymphocytes (1.98±0.63 vs 1.95±0.62, p=0.04) and mixed cells (0.55±0.20 vs 0.52±0.22, p<0.001). There were no difference in leukocyte counts between stroke-free and ICH cases. After risk factor adjustments, TLC (Hazards Ratio (HR) 1.4, 95% CI,1.2-1.7) and neutrophils (HR 1.3,1.1-1.5) were significantly associated to cerebral infarction. There was an inverse association between elevated TLC and ICH (HR 0.7,0.4-0.99).
Conclusion: Elevated total leukocyte count, lymphocytes and neutrophils were associated to increased incidence of cerebral infarction, whereas there was a negative association of increased total leukocyte count and ICH. The Results might underline differences between these stroke subtypes in underlying vascular pathology.

726 Etiology of stroke and risk factors

INTERMITTENT IS MORE PREVALENT THAN SUSTAINED ATRIAL FIBRILLATION IN ACUTE STROKE AND TIA PATIENTS

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Introduction: The prevalence of atrial fibrillation (AF) is estimated to be about 1% in the general population, rising significantly with age. Although AF represents a common reason for ischemic stroke (IS) and TIA, there is a lack of data on the relative prevalence of sustained (sAF) and intermittent (iAF) AF in these patients. The aim of our study was to evaluate the prevalence of sAF and iAF in a consecutive acute IS and TIA patient cohort.
Methods: Prospectively, consecutive patients with acute IS and TIA presenting in the emergency room (ER) were enrolled over a 6 months period. We documented whether patients had (A) a history of AF, (B) were newly diagnosed with AF in the emergency room, or (C) during a 3 months interval following the event. Differences between frequencies of AF diagnosis in association to the disposition of patients after ER work-up were assessed. Diagnosis of intermittent AF required at least two ECGs.
Results: 692 patients were enrolled (male: 52.2%; IS: 69.1%; TIA: 30.9%). A history of AF was present in 19.7% (sAF: 47.1%, iAF: 52.9%). In 26 patients AF was newly diagnosed in the ER (iAF: 61.5%). Further 36 patients were identified to suffer AF until the 3 months visit. Thus, the overall prevalence of AF in this population was 28.6% (iAF: 62.6%). IAF evaded diagnosis at ER presentation in 57%. The prevalence of AF exceeded significantly with age (p<0.001). Patients with iAF were significantly younger than those with sAF (p=0.004) and more often female (p=0.05). The presence of any AF was associated with higher initial NIHSS scores (p<0.001), and a higher Rankin score after 3 months in comparison to patients without (p<0.001).
Conclusions: In contrast to data from the general population, intermittent is more frequent than sustained AF in acute stroke and TIA patients. Because efficacious secondary prevention in AF with anticoagulants depends on establishing AF diagnosis, adequate cardiac work-up for iAF in these patients has to be developed.

DETECTION OF PAROXYSMAL ATRIAL FIBRILLATION IN PATIENT WITH ACUTE BRAIN ISCHEMIA COMBINING CARDIAC AND HOLTER MONITORING: PREVALENCE AND PREDICTORS

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Background: The yield of serial electrocardiograms (ECG) plus 72-hour cardiac monitoring and Holter monitoring in paroxysmal atrial fibrillation (PAF) detection is not well known.

Methods: Consecutive patients with stroke or transient ischemic attack (TIA) admitted to a Stroke Unit (SU) during 2009 were studied. Patients underwent serial ECG and cardiac monitoring in the first 72 hours. Furthermore, 24 hours-Holter monitoring were performed in patient with brain ischemia of unknown origin or if cardiac embolism was suspected. The presence of atrial fibrillation (AF) and PAF was recorded.

Results: three hundred seventy-five patients were included, 232 males. Mean age 69 (SD 13.5) years. Previous AF was present in 57 (15.2%) patients. ECG on admission showed not previously known AF in 20 (5.3%), 2 (0.5%) were PAF. Cardiac monitoring and serial ECG in the SU detected 9 (2.4%) cases more of PAF. Holter monitoring was completed in 98 patients, 5 with PAF in serial ECG/cardiac monitoring. Holter monitoring identified PAF in 24 cases, of them only 5 had been detected by ECG/cardiac monitoring. Holter monitoring detected 100% of PAF identified by the previous techniques. In total, 8% of patients were diagnosed of new PAF. In multivariate analyses, NIHSS on admission (OR 1.2 for each 1 year increase; 95% CI, 1-1.4), enlarged left atrial (OR 4.4; 95% CI, 1.2-14.6) and absence of carotid plaques by duplex ultrasound (OR 4; 95% 1.2-13) were predictors of PAF.

Conclusion: Holter monitoring increased by 3.8 fold the detection of PAF as compared to serial ECG plus cardiac monitoring in acute stroke patients. Stroke severity, enlarged left atrial and absence of carotid plaques are associated with PAF.

LOMBARDIA GENS REGISTRY OF MONOGENIC DISEASE: FINAL RESULTS

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Background: Monogenic disorders are rare, but probably underdiagnosed causes of stroke and their recognition is important to implement specific treatments or preventive measures. Lombardia GENS is a regional clinical and genetic network involving 36 stroke centers and 7 high technologies laboratories, for the diagnosis of 6 monogenic diseases associated with stroke, including: CADASIL, FABRY DISEASE, MELAS, FAMILIAL and SPORADIC HEMIPLEGIC MIGRAINE (FHM/SHM), HEREDITARY CEREBRAL AMYLOID ANGIOPATHY (H-CAA), MARFAN SYNDROME.

Methods: All stroke/transient ischemic attack patients fulfilling the clinical criteria for monogenic diseases, identified by the participant centres during the recruiting period (2008-2010), were included in the study. Demographic, clinical and familial history data and diagnostic criteria were collected within standardised forms. Nine trained monitors, attending twice a month all involved clinical centres, guaranteed continuous activity and data accuracy and completeness.

Results: Out of 289 stroke/TIA patients with suspected monogenic disease, 248 (86%) fulfilled inclusion criteria. The mean age was 55.2 (95%CI 52.2-57.2) and 50.8% were males. Stroke was ischemic in 76% and heamorragic in 23% whereas 29% of included patients presented with TIA. Ninentyfive (39%) underwent to genetic screening for CADASIL, 35 (14%) for Fabry disease, 65 (26.2%) for H-CAA, 17 (6.9%) for MELAS, 27 (10.9%) for FHM/SHM and 7 (2.8%) for Marfan Syndrome.

Diagnosis was confirmed in 5 (7%) of the patients enrolled with a suspicion of CADASIL, 1 (2%) of the patients with a suspicion of H-CAA, 2 (12%) patient with

a suspected MELAS (12%) and in 2 (11%) patients with suspected FHM. Genetic screening was negative in all patients with a suspect of Fabry or Marfan disease. Genetic analysis is still ongoing in 21% of cases.

Conclusions: Despite the relative small sample size of the study, the proposed diagnostic algorithm is easy to use, reliable and sensible for monogenic diseases and our experience could provide a diagnostic pathway model for the implementation of rare disease regional or national guidelines.

PREVALENCE OF FABRY DISEASE IN YOUNG ADULTS WITH CRYPTOGENIC ISCHEMIC STROKE

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Background: Identification of ischemic stroke (IS) etiology is central for secondary prevention. Despite investigation, etiology remains idiopathic in 30% of young adults with IS, of which, up to 4% may be accounted for by Fabry disease. Potential markers of Fabry disease include vertebrobasilar IS location and proteinuria. We sought to determine the prevalence of Fabry disease in our population of young patients with idiopathic IS.

Methods: Since 2001-02, consecutive individuals hospitalised for IS have been prospectively registered in a single-center neurovascular database and followed-up clinically. We reviewed our database and identified those aged 18-55 with idiopathic IS (with or without isolated patent foramen ovale). At their annual follow-up visit, IS survivors were screened for Fabry disease using a focused questionnaire, clinical examination and genetic sequencing of the α-GAL gene.

Results: We identified 143 cases of young individuals with idiopathic IS. We excluded 48 individuals who were deceased or lost to follow-up and two who declined study participation. We screened 93 cases, including 89 (96%) Caucasians and 4 (4%) Blacks, 70 (75%) French-Canadians and 33 (35%) with vertebrobasilar IS. None had angiokeratomas, acroparesthesia, or other clinical evidence of Fabry disease. One patient had idiopathic hypertrophic cardiomyopathy and another had proteinuria. By genetic sequencing of the α-GAL gene, no significant mutation was found in 54 cases (prevalence=0%; 95%CI=0.0-7.9%); Results of 39 cases are pending.

Conclusions: Even though these are preliminary data, our findings may suggest low prevalence of Fabry disease in our idiopathic IS population.

LOW ANKLE-BRACHIAL INDEX PREDICTS EARLY RISK OF RECURRENT STROKE IN PATIENTS WITH ACUTE CEREBRAL ISCHEMIA

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Background & Purpose: Low Ankle–Brachial Index (ABI) identifies patients with symptomatic and asymptomatic peripheral arterial disease (PAD). Recent data indicate that asymptomatic PAD in stroke patients may be independently associated with recurrent vascular events. We evaluated the association of low ABI with 1-month risk of recurrent stroke in consecutive patients with acute cerebral ischemia (ACI) in a single-center pilot study.

Subjects & Methods: Consecutive patients with acute ischemic stroke (AIS) or transient ischemic attack (TIA) and no previous history of PAD were prospectively evaluated with ABI measurements. Demographic characteristics, stroke risk factors and secondary prevention therapies were documented. An ABI <0.90 in either leg was considered as evidence of PAD, and an ABI ≥0.90 was considered as normal. Patients with elevated ABI (>1.30) suggestive of poorly compressible leg arteries were excluded.

Results: A total of 97 consecutive patients with ACI (63% men, mean age 64±14years, 72% AIS, 28% TIA) and ABI≤1.3 were prospectively evaluated. The median NIHSS-score at hospital admission was 7 points (interquartile range 6). Low ABI was identified in 13 cases (13%; 95%CI: 7%-22%), while recurrent stroke occurred in 4 patients (4%; 95%CI: 0%-10%) during the first month of ictus. Recurrent stroke was more prevalent in patients with low ABI (23% vs. 1%; p=0.007 by Fisher's exact test). The 1-month recurrence rate was higher in patients with

low ABI (23%; 95%CI: 0%-46%). After adjusting for demographic characteristics, vascular risk factors, baseline NIHSS-score and secondary prevention therapies, low ABI was independently associated with a higher 1-month stroke recurrence risk (HR: 22.8; 95%CI: 2.4-219.7; p=0.007).

Conclusions: Our pilot study indicates that asymptomatic PAD identified by ABI may constitute an independent risk factor for early recurrent stroke. This preliminary finding requires further independent validation in a multi-center setting.

731 Etiology of stroke and risk factors

FREQUENCY OF UNRECOGNIZED FABRY DISEASE AMONG SPANISH PATIENTS WITH STROKE. THE MULTICENTER FABRICIO STUDY

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Background: Fabry disease (FD) is an infrequent X-linked disorder caused by a mutation in the gene of the enzyme alpha-galactosidase-A (a-GAL). It has been suggested that FD is not unusual among patients with cryptogenic stroke. FABRICIO study Aims to investigate the existence of FD among adult stroke patients attended by neurologists in 11 Spanish hospitals.

Methods: Multicenter observational study conducted in 11 hospitals. a-GAL enzymatic activity and molecular diagnostic was determined in stroke patients (males ≤ 55 years or female ≤ 65 years). Only cryptogenic (ischemic or hemorrhagic), small-vessel disease or possible cardioembolism etiology strokes (SSS-TOAST criteria) were studied.

Results: 468 patients were enrolled in the prospective study (mean age 46.6 years, SD ±10.13, 66% were males). 225 (48%) suffered cryptogenic ischemic stroke, 99 (21%), small-vessel stroke, 60 (13%) possible-cardioembolism, 48 (10.5%) cerebral hemorrhage and 36 (7.5%) cryptogenic-TIA. We found 3 patients with an a-GAL mutation. Two of these mutations are considered as a cause of Fabry disease: A143T (enzyme activity-AE-0.36 nmol /h/spot), R118C (AE 0.33 nmol /h/spot) and a third is considered as a polymorphism: D313Y (AE 0.59 nmol /h/spot). Therefore, the prevalence of a-GAL mutations in our series is 0.64% but the prevalence of FD among our stroke patients is 0.42%. The two patients with FD causative mutations were women, one had suffered a brain haemorrhage and the other a lacunar stroke.

Conclusion: FD is rare among stroke patients in Spain. If neurologists would exclude FD in their stroke patients, our Results lead us to recommend FD screening not only in male patients with cryptogenic stroke, but also in women and patients with ischemic or hemorrhagic microangiopathy.

732 Etiology of stroke and risk factors

ARE YOUNG ISCHEMIC STROKE PATIENTS ADEQUATELY INVESTIGATED IN A GENERAL HOSPITAL?

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Background: There are very few specific guidelines for the management of ischemic stroke in young adults. Undetermined causes and rare causes of ischemic stroke are more frequent among young stroke patients than older stroke patients. Registries suggest that the cause of stroke cannot be identified in about 30% of young stroke patients. Young stroke patients are increasingly investigated in general hospitals. We sought to determine the adequacy of investigations among ischemic stroke patients under 45 years of age and to record the frequency of undetermined causes of ischemic stroke in this group of patients.

Methods: We retrospectively examined consecutive young ischemic stroke patient case notes for hospital admissions between 2005 and 2010 to record demographic details and the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. We developed an investigation protocol and recorded the adequacy of investigations in this group of patients.

Results: Over a three year period 20 patients were identified with new onset ischemic stroke under the age of 45 years. There were 15 men and 5 women, mean age 36.8 (SD 7.9) years. Three had a history of migraine with aura, 13 smoked cigarettes and 6 drank excessive amounts of alcohol. Five had a history of hypertension and

3 had diabetes mellitus. Five (20%) were classified as cardioembolic stroke, 3 (15%) large artery, 3 (15%) small artery, 2 had another cause and 7 (35%) had an undetermined cause of stroke. Only 1 patient was investigated for HIV and none for syphilis infections. Only 2 of the 7 undetermined cases had a transesopsheal echocardiogram.

Conclusion: In a general hospital undetermined causes of acute ischemic stroke in young adults are similar to frequencies in other registries. However, we have identified evidence of inadequate investigations, which have allowed us to develop local guidelines to improve the care of young stroke patients.

733 Etiology of stroke and risk factors

PERIPHERAL ENDOTHELIAL DYSFUNCTION RELATES TO ENDOGENOUS NO-INHIBITOR ASYMMETRIC DIMETHYLARGININE IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Endothelial dysfunction (ED) is a key pathophysiological feature in the development of chronic heart failure (CHF) and acute ischemic stroke. Asymmetric dimethylarginine (ADMA) has been implicated in the development of ED. We aimed to examine role of ADMA for peripheral endothelial function in patients with acute ischemic stroke in comparison to CHF patients and healthy controls.

Methods: We evaluated 60 patients with acute ischemic stroke of the middle cerebral artery. Stroke patients were classified according to TOAST: cardioembolic infarcts (CEI), macroangiopathic infarcts (MAI), lacunar infarcts (LAI), and stroke of undetermined etiology (UDE). Additionally, patients with stable, ambulatory treated CHF (n=46, LVEF=34±11%, mean ± SD), and controls (n=23) were studied. Endothelial function was assessed by EndoPAT2000 technology using reactive hyperaemia index (RHI).

Results: RHI was significantly decreased in stroke as in CHF compared to controls (1.8±0.3 vs. 1.8±0.4 vs. 2.2±0.4; ANOVA p=0.01). Decreased RHI was depended on TOAST classes (CEI: 1.7±0.4, MAI: 2.0±0.4, LAI: 1.8±0.5, UDE: 1.7±0.3, p<0.0001) and in CHF patients on NYHA classes (NYHA I-II: 1.9±0.4, NYHA III-IV: 1.6±0.3, p<0.01). L-arginine/ADMA ratio was significantly decreased in CHF and stroke (126.1±37.9 vs. 147.6±31.7 vs. controls: 161.5±26.1, p<0.0001) and decreased in parallel to severity of the heart failure (NYHA I-II: 136.7±33.3, NYHA III-IV: 109.7±39.7, p<0.01). In stroke L-arginine/ADMA ratio was lowest in CEI group (133.0±29.4, MAI: 151.1±28.6, LAI: 148.1±31.8, UEI: 167.9±14.0; p<0.0001). Lower L-arginine/ADMA ratio was predictive of ED in CEI group as well in CHF (r=0.324, p<0.05 and r=0.429, p<0.0001).

Conclusion: Peripheral ED occurs in patients with acute ischemic stroke to a similar degree as in CHF patients. The impaired vasodilator capacity relates to TOAST groups in stroke and to NYHA classes in CHF. ADMA impairs regulation of endothelium function in patients with stroke as in CHF.

734 Etiology of stroke and risk factors

RELATION BETWEEN THE DISTRIBUTION OF CEREBRAL ATHEROSCLEROSIS AND STROKE RISK FACTORS IN PATIENTS WITH EXTRACRANIAL CAROTID DISEASE

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Background: In Korean patients, atherosclerotic lesions are more often found in the intracranial rather than in the extracranial cerebral arteries compared to Caucasian patients. However, extracranial carotid artery lesions are increasingly recognized in recent years. Although some studies have shown Asians to have more intracranial diseases, patients with intracranial stenosis often have extracranial disease. The aim of this investigation was to determine the frequency of combined intracranial atherosclerotic lesions in patients with extracranial carotid disease and to analyze the differences in stroke risk factors between patients with pure extracranial carotid artery disease and those who have combined extra- and intracranial artery disease.

Methods: We reviewed 100 consecutive patients with extracranial carotid artery stenosis (defined as > 30% narrowing of diameter) or occlusion proven by a conventional angiography.

We investigated the distribution of atherosclerotic lesions and compared risk factors for atherosclerosis between the pure extracranial carotid occlusive group and the combined extra- and intracranial artery occlusive group.

Results: Among 100 patients with extracranial carotid occlusive lesions, combined intracranial stenosis (>30% narrowing of diameter) or occlusion was seen in 67 patients. Multivariate analysis showed that diabetes mellitus was the only factor that was associated with the combined extra- and intracranial artery occlusive groups (p<0.05).

Conclusions: The combined extra- and intracranial atherosclerotic lesions was were frequently seen in Korean patients. Diabetes mellitus may play an important role in the development of intracranial atherosclerosis in patients who have combined extra- and intracranial occlusive disease.

735 Etiology of stroke and risk factors

CERVICOCEPHALIC ARTERIAL DISSECTION: A COMPARATIVE ANALYSIS OF INTRACRANIAL AND EXTRACRANIAL DISSECTIONS

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Background: Spontaneous cervicocephalic arterial dissections (sCCADs) are important causes for stroke and subarachnoid hemorrhage. Whether intracranial and extracranial sCCADs patients have similar etiological factors or not, and how they are different in clinical and imaging characteristics are focused issues.

Methods: A total of 126 sCCADs patients who were firstly diagnosed according to imaging criterion were consecutively included. All patients carried out whole brain digital subtraction angiography (DSA); other head or neck imaging was used for determination if necessary. Intracranial and extracranial sCCADs patients were compared in aspects of epidemiology, clinical manifestations and imaging features.

Results: We included 47 patients with intracranial dissections (37.3%), 70 with extracranial lesions (55.6%), and 9 with dissections in both parts (7.1%). The demographic characteristics were not statistically different among the three groups of patients. History of minor trauma was more normally seen in patients with extracranial sCCADs (p<0.05), while other possible related risk factors had no statistical difference. Head and/or neck pain was the most common clinical manifestation in all patients. Cerebral ischemia was more common in the extracranial cerebral artery involved patients, while hemorrhage could only be seen in intracranial sCCADs (p<0.01). DSA showed that dissections which induced arterial stenosis or occlusion more involved extracranial cerebral arteries, while aneurysmal dilatations with or without stenosis were more common in intracranial posterior circulation arteries (p<0.01).

Conclusions: Intracranial and extracranial sCCADs may have similar susceptible population, risk factors and pathogenesis, but their lesion patterns and clinical manifestations have big differences.

736 Etiology of stroke and risk factors

LOWER SERUM CALCIUM LEVEL CONTRIBUTES TO LARGER HEMATOMA VOLUME IN ACUTE INTRACEREBRAL HEMORRHAGE PATIENTS

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Aims: Low serum calcium (Ca) levels have been reported to be associated with large infarct volume and poor outcomes after ischemic stroke. To investigate whether Ca level on admission is associated with hematoma volume, stroke severity and outcome in patients with acute intracerebral hemorrhage (ICH).

Methods: We enrolled consecutive ICH patients admitted within 24 hours after onset between 2004 and 2009. Total Ca levels were measured on admission and were divided into quartiles (Q1 (<9.1), Q2 (9.1-9.3), Q3 (9.4-9.7), Q4 (>9.7 mg/dl)). The relationships between Ca levels and following outcomes were examined using multivariate regression analysis; admission hematoma volume, admission NIHSS score, favorable outcome assessed by mRS ≤2 at discharge, and in-hospital death.

Results: 267 patients (90 women, 70±11 years) were studied. The median hematoma volume for each Ca level quartile (Q1 to Q4) were 18, 9, 10, and 9 ml (p=0.004), and NIHSS score were 16, 11.5, 11, and 8 (p=0.0009). After adjustment with age, sex, location of hematoma, history of hypertension and diabetes mellitus, habit of smoking and drinking, antithrombotic use, body mass index and previous stroke, the median hematoma volume (OR 11.14, 95% CI 4.93-17.35) and NIHSS score (OR 3.69, 95% CI 2.04-5.34) in Q1 was statistically significantly larger than that in Q4. 82 patients (30.7%) had favorable outcome (Q1:15.8, Q2:36.8, Q3:31.9, Q4:35.5%) and 21 (7.9%) died (Q1:19.3, Q2:4.0, Q3:4.2, Q4:6.5%). Ca levels on admission were not associated with the outcomes at discharge after adjustment for the above characteristics plus NIHSS, and was associated with mortality after adjustment without including NIHSS (OR3.73, 95% CI 1.22-12.82).

Conclusions: Lower Ca levels on admission were associated with larger hematoma volumes and higher NIHSS score among patients with acute ICH. Ca level may serve as a prognosticator for hematoma volume and clinical deficit.

