Intraoperative Hyperglycemia Is Associated with Increased Long-Term Postoperative Cognitive Abnormalities in Patients Undergoing Cerebral Aneurysm Clipping

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The goal of our investigation was to determine if elevated intraoperative blood glucose concentrations were associated with an increased risk of long-term neurologic dysfunction in a population of neurosurgical patients at high risk for cerebral ischemia. Data were obtained from the IHAST (Intraoperative Hypothermia for Aneurysm Surgery Trial) database. All 1000 patients who completed the trial had aneurysmal subarachnoid hemorrhage and were scheduled for surgical clipping of their aneurysm. They were neurologically intact, or nearly intact, prior to induction of anesthesia. Blood glucose concentration at the time of clip placement was correlated with neurocognitive changes at the completion of the 3-month study period as assessed by the Mini Mental Status Examination, Benton Visual Assessment, Oral Word Association Test, Complex Figure Test, Grooved Peg Board Test, and Trail Making Test. Data were corrected for treatment (hypothermia versus normothermia) and other variables including pre-operative neurologic status. Average blood glucose concentration at the time of aneurysm clipping was 132 +/-35 mg/dL. When compared to patients with a blood glucose concentration of ≤107 mg/dL (the lowest quartile), those with blood glucose concentrations ≥152 mg/dL (the upper quartile) had impairment of significantly more neurocognitive tests (p=0.019) at 3 months after surgery. Those with blood glucose concentrations 129–151 mg/dL and ≥152 mg/dL (the upper two quartiles) were more likely to have impairment of at least 1 test (p=0.009 and p=0.006 respectively). Intraoperative hyperglycemia is associated with subtle changes in neurocognitive function in neurosurgical patients at high-risk for ischemic brain injury.

In-Hospital Complications Following Acute Ischemic Stroke in the Registry of the Canadian Stroke Network, Phase 3

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Background: Stroke units decrease morbidity and mortality for stroke patients, possibly resulting from reduced in-hospital complications. We assessed the hypothesis that in-hospital complications are associated with less favourable outcomes and that variations across hospitals may relate to differences in care. Methods: All acute ischemic stroke patients admitted to 12 acute care hospitals in Ontario, Canada, were prospectively entered in the RCSN Phase 3. Detailed in-hospital data were collected retrospectively from chart abstraction upon hospital discharge (July 2003-Dec. 2004 data completed). Trained nurse coordinators performed data collection and entry into the Registry. Descriptive analysis of baseline demographics and detailed analysis of complication data was performed. Results: Data from 3220 patients were analysed. At least one complication occurred in 1177 (36.6%) patients. Neurological complications were seen in 568 (17.6%) patients; recurrent in-hospital stroke occurred in 107 (3.3%) and TIA in 34 (1.1%). Preventable complications (DVT, embolism, falls, pneumonia, skin ulcers, and UTI) were seen in 551 (17.1%) patients. Mortality was higher in patients with complications [346 (29.4%) deaths vs. 42 (2.1%) deaths; p<0.0001]. Median length of stay in patients with complications was longer (14 vs. 8 days; p<0.0001) and these patients were less likely to be discharged home (26.7% vs. 59.6%; p<0.0001). Increasing age and stroke severity (Canadian Neurological Score, Oxfordshire Classification and level of consciousness) were associated with a higher risk of complications. Risk-adjusted hospital complication rates varied significantly between sites. Conclusions: In-hospital complications following ischemic stroke are associated with worse outcomes. A proportion of complications are preventable. Inter-hospital variability in complication rates suggests that differences in stroke care are important though specific factors remain unidentified.

Gender Does Not Influence Functional Outcome or Recanalization Rates in Patients Treated with Intra-arterial Thrombolysis for Acute Stroke

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Background: Recent studies have indicated that women fare better than men with regard to arterial recanalization rates and functional outcomes following intravenous thrombolysis for acute ischemic stroke. It is not known if this gender advantage extends to ischemic stroke patients treated with intra-arterial thrombolysis. We investigated the effect of gender on clinical and angiographic outcomes after treatment with intra-arterial (IA) thrombolysis for acute ischemic stroke. Methods: We analyzed patients recorded in a prospectively maintained registry who had received intra-arterial fibrinolysis without concomitant intravenous or mechanical recanalization therapies at a university medical center from July 1, 1992 to June 30, 2005. Outcomes included achievement of angiographic recanalization (TIMI score), 7-day NIH Stroke Scale (NIHSS) score, 90 day modified Rankin Scale (mRS) score, and length of Hospital Stay (LOS). The independent effect of gender on outcome was evaluated by ordinal logistic regression (mRS), and least squares regression (NIHSS, LOS, TIMI), adjusting for thrombolytic dose and variables known to predict outcome after ischemic stroke. Results: Among 81 patients, mean age was 70 years, and 49% were female. Women were significantly older than men, but both sexes were matched in other clinical and demographic variables. Partial or complete recanalization (TIMI 2 or 3) was achieved in 73% of women and 73% of

men; complete recanalization (TIMI 3) in 10% of women and 15% of men. In unadjusted analysis, there was no significant difference in women versus men in the 7-day median NIHSS (12 vs. 4.5, p=.17), median 90 day mRS (3 vs. 2, p=.67), median LOS (8 vs. 8 days, p=.97) and median TIMI score (2 vs. 2, p=.56). After adjusting for covariates, there were no significant differences between men and women for all 4 outcomes studied. Conclusions: Unlike intravenous thrombolysis, IA thrombolytic treatment is not associated with greater recanalization rates and functional outcomes in women compared to men. The high local concentrations of fibrinolytic agent achieved by IA administration may overcome hemostatic and thrombus volume differences between the sexes, permitting equal outcomes among women and men.