737 Etiology of stroke and risk factors

FAMILY HISTORY ON SUBTYPE OF ARTERIAL THROMBOSIS DIFFER BETWEEN YOUNG WOMEN SUFFERING FROM MYOCARDIAL INFARCTION AND ISCHAEMIC STROKE: RESULTS FROM THE RATIO CASE-CONTROL STUDY

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Background: The use of the term "arterial thrombosis" or "cardiovascular event" implies that myocardial infarction (MI) and ischaemic stroke (IS) share a common aetiology and risk factors. If MI and IS are mere different manifestations of the same disease, a positive family history of early onset MI should be as prevalent in cases suffering from MI and IS.

Methods: The RATIO study is a population based case control study including women with MI (N=248), IS (N=203) and 925 healthy controls, matched on age, year of event and area of residence. All participants filled out a questionnaire on cardiovascular events in their family before the age 60. The prevalence of paternal and maternal history, as well as a strong history in first degree relatives (more than 33% affected) of MI or IS was assessed for all participants. Odds ratios, adjusted for matching factors, and corresponding 95% confidence intervals (OR; 95%CI) are used to compare the prevalences between MI and IS cases.

Results: Either a mother or father experienced a MI before the age of 60 in 40.3% of MI cases, 23.6% of IS cases and 18.3% of controls. This pattern was more differential for a positive maternal history and when both parents were affected (resp. 4.8%, 0.5%, 1%). A parental history for IS was present in 11.7% of MI cases, 10.8% of IS cases and 7.4% of controls. This pattern was not evident for both parents affected (resp. 1.2%, 1.0% 0.5%).

Affected family member		MI	IS	CON	CON	OR MI vs IS	95% CI
		N=248	N=203	N=925			
MI	Father	29.4%	19.7%	15.0%		1.82	1.12–2.97
	Mother	15.7%	4.4%	4.4%		3.75	1.71–8.26
	Father or Mother	40.3%	23.6%	18.4%		2.21	1.41–3.48
	Father and Mother	4.8%	0.5%	1.0%		14.8	1.82–120
	>33% of 1st degree	17.3%	8.8%	5.3%		2.12	1.07–4.19
IS	Father	5.6%	6.9%	3.9%		0.81	0.35–1.89
	Mother	7.3%	5.0%	4.0%		1.30	0.55–3.07
	Father or Mother	11.7%	10.9%	7.4%		1.01	0.53–1.93
	Father and Mother	1.2%	1.0%	0.5%		1.12	0.51–1.97
	>33% of 1st degree	2.7%	3.3%	2.1%		0.60	0.18–2.04

Conclusion: A positive family history for MI was more common in women who had an MI than those with IS, whereas a family history for IS was equally frequent between these two groups; the prevalence in controls was lowest. These findings support the notion that MI and IS have different aetiologies and risk factor patterns.

738 Etiology of stroke and risk factors

EVALUATION OF VARIOUS RISK FACTORS FOR ARTERIOSCLEROSIS RELATED TO THE CLASSIFICATION OF CEREBRAL INFARCTION

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Background: It is becoming clear that ischemic heart disease, low blood concentration of eicosapentaenoic acid (EPA) and low EPA/arachidonic acid (AA) ratio are independent risk factors, while a high EPA/AA ratio prevents stroke recurrence in patients with hypercholesterolemia. Risk factors for arteriosclerosis, i.e. carotid intima-media thickness (IMT), cardio-ankle vascular index (CAVI) and ankle-brachial index (ABI), may also be related to the onset of stroke, but there have been no well-organized reports. We evaluated the relationship of serum lipid level and risk factors for arteriosclerosis with the onset of stroke.

Methods: Parameters that are likely to influence the onset of stroke, namely total cholesterol, LDL-C, HDL-C, triglycerides, plasma fatty acid composition, EPA/AA ratio, IMT, CAVI and ABI were measured in patients who had suffered an acute cerebral infarction between February and August 2010. The analysis set included 66 males and 49 females with a mean age of 65.6 years. The disease was atherothrombotic in 54 cases, lacunar infarction in 36, cardiogenic cerebral infarction in 19, and non-classifiable in 6 cases. The statistical analysis of the data was carried out to verify the relationship between the parameters and arteriosclerosis and the onset of cerebral infarction.

Results: The incidence of lacunar infarction was significantly high in males with a CAVI ≥ 9.0 (48.8%) compared to those with a CAVI <9.0 (21.7%) (p=0.038). Multiple regression analysis indicated that EPA/AA ratio was the only Background factor strongly related with CAVI (p=0.064). The proportion of patients with an EPA/AA ≥ 0.5 was 82.6% in the group with a CAVI <9.0 and 60.5% in the group with a CAVI ≥ 9.0 (p=0.096). However, other serum lipid markers were not considered to be independent factors for lacunar infarction.

Conclusion: The Results indicated that the occurrence of lacunar infarction correlated with CAVI in males, and that an EPA/AA ratio less than 0.5 was an important factor for an increased CAVI.

739 Etiology of stroke and risk factors

INFLUENCE OF STROKE ETIOLOGY ON OUTCOME OF PATIENTS TREATED WITH INTRAVENOUS THROMBOLYSIS

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Background: The data about the benefit of intravenous thrombolysis (IVT) in various etiologic subgroups of ischemic stroke are scarce. The aim of this study is to evaluate the efficacy and safety of IVT in various stroke subtypes.

Methods: The stroke etiology classification was done according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria. The main outcome measures were: favourable outcome after 3 months (Modified Rankin Scale (mRS) score ≤ 2), occurrence of symptomatic intracerebral haemorrhage (sICH) according to ECASS III criteria and death.

Results: In our ward, from 2006 to 2010, 175 ischemic stroke patients were treated with IVT within 4.5h time window. According to the TOAST etiology, 26.9% of patients had large artery atherosclerosis (LAA), 23.4% cardio embolism (CE), 13.7% small vessel disease (SVD), 13.7% other determined etiology (71% cervical artery dissection), 5.7% unknown etiology, 4.0% multiple possible causes and 12.6% had incomplete diagnostic evaluation. Patients with LAA, SVD and CE were older than patients in other etiological groups (58.9±11.2 vs. 44.7±12.4, p<0.01). Hypercholesterolemia, hypertension and diabetes were more often in patients with LAA and SVD than in other etiological groups (68% vs. 50%, 89% vs. 59% and 24% vs. 10%, respectively). In comparison with other groups, patients with SVD had lower median baseline NIHSS score (8 vs. 11, p<0.05), no occurrence of sICH (0% vs. 9.2%, p<0.01), lower mortality (4,7% vs. 15.4%, OR 0.27; 0.03 to 2.15), and better functional recovery (87.5% vs. 61.6%, OR 4.4; 1.2-15.3). Tendency to good outcome in patients with SVD remained after adjusting for baseline clinical characteristics (OR 3.2; 0.93 to 11.1). In the adjusted multivariate model, group with other determined etiology of stroke also showed tendency to good outcome (OR 3.8; 0.92-16.6).

Conclusion: Among all patients with stroke treated with IVT, those with SVD had the best prognosis.

740 Etiology of stroke and risk factors

THE IMPACT OF SMOKING ON BLOOD PRESSURE VARIABILITY IN STROKE PATIENTS

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Introduction: Hypertension (HTN) is one of the most common modifiable risk factors for cerebro-vascular accidents (CVA); however, the mechanism by which HTN causes CVA is poorly understood. Recently, new evidence has emerged suggesting that visit-to-visit variability in systolic blood pressure (sBP) is a strong predictor of CVA. The question now is what are the factors impacting BP variability?

Aim & Method: The aim of this study was to assess the impact of smoking status on sBP variability in stroke patients.

Patients with diagnosis of CVA in the past 9 months were recruited from hospital wards or outpatient clinics, and classified into smokers, non-smokers and ex-smokers. They were visited by a nurse at home at 1, 6 and 12 month intervals to have their BP measured.

sBP variability was measured as the standard deviation (SD) of mean sBP. Mean sBP for each participant was measured as the average of the mean sBP of the three visits. Clin stat programme was then used to calculate paired t-test value, 95% confidence interval and 2-tailed probability (p value) for the following groups: 1. smokers v non-smokers; 2. smokers v ex-smokers; 3. non-smokers v ex-smokers.

Results: A total of 223 patients had 3 nurse-measured BP readings available, with 52 smokers, 84 ex-smokers, and 87 non-smokers. The mean sBP and variability [mean sBP (variability)] for smokers, ex-smokers and non-smokers were 143.62 (12.11), 135.43 (11.03), 138.37 (12.21), respectively.

We found no statistical significance in sBP variability for the 3 groups: smokers v non-smokers (p value 0.94, 95% CI -2.89 to 2.69), smokers v ex-smokers (p value 0.42, 95% CI -1.58 to 3.74), and non-smokers v ex-smokers (p value 0.31, 95% CI -1.11 to 3.47).

Discussion: The current study has found no evidence suggesting that smoking significantly impacts stroke patients' sBP variability. So, although smoking increases the risk of CVA, it does not do so by impacting BP variability.

741 Etiology of stroke and risk factors

RISK STRATIFICATION WITH CHA2DS2-VASC SCORE MIGHT REDUCE ISCHEMIC STROKE IN PATIENTS WITH ATRIAL FIBRILLATION

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Background: Risk stratification schemes to predict ischemic stroke and thromboembolic events in patients with atrial fibrillation (AF) are important for indicating antithrombotic therapy. The CHA2DS2-Vasc score is the most complete stratification scheme which was recently recommended by European Society of Cardiology guideline. We have retrospectively compared two risk stratification schemes in patients admitted with ischemic stroke due to AF.

Methods: We assessed 215 patients admitted by ischemic stroke at a tertiary hospital between September 2004 and March 2006. Thirty-five patients with AF and ischemic stroke were identified. Data were collected using clinical questionnaires at admission. Patients were divided in three age groups (<65 years, between 65 and 79 years and 80 years or older) and we applied CHADS2 score and CHA2DS2-VASc score.

Results: AF increased significantly with age, reaching 27% of 80 years or older patients, and this group was mostly composed by women (81% of total). Among these 35 patients which had ischemic stroke and AF, no patients had CHADS2 score of 0 and nine had score of 1 (25,5%). All patients with CHADS2 score of 1 had CHA2DS2-VASc score ≥ 2, leading to indication of oral anticoagulation.

Conclusion: Risk stratification by CHA2DS2-VASc score would have optimized indication of oral anticoagulation in our patients. We suggest complementation of risk stratification by applying CHA2DS2-VASc score in all patients with CHADS2 score of 0 and 1.

742 Etiology of stroke and risk factors

THE EUROPEAN UNSTABLE CAROTID PLAQUE STUDY (EUCAPS)

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Background: A significant proportion of strokes are thromboembolic, arising from an atherosclerotic carotid plaque. In current clinical practice treatment primarily involves identification of the severity of luminal stenosis. It is increasingly clear, however, that this alone may not be the best predictor of risk. Strokes may occur as a result of non-stenotic carotid disease, and conversely, patients with significant carotid stenosis may remain asymptomatic throughout their life-time. Recent research has shown that inflammation plays a key role in plaque destabilization and increases the risk of artery to artery embolisation. The main goal of The European Unstable Carotid Artery Plaque Study (EUCAPS) is to register data which will enable the identification of new markers of plaque instability. EUCAPS has established a robust method for registering and storing patient data without the use of national identity numbers and with mechanisms to handle these conversions electronically with a high level of security.

Methods: EUCAPS is a prospective study which registers data regarding patients with symptomatic (unstable) and asymptomatic carotid artery plaques. It includes clinical details with a follow-up at 6 and 12 months, serum markers and mediators of plaque instability, carotid ultrasound findings, CT angiography and where available carotid 3-Tesla MRI with dedicated carotid coils, and imaging of metabolic activity using FDG-PET. Lastly, the histology and immunohistochemistry of plaques removed by endarterectomy will be examined.

Conclusion: Results from this study may contribute to identification of new markers for plaque instability in atherosclerotic carotid stenosis. Better prediction of risk in carotid artery disease would result in more accurate selection of patients to different prophylactic treatments. Interested hospitals are invited to participate in EUCAPS.

743 Etiology of stroke and risk factors

OXIDATIVE MODIFIED LDL PARTICLES IN ASYMPTOMATIC CAROTID STENOSIS

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Background: Oxidative modified low-density (oxLDL) lipoprotein particles are considered to have a major role in atherogenesis by inducing the formation of foam cells and the process of inflamation and thrombogenesis. The aim of this study was to evaluate the serum level of oxLDL particles in clinicaly asymptomatic patients with carotid artery stenosis.

Methods and Results: The investigation included 52 patients of both gender with carotid artery stenosis. Thirty of them were symptomatic, while twenty two were asymptomatic. All patients were divided in subgroups according to the severity of color-duplex ultrasonography of carotid arteries, using a standard five-graded scale. OxLDL was determined by spectrometric measurment of malon-dialdehyde in isolated LDL fraction, which was determined by enzimatic method. The mean value of oxLDL in the whole symptomatic group was 0,57 μmol/l and in the whole asymptomatic group was 0,22 μmol/l, which was statisticaly highly significant difference (p<0,01) The difference between each subgroup did not reach statisticaly significant level, except for the group with 5th level graded stenosis vs the asymptomatic group with low-graded stenosis (p<0,05).

Conclusion: OxLDL particles have important pathogenic role not only in the process of atherogenesis, but also in the pathogenesis of ischemic cerebral lesion and reperfusional cerebral lesion.

744 Etiology of stroke and risk factors

ATHEROSCLEROTIC LESIONS IN LYMPHOMA SURVIVORS TREATED WITH RADIOTHERAPY COMPARED WITH NON-IRRADIATED PATIENTS WITH STROKE AND TIA

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Background: Radiotherapy may cause premature atherosclerosis in Hodgkin's lymphoma survivors (HLSs). We compared the extent of atherosclerosis in HLSs treated with mantle field radiotherapy with non-irradiated patients and determined whether atherosclerosis within the radiation field was predicted by traditional risk factors independent of radiation.

Methods: Forty-three HLSs (median age 50 years, range 38 – 63) treated with mantle field radiotherapy were included. Cardiovascular risk factors were registered at first follow-up (FU-1) a median of 10 years (5 – 13) after treatment. A second follow-up (FU-2) occurred at a median of 23 years (18 – 27) after treatment. At FU-2, in-field atherosclerosis was assessed by computed tomography with calculation of coronary artery calcium volume score (CACS) and pre-cranial artery atherosclerosis score (PAS). Peripheral endothelial dysfunction was assessed by ante-brachial strain-gauge plethysmography. CT angiography of pre-cranial vessels was also performed in 43 age – and gender matched non-irradiated patients with a history of a cerebral ischemic event.

Results: There were more atherosclerotic lesions in HLSs (n=141) than in non-irradiated patients (n=73, p = 0.001) but no difference in the proportion of calcified plaques (120/141 (85%) and 65/73 (89%), p = 0.57). Multiple linear regression analyses showed that cholesterol was a predictor of CACS (beta 308 (95% CI 213 – 403), p < 0.001), PAS (beta 3.67 (95% CI 2.29 – 5.04), p < 0.001) and peripheral endothelial dysfunction (beta 2.74 (95% CI 0.47 – 5.01), p = 0.02).
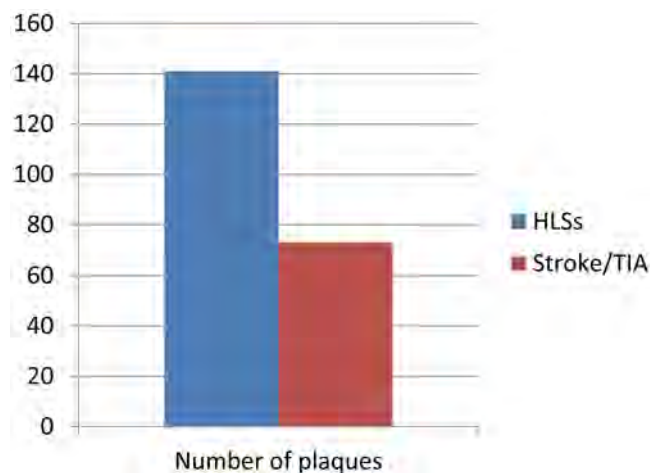
Figure 1. Atherosclerotic plaques in 43 Hodgkin's lymphoma survivors (HLSs) treated with radiotherapy median 23 years earlier compared with 43 patients with a recent stroke or TIA.
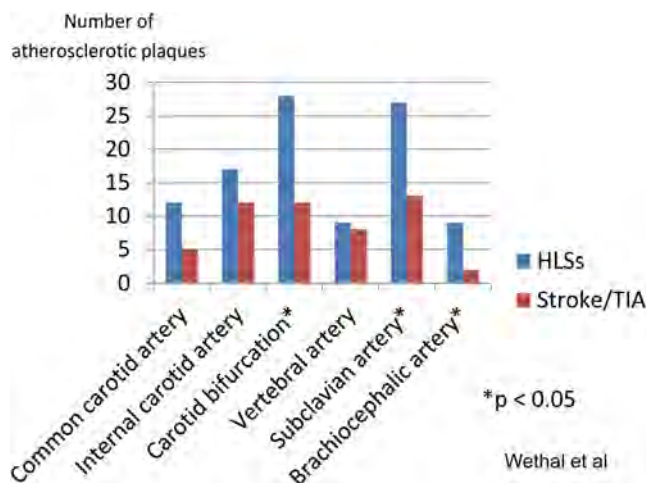
Figure 2. Distribution of atherosclerotic plaques in 43 Hodgkin's lymphoma survivors (HLSs) treated with radiotherapy median 23 years earlier compared with patients compared with 43 patients with a stroke or TIA.

Conclusions: Atherosclerotic lesions developed more frequently in irradiated arteries. Statin therapy may be important in preventing premature atherosclerosis in HLSs.

745 Etiology of stroke and risk factors

STROKE REGISTRY IN THE NETHERLANDS. SET UP AND FIRST RESULTS

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Background: Helsingborg declaration 2006 states: "All Member States should establish a system for routine collection of data needed to evaluate the quality of stroke management, including patient safety issues". Kennisnetwerk CVA Nederland started collecting data from its members, 60 of about all 90 stroke services participate. The Network is a not-for-profit foundation, established in 2006 in order to improve care for stroke patients through implementation of Helsingborg Declaration.

Methods: Data were collected on 2005, 2006, 2007 and 2008: age, type of stroke (hemorrhage or infarction), thrombolysis, door to needle time, mortality at 1 month, functional outcome (mRS), and mortality at 3 months. All data were collected at group level, individual patients were not identifiable.

Results: 19 stroke services gave information on 2005 en 2006, 28 on 2007 and 34 on 2008, with respectively 7393, 7545, 11323 and 13402 patients. Average age was 71,5 years and 50 percent was female.

Data on thrombolysis were presented by 17 (2005), 18 (2006), 28 (2007) and 33 (2008) stroke services. The percentages thrombolysed stroke patients varied from 0,4 to 23, median 5,5 to 8,1.

Four stroke services presented door to needle time over 2005 and 2006, 14 on 2007 and 26 on 2008. The averages ranged from 42 to109 minutes. Median was 73 minutes in 2005, 80 in 2006, 68 in 2007 and 61 in 2008. One month mortality was around 11%.

Conclusion: We are in the process of developing a nationwide system on quality of care and outcome for stroke patients. Currently we have data on about 30% of all hospitalized stroke patients and we expect to cover 80% in the year 2015. The Results suggest improving stroke care, with more patients being thrombolysed within shorter time frame each year. The data quality should lead to caution in interpretation, yet the Results are encouraging. Further developments will include the use of individual patient data.

Literature: Kjellström T, Norrving B, Shatchkute A. Helsingborg declaration 2006 on European stroke strategies. Cerebrovasc Dis 2007; 23: 231-4.

746 Etiology of stroke and risk factors

BLOOD PRESSURE LEVEL AMONG NON-HYPERTENSION POPULATION IN A CERTAIN RURAL COMMUNITY IN SHANGHAI

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Background: There exists a substantial portion of individuals with elevated blood pressure among non-hypertension population that are potential candidates for cardio-vascular diseases. So we conducted a cross-sectional analysis of non-hypertension population in rural community in Shanghai and compared the distribution of blood pressure among different age and gender groups in order to obtain the baseline data of stroke risk factor profile and the contribution of blood pressure level among normal people.

Methods: Cluster random sampling was employed among 10,000 people in a certain rural community in Shanghai and those elder than 35-year-old meanwhile without a history of hypertension were selected to be investigated. The average blood pressure was compared among different age and gender groups and the detection rate of hypertension was analysized.

Results: 5172 cases were included (mean age 53.3±12.7, 2454 male and 2718 female). The average systolic pressure was 123.88±11.99mmHg in male and 120.12±12.72mmHg in female while those of diastolic pressure were 77.38±6.66mmHg in male and 75.04±4.45mmHg in female. There were significant differences between gender groups both in systolic and diastolic pressure (p<0.001). The level of blood pressure increased along with the age among the subjects except of males elder than 75-year-old.The overall detection rate of hypertension was 12.7% and it was found increased with age.

Conclusion: Both systolic and diastolic pressure were higher in male than in female and the pressure increased with age and the detection rate of hypertension was high which was also increased with age among non-hypertension population.

747 Etiology of stroke and risk factors

CARDIOEMBOLIC STROKE IN HOSPITAL SÃO LUCAS, PORTO ALEGRE-BRAZIL

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Introduction: Stroke is a leading cause of mortality and disability in Brazil. Among the risk factors for cerebrovascular disease some have more influence in certain stroke subtypes. There is little data available in the literature on the prevalence of stroke subtypes in Latin America.

Previous studies show a high frequency of stroke caused by cardioembolic sources in other countries.

Materials and Methods: We analyzed data from 688 patients with acute ischemic stroke (52.3% women, mean age 65.7 years) who were enrolled in a stroke data bank. Standardized data assessment and stroke subtype classification were used.

Results: One of the most common stroke subtype was cardioembolism (n:195, 28.3%). Among the 195 patients with cardiac sourced, 48% were caused by arrhythmia, 23% were caused by valvular disease, 14% occurred in post-myocardial infarction and other ethiologies occurred in 15% of the cases.

In these patients, the most important risk factors were hypertension and dyslipidemia.

Discussion: The population of South America is diverse in its ethnicity and few studies describe the distribution of risk factors among stroke subtypes in this population.

Conclusion: Few data are available about stroke epidemiology in Latin America. Cardioembolic stroke patients represent an important percentage of cases of stroke.

748 Etiology of stroke and risk factors

MOYAMOYA IN CHILDREN WITH SICKLE CELL ANEMIA AND CEREBROVASCULAR OCCLUSION

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Introduction: Cerebro-vascular disorders are frequently associated with sickle cell disease (SCA), mainly in homozygous children. Moya Moya syndrome describes an angiographic pattern consisting of progressive development of collaterals after occlusion of large cerebral vessels. It represents a relatively uncommon neurovascular complication of SCA.

Case Reports: We report 3 cases of Moya Moya patterns diagnosed after a first neurological episode in patients with SCA with a mean age of 14 years. Clinical presentations were recurrent transient ischemic attacks, minor stroke and seizures. One patient suffering of chronic headaches had silent cerebral infarction. Magnetic resonance angiography revealed anterior bilateral stenosis of the circle of Willis and presence of a new vascular network. There was an increased transcranial Doppler ultrasound velocity in one patient, coagulopathy with protein C deficiency in the second patient and an associated beta thalassemia in the third one. Two patients have been compliant with chronic transfusion since their recurrent events. Only one received hydroxyurea therapy. After 5 years of follow-up, no patient experienced new stroke episode.

Discussion and Conclusion: Sickle cell disorders are relatively frequent in Tunisia observed in 1 to 2% of the population. Ischemic stroke occurs in 7% to 11% of children with homozygous SCA before the age of twenty years. Moya Moya is a rare radiological syndrome consisting of progressive development of collaterals after occlusion of large cerebral vessels. It can be primitive or symptomatic of various medical conditions including SCA. The pathogenesis remains unclear. Transfusions are more effective for stroke prevention. Hydroxyurea is also used with promising Results, but no radiologic or MRI data about these patients were provided. Surgical revascularization techniques remain yet controversial. More data are needed to provide optimal indications for the treatment of Moya Moya related to SCA disease.

749 Etiology of stroke and risk factors

STROKE OCCURRING ON WARFARIN THERAPY IS FREQUENTLY NOT RELATED TO UNAPPROPRIATE ANTICOAGULATION: WHO IS THE REAL GUILTY?

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Background and purpose: Not all stroke in patients taking warfarin are cardioembolic in origin. We sought to investigate the real impact of a correct/ not-correct anticoagulation in the pathogenesis of stroke in a group of consecutive patients.

Methods: 160 consecutive patients (90 M, 70 F, median age: 78.1) on warfarin therapy with first-ever stroke were evaluated retrospectively: it was assumed in 66,3% cases for non valvular atrial fibrillation, in 26% for cardiac valvular disease,

in 4,2% for myocardial infarction, in 3,5% for dilatative cardiomiopathy. All patients were investigated by cranial CT scan to detect hemorrhagic or ischemic stroke and by instrumental evaluations to establish the ethiopathogenetic diagnosis of the ischemic event according to TOAST criteria. INR values at admission were considered.

Results: 135 (84,4%) patients presented ischemic events, and 25 (15,6%) haemorrhagic stroke. 72/135 (53.3%) ischemic patients showed INR values under therapeutic range (<2): 70% were cardioembolic (CE), 18,8% lacunar (La) and 12,2% with large arteries atherosclerosis (LAA). 45/135 (33.3%) patients showed INR values in range (2-3): 31.3% CE, 48.9% La and 18.8% with LAA. 18/135 patients (13.4%) showed INR values over the range (>3): 11.2% CE, 50.7% La and 38.1% with LAA. Of the 25 hemorrhagic patients, 54.5% showed INR values under range, 36% in range and 9.5% over range.

Conclusion: Our study documents that only half of patients with ischemic occurring on warfarin therapy present INR values under the therapeutic range, while the other half has normal or high values, especially in non-CE events. This may be related to the role of the etiophatogenetic diagnosis and suggests that the anticoagulant treatment represents only a part of cerebrovascular prevention. Similarly, only 9,5% of cases with hemorrhagic stroke present INR values over range, so that not only excessive anticoagulation but also other risk factors may lead to cerebral hemorrhage.

750 Etiology of stroke and risk factors

PREVALENCE AND RISK FACTOR RATES OF INTRACEREBRAL HEMORRHAGE – HYPERCHOLESTEROLEMIA IS THE LEADING RISK FACTOR?

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Background and purpose: The aim of this study was to identify and measure the effects of related risk factors, age, gender, use of antiaggregant or/and anticoagulant agents on the incidence rates of intracerebral hemorrhage (ICH) in patients that were hospitalized in the clinic of neurology department of Cerrahpasa Medical Faculty between January 2005 and December 2010.

Methods: Data was collected from patients hospitalized in our university hospital clinic between January 2005 and December 2010. The patients with ICH were assessed through history of hypertension (HT), diabetes mellitus (DM), smoking, alcohol intake, atrial fibrillation (AF), usage of anticoagulant and/or antiaggregant agents, hypercholesterolemia and obesity.

Results: A total of 4449 patients were included in this study. 1378 (31%) of these patients were diagnosed as having cerebrovascular disease and 165 (3.7%) had intracerebral hemorrhage. 165 patients with ICH were distributed as 66 (40%) females and 99 (60%) males. The mean age of females was 64 (between 29 and 102), males was 61 (between 30 and 94). We identified the risk factors of ICH as; hypercholesterolemia (LDL over 100 mg/dl) in 93 (56.3%) patients, [LDL between 100-120 in 27 (16.3%), LDL between 120 -140 in 24 (14.5%) and LDL over 140 in 42 (25.5%) patients]. HT in 81 (49%) patients, use of antiaggregant and/or anticoagulant agents in 62 (37.5%); smoking in 44 (26.6%); DM in 23 (14%) patients; obesity (Body Mass Index 30 kg/m^2 and over) in 19 (11.5%); AF in 15 (9%) and alcohol intake in 9 (5.4%) patients.

Conclusions: Results of this data show that hypercholesterolemia and hypertension are the leading risk factors in ICH. Use of antiaggregant and/or anticoagulant agents may be associated with an increased incidence of ICH also. Our aim now is to further evaluate our data on hypercholesterolemia: the use of statins and the coalescence of other risk factors in that patient group with ICH.

752 Etiology of stroke and risk factors

RISK FACTORS FOR ISCHEMIC STROKE AMONG HYPERTENSIVE PATIENTS

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Background: Hypertension is the most important modifiable risk factor for ischemic stroke. Several other modifiable risk factors contribute to a variable degree to the burden of stroke. The aim of the present study was to evaluate risk factors for stroke in hypertensive patients followed-up in the Hypertension Outpatient Clinic of a University Department.

Methods: The medical notes of the most recent visit of 1,810 hypertensive patients (40.4% males, age 56.5±13.5 years) who attended at least once the Hypertension Outpatient Clinic of our Department were analyzed.

Results: Eighty-two patients (4.5%) had a history of stroke. These patients were older (61.1±12.7 vs. 56.3±13.5 years; p<0.005), had more frequently type 2 diabetes mellitus (T2DM, 31.2 vs. 7.4%; p<0.001) and had marginally lower body mass index (BMI, 28.2±3.9 vs. 30.2±5.7 kg/m^2; p=0.055) than patients without a history of stroke. In contrast, low density lipoprotein cholesterol (p=0.73), high density lipoprotein cholesterol (p=0.51) and triglyceride levels (p=0.66) did not differ between the 2 groups. In addition, systolic and diastolic blood pressure levels were similar in the 2 groups (p=0.43 and p=0.47, respectively).

Conclusions: Our cross-sectional study suggests that age and T2DM are the most important risk factors for stroke among hypertensive patients. The prevalence of stroke is high even among non-elderly hypertensive patients. The trend for an inverse association between BMI and stroke might be due to malnutrition after stroke. In agreement with previous population-based studies, dyslipidemia did not appear to contribute significantly to the burden of stroke. Given the aging of the population, the prevention and aggressive management of hypertension and T2DM, especially when these risk factors coexist, are needed to reduce the incidence of stroke and the associated morbidity and mortality.

753 Etiology of stroke and risk factors

HELICOBACTER PYLORI SERUM ANTIBODY TITERS IN PATIENTS WITH ISCHEMIC STROKE

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Background & Aims: Helicobacter pylori infection has been associated epidemiologically and pathogenetically with athreosclerosis of coronary arteries but there is lack of data regarding possible association between chronic infection with this organism and cerebral ischemia. In this study we evaluated the association between this antibody and cerebral ischemic stroke.

Methods & Materials: This was a cross-sectional study that was performed in AlZahra hospital, Isfahan, Iran. 96 patients with ischemic stroke were enrolled in this study. Patients with a known cardiac source for cerebral embolism, those with major risk factors for atherosclerosis and symptoms related to peptic ulcer disease were excluded. Control group were selected from healthy blood donors. IgG and IgA antibodies to Helicobacter pylori were detected using a rapid enzyme linked immunosorbent assay. Statistical analyses were performed with the SPSS 15.0 software package with t-test and chi-square test.

Results: Patients and controls were similar regarding age and gender. There were 21 cases of HTN and 5 cases of DM among patients. Patients and controls were similar regarding serum IgA and IgG titers as well as positivity. There were 13 and 15 cases of positive IgA and 44 and 39 cases of positive IgG among patients and controls, respectively. Also, there were 7 and 9 cases of both positive IgA and IgG in among patients and controls, respectively. No differences were found between the two groups in IgA or IgG titers or positivity (P > 0.05).

Conclusions: The Results of the present study showed that patients with stroke are not different from healthy age and sex matched controls in regarding either H.Pylori IgA or IgG positivity or the antibody titers. Genetic typing of H.Pylori and comparing patients with stroke with controls and diagnosis of H.Pylori with other more specific and sensitive tests such as stool antigen test are recommended.

Keywords: Helicobacter, infection, inflammation, athreosclerosis, stroke

754 Etiology of stroke and risk factors

THE IMPACT OF GENDER ON BLOOD PRESSURE VARIABILITY IN STROKE PATIENTS

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Introduction: Hypertension (HTN) is one of the most common modifiable risk factors for cerebro-vascular accidents (CVA); however, the mechanism by which HTN causes CVA is poorly understood. Recently, new evidence has emerged suggesting that visit-to-visit variability in systolic blood pressure (sBP) is a strong predictor of CVA. The question now is what are the factors impacting BP variability?

Aim: The aim of this study was to assess the impact of gender on sBP variability in stroke patients.

Method: Patients with diagnosis of CVA in the past 9 months were recruited from hospital wards or outpatient clinics. They were visited by a nurse at home at 1, 6 and 12 month intervals to have their BP measured.

sBP variability was measured as the standard deviation (SD) of mean sBP. Mean sBP for each participant was measured as the average of the mean sBP of the three visits.

Clin stat programme was then used to calculate paired t-test value, 95% confidence interval and 2-tailed probability (p value), comparing men to women.

Results: A total of 223 patients had 3 nurse-measured BP readings available, with 130 men and 93 women. The mean sBP and sBP variability [mean sBP (variability)] for men and women were 138.86 (10.77), and 137.97 (13.11), respectively. We found women to have statistically significant higher sBP variability compared to men, with p value 0.0254 (95% CI 0.290-4.389).

Discussion: These Results show women to have greater sBP variability than men, hence increasing their risk of stroke. What remains to be found is the pathophysiology of this gender difference.

755 Etiology of stroke and risk factors

ATRIAL FIBRILLATION DETECTED BY ECG DATABASE SCREENING OF ISCHEMIC STROKE PATIENTS

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Introduction: Atrial fibrillation (AF) is an established risk factor for ischemic stroke. History-taking at acute stroke onset has limited reliability regarding verification of prior AF which may cause underdiagnosis of AF. The aim of our study was to assess the prevalence of AF in first-ever ischemic stroke patients using retrospective review of digital ECGs stored in hospital database. We also evaluated previous or ongoing treatment with oral anticoagulants (OAC).

Methods: The study material comprised 336 consecutive pts (age 74±11 y, 200 men) with first-ever ischemic stroke enrolled in Lund Stroke Register during 1 year. Medical records were reviewed for AF history, previous or at stroke onset ongoing OAC treatment, stroke severity by NIH stroke severity scale (NIHSS) and cardiovascular risk profile by CHA2DS2-VASc scale. Regional ECG database containing all ECGs taken in the hospital catchment area, including primary care outpatient clinics, starting from 1988 were reviewed for documented AF episodes prior to the stroke admission.

Results: In total, 1890 ECGs were reviewed (5,6±7,8 per pt). By index admission, 98 pts (29,2%, 59 men) had prior or current AF ("AF pts"): 70 pts (20,8%) on admission ECG; 22 pts (6,5%) on retrospective ECG, 14 of whom had no prior AF history mentioned in their admission medical records; and 6 pts (1,8%) had AF history without ECG documentation. AF patients were older (80±8 vs 72±12 y, p<0.001), had higher CHA2DS2-VASc score (4,0±1,6 vs 3,2±1,7, p<0.001), higher NIHSS score (9,0±9,3 vs 5,4±6,4, p<0.001) and higher in-hospital mortality (8.2% vs 1.7%, p=0.007) than patnients without AF. Twelve of 98 AF patients received OAC prior to stroke (12, 2%), of whom only 7 were treated with OAC at stroke onset (INR<2.0 in 3 of 7 patients at admission).

Conclusions: A vast majority of AF patients suffering from ischemic stroke are not receiving adequate OAC therapy at stroke onset. Retrospective review of ECGs from clinical databases allows detection of otherwise unknown AF cases. This approach may detect more patients with AF and thereby enhance OAC therapy to prevent stroke.

756 Etiology of stroke and risk factors

METABOLIC SYNDROME COMPONENTS ARE PREDICTORS OF BOTH INTRACRANIAL AND EXTRACRANIAL STENOSES IN A BRAZILIAN POPULATION WITH ISCHEMIC STROKE

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Background: Metabolic syndrome (MS) is a multiplex risk factor for vascular diseases which can be easily assessed by physical examination and basic laboratory evaluation. The contribution of MS and its various components as risk factors for intracranial and extracranial stenoses (ICS and ECS) is not well known. We aimed to determine the prevalence of MS and to identify which components better predict ICS and ECS in patients with ischemic stroke.

Methods: Consecutive patients admitted to a university-based outpatient stroke clinic were submitted to 64-slice spiral CT angiography (CTA) of the intracranial and extracranial brain vessels. Patients with a contraindication to CTA (iodine allergy or renal failure) were excluded. MS was defined by at least three of the following: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, history of hypertension and diabetes. Multivariable logistic regression analysis was performed including variables with a possible (P<0.1) association in univariable analyses, searching for predictors of ICS and ECS.

Results: Thirty-seven patients were studied, mean age 60±13 years, 60% female. The prevalence of ICS, ECS and MS was 33%, 41% and 62%, respectively. Critical (>70%) stenoses were present in 13% (ICS) and 11% (ECS) of patients. In multivariable analyses, only hypertriglyceridemia remained a predictor of ICS (OR=18.2; 95% CI=1.8-200.0, P=0.015), while hypertension was the only predictor of ECS (OR=30.4; 95% CI=1.2-778.4, P=0.039).

Conclusion: Different components of the MS are associated with ICS or ECS. These findings may have implications for secondary preventive strategies towards atherosclerotic stroke.

757 Etiology of stroke and risk factors

ASCO CLASSIFICATION APPLIED IN A BRAZILIAN POPULATION

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Background: Stroke is the leading cause of death in Brazil and functional disability around the world. However, there is few data about acute stroke surveillance and its epidemiology and etiological profile in Brazil. Indeed, most of the studies are restricted to a subgroup of patients, without continuous follow-up. We aimed to assess a group of acute ischemic stroke patients in the Emergency Unit of a tertiary hospital of a middle-sized city in Brazil included in a local registry (REAVER), using the phenotypic classification ASCO.

Methods: We reviewed charts of patients with cerebrovascular disease that presented to our center between January2006 and June2008. Neuroimaging and laboratory tests were evaluated to categorize patients in each phenotype ASCO, as following: A=atherosclerosis; S=small vessel disease; C=cardiac disease; O=other causes. For each phenotype, a score is used, depending on the presence and its relationship to the stroke causality. Each of the 4 phenotypes is graded 1, 2, or 3. One for definitely a potential cause of the index stroke, 2 for causality uncertain, 3 for unlikely a direct cause (but disease is present). When the disease is completely absent, the grade is 0; the grade is 9 for insufficient workup.

Results: We observed that 16,3% of the patients were classified as A1; 18,6% as S1, 34,3% as C1 and 7,3% as O1, whereas 37,5% were assigned to S3 and 44,1% were classified as A9.

Conclusions: The ASCO classification can be used in a collective way, for a phenotypical classification of a large group of patients included in a registry. We could observe that in our casuistry the cardioembolic etiology has a great importance. On the other hand, we have a low incidence of stroke due to lacunar disease, despite the high incidence of oligossymptomatic or silent small vessel disease. Additionally, the ASCO system helped identify that the athethrombotic etiology had still been insufficiently investigated, being probably underdiagnosed in this population.

758 Etiology of stroke and risk factors

PHYSIOLOGICALLY EQUIVALENT TEMPERATURE AND STROKE ATTACK RATES

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Background: Although studies have examined effects of temperature on stroke rates, the incorporation of other climate parameters may be more meaningful. We examined the association of physiological equivalent temperature (PET), a thermal index based on the human energy balance (including the effect of air temperature, humidity, wind speed and cloud cover), on stroke attack rates.

Method: Stroke events registered by the Cardiac and Stroke Outcomes Unit from 1996 to 2008 in 4 coastal local government areas of the Hunter region of New South Wales were linked with weather data obtained from the Australian Bureau of Meteorology. Calculated PET (°C) and temperature (min, max) data from the day of and preceding admission were allocated into categories.

Results: There was no effect of high air temperatures or PET on stroke attack rates (N=4662). However, the lowest categories of PET, and minimum and maximum temperatures were all associated with higher stroke rates, greatest on days with PET <15°C (mean [SD] 12.7 [1.8]°C). Compared with the highest stroke rate category,

reductions in risk were of 10% (p=0.002) for 15-19°C, 16% for 20-24°C (p<0.005), 13% for 25-29°C (p<0.005), 20% for 30-34°C (p<0.005), 18% for 35-39°C (p<0.005),19% for 40-44°C (p=0.01) and 18% (p=0.07) for ≥45 °C.
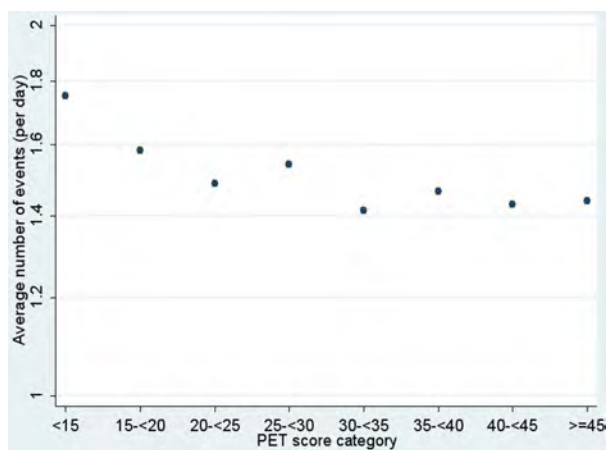
Discussion: An association of high stroke rates with days of low PETs, possibly due to behavioural (e.g. access to air conditioning) or physiological adaptations, could explain the discrepancy between out negative finding and that of previous studies showing positive associations between high temperatures and stroke admissions.

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759 Etiology of stroke and risk factors

INTRACRANIAL ARTERIAL STENOSIS AND CLINICAL RISK FACTORS IN ACUTE STROKE PATIENTS
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Background and Aims: Intracranial arterial stenosis are relatively common findings of stroke patients in Asia area. We reviewed stroke database to investigate clinical risk factors related to intracranial arterial stenosis, including carotid disease, and peripheral arterial disease which reflects advanced atherosclerosis.
Methods: Acute stroke patients at the National Health Insurance Corporation Ilsan Hospital from January 2008 to December 2010 with available transcranial Doppler (TCD) examination, carotid ultrasound and ankle-brachial indexes (ABI) formed the analysis cohorts. Retrospective review was performed.
Results: A total of 642 patients were included during that period, 212 patients with incomplete TCD study due to poor insonation windows were excluded (33%). According to TCD criteria, 3 groups of intracranial arterial stenosis are defined: 0 vessel stenosis is in 220 patients (51%), 1-2 vessels in 125 patients (29%), more than 3 vessels in 85 patients (20%). As the arterial number of intracranial stenosis increased, ABI is decreased (P=0.013) and the size of carotid artery plaque is increased (P=0.011). Among the risk factors, Diabetes, age, past stroke history are increased (P=0.0000, P=0.006, P=0.05) and HDL cholesterol showed tendency of decrease (P=0.033). However hypertension, smoking, total cholesterol, LDL cholesterol, triglyceride and sex are not correlated with intracranial arterial stenosis.
Conclusions: Among the acute stroke patients, about a half of them have intracranial arterial stenosis and these patients tend to have higher burden of advanced atherosclerosis as evidenced by a higher prevalence of Diabetes, large sized plaques of carotid artery and peripheral arterial occlusive disease.

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760 Etiology of stroke and risk factors

CLINICAL, ANGIOGRAPHIC, AND HIGH-RESOLUTION MR IMAGING RISK FACTORS FOR CAROTID STENOSIS PROGRESSION
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Background: Carotid stenosis (CS) progression is associated with a higher risk of ischemic event, and progression is often used to select patients for endarterectomy.

We sought for clinical, angiographic, and plaque high-resolution MRI risk factors for CS progression.
Methods: HIRISC is an ongoing cohort study of patients with nonsurgical ≥50% (ECST) recently symptomatic CS or ≥50% (NASCET) asymptomatic CS. In addition to the clinical follow-up (FU) planned by the protocol, patients from our centre had routine ultrasounds FU. Patients were prospectively imaged in 1.5-T MR units using a standardized protocol. Two observers, blinded to clinical data, independently examined initial arterial work-up, and plaque MRI. Intraplaque haemorrhage (IPH), calcifications, cap rupture, and high lipid content (mean ratio lipid/plaque surface ≥40%) were recorded. Stenosis was categorised by the NASCET method as follows: <50%, 50-69%, ≥70% at baseline and at each FU visit, using validated morphologic and hemodynamic criteria. CS progression was defined by any increase in NASCET category or occlusion.
Results: Among 131 patients, 20 had no ultrasound FU, 2 had FU < 6 months, 2 had no MRI available. After a median (IQR) FU of 2.1 years (0.9-3.9), 11/107 (10.3%) had CS progression: <50% group: 3/41, 50-69% group: 6/57 (OR=1.5; 0.4-6.3), ≥70% group: 2/9 (OR=3.6; 0.5-25.8). Compared with patients without CS progression, those with progression were older (age>75: OR=2.9; 0.8-10.7), had more severe atherosclerosis (contralateral CS≥70%: OR=2.5; 0.4-14.8; carotid artery tandem lesion: OR=5.1; 0.8-31.9), and were more likely to have cap rupture (OR=2.7; 0.7-9.5) and high lipid content (OR=4.1; 0.7-23.9) on plaque MRI. No relation was found with IPH. However, no association was statistically significant. Results were unchanged after adjustment for potential confounders.
Conclusions: Age, severity of atherosclerotic disease, cap rupture and high lipid content may predict CS progression.

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761 Etiology of stroke and risk factors

BRAIN-DERIVED NEUROTROPHIC FACTOR AND ITS RELATED FACTORS AFTER ISCHEMIC STROKE - RESEARCH FOR BIOMARKERS IN ISCHEMIC STROKE (REBIOS) -
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Background: There is no biomarker clinically available for diagnosis of ischemic stroke so far. In the present study, we aimed to discover blood biomarkers for ischemic stroke and examined their significance in pathophysiology of ischemic stroke.
Methods: We designed Research for Biomarkers in Ischemic Stroke (REBIOS) study, and 173 patients with cerebral infarction (atherothrombotic (AT) 34, cardioembolic (CE) 50, lacunar (Lac) 45, and unclassified (Unc) 44 cases) were recruited from the Fukuoka Stroke Registry, a prospective multi-centered study for acute stroke in Japan. Blood samples were obtained at 5 points after the stroke onset, day 0 (within 24 hours), 3, 7, 14, and 90. Ninety molecules were measured by HumanMAP® v1.6 (Rules-Based Medicine, Inc.). Age and sex-matched healthy subjects were enrolled from the Hisayama study in Japan as the control (n=171).
Results: We identified BDNF (brain-derived neurotrophic factor) as one of the biomarkers that increased immediately after the stroke onset (3.03±0.18ng/ml, mean ± SEM), compared with the control (2.06±0.11ng/ml, P<0.0001). BDNF levels in Lac were highest among the 4 subtypes throughout the observation period. At day 0, BDNF values were positively correlated with epidermal growth factor (EGF) values (r2=0.665) and LDL cholesterol, while inversely correlated with age. BDNF values remained high level at day 90 in the good prognosis group (modified Rankin scale (mRS) 0-2, 3.14±0.25ng/ml), while those were significantly decreased in the poor prognosis group (mRS 3-6, 2.31±0.26ng/ml).
Conclusions: Plasma BDNF levels could be a biomarker useful for diagnosis of ischemic stroke and be associated with functional prognosis. BDNF values were positively correlated with EGF and LDL cholesterol levels, and thus may play some roles in mediating neuronal recovery through cholesterol metabolism in ischemic stroke.

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762 Etiology of stroke and risk factors

SIGNIFICANT ASSOCIATION BETWEEN NOCTURNAL HYPERTENSION AND CEREBRAL MICROBLEEDS IN HYPERTENSIVE STROKE PATIENTS
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Background: Cerebral microbleeds (CMBs), indicative of cerebral small-vessel disease, may occur with increased frequency in patients with hypertension. However, little is known about the relation of CMBs with specific blood pressure (BP) levels. Objective: We assessed the relation between ambulatory measured BP and the presence of CMBs in a cohort of acute noncardioembolic stroke patients.

Methods: A total of 53 hypertensive patients (37 males, age 64.0±9.0 years) underwent 24-hour ambulatory BP monitoring two weeks after stroke onset (off-antihypertensive medication) and brain MRI to detect CMBs. We performed logistic regression analyses to relate the following BP components to CMBs: the mean 24-hour, awake, and sleep BP; morning, evening, lowest, prewake BP; morning surge, nocturnal BP fall. Models were adjusted for age, gender, and additionally for cardiovascular risk factors.

Results: We detected CMBs in 26 patients (49.1%). Elevated nocturnal diastolic BP rather than systolic BP was independently associated with CMBs at one SD increment in BP (OR 2.63; 95% CI, 1.26-5.50; P=0.01). The odds ratio for CMBs in reverse dipper group was 6.67 (95% CI, 1.32-33.69; P=0.022). CMBs were not associated with morning surge.

Conclusions: CMBs are frequently found in stroke patients with hypertension, and are independently associated with elevated nocturnal diastolic BP as well as nocturnal BP fall status.

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763 Etiology of stroke and risk factors

INFLAMMATORY MARKERS AND X-RAY SUB-GROUP ANALYSIS IN PATIENTS FOLLOWING ACUTE ISCHAEMIC STROKE/TIA

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Introduction: Little is known about inflammatory markers correlation with CT head scan sub-groups, it might be that the pathological process involved in small vessel disease may differ significantly from discreet cerebral infarct.

Methodology: 113 patients were included, those with cardio-embolic disease and inflammatory processes were excluded. HS-CRP, D-dimer and monocyte count were taken during the acute phase. CT scans of head on admission were reviewed by an experienced Consultant radiologist and were divided into (1) normal CT, (2) discreet cerebral infarct, (3) small vessel disease +/- cerebral infarct. Risk factors were treated according to ESC guidelines. Patients were followed for up to two years and vascular events were recorded including death, coronary events, cerebro-vascular events etc. as per REACH registry.

Results: Inflammatory marker data is subject to attrition rates. There is no significant difference in the value for the inflammatory markers between these three x-ray sub-types.

Table 1. Events in Sub-Groups

	D-dimer		MC		HS CRP	
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Normal	202.7	(163.2)	0.414	(0.150)	9.20	(21.5)
Infarct	232.4	(161.2)	0.493	(0.192)	13.92	(21.1)
SVD+/- infarct	213.7	(143.5)	0.440	(0.130)	16.12	(27.8)

A straightforward cross-tabulation of Vascular Events in subjects within each sub-group yields the table.

Table 2

	Normal	Cerebral Infarct	SVD (+/- cerebral infarct)
Event			
No	29	40	17
Yes	5	9 13	

The observed proportions of subjects experiencing an event clearly vary considerably, and the hypothesis that there are equal proportions of events in each sub-group is rejected (chi-squared=8.6, degrees of freedom=2, p=0.013). It is clear that the proportion is lowest in the Normal sub-group, highest in the SVD sub-group; the proportion for Infarct sub-group is between the two others, and different from either.

Conclusion: Small vessel disease seems to incur high risk. No inflammatory correlation demonstrated with CT sub-type.

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764 Etiology of stroke and risk factors

YOUNG ADULTS OFTEN SHARE SIMILAR STROKE ETIOLOGIES WITH THE ELDERLY: RECENT LESSONS FROM THE APPLICATION OF THE NEW ASCO STROKE SUBTYPE CLASSIFICATION

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Background: Young adult stroke patients have long been reported to suffer from rather different etiologies than the elderly but subclassification of stroke was biased by insufficient work-up and the TOAST classification disregarding concomitant sources of stroke as "undetermined" in about one third of the patients.

Methods: The ASCO classification was compared with the TOAST classification in a prospective series of young adult patients <45 years of age admitted to our Stroke Unit. All patients received full stroke work up according to the ESO guidelines, which was documented in our stroke registry: Neurological examinations, brain MRI and MRA, ultrasound cerebrovascular imaging, ECG-monitoring, blood tests etc. Most of the patients (70.2%) also received transesophageal echocardiograms (TEE). All risk factors were recorded in detail.

Results: 104 patients (46 men, 58 women) with mean age of 38±6.9 years were included in the study. Mean NIHSS score (±SD) was 3±5 on admission and 1±4 on discharge. The classification using TOAST/ASCO (grade 1) was: Macroangiopathic 26%/8.7%, cardiac origin 21.2%/10.6%, microangiopathic 9.6%/9.6%, other causes 3.8%/13.5% and undetermined 39.4%/19.2% (for A0S0C0O0). 29 of 74 patients with TEE (39.2%) had a patent foramen ovale (PFO). The most common risk factors were smoking (55.2%), hypertension (31.4%) and hyperlipidemia (27.6%). Hypoplastic posterior circulation (21.9%) and migraine (21.0%) were also quite common.

Conclusions: According to the ASCO classification young adult patients with ischaemic stroke share the characteristics of atherosclerosis with an elderly ischaemic stroke population much more than hitherto assumed. In addition, provided TEE/TCD studies are regularly performed, a significantly elevated percentage of young patients reveal comorbidities with PFOs, vascular abnormalities in the posterior circulation and migraine. The ASCO classification should be preferred for a better classification of stroke subtypes.

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765 Etiology of stroke and risk factors

SHOULD PATIENTS WITH STROKE/TIA FROM PRESUMED LARGE-ARTERY ATHEROSCLEROSIS BE MORE AGGRESSIVELY INVESTIGATED FOR A CARDIOEMBOLIC CAUSE IF CAROTID AND CORONARY VESSEL IMAGING SHOW LITTLE DISEASE?

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Background: As per TOAST classification 25% of ischaemic stroke remain of undetermined aetiology. Most patients over 50 years with vascular risk factors do not under go further vascular imaging other than carotid vessels. The yield of trans-thoracic echo cardiogram (TTE) is poor and routine ECG is likely to miss paroxysmal Atrial Fibrillation (PAF).

Method: We investigated 75 patients under 65 years for concurrent coronary artery disease following ischaemic stroke or TIA with CT coronary calcium score. 23 patients between 50 and 65 years with negligible scores (less than 10) were reviewed for the possible aetiology of the ischaemic event. All were investigated for other large artery disease using Carotid Doppler, CT angiography or contrast enhanced MRA. All had a 72 hour R test to detect PAF.

Results: Average age was 58.4 years with 17 being male. 15 (65.2%) had no coronary calcium. 8.7%, 69.6%, 43.5% had Diabetes, Hypertension and Hypercholesterolemia. Only 1 had detectable carotid artery disease. 2 (8.7%) had PAF and were warfarinised. 11 TTE were done and all were negative.

Conclusion: Determining the aetiology of the ischaemic event is important as this will direct treatment. In our cohort only 1 had significant proven large artery disease and 2 (8.7%) were anti coagulated due to 72 hour cardiac rhythm analysis. The remaining 20 (87%) had proven absence of large artery disease and hence aetiology

strongly shift towards cardio embolic source. Transoesophageal echocardiography (TOE) studies reports a strong association between aortic atheroma and the development of stroke. TOE also strongly influence secondary prevention and can lead to anti coagulation in up to one third of patients. Therefore even patients between 50 and 65 years with no large artery disease would benefit from TOE and ideally 7 day cardiac rhythm analysis to detect cardio embolic aetiology.

766 Etiology of stroke and risk factors

DIFFERENCES OF THE TIME RATE OF BLOOD PRESSURE VARIATION BETWEEN PATIENTS WITH ISCHEMIC STROKE AND INTRACEREBRAL HAEMORRHAGE

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Background: Time rate of blood pressure (BP) variation is a measure of the speed of BP fluctuations derived from a computerized analysis of 24 hour ambulatory blood pressure monitoring (ABPM). Previous studies have demonstrated that the rate of BP variation is associated with increased target organ damage. The aim of our study was to compare the time rate of BP variation between patients with ischemic stroke (IS) and intracerebral haemorrhage (ICH).
Methods: A total of 109 consecutive acute stroke patients underwent 24-h ABPM. Patients with atrial fibrillation were excluded from the study. The time rate of BP variation was defined as the first derivative of the BP values against time. All demographics, risk factors and BP parameters were documented. Patients were divided into two groups: IS group and ICH group. Statistical analyses were performed using independent sample t-test and x2 tests.
Results: Our study population consisted of 94 (86,2%) with IS and 15 (13,8%) with ICH. There were no statistically significant differences regarding baseline characteristics, risk factors and 24-h BP values between the two groups. The morning surge rate of systolic BP variation was significantly higher in ICH group (0.774mmHg/min; 95% CI 0.592-0.682) than in IS group (0.615mmHg/min; 95% CI 0.468-0.538). Both groups did not differ significantly regarding diastolic rate of BP variation.
Conclusion: Patients with ICH presented significantly higher time rate of systolic BP variation during the morning surge period than patients with IS.

767 Etiology of stroke and risk factors

TEMPORAL DISTRIBUTION AND MAGNITUDE OF THE VULNERABILITY PERIOD AROUND STROKE DEPEND ON SUBTYPE

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Introduction: Although there are several studies regarding the course of recurrent cerebrovascular events in patients with ischemic stroke, there are only scarce data on the evolution of premorbid events with time. Aim is to analyze the rate and time distribution of pre- and postmorbid cerebrovascular events in a single ischemic stroke population, and whether it depends on the underlying etiology of the index stroke.
Methods: All acute strokes registered in ASTRAL between 2003 and 2010 were included in the study. The event that led to admission was considered the index stroke. The most recent or the first recurrent of any of the following four cerebrovascular events was used: ischemic stroke, transient ischemic attack, intracranial haemorrhage and subarachnoid haemorrhage. Frequency distribution and cumulative relative distribution graphs of the most recent and first recurrent event were drawn in weekly and daily intervals for all strokes, and each type.
Results: 539 (24.5%) out of 2203 patients had a previous cerebrovascular event. When comparing identical time points before and after the index stroke, the frequency of events was mostly reduced in the first week after (vs. before) the stroke (1.0% vs. 4.2%, p<0.001), and the first month (2.7% vs. 7.4%, p<0.001), and then ebbed out somewhat over the first year (8.4% vs. 13.1%, p<0.001). On a daily basis the peak frequency was noticed at day -1 (1.6%) with a subsequent reduction to 0.7% at the day of the index stroke, and to 0.17% the first 24h hours after. The event rate in patients with atherosclerotic stroke was particularly high around the index event, but the cumulative recurrence rate over one year was similar in all stroke types, including lacunar.
Conclusions: We confirm a short window of increased vulnerability in ischemic stroke patients, and show a 4-, 3- and 2-fold reduction of cerebrovascular events at 1 week, 1 month and 1 year respectively after a stroke when compared to

identical pre-stroke periods. This break in the "stroke wave" is particularly striking after atherosclerotic and lacunar strokes and probably illustrates the efficiency of secondary stroke prevention.

768 Etiology of stroke and risk factors

DIFFERENCES IN THE IDENTIFICATION OF CEREBROVASCULAR PHENOTYPES BETWEEN TWO ETIOLOGICAL STROKE CLASSIFICATIONS: TOAST AND ASCO

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Backround: The classifications of stroke are based on identifying their most likely cause. A new classification capable to describe a "stroke phenotyping" has been recently proposed: ASCO; A, atherosclerosis; S, small vessel disease; C, cardiac source; O, other cause. Each one is graded 1, 2, 3 (according to the degree of causality), 0 or 9 if the disease is absent or is not possible due to insufficient workup. The main objective is to analyze and contrast the Results of TOAST classification to the phenotype of cerebrovascular disease in the ASCO classification.
Methods: Observational study of the first 30 ischemic stroke patients admitted to our Stroke Unit in 2010. The clinical records were given to two stroke expert neurologists, two general neurologists and two resident neurologists, who classified each stroke patient according to TOAST and ASCO classifications.
Results: ASCO classification identified atherothrombotic, small vessel disease and cardiac source in 95 to 100% (minimum and maximum percentage between the six observers) of the patients classified as such according to TOAST. In 80% to 94% of patients with cardiac source C1 by ASCO (definitively cause of stroke), presented scores of 1-3 in the other items (A, S, O). Evidence of atherosclerosis and small vessel disease (scores 1-3) were observed in 63%-80% of strokes caused by cardioembolism according to TOAST, and ASCO revealed evidence for other stroke etiologies in most of strokes of undetermined origin by TOAST (50%-80%, 40%-75%, and 40%-99%, for atherosclerosis, cardioembolism and small vessel disease, respectively).
Conclusion: ASCO classification identified the principal cause of stroke and the potential burden of other diseases associated with stroke risk and ignored in other classifications.

769 Etiology of stroke and risk factors

CONNECTION BETWEEN FATAL INTRACEREBRAL HAEMORRHAGE AND FACTOR XIII VAL34LEU POLYMORPHISM

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Introduction: Blood coagulation factor XIII (FXIII) plays a key role in the protection of fibrin against fibrinolysis, in the crosslinking of fibrin and its mechanical strength. Inasmuch as no earlier papers studied the connection of the FXIII A-subunit Val34Leu polymorphism with fatal primary intracerebral haemorrhages (PICH), we studied the prevalence of this polymorphism in stroke patients with fatal PICH and population control matched for age and gender.
Methods: The population control group consisted of 1146 healthy individuals. The prevalence of genotypes, Leu34 carriers and Leu34 allele frequencies were studied in this group according to genders and tertiles. The prevalence of this polymorphism was also determined for patients with fatal PICH (n=98, female/male:41/57) and controls (n=98 female/male:41/57). DNA was obtained from peripheral white blood cells in case of controls and from paraffin embedded tissue sections in case of patients died of PICH. FXIII-A Val34Leu polymorphism was identified by real-time PCR using fluorescence resonance energy transfer detection and melting curve analysis.
Results: We analyzed control group according to gender and tertiles and observed no difference for genotypes, Leu34 carriers or Leu34 allele frequency. However, as fatal PICH group compared to aged and sex matched controls, the Leu/Leu genotype was more frequent in total [OR: 5.65 (1.8-17.3)] or male subgroups [OR: 8.12 (1.7-37.9)]. The odds for increasing the risk of PICH against the control group were: total OR: 3.38 (1.9-5.7), males OR: 3.5 (1.7-7.0), females OR: 2.9 (1.1-7.0).
Discussion: The Leu34Leu homozygous variant of the FXIII Val34Leu polymorphism significantly increased the risk of fatal PICH stroke.

SERUM CONCENTRATIONS OF TNF ALPHA AND INTERLEUKINS 6 AND 10 IN PATIENTS WITH ICA STENOSIS

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Background: Few published reports about the prognostic value of inflammatory markers in patients with ICA stenosis together with the knowledge about inflammatory processes in the development and progression of atherosclerosisled us to further explore those problems. The aim of the study was to assess serum concentrations of TNF alpha and interleukins 6 and 10 in patients with ICA stenosis.
Methods: 65 patients (20 females and 45 males) aged 55-80 years with ICA stenosis (>50%) where enrolled to the study. The control group consisted of 30 patients (20 females and 10 males) aged 50-78 years. In 39 patients the stenosis was symptomatic. All patients underwent clinical examination. In all patients stroke risk factors were identified and laboratory tests were performed (blood count, sedimentation rate, TNF alpha, interleukin 6, interleukin 10, creatinine, glucose, CRP, fibrinogen serum concentration, lipidogram and general urine examination). The extent and the morphology of the ICA stenosis were assessed with the Color Coded Duplex.
Results: Mean interleukin 6 serum concentration (13,65 pg/ml) was higher in patients with ICA stenosis then in healthy individuals (5,88 pg/ml) (p=0,001). There were no statistical differences between mean TNF alpha (14,32 pg/ml) and interleukine 10 (3,72 pg/ml) serum concentration in patients with carotid stenosis and the control group (TNF aplha – 11,78 pg/ml; intereukine 10 – 3,18 pg/ml). There were no statistical differences between mean TNF alpha interleukin 6 and interleukine 10 serum concentration in patients with symptomatic carotid stenosis and patients with asymptomatic carotid stenosis. In the group of patients with ICA stenosis the elevated TNF alpha levels were significantly related to increased interleukin 6 levels (p=0,00002). At the same time increased interleukine 6 levels were statistically related to elevated interleukine 10 levels (p=0,0008).
Conclusion: Increased interleukine 6 concentrations in the serum of patients with atheromatic ICA stenosis suggest their involvement in that pathology.

CANNABIS: A NEW RISK FACTOR FOR ISCHEMIC STROKE?

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Background: There is a temporal relationship between cannabis use and stroke in case series and population based studies. We aimed to determine the prevalence of cannabis use in younger stroke patients and, in a subset of patients aged 40-55 years, whether this differed from control patients.
Methods: Consecutive stroke patients aged 18-55 years had urine screens for illicit drugs between January 2009 and January 2011. Ethics committee approval was only obtained to drug-screen a control cohort of patients aged 40-55 years who were admitted under the internal medicine service with non-cardiovascular diagnoses. Control drug screens were performed on residual urine samples collected for other reasons and all identifying information was removed before testing.
Results: One hundred and fourteen of 173 (66%) stroke patients [73 (64%) men and 41 (36%) women; mean (SD) age 44.8 (8.6) years], had urine drug screens. Ninety-nine of 114 (87%) patients had ischemic stroke (IS) and 15 (13%) had intracerebral hemorrhage (ICH). Seventeen of 99 IS patients (17%; 13 men and 4 woman) tested positive for cannabis, and one patient each tested positive for methamphetamines or opiates. There were no baseline differences in age, sex, ethnicity or vascular risk factors (including tobacco use or cardiac arrhythmia), between those with and without positive drug screens (Chi-squared, p>0.10). All 15 ICH patients had negative drug screens. Thirteen of 77 (17%) IS patients aged 40-55 years tested positive for cannabis compared with only six of 77 (8%) control patients (Chi-squared p=0.04).
Conclusion: Recent cannabis use is high in younger IS patients and, at least in patients aged 40-55 years, is double the rate seen in patients admitted to hospital with non-stroke diagnoses. While these findings require independent confirmation, this study suggests that cannabis may be a risk factor for IS.

PREVALENCE OF INTRACRANIAL OCCLUSIVE DISEASE IN PATIENTS WITH ISCHAEMIC STROKE AND TRANSIENT ISCHAEMIC ATTACK

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Background: Large artery intracranial occlusive disease (LAICOD) causes 8-10% of strokes in North America and 30-50% in Asia. We aimed to determine the prevalence of LAICOID in ischaemic patients using CTA.
Methods: Retrospective study of consecutive stroke and TIA patients from 09/2006 to 08/2008 who had CTA at the Utrecht Stroke Center. The demographics, cerebrovascular risk factors, clinical presentation (OCSP) and the presence of extracranial internal ICA stenosis were obtained from a database. We assessed presence of occlusion or stenosis of intracranial ICA and MCA on 3 mm-reconstruction axial scans CTA images. Clinical and demographic characteristics were compared between patients with or without LAICOID.
Results: We studied 220 patients (187 with stroke, 33 with TIA): mean age was 65 years, 57,3% were male. Intracranial stenosis was found in 6,4% (CI 3,9-10,4), intracranial occlusion in 34,5% (CI 6-41,0), both occlusion and stenosis in 2,3% (CI 1-5). Clinical characteristics (age, sex and cerebrovascular risk factors) did not discrimate between patients with or without intracranial pathology. In univariate analysis we found an association between intracranial occlusion and stroke (as compared to TIA): OR 3,43 (CI 1,19-10,63); intracranial occlusion and stroke subtype TACI-PACI (as compared to LACI): OR 23,14 (CI 7,9-90,7); intracranial occlusion and extracranial ICA atherosclerosis: OR 40,12 (CI 11,02-173); intracranial occlusion and timing of CTA (<24 h versus >24 h): OR 3,07 (CI1,17-9,44). In the multivariate analysis the predictors of intracranial occlusion or stenosis were stroke subtype TACI -PACI: OR 6,7 (CI 2,9-15,4) and extracranial ICA pathology: OR 25,6 (CI 7,2-90,9).
Conclusion: Prevalence of intracranial stenosis is similar to that shown by previous studies in white population. LAICOID includes two different kinds of disease: stenosis as result of atherosclerotic disease and occlusion caused by an embolic mechanism.

ASSOCIATION OF RS4578424DNA MARKER ON CHROMOSOME 15 WITH TOTAL STROKE RISK IN MOSCOW SLAVONIC POPULATION

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Background and purpose: A number of previous genome wide association studies recently identified some genome variants to be associated with stroke in local populations. The aim of our study was to assess the individual risk of stroke development in Slavonic population.
Methods: We performed a case-control association study in 694 stroke patients from Moscow Slavonic population and 715 controls from the same population. Standard examinations including CT, MRI, duplex, Echo-CG, CTA, and MRA were performed to identify the stroke cases. The stroke subtypes were diagnosed according to the TOAST criteria. Whole genome associative study was performed using DNA microarrays HumanCyto12 v. 2 ("Illumina", USA), allowing typed more than 300, 000 SNP and CNV regions also.
Results: The resulting raw data were processed using software packages Genome Studio, PLINK, Helix Tree and eventually found several SNPs associated with the development of acute stroke. The most statistically significant association with the rs4578424DNA marker, located on gene TUB locus on chromosome 15. This gene encodes a protein that participates in the system of signal transduction through G proteins, and may be associated with violation of lipid metabolism.
Conclusion: Our data suggest the association of rs4578424 on chromosome 15 with total stroke risk formation.

774 Etiology of stroke and risk factors

CLINICAL APPLICABILITY OF THE A-S-C-O CLASSIFICATION IN THE DIAGNOSIS OF ISCHEMIC STROKE AND TRANSIENT ISCHEMIC ATTACKS

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Background: A-S-C-O is a new approach to stroke subtyping that introduces a complete "stroke phenotyping" classification. Patients are characterized by A-S-C-O: A: atherosclerosis, S: small vessel disease, C: cardiac source, O: other cause, and graded according to causality likelihood (1 = definitely a potential cause, 2 = Causality uncertain, 3 = Unlikely a direct cause (but disease is present), 0 = no disease, 9 = insufficient work-up). Our aim was to compare A-S-C-O with the Spanish Neurology Society/Cerebrovascular Study-Group (SNS/CSG) etiologic classification, and to evaluate its clinical applicability in daily practice.

Methods: Etiologic diagnosis of patients with ischemic stroke/TIA admitted in our Stroke Unit for 4 months of 2009 were reviewed. Patients were re-classified according to the A-S-C-O classification.

Results: We identified 120 patients. Subtypes according to SNS/CSG criteria: atherothrombotic 11%, Small vessel: 22%, cardioembolic 33%, Infrequent: 2%, undetermined 32%. According to A-S-C-O, 17% of patients scored A1, while only 4% were "purely atherothrombotic" (A1-S0-C0-O0), 58% of patients presented some degree of atherosclerosis (A1, A2 or A3). 15% scored S1. Some degree of small vessel disease (S1, S2 or S3) was detected in 69% of patients. 30% of patients scored C1 but only 8% were "purely cardioembolic" (A0-S0-C1-O0). 2% of cases scored O1, and in 10% no cause was detected (A0-S0-C0-O0). 65% patients were classified in more than one category.

Conclusions: A-S-C-O classification allows a more precise and complete etiology characterization of stroke patients. It can offer treatments tailored to each case and allows to monitor risk factors and potential causes of stroke. This subtyping system might be used in the daily clinical practice, although it may complicate decision-making.

775 Etiology of stroke and risk factors

PREDICTORS OF NEW ONSET ATRIAL FIBRILLATION IN PATIENTS WITH CRYPTOGENIC STROKE: A RETROSPECTIVE COHORT STUDY

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Introduction: A significant proportion of stroke of undetermined aetiology is due to undiagnosed atrial fibrillation (AF). The present study sought to evaluate in-hospital factors associated with new-onset AF after hospital discharge in patients with ischemic cryptogenic stroke.

Methods: One hundred and forty three patients with ischemic cryptogenic stroke were followed-up. AF was diagnosed as an irregular non-sinus rhythm lasting > 30 minutes detected by either 24-h ambulatory ECG monitoring or 12-lead surface electrocardiogram. Clinical, biological and echocardiographic characteristics of these patients were retrospectively recorded and used to produce a grading score for predicting AF.

Results: Over a median follow-up period of 839 days, 21 AF (15%) were diagnosed. In multivariate analysis, factors associated with AF were NIHSS ≥ 2 (1 point), baseline troponin levels ≥ 0.02 μg/l (1 point) and left ventricular end diastolic diameter ≥ 50 mm (2 points). A score ≥ 3 identified patients with new-onset AF with a sensitivity of 76% and a specificity of 78% (AUC: 0.867; p< 0.001).

Conclusions: In ischemic cryptogenic stroke, this score may help screen for patients at high risk of new onset AF after hospital discharge. These Results warrant attempt at replication in further prospective studies.

776 Etiology of stroke and risk factors

PROGRESION OF D-DIMER AND MONOCYTE COUNT OVER TWO YEARS IN PATIENTS WITH ACUTE ISCHAEMIC STROKE/TIA

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Introduction: It is recognised that inflammatory markers are elevated during acute TIA/ischaemic stroke. However, progression of said markers during treatment with statins, anti-platelet agents and risk control is less well documented. The peripheral monocyte is obviously related to the plaque macrophage and its behaviour is interesting.

Methodology: 113 patients with a clinical diagnosis of stroke/TIA were included. Those with cardio-embolic disease and inflammatory processes were excluded, as were those with D-dimer levels >1000. These samples were measured in duplicate over a period of two years. Risk factors were treated according to ESC guidelines.

Results:

Month	D-dimer		Monotype Count	
	Mean	**(SD)**	**Mean**	**(SD)**
0	218.5	(156.1)	0.455	(0.167)
4	167.8	(119.8)	0.436	(0.154)
8	150.0	(117.5)	0.434	(0.148)
12	157.4	(131.3)	0.459	(0.152)
16	133.3	(83.1)	0.483	(0.174)
20	139.6	(124.4)	0.490	(0.176)
24	127.1	(110.1)	0.486	(0.174)

Conclusion: Data is subject to attrition rates typically seen in studies of this length based on repeated measures. D-dimer – the data exhibits considerable skewness with a marked trend over time (P=0.001); formal analysis is therefore based on a logarithmic transformation. The trend is characterised by an initial significant fall with further smaller (non-significant) decreases over time. Monocyte count – considerable variablility over time and hypothesis of a constant mean is rejected (P<0.001). The pattern over time is complicated, an initial fall is followed by a larger increase after which mean values remain relatively constant. It remains to be seen if low value inflammatory markers confers a better prognosis for the patient.

777 Etiology of stroke and risk factors

RELATIONSHIP BETWEEN ANKLE-BRACHIAL INDEX AND CEREBRAL ATHEROSCLEROSIS IN ACUTE ISCHEMIC STROKE

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Background and purpose: Low ankle-brachial index (ABI) is known to be a marker of peripheral artery disease (PAD). It is the ratio of tibial artery systolic blood pressure to brachial systolic artery pressure. Because ABI reflects the status of atherosclerosis, the ability of ABI to predict other cardiovascular disease events as well as peripheral artery disease is reported in several population-based studies. Also, some studies suggested that low ABI can be an indicator of stroke events. In this study, we aim to reveal the relationship between ABI and cerebral atherosclerosis using brain magnetic resonance angiography (MRA). Furthermore we aim to determine the concomitant presence of PAD in patient with acute ischemic stroke.

Methods: Men who admitted with diagnosis as acute cerebral infarction or transient ischemic attack (TIA) were included during July, 2009 to July, 2010. Healthy controls were included at the same time. ABI was measured at both posterior tibial and brachial artery. We selected the highest value of ABI among them. All of them were examined brain MRA.

Results: Total 73 people were included. 32 patients were diagnosed as acute ischemic stroke or TIA. 41 controls did not have medical history of PAD and cerebrovascular accident. There were no differences in sex, age, presence of diabetes, and lipid profile (total cholesterol, serum triglyceride, LDL-cholesterol and HDL-cholesterol) between two groups. Statistically significant differences were shown in three variables- presence of hypertension (σ=0.019), current smoker (σ=0.005) and cerebral artery stenosis in the brain MRA (σ=0.002). They are well known to be typical risk factors of stroke as established before. ABI was correlated with cerebral atherosclerosis significantly (σ=0.022). Low ABI (<0.9) was larger in numbers in the groups of cerebral atherosclerosis presence.

Conclusion: The Results of this study showed low ABI would be relation to cerebral atherosclerosis in acute phase of ischemic stroke.

778 Etiology of stroke and risk factors

CLINICAL, FAMILIAL AND RADIOLOGICAL CHARACTERISTICS IN CADASIL PATIENTS AND NOTCH3 NEGATIVE PATIENTS

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Background: CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) is a rare disease resulting from NOTCH3 gene mutations on 19th chromosome, which causes small vessel disorder in brain. To define the clinical and radiological characteristics of CADASIL patients with NOTCH3 gene mutation and NOTCH3 negative patients might better explain the phenotpical and genetical features of CADASIL.
Methods: A total of 2169 patients with the diagnosis of ischemic stroke investigated in our Stroke Unit between years 1996 and 2010 were examined.
Results: There was 1175 males, and 994 females with a mean age of 61.8+12.9 years (ranging between 17 and 96 years). Of these, only 10 patients (6 males, 4 females, between 41 and 71 years) were suspected to have CADASIL on the basis of clinical and radiological findings. Genetic study could not be performed in one patient, and another patient died before genetic examination. The remaining 8 patients were tested genetically, and NOTCH3 gene mutation was detected in 4 patients, while no mutation was detected in 4 patients. One of the mutations was newly defined (heterogenous mutation on exon 4, rs1043994). The mean follow-up duration of these patients was 3.8 years (ranging between 9 months and 10 year). Although the cranial MRI findings were similar, clinical characteristics showed some differences, including younger age at onset and the presence of dementia in family history of patients with NOTCH3 gene mutations.
Conclusions: The diagnostic criteria for the molecular genetics of CADASIL is now known, though pregenetic criteria is not well-defined. As the data on CADASIL patients and NOTCH3 negative patients are gathered, the clinical and radiological comparisons might help to reveal some other aspects of the disease.

779 Etiology of stroke and risk factors

EVALUATION OF ECHOCARDIOGRAPHY RESULTS IN PATIENTS WITH ACUTE CEREBROVASCULAR ACCIDENTS (CVA)

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Background and objective: Cerebrovascular accidents are one of the most common causes of disability and mortality in human population all over the world. Several factors such as age, sex, hypertension, hyperlipidemia and heart diseases are risks of stroke. Considering high prevalence of cerebrovascular accidents and its related risk factors and specially heart diseases, we decided to study echocardiography findings in patients with cerebrovascular accidents.
Materials and Methods: This descriptive study was conducted on 372 cerebrovascular accidents patients who were admitted in Zanjan Vali-e-asr hospital. The data such as gender, age, type of cerebrovascular accidents, underlying disease and findings of echocardiography, were collected through questionnaire and then they were analyzed using appropriate software.
Results: Out of 372 patients including 181 men (48.6%) and 191 women (51.4%). Systolic function in 321 cases (86.3%) were normal and 51 cases (13.7%) were abnormal. Diastolic function in 304 cases (81.9%) were normal and 68 cases (18.1%) were abnormal. 22 cases had mitral stenosis and 198 case had mitral regurgitation and 23 cases had both of them. 9 cases had aortic stenosis, 80 cases had aortic regurgitation and 5 cases had both of them. 165 cases had tricuspid regurgitation and 1 cases had both regurgitation and stenosis. 63 cases had ejection fraction below 40%. only, one case had clot.
Conclusion: Control of heart diseases, reduces occurrence of CVA. Also, echocardiography technique determines many of heart problems, and we can prevent of occurrence of cerebrovascular accidents by treatment of them.
Keywords: stroke, echocardiography, risk factors

780 Etiology of stroke and risk factors

STROKE OR TRANSIENT ISCHEMIC ATTACK AMONG OUR CASES FOLLOWED-UP FOR OSAS

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Background: The Results of many studies underline the association between sleep related breathing disorder (SRBD) and cerebrovascular disorders. The SRBD, mostly obstructive sleep apnea syndrome (OSAS), is proved to be an independent risk factor of stroke and is related to poor outcome and increased long-term stroke mortality. The present study evaluated the frequency of stroke or transient ischemic attack in our OSAS patients.
Methods: Since 1995, 12,548 questionnaires have been completed by the clients of our center. In 6,356 cases this was followed by cardiorespiratory polygraphy, intended for assessing the severity of OSAS objectively. Subjects were categorized according to the following criteria: preclinical OSAS (AHI=5-10); mild OSAS (AHI=11-20); moderate OSAS (AHI=21-40); severe OSAS (AHI>40). The prevalence of stroke or transient ischemic attack was ascertained in the patient population studied.
Results: Verifying the independence of stroke or transient ischemic attack from severe OSAS using Pearson's chi square test revealed that in this population the occurrence of stroke or transient ischemic attack is influenced by OSAS severity (df: 3; p<0.0001). According to evidence from a prospective study, the risk of concomitant stroke or transient ischemic attack was 1.5 times higher in severe, than in mild or preclinical OSAS (RR: 1.58) in our cohort. The odds ratio for OSAS accompanied by stroke or transient ischemic attack was higher for all RDI classes in younger (aged <50 years), than in elderly (>50 years old) patients. Furthermore, the relative influence of BMI was smaller in the subset of younger patients.
Conclusion: RDI is independently associated with the presence of stroke or transient ischemic attack – as well as with BMI and age – as seen in our patient population. The odds ratio (OR) for OSAS and stroke or transient ischemic attack is higher in the younger (≤50 years old) age group, than among the elderly. Therefore, young patients suffering from severe OSAS stand a higher chance of undergoing stroke or transient ischemic attack.

781 Etiology of stroke and risk factors

EVALUATION OF FACTOR V LEIDEN'S ROLE IN ISCHEMIC STROKE AMONG YOUNG ADULTS IN IRAN

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Objectives: Several investigations have suggested different risk factors for ischemic stroke in young adults. In spite of extensive diagnostic studies, the primary cause remains unknown in some cases.Resistance to activated protein C (APC) is the most prevalent inherited risk factor for venous thromboembolism. Studies on factor V Leiden as the main cause of resistance to APC that has been done for clarifying the role of it in stroke are controversial. The current study is verifying the frequency and effect of factor V Leiden's mutation in ischemic stroke among young people in Iran.
Methods: This case-control study was performed during 14 months (September 2007- December 2008) in Alzahra university hospital. After taking medical history and clinical investigations, 76 young adults (15-45 years) were included in the study. Twenty two patients with ischemic stroke (15 male, 7 female) and without classic stroke risk factors enrolled in the case group and 54 healthy young individuals (17 male, 37 female) were included in the control group. After filling consent form, 1mL of their venous blood stream were obtained and sent to genetics department laboratory for DNA extraction, PCR and gel electrophoresis.
Results: No factor V Leiden mutation was found in the case group. There was one individual that was carrying the mutation as heterozygous. (Relative frequency=1.85%)
Discussion: Based on our study, we concluded that in spite of determined role of factor V Leiden in venous thromboembolism, it might not be considered as an independent risk factor for ischemic stroke in Iranian individuals who are healthy regarding to other aspects.

782 Etiology of stroke and risk factors

STROKE IN CHILDREN, CLINICAL, LABORATORY AND RADIOLOGICAL STUDY

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Stroke is considered as one of the top 10 causes of death and chronic morbidity in children.

Twenty eight children (72.% males and 28% females) diagnosed as CVS (82.1% infarction, and 17.9% hemorrhage) by clinical and imaging tools were included in our study aiming at identification of the variability of their clinical presentations according to age and sex, risk factors, and radiological findings, and outcome. All patients underwent the following investigations; CT, MRI, MRA, MRV, carotid and vertebral doppler/douplex studies and conventional angiography if needed, in addition to echocardiography and other lab investigations for search of the leading risk factors.

Partial anterior circulation stroke (hemiparesis and seizures) was the commonest clinical presentation. The most commonly identified risk factors in our patients included; prothrmbotic coagulopathy, cardiac problems, autoimmune diseases, infections, aneamia, combination of the above and other much rarer risk factors. Moderate disability according to modified Ranken scale was the common 6 month outcome that showed significant negative correlation with baseline Glasgow coma scale.

The above mentioned risk factors should be routinely screened in childhood stroke taking in consideration that the baseline coma scale is the single most important predictor of outcome.

783 Etiology of stroke and risk factors

ISCHEMIC STROKE IN YOUNG ADULTS AND GENETIC THROMBOPHILIC MUTATIONS – A CASE SERIES

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Background: Inherited thrombophilia is an increased predisposition to thrombosis related to protein gene mutations in the coagulation process. The literature contains no solid evidence to support an important relationship between the other thrombophilic defects reviewed and the risk of arterial thrombosis. The aim of our case series was to determine the relationship between ischemic stroke and genetic thrombophilic mutations in young adults.

Methods: The study was performed at the Department of Neurology, Osijek University Hospital Center, Osijek, Croatia during 1 year. In 19 ischemic stroke patients (10 males and 9 females) aged less than 50 years we tested genetic markers for thrombophilia (Factor V Leiden, Factor II Prothrombin, Plasminogen Activator Inhibitor-1 (PAI-1), Methylenetetrahydrofolate Reductase (MTHFR)). We used Oxford Classification of Stroke.

Results: We found a gene mutation for PAI-1 in all of our patients, compared to 12 patients with the MTHFR enzyme mutation and only one patient with Factor V Leiden mutation (none with Factor II mutation). In 17 patients we detected an increased serum level of total or LDL- cholesterol and/or cigarette smoking. Mean age for stroke occurrence was 40.7 years (43 for females and 38.6 for males). In 7 patients only with PAI-1 mutation stroke occurred at mean age of 43.1 years, compared to earlier stroke occurrence (at mean of 39.2 years) in patients with both PAI-1 and MTHFR mutations. Male patients had an usual pattern of territorial distribution of stroke, while female patients had more strokes in the posterior cerebral circulation area.

Conclusion: We found in young adult patients with ischemic stroke a greater proportion of PAI-1 gene mutation (100%) than other mutations of genetic markers for thrombophilia. Territorial distribution of ischemic stroke in young female patients with thrombophilic gene mutations may indicate a predilection for the impairment of posterior brain circulation.

784 Etiology of stroke and risk factors

FREQUENCY OF ISCHEMIC STROKE IN PATIENTS WITH MIGRAINE

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Introduction: Migraine is an episodic, paroxysmal disorder accompanied with different neurological, gastrointestinal and vegetative changes. Results of the recent studies have shown certain correlation between transitory clinical manifestation with focal reduction of cerebral circulation and possible ischemic lesions in patients with migraine.

Methods and Results: The purpose of this study was to evaluate the possible presence of the structural lesions of brain parenchyma in patients with migraine with MRI. This study included patients which according to known criteria had migraine preceded or not by an aura. All patients underwent MRI examination without and with contrast media (Gadolinium dimeglumine Gd-DTPA). Examination was performed in 80 patients with common migraine and in 60 patients with migraine preceded by an aura and focal neurological manifestations. Patients with serious risk factors for ischemic brain disease were excluded.

In 9 (11,25%) patients with classic form migraine MRI was recorded T2-weighted enhancement of signal intensity of white matter, and only in 4 (5,00%) patient focal change of signal intensity what is characteristics for ischemic lesions of brain parenchyma.In patients with migraine preceded by an aura and focal neurological manifestations (deficits) MRI showed T2-weighted change of signal intensity of white matter in 12 (20,00%) patients, and focal ischemic brain lesions in 7 (11,6%) patients.

Conclusion: Our Results showen that MRI necessary examination in complicated migraine patients and in patients with frequent and serious attacks.

785 Etiology of stroke and risk factors

POTENTIAL CAUSES OF STROKE IN ELDERLY HYPERTENSIVE PATIENTS

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Background: Hypertension is the main cause of stroke in the general population. Elderly hypertensive patients (EHP) constitute the most important subgroup population at risk for stroke. As age advances, two thirds of population will develop hypertension. Stroke is the most common cause of cardiovascular (CV) events in developing countries and the third one in developed ones. Our objective was to evaluate potential causes of stroke in EHP.

Methods: Consecutively, 487 EHP ≥ 70 years old (YO), mean age: 79.27 YO (70-101), evaluated in our geriatric department were included in this analysis. Mean: height, 1.58 m; weight, 67.47 kg, BMI, 26.73 kg/m². Six percent experienced a stroke with at least mild sequel, as opposed to coronary disease, whose prevalence was 24.1%.

Results: The univariate analysis included all traditional CV diseases and risk factors. But, in the multivariate regression analysis, only diabetes mellitus, atrial fibrillation (AF) and male sex showed statistical significance as a potential cause of stroke in EHP (table).

Table 1. Potential causes of stroke in EHP

Parameter	OR	95%CI	p-value
Male Sex	2.190	0.997–4.808	*0.0508*
Diabetes	3.251	1.481–7.134	*0.0033*
Atrial Fibrillation	2.435	1.061–5.588	*0.0358*

Conclusions: Diabetes was the most important cause of stroke in EHP and tripled that risk.

Atrial fibrillation increased the risk of stroke 2.4 times, although the kind of stroke linked to AF (cardioembolic) presents a different mechanism compared to other potential causes.

Among men, the prevalence of stroke doubled as compared to women.

786 Etiology of stroke and risk factors

THE MECHANISN OF CARDIOEMBOLIC STROKE BY INCREASED INTRATHORACIC PRESSURE

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Background: Because an increase in intrathoracic pressure (ITP) is frequently encountered during many daily straining activities, its hemodynamic effects have been studied extensively. It have been suggested that paradoxical embolization through a patent foramen ovale (PFO), caused by elevated ITP, could lead to stroke. However, very little is known about the effects of raised ITP on the incidence of stroke.

Methods: We retrospectively reviewed acute ischemic stroke patients who were admitted in Korea University Ansan Hospital from 2007 to 2009. Among them, the patients with cardioembolic stroke were selected and the situation of stroke occurrence and the presence of ITP were assessed.

Results: A total of four patients with cardioembolic stroke had the presence of ITP. The mean age was 31.50±10.66 years (range 22-45 years) and two of them (50%) were female. All four young patients were found to have a potential cardiac source

of embolism. Despite a thorough work-up, no other possible cause of stroke was identified. In all cases the stroke was preceded by an increase in ITP that occurred during coughing, vomiting, or sexual intercourse.

Conclusions: The increased ITP due to cough, vomiting, or sexual intercourse may precipitate embolization in patients with PFO, atrial fibrillation, or papillary fibroelastoma. We suggest that cardioembolic stroke is expedited by elevated ITP.

787 Etiology of stroke and risk factors

AIDS- A NEUROVASCULAR EMERGENCY?

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Background: HIV infection should always be considered in case of stroke in young patients especially in absence of vascular risk factors.

HIV induced vasculapathy appears multifactorial and may result from immunologic abnormalities or exposure to a variety of xenoantigens, HIV itself and other infectious agents or drugs. Forms of vasculitis were reported in HIV-infected patients. Also it has been described the vasculopathy of important arteries with multiple aneurysms formation or the occlusive disease. The most common presentations include ischemic stroke, intracranial hemorrhage and seizures.

Case report: We present the case of a 27- years old right handed man, without any relevant medical history (except ophtalmic zoster 6 months before) and without known vascular risk factors, referred to our hospital for language disturbances and right limbs weakness with sudden onset.

Neurological examination revealed an alert patient, presenting mixed aphasia, right hemiparesis, right facial weakness and generalized micropolyadenopathy. IRM relieved acute left putaminal acute ischemic lesion. Doppler examination of extra and intracranial blood vessels, ECG, echocardiography were normal. Blood testing showed an HIV-RNA load of 2 millions copies/ml and CD4 lymphocyte count of 100cell/mmc (AIDS- B3). CSF examination (cell count, protein, glucose level, other agents) was normal.

Neurological course was favorable under treatment with aspirin and statins added to antiretroviral therapy with lamivudine, zidovudine and efavirenzum.

Discussion: In a prospective study on HIV seropositive patients, prevalence of ischemic stroke is five time higher than in seronegative general population of the same age. The prevalence increases with CDC stage (third stage is associated with the higher prevalence. The particularity of our case is a neurologic lesion not so typical for vasculopathy HIV-related in patient with no vascular risk factor but mild presentation of AIDS.

Atrouni, S., 247
Attia, J., 300
Attygalle, T.N., 164, 284, 316
Au, W.C., 172
Audebert, H., 76, 278
Audebert, H.J., 34, 183
Auer, D., 5
Auer, D.P., 53, 84
Auffermann, W., 150
Augusto, L., 114
Auntai, P.A., 49
Aurangzeb, S., 268
Avelar, W.M., 120
Awad, I., 88
Awano, H., 215, 222, 315
Ayerbe, L., 46, 246
Ayis, S., 46
Ayis, S.A., 77
Aymerich, N., 214
Ayo-Martín, O., 104
Ayres-Basto, M., 160
Azevedo, E., 79, 114, 115, 151, 160, 179
Azzini, C., 230

Baas, A.F., 39
Baas, H., 102
Bachmann, G., 144, 295
Bacigaluppi, M., 143
Badhwar, J., 231
Badimon, L., 8, 91, 137, 145
Badruddin, A., 131, 162, 165, 175
Bae, H.J., 219
Bae, H.-J., 40, 212
Bae, H.J., 74, 75, 243, 261
Baek, S.H., 116, 140, 247
Baert, I., 189
Baeza, J., 178
Bafadhel, L., 303
Bagoly, Z., 291
Bahnemann, M., 11
Bähr, M., 140
Baik, M.W., 173
Baker, R., 40
Bakker, D.C., 226
Bal, S., 128, 273
Bal, S.P., 29, 52, 59
Balami, D., 212, 292
Balami, J., 239, 245
Balci, K., 281
Balducci, A., 296
Balestrino, M., 81
Baligh, E., 163
Balkaya, M., 26, 124
Ball, J., 115
Ball, S.P., 255
Ballesteros, I., 138
Ballet, S., 274
Baloyannis, S.I., 160
Balseanu, A.T., 142
Baltatzi, M., 313
Bammer, R., 67
Bandaru, V.S.K., 96
Banerjee, G., 296

Banerjee, S., 176, 296
Bangad, S., 123
Bar, M., 224, 254
Baracchini, C., 244
Barber, P.A., 318
Barinagarrementeria, F., 51
Barker, J., 296
Barlinn, K., 183, 250, 264, 287
Baron, A.F., 60
Baron, J.C., 3, 90, 93
Baron, P., 307
Baronnet, F., 197
Barral, D., 28, 144
Barreal, L., 201
Barrera, A., 190
Barreto, M., 205
Barrick, T.R., 83
Barrie, E., 192, 221
Barros, A.D.M., 314
Barros, P., 79, 110, 179
Barrows, R.J., 160
Barth, A., 176
Bartko, D., 177, 292
Bartkova, A., 175, 261
Bartz, M., 279
Baruch, A., 201
Basile, A.M., 81, 244
Bassile, C.C., 191
Bastawrous, M.M., 188
Bastiansen, M., 292
Bastin, M., 213
Bath, M.W., 184
Bath, P., 75
Bath, P.M., 73
Bath, P.M.W., 5, 16, 51, 141, 182, 184, 299
Battaglia, G., 136
Baturova, M.A., 314
Bauer, P., 134
Bauermann, T., 98
Baumann, A.M., 34
Bavarsad Shahripour, R., 128, 216, 284
Bayley, M., 42, 43, 198, 242
Bayounis, M., 291
Bazan, R., 109, 120, 198
Bäzner, H., 175
Bazzan, R., 194
Beagan, M.L.C., 79
Beare, R., 166
Beauchamp, R., 193, 194
Beaulieu, C., 95
Becher, H., 207, 246
Beck, A., 21, 156
Beck, C., 14, 257
Beck, J., 96, 176, 288
Beckmann, C., 75
Beenen, L.F.M., 33
Begue, R., 270
Behnke, S., 22
Behrens, J., 203
Behrens, J.R., 225
Beitzke, M., 4
Bejot, Y., 283

Béjot, Y., 299
Belham, M., 32, 145, 206
Bell, R., 208
Bello, L.A., 292
Bellon, R., 6
Bembenek, J., 218
Ben Abdelaziz, I., 312
Ben Mustapha, M.A., 312
Benbir, G., 320
Bende, C., 102
Benecke, R., 104, 218
Benes, V., 224
Bengel, D., 233
Benjamin, M., 44
Bentley, P., 75, 185, 306
Benyounes, N., 61
Beraldo, F.A., 205
Beray-Berthat, V., 274
Bereczki, D., 206, 213
Berentey, Z., 262
Beretta, S., 35, 140
Berg, L., 204
Berge, E., 16, 186, 226
Berger, K., 38, 40, 89, 239
Bergmann, J., 134, 190
Bergström, A.L., 191
Berisavac, I.I., 310
Berlis, A., 132
Berlit, P., 127
Bermejo, B.B., 214
Bermúdez i Badia, S., 190
Bermudez i Badia, S., 42
Bermúdez i Badia, S., 191
Bernardino, S., 110, 251
Bernhardt, J., 1, 58, 195, 240, 251
Bernstein, R.A., 297
Berrouschot, J., 48
Bersano, A., 307
Bertasi, E., 56
Berthet, C., 27
Bertolami, M.C., 321
Bertora, P.L., 83
Bertotti, M.F.Z., 109
Bertz, A.K., 86
Beslac Bumbasirevic, L., 215, 310
Beslac-Bumbasirevic, L., 235, 257
Betlehem, J., 180, 181, 213
Betrand, T., 60
Bettex, Y., 222
Betting, L.E.G.G., 120
Beusmans, G., 312
Bevilacqua, F., 312
Bezerra, W.M., 205
Bhalla, A., 63, 225, 246
Bhalla, V., 111
Bhasin, A., 56
Bhatia, R., 56
Bhattacharjee, M., 66
Bhogal, M., 193, 194
Bhullar, R.S., 133, 189, 242
Bianchi, S., 81
Bienek, A., 214
Biessels, G.J., 74, 159, 161, 318

Bigalke, B., 279
Bigi, S., 275
Billard, J., 60
Birns, J., 225, 246
Bivard, A., 86, 91
Blackburn, D.J., 303
Blacker, D.J., 266
Bladin, C., 86, 223
Blake, M., 164, 287
Blanco Rojas, L., 148
Blanco, M., 6, 53, 153, 154, 280
Blankenberg, G., 119
Blasco, J., 125, 127
Blight, A., 102, 117
Blinzler, C., 254
Blomstrand, C., 54
Boada, C., 140
Boaz, A., 178
Bode-Böger, S.M., 10, 308
Bodechtel, U., 287
Boden-Albala, B., 191
Bodenant, M., 235
Bogiatzi, C., 115, 163, 294, 307
Bogosavljevic, V., 235, 257, 310
Bogousslavsky, J., 14
Bojar, M., 31
Bokemark, L., 45, 231, 294, 295
Bolam, B.L., 294
Bolanos, J.P., 50
Bolognese, M., 31, 54, 241, 247
Boltshauser, E., 275
Bonafe, A., 22
Bonati, L., 268
Bonati, L.H., 14, 48
Boncoraglio, G., 199, 307
Boncz, I., 180
Bondarenko, E.A., 318
Bonifati, D.M., 244
Bonnet, A.L., 117
Bonneville, F., 69, 85
Bonvin, C., 240, 257
Booth, J., 198
Borando, M., 136
Boras, E., 145
Bordet, R., 185
Borges, J.L., 321
Borges, M.A., 321
Borhani Haghighi, A., 177
Bornstein, N.M., 130, 255, 279
Börsch, S., 246
Borsotto, M., 142
Bosboom, W.M.J., 289, 290
Bose, A., 6
Bösel, J., 219
Boskovic, Z., 321
Boss, H.M., 289, 290
Bosutti, A., 8
Bots, M.L., 71
Böttcher, C., 26
Bottin, L., 34
Boulahri, B.T., 120, 156, 216
Bouley, J., 139
Bourazza, B.A., 120, 156, 216
Bousquet, S., 103

Chotmongkol, V.C., 49
Chousein, S., 294
Chowdhury, M.R., 225
Christensen, A., 13, 96
Christensen, D., 300
Christensen, H., 13, 96
Christensen, S., 11, 161
Christiansen, L.K., 204
Chung, A.W., 83
Chung, D., 130, 132
Chung, P.W., 163
Chung, P.-W., 98
Chung, S.Y., 176
Churilov, L., 1, 195, 269
Ciccone, A., 134
Cieza, A., 190
Cifkova, R., 286
Ciolli, L., 81, 301
Cipolotti, L., 44, 299
Cislaghi, G., 83
Clarke, J.R., 220
Clarke, W., 44
Claro, S., 304
Clavera, B., 305
Cloud, G., 81
Clouth, B., 122
Cluckie, G., 225
Coates, V., 218
Coelho, D., 321
Coenen, M., 190
Coert, B.A., 22
Cogez, J., 117
Cognard, C., 192
Coker, B., 77
Cola, P.C., 194, 198
Collas, D.M., 266
Collins, D.R., 8, 9, 85, 139, 142, 227, 245
Collinson, S.L., 44
Comanescu, A., 118
Combor, I., 177, 292
Comi, G., 143, 307
Compter, A., 65
Conley, A.M., 192
Connaughton, J., 227, 245
Connolly, D., 194
Connolly, F., 34
Connolly, S.B., 296
Conroy, R., 289
Conti, E., 140
Conwit, R., 73
Cook, D.J., 139
Cooper, K., 266
Coote, S., 223
Copeland, C., 229
Cordeiro, G., 147
Cordenier, A.K.M., 185
Cordido Henriquez, F., 319
Cordonnier, C., 3, 21, 185, 235
Correas, E., 307
Correia, M., 36, 267
Correnti, A., 261
Corzo, C., 304
Corzo, C.C., 120, 297

Coscojuela, P., 15, 20, 36, 152, 239
Costa, E., 154
Costa, H., 115
Costa, J.C., 312
Costalat, V., 22
Cote, R., 214
Cotter, P.E., 32, 145, 206
Coughlan, K., 223
Coughlan, T., 8, 9, 85, 139, 142
Coughlan, T.L., 227, 245
Couillard, P.L., 173
Coulon, G., 259
Coulter, J.I., 67
Counsell, C.E., 38, 276
Couratier, F., 285
Courcoutsakis, N., 307
Courlander, J., 312
Coutinho, J.M., 22
Coutts, S.B., 67, 68
Couvreur, G., 283
Couvreur, T., 289
Coward, L.J., 164, 284, 316
Craig, L.E., 58
Crespo, J., 137
Crichton, S., 63, 273
Crowe, M., 183, 286
Crozier, S., 106, 248
Cruz Culebras, A., 258, 264
Cruz-Culebras, A., 108
Cruz-Flores, S., 186, 231
Cruz-Herranz, A., 306, 307
Csiba, L., 76, 189, 236, 291
Csoboth, I., 213
Cuadrado Godia, E., 60
Cuadrado, E., 260
Cuadrado-Godia, E., 174, 211, 281
Cuadras, P., 11, 260
Cuartero, M.I., 138
Cuciureanu, A., 119
Cuciureanu, D.I., 119
Cucos, L., 303
Cuello, J.P., 242, 319
Culafic, S., 321
Cunha, L., 147
Curtze, S., 74
Cuthbertson, F., 43
Cuxart, A., 190
Czech-Zechmeister, B., 138
Czerny, D., 23, 132, 224
Członkowska, A., 282, 305
Czlonkowska, A., 76, 77, 218

D'Ambrogio, S., 222
D'anna, L.D., 210
D'Este, C., 87, 88, 233
da Silva, L.K., 110
Dacey, L., 270
Dachenhausen, A., 46, 77
Dahl, A., 158
Dahl, A.E., 195
Dahms, M.J., 107
Dai, D., 38, 276
Dai, G., 26
Dalal, P.M., 66

Dale, S., 87, 88, 233
Dalis, M., 150
Dallongeville, J., 35
Dalloz, M.-A., 206
Dalloz, M.A., 34
Dalmeida, W., 126, 255
Dalvandi, A., 204
Daly, D., 189
Daly, P., 227, 245
Damarin, V., 76
Danburam, A., 212
Dang, C., 26
Dani, K., 12, 91, 94, 95, 97, 134
Dani, K.A., 92
Daniel, W.G., 129
Danielson, E., 204
Dános, Z., 206, 213
Daolio, M., 134
Darkhabani, M.Z., 165
Darlix, A., 103
Das, G., 166
Dávalos, A., 11, 37, 124, 138, 146, 260, 263, 280, 288
Davalos, A., 174
Davies, E.A., 270
Davies, P., 220
Davies, R., 122
Davis, S.M., 11, 86, 161, 182
Dawid, M., 122
Dawood, A., 246
Day, E., 220
De Arce, A.M., 20
de Bakker, P.I.W., 39
De Boni, A., 244
de Borst, A.G., 87
de Borst, G.J., 72
De Curtis, M., 140
de Fays, K., 178, 288
De Geyter, D., 62
de Jong, F.J., 62, 63
De Keyser, J., 125, 185, 226, 272
de Koning, I., 301
de Kort, P.L.M., 277
de la Ossa, N., 67
de La Sayette, V., 117
de Laat, K.F., 82, 83
de Lau, L.M.L., 39, 301
de Leeuw, F.E., 52, 82, 273
de Leeuw, F.-E., 83
de Leeuw, P.W., 83
de Maat, M.P.M., 39
de Melker, E.C., 289
De Raedt, S., 125, 272
de Ridder, I.R., 62, 63
de Rooij, N.K., 153
De Silva, D.A., 54, 273, 275
De Smedt, A., 125, 272
de Souza, C.P., 110
De Stefano, N., 81
De Vito, A., 230
de Vries, J., 15
De Vries, T.M., 226
Deary, I.J., 147, 213, 302
Deb, M., 10, 258

Debette, S., 35
Debruxelles, S., 109
Deepak, T., 85
Degnan, A., 79
Deif, R., 163
Deijle, I.A., 289
Dejaeger, E., 189
Del Bene, A., 81
Del Giudice, C., 227
Del Rios, M.M., 307
Delavaran, H., 193
Delcourt, C., 37, 63
Delgado, R., 67, 68
Delgado-Esteban, M., 50
Delgado-Mederos, R., 20, 137
Dellinger, R.P., 5
Deltour, S., 61, 120, 232, 248
Deltour, S., 106
Deluca, C., 244
Demaerschalk, B.M., 224
Demant, M.N., 209
DeMarchis, G.M.D.D., 220
Dembo, T., 298
Demchuk, A.M., 10, 29, 52, 59, 67, 68, 86, 128, 255, 273
Deme, S.M., 166
Demmler, H., 321
den Hartog, G.J., 87
den Hertog, H.M., 55, 63, 283, 293, 301
Dengler, R., 10, 153
Dennis (Professor), M., 240
Dennis, M., 81
Dennis, M.S., 126
Deplanque, D., 70
Dequatre, N., 21
Derdeyn, C.P., 44
Derelle, A.L., 103
Desmond, P., 161
Desmond, P.M., 11
DeTaboada, L., 24
Dettmers, C., 56
Deutsch, K., 180, 181
Devuyst, G., 14
Dewey, H.M., 269
Dharmasaroja, P., 257
Dheeraj, K.V., 189
Dhillon, B., 147, 188
Di Angelantonio, E., 32
Di Lazzaro, V., 253
Di Legge, S., 227, 228
Di Matteo, A., 244
Di Piero, V., 83, 157
Diallo, A., 106
Dias, V.P., 251
Diaz Otero, F., 242, 264
Díaz Otero, F., 258, 319
Díaz, R., 11
Díaz-Maroto, I., 104
Díaz-Otero, F., 35
Diaz-Otero, F., 35, 222, 227, 232
DiCarlo, A., 80
Diccini, S., 205
Dichgans, M., 7, 9, 97, 210, 274

Hommel, M., 57
Hommet, Y., 60
Homuth, G., 142
Hong, C.S., 173
Hong, J.M., 149, 243, 262
Hong, K.S., 261
Hong, Y.H., 243
Hong, Z., 312
Hopkins, S., 153
Horgan, G., 305
Horie, Y., 87
Horiuchi, Y., 298
Hornberger, E., 119
Hornnes, N., 290
Horsch, A.D., 74
Horváth, E., 235
Horvath, R., 160
Horvath-Mechtler, B., 122
Hoseini, T., 313
Hosomi, M., 188
Hosomi, N., 38, 74
Hosseini, A.A., 84
Hosseini, H., 109
Hosten, N., 36
Hotter, B., 29, 93, 135, 158
Houlihan, P., 292
Houshmandzad, S., 129
Howarth, R.C., 79
Howells, D.W., 182
Hsaini, H.Y., 120, 156, 216
Hsieh, C.F., 281
Hsieh, Y.W., 197
Hsu, L.C., H.H. Hu, 286
Huang, B., 193, 194
Huang, C.C., 312
Huang, J., 88
Huang, J.Y., 312
Huang, Y., 37, 63
Huang, Y.N., 180
Huddle, D., 6
Hueb, J.C., 109
Huertas, R., 308
Hughes, D., 40
Hughes, G., 286
Huijbregts, M., 42, 198
Huijts, M., 149
Hulme, S., 153
Humbert, F., 56
Hung, J.W., 197
Hunter, A., 271
Hunter, K., 5
Hurtado, O., 146
Hutchinson, P., 153
Huttner, H.B., 155, 156, 254
Hvidberg, M., 40
Hwang, S.H., 285
Hwang, S.Y., 100
Hwang, Y.H., 219, 237

Ibarra, B., 20, 152, 239
Idrovo, L., 80
Igase, K., 91
Igase, M., 293
Igual-Camacho, C., 202

Iihara, K., 29, 268
Ikeda, Y., 87
Ikram, M.A., 39
Illanes, S., 25
Ilsen, H., 125
Imahori, T., 170
Imamura, H., 170, 171
Imamura, T., 171
Ince, B., 320
Indredavik, B., 195
Ingall, T.J., 224
Inoue, T., 128
Inoue, Y., 309
Inzitari, D., 81, 223, 301, 302
Ip, H.L., 172
Iqbal, A., 106
Irani, I., 164, 284
Isa, K., 267
Ishihara, S., 267
Ishikawa, T., 170
Ishitsuka, K., 315
Ishitsuka, T., 128, 266, 276
Ismail, A., 96
Ismail, F., 193, 194
Isomura, T., 315
Itabashi, R., 300
Ito, M., 300
Ito, T., 107, 300, 310
Ito, Y., 216
Ivanova, G.E., 141, 188, 192, 199
Iwata, T., 99, 172, 221, 224
Iwata, T.I., 107, 233

Jaakmees, H., 250
Jack, C.I.A., 212
Jackson, C.A., 3
Jacobi, C., 125
Jacquiau, G., 232
Jacquin, A., 283, 299
Jadhav, V., 260
Jaeger, H.R., 3, 44, 299
Jafaar, I., 125
Jafar, A.H., 116
Jafar, Y.A., 116
Jagodzinska, J., 285
Jaigobin, C., 32
Jaillard, A., 57
Jakobs, A., 169
Jallo, J., 208
James, M., 113
Jančuljak, D., 321
Jander, S., 141
Janes, F.J., 210
Jang, M.S., 74, 75, 212, 243
Jang, S.H., 174
Jansen, O., 23
Januel, A.C., 28
Jarkass, H., 247
Jatuzis, D., 16, 76
Jax, F., 268
Jayakanthi, C., 281
Jeannet, P.Y., 275
Jeerakathil, T., 47, 95
Jefferson, S., 58

Jeffery, R., 105
Jegzentis, K., 80, 135
Jehna, M., 82
Jenetzky, E., 31, 306
Jenkinson, D., 180, 220
Jensen, M.B., 155
Jensen, S.S., 40
Jern, C., 39, 54
Jesic, A., 236
Jesus, P.A.P., 314
Jeyaraj, P., 271
Jianu, D.C., 166
Jianu, S.N., 166
Jie, S., 10, 165, 173, 230
Jimena, S., 211
Jimenez Caballero, P.E., 238
Jimenez, J., 260
Jiménez, M., 154, 260
Jimenez, M., 18, 140
Jiménez-Caballero, E., 67, 68
Jimenez-Conde, J., 174, 211, 281
Jiménez-Xarrié, E., 137
Jin, A.Y., 137
Jin, Z., 141
Jinnouchi, J., 128, 266, 276
Jiwa, N.S., 151
Jog, M., 193, 194
Johansson, E.P., 13, 68
Johansson, U., 43
Johnsen, S.H., 84, 159
Johnsen, S.P., 300
Johnson, D., 102
Johnson, R.R., 72
Johnston, D.E., 254
Jolic, S.Z., 235
Jolley, D., 166, 266
Jones, A., 222
Jones, K., 239
Jones, P.S., 90
Jones, S.P., 200, 234
Jongen, L.M., 14
Jonszta, T., 23, 132, 254
Joo, K.D., 100, 234
Jood, K., 39, 54
Jost, V., 125
Joud, A., 103
Joung, J.J., 100
Jouvent, R., 193
Jovanovic, D.R., 215, 235, 257, 310
Joye, D., 222
Jun, S.M., 219, 230, 245
Jung, C.K., 74
Jung, S., 165
Jung, S.J., 220
Jungehuelsing, G.J., 158
Jungehuelsing, J., 29
Jungehulsing, G.J., 135
Jungehülsing, G.J., 80, 210
Junk, J.D., 143
Jurcau, A., 119, 131
Jüttler, E., 62
Jwad, A., 108

Kablau, M., 31, 54, 241, 247, 256
Kabore, R., 69, 285
Kadlecova, P., 76
Kadojić, D., 321
Kaiser, J., 142
Kaji, M., 214
Kaker, P., 269
Kakoulidis, E., 214
Kalandadze, I., 142
Kalaw, A.J.L., 33
Kaliatzakis, I., 214
Kallingal, J., 75, 115
Kallis, C., 299
Kallmünzer, B., 21, 156
Kálnoki Gyöngyössy, I., 235
Kamal Ebrahim, H., 320
Kamali, M., 195
Kamiński, B., 282, 305
Kaminska, K., 249
Kamouchi, M., 215, 222, 315
Kampondeni, S., 280
Kandiyil, N., 53, 84
Kang, D.H., 237
Kang, D.-W., 4, 161, 219, 248
Kang, H.D., 234
Kang, J.H., 212
Kang, K., 114
Kannan, A., 105, 164, 287
Kanovsky, P., 175, 261
Kao, H.W., 278
Kapeller, P., 271
Kappelle, L.J., 55, 65, 72, 74, 209
Kappelmayer, J., 291
Kapral, M., 188
Kapral, M.K., 214
Kaps, M., 73, 144, 210, 295
Kar, A., 104, 176
Karageorgiou, C., 213
Karageorgiou, K., 214, 264
Karapanayiotides, T., 14
Karaszewski, B., 126
Kardos, L., 236
Karimi, M., 124, 177
Kario, K., 21, 253, 262
Karlinski, M., 218
Karlinski, M.A., 77
Karlsson, S., 54
Karlström, L., 14
Karpinska, A., 9
Karpova, O.V., 7
Kartvelishvili, T., 142
Karunaratne, D., 111
Kastaun, S., 295
Kaste, M., 50, 52, 59, 247
Kastrup, A., 173, 220
Kaszás, N., 235
Katada, F., 216
Katagi, R., 293
Kataoka, Y., 300
Katayama, Y., 228
Kato, Y., 298
Katsibari, C., 115, 163, 294, 307
Katsiki, N., 313
Katsura, N., 159

Katz, J., 180
Kauert, C., 176
Kaur, P., 133, 189, 242
Kaushal, R., 231
Kavanagh, S.J., 78
Kavangh, E.C., 67
Kawarai, T.K., 148
Kayserili, H., 320
Kazibutowska, Z., 318
Kazmierski, R., 282
Keane, R.A., 290, 292
Kebets, V., 44, 299
Kechaou, M., 312
Kee, Y.K., 250, 269
Kehler, U., 109
Kehrer, M., 4, 8
Keil, U., 286
Keller, L., 228
Kellert, L., 220
Kellner, P.A., 34
Kelloway, L., 200, 202
Kelloway, L.J., 200
Kelly, D., 243
Kelly, H., 1
Kelly, P.J., 60, 62, 67, 112, 183
Kemeny, V., 14
Kemmling, A., 10, 84, 169
Kennedy, F., 71
Kennedy, J., 143
Kent, D.M., 32, 186
Kent, L., 245
Kent, T.A., 126, 255, 263
Kenton, A., 196
Kepplinger, J., 287
Kéri, A., 206, 213
Kern, R., 27, 92, 94, 119, 270
Kerr, D.M., 75
Kerr, M., 189
Kerry, S.M., 310, 313
Kesani, M., 250, 264
Kesavadas, C., 271
Kessels, R.P.C., 52
Kessler, C., 36, 142
Ketzel, M., 40
Khadjooi, K., 196
Khajeh, L., 155
Khalil, A., 206
Khankeh, H.R., 204
Kharbanda, R.K., 143
Khaw, A.V., 36
Kheradmand, E., 320
Khokhar, A., 284, 316
Khoumri, C., 299
Kiechl, S., 8, 120, 218, 258
Kiefer, C., 165
Kielstein, J.T., 10
Kiemeney, L.A., 39
Kiernan, T., 224
Kijima, C., 228, 232
Kilkenny, M., 72
Killer, M., 23
Kim, B.J., 40, 51, 55
Kim, B.M., 174
Kim, C.-K., 315

Kim, C.K., 40, 51, 55
Kim, D., 261
Kim, D.H., 219, 230, 245
Kim, D.I., 174
Kim, D.K., 100, 298
Kim, E.G., 261, 285
Kim, E.H., 237
Kim, G., 58
Kim, G.M., 298
Kim, H.K., 176
Kim, H.O., 100
Kim, H.Y., 130, 132, 319
Kim, J.H., 243
Kim, J.S., 4, 219, 248
Kim, K.B., 100
Kim, M.K., 108, 303
Kim, M.S., 155, 172, 174
Kim, N., 75
Kim, N.Y., 74, 243
Kim, S.J., 261
Kim, S.R., 173
Kim, S.W., 219, 230, 245
Kim, S.Y., 243
Kim, T.W., 272
Kim, W.J., 74, 243
Kim, W.S., 298
Kim, Y.H., 141
Kim, Y.J., 285
Kim, Y.S., 130, 132, 237
Kim, Y.W., 173
Kimura, K., 21, 29, 253, 262, 268
King, A., 153
Kinsella, J.A., 8, 9, 85, 139, 142
Kiphuth, I.C., 155, 156, 254
Kippnich, U., 226
Kirawa, U., 292
Kirchhof, P., 33
Kirchmayr, M., 218, 258
Kirsch, M., 36
Kiselev, V.G., 93
Kita, Y.K., 148
Kitazono, T., 215, 222, 266, 276, 315
Kitsios, G.D., 186
Kiyohara, Y., 215, 222, 315
Kjekshus, J., 311
Klærke-Mikkelsen, I., 90
Kleemann, T., 207
Klein, F.G., 230
Klein, I., 126
Klein, I.F., 70
Kleinman, J., 67
Kleinschmidt, A., 197
Kleinschnitz, C., 25
Klijn, C.J.M., 2
Klochihina, O.A., 208
Kloppenborg, R.P., 82
Klos, M., 35
Kloska, S.P., 155, 156
Klotz, J.M., 244
Kmieckowiak, M., 282
Knash, M., 95
Knauf, J., 173
Knauth, M., 23, 173

Knibb, J.A., 70
Knoflach, M., 8, 120, 218, 258
Ko, Y.C., 155, 172, 212, 243
Kobal, J., 156
Kobayashi, A., 76, 77, 155, 218, 282, 305
Kobayashi, M., 164
Koch, G., 227, 228
Kocher, M., 261
Kochetov, A.G., 7
Koehler, J., 49, 129
Koennecke, H.C., 38
Koerner, R.J., 254
Koga, M., 21, 253, 259, 262, 265
Koh, L.H., 275
Koh, S.-H., 132
Koh, Y., 75
Koh, Y.C., 74
Kohara, K., 293
Kohno, M., 38
Köhrmann, M., 6, 155, 156, 161, 254
Koivunen, R.-J., 152
Kojan, S., 291
Kokaia, Z., 193
Kokuba, K., 267
Kokubo, Y., 65
Kolbaske, S., 104, 218
Kollerits, B., 190
Kollmar, R., 21, 129, 156, 229
Kolomentsev, S.V., 251
Kolominsky- Rabas, P.L., 64
Kolominsky-Rabas, P.L., 207
Komitopoulos, N., 213
Komoltri, C., 146
Koneski, P., 210
Kong, T.S., 174
Konieczna-Brazis, M., 256
Kono, T., 74
Kontzevoy, V.A., 302, 303
Koo, J.S., 219
Kooijman, R., 62
Kool, H.A., 74
Kopczynski, M.C., 235
Kopitzki, K., 86
Korbel, E., 241
Körner, H.K., 143
Koroboki, E., 38, 283
Kõrv, J., 16, 76, 246, 250
Kory-Calomfirescu, S., 166
Koscica, N., 136
Koshcheev, A.Y., 175
Kostic, S., 321
Koton, S., 80, 255, 279
Koudstaal, P.J., 39, 55, 283, 293, 301
Kougkas, E., 214
Kouperberg, E., 165
Kouzi, I., 213
Kovacs, K., 160
Kovács, K.L., 206, 213
Kovrazhkina, E.A., 141, 192, 199
Kowalczyk, K., 279
Kozak, J., 261

Kozmann, G., 191
Krack, L., 118
Krahulik, D., 175
Krajca, J., 23, 132
Krajina, A., 254
Kral, M., 23, 175, 261
Krátky, M., 121
Krause, T., 11
Kravchenko, M.A., 297
Krebes, S., 34
Kreis, A., 250
Kremer, C., 236
Kremer, H.P.H., 226
Krendl, R., 271
Krespi, Y., 76
Kress, B., 125
Krewer, C., 134
Kribben, A., 150
Krieger, D.W., 13, 96
Krishnamurthy, V., 318
Kristiansen, L.C., 40
Kriszbacher, I., 180, 213
Kroeger, J., 104
Kronenberg, G., 124
Kroon, A.A., 83
Krsmanovic, Z., 311, 321
Kruetzelmann, A., 49
Kruetzelmann, A.C., 93
Krumm, R., 10, 84
Krupinski, J., 8, 91, 145
Kruse, C., 271
Krützelmann, A., 14, 49, 257
Kubo, S., 258
Kuchelmeister, K., 154
Kudo, K., 159, 164
Kueker, W., 111, 171
Kuesel, T., 28
Kufner, A., 12
Kuhlen, D., 176, 288
Kulagin, P.A., 132
Kuliha, M., 23, 132, 224, 254
Kullamaa, S., 250
Kumar, A., 122
Kumar, G., 75
Kumaran, S., 56
Kumstýřová, T., 31
Kumwenda, J.J., 280
Kundu, A.K., 164, 284, 316
Kung, T., 308
Kuramatsu, J.B., 155, 156
Kuramoto, Y., 170, 171
Kurča, E., 121
Kureck, I., 246
Kuriyama, M., 258
Kurre, W., 127
Kustova, M.A., 260
Kutlubaev, M.A., 183
Kuzmanovic, I., 257
Kvaløy, S., 311
Kwarciany, M., 279
Kwok, C.S., 44, 276
Kwon, D.H., 308
Kwon, D.Y., 321
Kwon, H.-M., 55, 315

Mack, W.J., 73
MacLeod, M.J., 12, 91, 92, 94, 95, 97, 134, 305
Macleod, M.R., 3, 182
Macrez, R., 5, 60
MacSweeney, S.T., 53, 84
Madai, V.I., 89
Maddah, S.S.B., 204
Madhavan, P., 8, 85
Madou, R., 117
Maeda, T., 300
Maeder, P., 72
Magalhães, R., 36
Magin, P., 300
Magkou, D., 313
Magnin, B., 120
Magnus, T., 137
Magos, T., 191
Magy, L., 285
Magyar, T., 291
Mahagne, M.H., 260, 295, 296
Mahesh, K., 271
Mahlzahn, U., 90
Mahmood, A., 237, 261, 269
Mahmood, S., 250, 269
Maigana, M., 212, 292
Maimon, S., 130
Mainar, E., 22, 168
Maisch, B., 65
Maisterra, O., 15, 20, 124, 128, 152, 239, 287
Majer, R., 316, 319
Majoie, C.B., 22
Majoie, C.B.L.L., 33
Major, L., 262
Majoros, A., 206, 213
Makihara, N., 315
Makinde, K., 316, 319
Makotrova, T.A., 259
Mali, W.P., 14
Mali, W.P.T.T., 72
Malik, N., 164, 284, 316
Malojcic, R., 286
Maltenfort, M., 208
Maltezos, E., 307
Malzahn, U., 38
Mamun, M., 170, 237, 261
Mamutse, G., 110
Man, B.L., 172
Mandava, P., 126, 255, 263
Mandeville, J.B., 26
Mangiafico, S., 223
Manios, E., 317
Mann, A., 319
Mansour, O., 132
Manthei, G., 169
Mantovani, A., 8
Manzano, J.J.F., 54
Marcati, E., 240
Marchand-Leroux, C., 274
Marczynski, U., 107
Mares, J., 175
Mares, R., 296, 297
Margaill, I., 274

Mariani, M., 176
Mariano-Gâmbaro, D.C., 314
Marin, M., 193
Marín, R., 137
Marín-Bueno, R., 20
Marinho, C., 57
Marinkovic, I., 236, 244
Marjot, T., 306
Markoula, S., 214
Markus, H.S., 71, 83
Marnane, M., 62, 67, 112
Marosfoi, M., 262
Marota, J.J., 26
Marousi, S., 213, 214, 264
Marquardt, L., 31, 40
Marques, M.E.A., 109
Marquez, J.M., 166
Marra, S., 296
Marro, B., 34, 206
Marrone, A.C.H., 312
Marrone, B.F., 312
Marrone, L.C.P., 312
Marsden, D.L., 232, 314
Marsden, P., 227, 245
Marshall, I., 126
Marshall, R.S., 41, 44, 191
Martens-Lobenhoffer, J., 10, 308
Martí-Fàbregas, J., 20, 137
Marti-Fabregas, J., 308
Martin, P.J., 32, 113, 145, 206
Martínez Sánchez, P., 258, 264
Martinez, A.B., 308
Martinez, F., 164
Martinez, P., 232
Martínez, P., 317
Martinez-Gonzalez, N., 3
Martinez-Martinez, M., 80, 307
Martínez-Ramírez, S., 20, 137
Martínez-Sánchez, P., 35, 67, 68
Martinez-Sanchez, P., 35, 80, 109, 306, 307
Martino, G., 143
Martins, J.R.M., 112
Martins, O., 212
Martins, S.O., 321
Martins-Neto, G.P., 314
Martí-Vilalta, J.L., 137
Marton-Simora, J., 180, 181
Martus, P., 210
Marumoto, K., 188
Marx, J., 98
Marzahn, U., 11
Mas, J.L., 32, 54, 315
Masayasu, M., 258
Mascoli, F., 230
Masjuan, J., 35, 108, 222, 227, 232, 258, 264
Masjuán, J., 35, 67, 68
Maslowska, B., 256
Massano, J., 151
Massodinezhad, S., 249
Massuet, A., 11
Massy, Z.A., 51
Mastroiacovo, F., 136

Mat'oška, V., 31
Mateos, V., 117, 120
Mateus, S., 304
Mathiesen, E.B., 84, 159
Mathieson, P., 245
Mathys, J., 165
Matias, G., 149, 271
Matias-Guiu, J., 121, 231, 256
Matias-Guiu, J.A., 121, 231, 256
Matosevic, B., 120, 218, 258
Matou, S., 8, 145
Matsubara, I., 91
Matsuki, T., 128, 266, 276
Matsumoto, M., 38, 74, 268
Matsuo, R., 215, 222
Mattioni, A., 161, 318
Mattle, H., 32
Mattle, H.P., 15, 126, 275, 288
Mattle, H.P.M., 220
Matz, K., 46, 77
Matzarakis, A., 314
Mauer, C., 155, 156
Maul, S., 11
Mausberg, A.K., 141
Maxwell, S.S., 3
May, C.R., 220
May, J.A., 53
May, Z., 262, 320
Mayer, O., 286
Mayer, S.A., 21, 283
Mayer, T.E., 171
Mayol, A., 18, 140
Mayr, A., 8
Mazeto, G.M.F.F., 109
Mazighi, M., 70, 126
Mazzetto-Betti, K.C., 90
McAdam, J.J., 234
McArthur, K., 79
McBride, W., 208
McCabe, D., 227
McCabe, D.J.H., 8, 9, 85, 139, 142, 245
McCann, E., 270
McCarron, M., 185
McCarron, M.O., 185, 218, 308
McCarthy, T., 24
McColgan, P., 185
McColl, E., 198
McCormack, P.M.E., 62
McCrae, K.R., 25
McCrum-Gardner, E., 218
McElduff, P., 87, 88, 232, 300, 314
McGee, H., 289
McInnes, E., 88
McIntosh, J., 197
McKee, J., 185, 308
McKevitt, C., 63, 77, 80, 225
McKevitt, C.J., 179, 196
McKimm, A., 30
McLoughlin, A.S., 220
McLoughlin, A.S.R., 234
McManus, J., 227, 245
McMeekin, P., 34
McQuaige, F.B., 79

McVerry, F., 12, 91, 94, 95, 97, 134
Mead, G.E., 183
Meagher, S., 6
Meairs, S., 19, 25, 27, 131, 146
Meder, J.F., 315
Medina-Baez, J., 109
Mehrhof, F., 65
Mehrholz, J., 203
Mehta, A., 75
Mehta, Z., 43, 45, 69, 70, 73, 147
Meisel, A., 38, 46, 135, 179
Mejias, V., 308
Melander, O., 39
Meler, P., 24
Mellinghoff, C., 220
Mellon, L., 292
Melms, A., 279
Melnikova, E.V., 132, 138, 144
Melo, T.G., 215, 310
Menassa, M., 283
Mendes, A., 160
Mendez-Pereira, V., 257
Mendonça, N., 147
Mendonça, T., 79, 114, 179
Menon, B.K., 10, 29, 52, 59, 86, 95, 128, 255, 273
Mensink, G.B.M., 40
Menzel, T., 31, 54, 241, 247
Menzel, T.J., 119
Mercé, J., 296, 297
Mercurio, A., 157
Meretoja, A., 50, 59, 74
Mériaux, S., 274
Merkely, B., 138
Merlos, M.E., 51
Merlos-Benitez, M., 272
Merrien, F.M., 210
Merwick, A., 62, 67, 112
Meseguer, E., 70, 126
Mesiano, T., 244
Metcalf, A.K., 30, 276
Metcalf, K., 110
Metello, M., 115
Metso, T., 35
Meves, S.H., 40
Meyding-Lamadé, U., 125
Mezili, A., 213, 214, 264
Michalak, S., 282
Michalik, J., 121
Michalski, D., 228
Michel, P., 32, 48, 72, 222, 227, 257, 317
Michels, P., 28
Michou, E., 58
Micieli, G., 307
Middelhoff, M., 25
Middelkoop, I., 312
Middleton, S., 87, 88, 233
Mihajlovic, S., 242
Mihelj, M., 190
Miki, T., 293
Miklavčič, P., 156
Mikulik, R., 76, 77, 224

Milcareck, B., 5
Milhaud, D., 22
Milia, P., 282
Milian, M., 296, 297
Millán, M., 11, 37, 124, 260, 280, 288
Millan, M., 174
Millan-Nuñez, M.V., 206
Miller, R., 193, 194
Milligan, J., 286
Milo, R., 249
Milošević, Z., 156
Minematsu, K., 21, 29, 219, 253, 259, 265, 268, 309
Minnerup, J., 25, 136, 239
Miralles, A., 117
Mirgholami, A.R., 98
Misaggi, G., 71
Mischenko, K.A., 132
Missimer, J., 272
Mistri, A.K., 48
Mistry, S., 58
Mitchell, E.A., 218
Mitchell, K.A., 79
Miteff, F., 86
Miyagi, T., 29, 253
Miyakoshi, K., 188
Miyamoto, Y., 65
Miyashita, F., 219, 309
Miyazaki, Y., 99, 172, 221, 224
Miyazaki, Y.M., 107, 233
Mizuma, A., 221
Mizusawa, H., 214, 216
Mizutani, T., 176
Mlynash, M., 67
Mocquard, Y., 210
Modi, J., 29, 68, 95, 128
Moehring, M., 183
Moens, M., 272
Moffatt, U., 243
Mogoanta, L., 142
Mohammadiani Nejad, E., 284
Mohammadifard, M., 98
Mohammed, A.A., 212
Mohan, K.M., 207
Mohanty, S., 56
Mohs, C., 125
Mokry, J., 43
Moldes, O., 7, 19, 28, 144, 280
Moldoveanu, E., 119
Molina, C., 128, 255
Molina, C.A., 15, 20, 24, 36, 124, 152, 239, 287
Möllmann, H., 295
Molshatzki, N., 64, 183
Molshatzky, N., 279
Molshazki, N., 43
Momjian-Mayor, I., 240, 257
Moniche, F., 18, 140
Mono, M., 176
Mono, M.L., 32, 288
Mono, M.L.M., 220
Montaner, J., 24, 140
Moore, D., 171

Moore, D.F., 307
Moore, D.J., 8, 85
Mora, J., 91
Mora, P., 157, 186
Morado, M., 109
Moraga, A., 138
Morais, R., 79, 179
Morales, A., 121, 164
Moran, R., 203
Morchon, S., 269
Mordasini, P., 96, 165
Moreau, T., 283
Moreno, A., 103, 121, 164
Moretti, M., 81
Moretto, G., 244
Mori, E., 300
Mori, K., 159, 164
Mori, T., 172, 221, 224
Mori, T., 99
Mori, T.M., 107, 233
Moriya, Y., 221
Moro, C.H.C., 210, 213
Moro, M.A., 138, 146
Moroney, J., 62
Moroney, J.T., 67
Morris, R.G., 83
Morris, Z., 147, 213
Morrish, W.F., 173
Mosqueira, A., 116
Mostafaei, S., 49
Mostafaie, S., 129, 211
Mostertz, J., 142
Motta, E., 318
Mottier, D., 210
Motto, C., 134, 307
Mounach, M.J., 216
Mourad, M.A., 281
Mourand, I., 22
Mourdisen, K., 90
Mouridsen, K., 93, 97
Mousavi, S.A., 313
Moussouttas, M., 208
Moynagh, M.R., 67
Moyses-Neto, M., 110
Moytl, M., 286
Mpakalakou, A., 213
Mpotsaris, A., 23
Mrabet, A., 312
Mrabet, H., 312
Mualem, E., 6
Mudd, P., 113
Mueller, C., 144
Muengtaweepongsa, S., 100
Muir, K.M., 12, 134
Muir, K.W., 1, 91, 92, 94, 95
Muir, K.W.R., 97
Müller, F., 134, 190
Müller-Jensen, A., 49
Müller-Tasch, T., 65
Mulroy, M., 290, 292
Munih, M., 190
Muñoz, A., 231
Muñoz, R.M., 214
Munro, F.A., 188

Murakami, N., 107
Murakami, Y., 63
Murata, Y., 26
Muresan, I.-P., 206
Muresan, I.P., 34
Muresanu, D.F., 166
Murillo, L., 51
Murin, J., 292
Murphy, D., 240
Murphy, R., 227, 245, 292
Murphy, R.P., 8, 9, 85, 139, 142
Murphy, S., 62, 67, 227, 245
Murray, A., 12, 91, 94, 95, 97, 134
Murray, C., 213
Murray, G.D., 16, 226
Muskovich, K., 297
Muszbek, L., 291, 317
Myint, P.K., 44, 276
Myllane-Fernandes, P., 57, 314

Naccarato, M., 136
Naegele, B., 57
Næss, H., 244
Nagahiro, S., 29, 268
Naganuma, M., 262
Nagao, T., 29, 228, 268
Nagashima, G., 170
Nagata, E., 221
Nagata, K., 300
Nagatsuka, K., 65, 259, 265
Nagel, E., 279
Naggara, O., 315
Naglie, G., 42, 198
Nagy, G., 180, 181
Nagy, Z., 138, 191
Nah, H.-W., 4
Najafi Nashali, M., 49
Nakachi, K., 267
Nakagawara, J., 21, 29, 253, 262, 268
Nakamura, A., 315
Nakamura, K., 315
Nakamura, T., 74
Nakazaki, M., 99, 172, 221, 224
Nakazaki, M.N., 107, 233
Nalbantoglu, M., 313
Namekawa, M., 253
Nannucci, S., 81, 301
Naoumis, D., 267
Napolitano, S., 227
Nappini, S., 223
Narasimhalu, K., 273, 275
Narata, A.P., 257
Nardai, S., 138
Nardetto, L., 81
Nardi, K., 185, 282
Narkiewicz, K., 279
Narumi, S., 159, 164
Nascimento, C., 57
Nasim, A., 195
Nasr, N., 53, 69
Navarro, M., 103, 121, 164
Naya, T., 38
Naylor, A.R., 171

Nechipurenko, N.I., 151
Nedelko, V., 56
Nedelmann, M., 144, 154
Nedeltchev, K., 32, 275, 288
Nedeltchev, K.N., 220
Nederkoorn, P.J., 1, 14, 33, 82
Nedregaard, B., 311
Neggers, S., 155
Nemeth, L., 180
Nencini, P., 223
Nesi, M., 223
Neskovic, M., 242
Neto, F.S., 321
Neto, I., 75
Neto, L., 110
Neumann, T., 65
Neumann-Haefelin, T., 244
Newton, J.L., 254
Ng, K.W., 13, 165, 173, 187, 229, 230
Ngamroop, R.N., 181
Nguyen, D.K., 245
Ní Chróinín, D., 60, 67, 183
Ni Chroinin, D., 62
Nichelatti, M., 134
Nichol, L., 200
Nicholas Chew, W.M., 204
Nicolae, H., 322
Nicolaides, A.N., 160
Nicoletti, F., 136
Niculescu, I., 322
Niederkorn, K., 4
Niederstadt, T., 10
Niesen, W., 130
Nieuwenhuis-Mark, R.E., 277
Niewada, M., 282, 305
Nighoghossian, N., 90, 93
Nijjer, S.S., 296
Nikolaou, G., 214, 264
Nilanont, Y., 146, 232, 269
Nilsson, M., 39
Ning, C., 10, 173
Niranjan, K., 195
Nishimura, K., 216
Nithi, K., 105
Nixdorf, K.E., 155
Noda, T., 262
Nogoshi, S., 170
Nogueira, R.G., 276
Nolte, C., 90
Nolte, C.H., 12, 76, 225, 301
Nombela, F., 35, 115, 116, 258, 264
Noone, I., 183, 286
Noraddin, A., 249
Norris, D.G., 82
Norris, J., 71
Norrving, B., 39, 81, 193, 210, 241
Nosál', V., 121
Nourian, A., 124
Novak, D., 190
Novak, E., 293
Nowak, E., 210
Nowe, T., 62, 80, 81, 286
Nowinski, W.L., 282

Storto, M., 136
Stott, D.J., 79, 302
Stracke, P., 127
Straka, M., 67
Stratton, S., 73
Strause, I., 130
Strbian, D., 50, 59, 74, 247
Streeter, J., 24
Strömberg, S., 14
Stromillo, M.L., 81
Struffert, T., 6
Stukova, L.N., 132
Stummer, W., 169
Sturm, J., 37, 300
Sturzenegger, M., 272
Stylou, L., 163
Su, W., 42
Suárez-Calvet, M., 137
Suárez-Luis, I., 270
Suchomel, P., 224
Sudlow, C.L.M., 3
Sueda, Y., 74
Sugimori, H., 266, 276
Sugiura, S., 107
Suh, C.K., 237
Suhr, J., 279
Suissa, L., 260, 295, 296
Sujjanunt, J., 269
Sukiennik, J., 125
Suman, A., 96
Sun, L., 19
Sung, S.F., 178, 282
Suñol, A., 288
Suppa, P., 150
Suri, F.K., 260
Suslina, Z.A., 297
Sutton, C., 198
Sutton, C.J., 212, 220
Suvorov, A.Y., 141, 199
Suzuki, A., 29, 268
Suzuki, K., 215, 222, 315
Suzuki, S., 128
Švigelj, V., 76
Swendsen, J., 302
Sykora, M., 152, 219, 220,
    223, 225
Sylaja, P., 271
Syme, P., 305
Szabo, K., 27, 92, 94, 241, 270
Szakacs PhD, Z., 320
Szakács, Z., 100
Szakacs, Z., 262
Szalai, M., 213
Szasz, G., 262
Szczuchniak, W., 234, 236
Szegedi, N., 100, 262
Szentpetery, L., 262
Szikora, I., 262
Szilágyi, G., 100
Szilagyi, G., 262
Szili, R., 213
Szilvasi, P., 262
Szima, G., 189
Sztajzel, R.F., 240, 257

Taba, P., 250
Tabasi, M., 124
Tabatabae, A., 124
Táborskú, L., 31
Tabusadani, M., 188
Tadano, M.T., 148
Tafani, M., 28
Tagaris, G., 264
Taheraghdam, A., 129
Tahira, F.A.C., 205
Tai, B.C., 79, 208
Taimkao, S.T., 181
Tairova, R.T., 143
Tajiri, H., 99, 172, 221, 224
Tajiri, H.T., 107, 233
Takada, T., 170
Takagi, S., 29, 221, 228, 232, 268
Takahashi, K., 188
Takahashi, T., 107
Takahashi, W., 221, 228, 232
Takamatsu, K., 258
Takashi Takebayashi, 188
Takebayashi, T., 188
Takeda, H., 298
Takizawa, S., 221, 228, 232
Takubo, H., 228
Talisumak, T., 35
Tallerman, C., 235
Tallon, E., 286
Tamazyan, R., 54
Tan, E., 162
Tan, K.M., 183, 286
Tan, L.C.S., 208
Tanahashi, N., 29
Tanahasi, N., 298
Tanislav, C., 73, 210
Tanne, D., 43, 64, 66, 183, 255, 279
Taqi, M., 131, 175
Tarassenko, L., 239, 245
Tardy, J., 17, 28
Tassinari, T., 253
Tatlisumak, T., 48, 50, 52, 74, 152,
    210, 247
Tatschl, C., 77
Taylor, R.A., 260
Taylor, R.G., 221
tDodick, D.W., 224
Tegos, T.J., 160
Teixeira da Silva, M.H., 304
Teixeira, N.B., 235
Tejada, J., 305
Tejada-Garcia, J., 105
Teljemark, J., 254
Telman, G., 165
Tembl, J., 168
Tembl, J.I., 22, 308
Teo, B.C., 33
Teoh, H.L., 10, 13, 44, 79, 107, 145,
    162, 165, 173, 187, 215, 229,
    230
Terayama, Y., 159, 164
Terborg, C., 49, 169
Terént, A., 16
Terent, A., 70

Terni, E., 174, 312
Tettenborn, B., 113
Teuschl, Y., 46, 304
Thaler, D.E., 32
Tham, K., 58, 191
Thiem, U., 40
Thieme, H., 203
Thien, T., 226
Thijs, V., 3, 16, 35, 81
Thomalla, G., 14, 49, 92, 93, 97,
    161, 257
Thomas, A., 213
Thomas, J., 108
Thomas, L., 198
Thomas, P., 316, 319
Thomas, R., 91, 126
Thomas, R.G., 12, 94, 95, 97, 134
Thomas, R.G.R., 92
Thomassen, L., 244, 310
Thomson, R.G., 34, 77
Thonke, S., 102
Thorpe, K., 43
Thuy, M., 1
Tiainen, M., 59, 74
Tiamkao, S.T., 49
Tierney, S., 8, 9, 85, 139, 142
Timofeev, D.Y., 318
Timsit, S., 210
Tinazzi, M., 244
Tinchon, A., 114, 122
Tirel-Badet, A., 210
Tistad, M., 43, 58, 191
Titiva, L., 259
Tjønneland, A., 40
Tobenamed, A., 8
Tobenamed, B., 8
Tobin, W.O., 8, 9, 85, 139, 142
Todica, O., 150
Todo, K., 170, 171
Tokami, H., 315
Tokashiki, T., 267
Tokucoglu, F., 251
Tola, M.R., 230
Tolosa, E., 137
Tomandl, B.F., 220
Tomek, A., 31
Tomic, G., 45
Toni, D., 240, 253, 261
Toor, G.K., 189
Topakian, R., 278
Töpper, R., 49
Toratani, N., 107
Torres, M.J., 67, 68
Toscano, M., 83
Touboul, J.P., 71
Touboul, P., 70
Tountopoulou, A., 47
Tourdias, T., 89, 109, 158, 161
Touze, E., 35
Touzé, E., 54, 315
Toyama, K., 310
Toyoda, K., 21, 65, 219, 253, 259,
    262, 265, 309
Trampisch, H.J., 40

Travasarou, M., 213, 214, 264
Tresserras, R., 241
Trobbiani, K., 294
Troester, D., 131
Tropepi, D., 227
Truelsen, T., 209
Tryc, A., 47
Tryc, A.B., 10, 256
Tsabari, R., 255
Tsai, F.Y., 275, 278
Tsai, J.Z., 99
Tsai, L.-H., 8
Tsai, S.H., 250
Tschirner, A., 136
Tseng, M.C., 178, 282
Tsim, S., 270
Tsiskaridze, A., 142
Tsivgoulis, G., 115, 163, 182, 187,
    294, 307
Tsuchiya, A., 170
Tsukita, K., 300
Tsygan, N.V., 166, 251
Tuemmler, J., 47
Tukiendorf, A., 282
Tuna, A., 36
Tunde, I.A., 212, 292
Turc, G., 315
Turhan, G., 308
Tuta, S., 151
Tymchuk, S., 67
Tymianski, M., 139
Tyrrell, P., 58, 78, 153, 249
Tziomalos, K., 313
Tzourio, C., 5

Ubelacker, A., 135
Uchino, K., 183
Uchiyama, S., 29, 87, 228, 268
Uebele, M., 98
Ueda, T., 170
Uehara, T., 29, 268
Ueno, Y., 170, 171
Uesugi, T., 221
Uljarevic, V., 242
Ullman, N., 88
Umachandran, V., 122
Ünal, A., 148
Urano, Y., 87
Urban, P.P., 49, 98
Urbanek, C., 207
Urra, X., 127
Ustrell, X., 296, 297
Uyguner, O.Z., 320
Uyttenboogaart, M., 125, 272

v Gorp, E., 312
Vadasdi, K., 235
Vadikolias, K., 115, 163, 294, 307
Vail, A., 153
Vairale, J.Y., 66
Vajda, Z., 175
Valabregue, R., 56
Valdés Hernánde, M.C., 148
Valdueza, J.M., 109

Valente, M.V., 210
Valenti, R., 81
Valenti, R., 301
Valenzuela, F., 115
Valero, J., 269
Vallat, J.M., 285
Vallejo, M.T., 19
Valle-Pereda, M., 120
Valvassori, L., 134
van Alebeek, M., 273
van de Beek, D., 1
van den Berg, B.T.J., 289
van den Berg, H.A.C., 83
van den Berg-Vos, R.M., 289, 290
van den Herik, E.G., 39, 55, 301
van den Meiracker, A.H., 55
van den Munckhof, P., 22
van der Bom, J.G., 4
van der Graaf, Y., 82, 209
van der Kolk, A.G., 159
van der Lugt, A., 14
van der Veen, M., 289
van der Vlugt, M.J., 273
van der Worp, H.B., 14, 65, 72, 87
van der Zee, D., 61
van Dijk, E.J., 52, 273
van Dooren, M., 83
van Duijn, C.M., 39
van Kessel, M.A., 182
van Kooten, F., 155, 182
van Landegem, W., 117
van Melkebeke, D., 117
van Norden, A.G.W., 82, 83
van Oostenbrugge, R.J., 149, 150
van Oudheusden, L.J.B., 82
van Overbeek, E.C., 150
van Overbeeke-Bakker, M.J., 33
van Rijsbergen, M.W.A., 277
van Rooijen, N., 141
van Schaik, S.M., 289, 290
van Seeters, T., 74, 161, 318
van Uden, I.W.M., 82
van Westen, D., 193
van, R.J., 83
van' t Hof, F.N.G., 39
Vanacker, P., 289
Vandermeeren, Y., 3, 178
Vandi, Z., 292
Vanhooren, G., 289
Vanlandewijck, Y., 189
Vanroy, C., 189
Vargas, B., 224
Vargas, P., 56
Varoquaux, G., 197
Vasconcelos, J.M., 297
Vasdekis, S., 163
Vashadze, T., 142
Vassilopoulou, S., 264, 267, 298
Vastagh, I., 206, 213, 235
Vaverka, M., 175
Vazquez Alén, P., 319
Vázquez Allen, P., 242
Vazquez Sanchez, F., 105

Vázquez, F., 305
Vazquez, F., 308
Vazquez, J.F., 22
Vazquez, V., 22, 168
vd Laar, T., 312
Veljancic, D.M., 311
Veloso, M., 110, 251
Velthuis, B.K., 74, 153
Veltkamp, R., 19, 25, 31, 306
Vemmos, K., 38, 213, 214
Vemmos, K.N., 267, 283
Vemmou, A., 38, 267, 283
Venker, C., 127
Venketasubramanian, N., 10, 13, 33, 44, 79, 165, 187, 208, 229, 230
Ventura, L.M.G., 314
Vér, C., 189
Vera, R., 108
Verhagen, A.P., 182
Verheyden, G., 203
Vermeij, J.-D., 1
Vermeulen, M., 33
Verschure, P., 42
Verschure, P.F.M.M., 190, 191
Veverka, T., 23, 175, 261
Veyssiere, J., 142
Viaccoz, A., 240, 257
Viader, F., 117
Viakhireva-Dovganiuk, I., 210
Viana-Baptista, M., 149, 271
Vibbert, M., 208
Vibo, R., 246, 250
Vicente Peracho, G., 319
Vicenzini, E., 83
Videen, T.O., 44
Viguier, A., 69, 259
Vilar, C., 308
Vilionskis, A., 76
Villafani, J., 305
Villafani-Echazu, W.J., 105
Villanueva Osorio, J.A., 242, 319
Villaplana-Alcázar, M., 202
Villemagne, V.L., 89
Villinger, K., 11
Villringer, A., 90
Villringer, K., 90
Viñas, J., 296, 297
Viñas, M.J., 214
Viosca-Herrero, E., 202
Virat-Brassaud, M.E., 283
Visser, F., 159
Visseren, F.L.J., 209
Vivancos Mora, J., 258, 264
Vivancos, J., 35, 116, 222, 227, 232, 263
Vivas, E., 124, 174
Vivien, D., 5, 60
Vlachova, I., 175
Vlak, M.H.M., 4, 184
Vlasov, T.D., 138, 144
Voisin, S., 259
Volceka, D., 285
Volkening, K., 134, 190

Vollmar, F.L.V., 25
Volonghi, I., 43
Volsek, M., 150
von Haehling, S., 279, 308
von Koch, L., 58, 191
von Kummer, R., 15
von Rappard, J., 113
von Weitzel-Mudersbach, P., 300
Vondrackova, D., 224
Vora, N., 231
Vosko, M.R., 28
Voumvourakis, K., 163
Voznyuk, I.A., 166, 251
Vroomen, P.C.A.A., 61, 226
Vucurevic, G., 98
Vukasinovic, N., 257
Vukasinovic, N.P., 235, 244
Vulpe, G., 322
Vysata, O., 241

Wachirutmanggur, L., 146
Wachsmuth, L., 25
Wachter, R., 65
Wagner, A., 306
Wagner, G., 4
Wagner, M., 224
Wahlgren, N., 23, 77, 253, 261
Wahlgren, N.G., 182
Wainwright, J., 249
Wakhloo, A.K., 15
Wakisaka, Y., 215, 222
Wakui, D., 170
Walker, M., 5, 189
Walker, M.F., 190
Wallace, S.C., 158
Wallin, A., 45
Walsh, S., 292
Walsh, S.U., 290, 292
Walter, S., 22
Walter, T., 295
Walter, U., 218
Wandurraga, L.R., 51
Wang, C.X., 153
Wang, J.G., 180
Wang, K.W., 99
Wang, L., 127
Wang, Q.S., 253
Wang, T.M., 197
Wang, W.J., 153
Wang, X., 61, 148, 312
Wang, Y., 208
Wang, Y.J., 101, 153
Wang, Y.L., 153
Wang, Z., 144
Wani, M., 270
Warach, S., 161, 165, 182
Warburton, E.A., 90
Ward, J., 87, 88, 233
Wardlaw, J., 91, 94, 95, 97
Wardlaw, J.M., 12, 92, 98, 126, 134, 147, 148, 183, 213
Wartenberg, K.E., 283
Wasser, K., 173

Watabe, W., 315
Watanabe, H., 170
Watanabe, M., 65
Watkins, A., 316, 319
Watkins, C., 198
Watkins, C.L., 180, 200, 212, 220, 234
Watson, T., 232
Watt, M., 271
Webb, A.J.S., 2, 72
Weber, J., 132
Weber, P., 275
Weber, T., 49
Weber, W., 23
Weck, A.W., 220
Weder, B., 272
Weekes, C.E., 273
Wehner, W., 263
Wehrli, E., 275
Wei, J.W., 180
Weibrich, C., 98
Weigand, J., 47
Weiller, C., 130, 197
Weimar, C., 32
Wein, T., 193, 194
Weinman, J., 288
Weinstein, G., 43
Weinstein, H.C., 289, 290
Weinzierl, U., 129
Weir, C., 91, 94, 95, 97
Weir, C.J., 12, 134
Weise, J., 171
Weissenborn, K., 10, 47, 153, 256, 258
Weisskopf, F., 268
Weisstanner, C., 170
Welch, S., 43
Wellwood, I., 80, 301
Werneck, I.V., 90, 262, 314
Werner, R., 107, 119, 246
Werring, D.J., 3, 44, 299
Wersching, H., 89, 239
Wessels, C., 154
West, C., 30
West, K., 171
Westendorp, W.F., 1
Wester, P., 13, 68
Wethal, T., 311
Wetterling, F., 19
Wetzel, S.G., 14
White, J.H., 300
Whitehead, L., 190
Whiteley, W.N., 126
Whittle, I., 186
Wick, G., 8
Widmann, C., 142
Wieberdink, R.G., 39
Wiebringhaus, R., 230
Wiedmann, S., 81, 301
Wiest, R., 272
Wijmenga, C., 39
Wilczak, N., 272
Wilkinson, B., 72