Incidence of Aphasia in Acute Stroke Patients: Prosit Study

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Background/Objective: Post stroke disability has been always related to motor impairment but there are some evidences that cognitive disturbances such as aphasia may contribute to stroke patients outcome. Data about the incidence and the contribute of aphasia on disability in stroke are still lacking. The aim of this study is to evaluate the incidence of aphasia and to compare clinical and demographic features in patients with and without aphasia. The populations studied is part of the Italian PROSIT study conducted during 2001. Methods: 15 researchers evaluated retrospectively 12.206 acute stroke patients'clinical records registering demographic, clinical and neurological conditions. From the initial series unconsciousness patients (2567) were excluded in order to avoid bias in aphasia estimation. The presence of aphasia was registered when reported on the first neurological examination. Non specific test for aphasia diagnosis were used. The 2 years follow-up was completed in 98% of patients. Results: Out of 9953 stroke patients 26% were aphasic. Of these patients the 74% presented arm and/or limb weakness that was in 82% on the right side, in 16% on the left side, in 2% bilateral. Aphasia seemed to be more frequent in women than man (53% vs 47%) and in patients older than 75 y.o. (59% vs 46%). Aphasic patients had a more severe stroke than non aphasics: 33% of aphasics compared to 15% of non-aphasics (p = 0.000) presented plegia in arm and/or limb and 14% of aphasics compared to 12% of non aphasics (p = 0.006) presented an ICH at CT scan. Aphasics died more frequently than non aphasics during hospitalisation and at follow up (10% vs 4% and 26% vs 16% respectively) and presented a more severe long term disability (Rankin scale score > 2) than non aphasics (48% and 34%, respectively). Conclusions: This is the first study evaluating the incidence of aphasia in a wide Italian population of acute stroke patients. We found the presence of aphasia in 26% of acute stroke patients according to previous reports in other countries. The presence of aphasia is a component of long term disability in stroke patients. These findings suggest the need to plan speech rehabilitation programs all aphasic patients in order to reduce their long-term disability.

5-Year Results of Carotid Stenting in High-Volume Centers: A Comparison of 2 Different Age Groups in Patients with Asymptomatic Carotid Stenosis (ELOCAS Registry)

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Background: The 5-year-results of the ACST Trial have shown a significant benifit of immediate carotid endarterectomy for patients with asymptomatic stenoses aged <75, but not for those ≥75 years of age. We compared the acute and long-term results of carotid stenting of asymptomatic stenoses in these two age groups as observed in 4 high-volume centers. Patients: Between 1993 and 2004, 1268 patients with an asymptomatic lesion were treated with stent implantation. Results of carotid stenting of 826 asymptomatic stenoses in patients aged <75 were compared to the results of 442 asymptomatic lesions in patients ≥75 years of age. There were no other significant differences in baseline characteristics. Methods: We used embolic protection devices in 86.8% and 85.3% procedures, respectively. 95.4% and 91.9% of the patients were treated with stent implantation. Results: Concerning the patients aged ≥75, the procedure was technically successful in 824/826 lesions (99.8%). Within 30 days after intervention 1 patient developed a major stroke, 1 patient suffered a fatal major stroke and 1 patient died due to non-cerebral cause. The major stroke/death rate at 30 days was 0.4%. During follow-up (after 30 days) the following events occurred: major stroke in 3, fatal major stroke in 1 and non-cerebrovascular death in 11 patients. Annual rate of major stroke/cerebral death was 0.4%. In patients ≥75 years the procedure was technically successful in 440/442 (99.5%). Within 30 days of the procedure 3 major strokes, 2 fatal major strokes and 4 non-cerebral deaths occured. The major stroke/death rate at 30 days was 2.0%. During follow-up the following events occurred: fatal major stroke in 2 and non-cerebrovascular death in 27 patients. Annual rate of major stroke/cerebral death was 1.0%. The differences between both groups were not significant. Conclusion: Carotid stenting is a successful technique to prevent stroke and can be performed safely in patients ≥75 years. Peri-procedural and long term risks seem to be higher in the elderly although the difference was not significant . This has to be weighed up with the higher risk of surgery and natural course of the disease in elderly patients.

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Decrease in Blood Pressure During the Acute Phase of Ischemic Stroke Is Associated with Poor Functional Outcome

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OBJECTIVE: Management of blood pressure (BP) during the acute phase of stroke is controversial. In this prospective, multicenter, observational study we sought to investigate the influence of BP and its changes during the acute phase of ischemic stroke on functional outcome. PATIENTS AND METHODS: Out of 1112 patients admitted in 12 hospitals within 24h from symptoms onset, 1028 patients fulfilled the inclusion criteria, and 902 were valid for the primary variable analysis. BP was registered in the emergency department (ED, average value of all readings), at admission in the stroke unit, and then at fixed intervals after stroke. Ischemic stroke was confirmed by cranial CT at admission. Canadian Stroke Scale (CSS) score was evaluated at the same intervals than BP determinations. Treatment of BP at the ED did not follow specific guidelines. The primary variable was the rate of poor outcome defined as a modified Rankin Scale (mRS) score >2 at 3 months. RESULTS: Poor outcome was recorded in 286 (31.7%) patients. A J-shaped effect was observed: the adjusted ORs of poor outcome for systolic BP (SBP) in the ED <110 and >180 mmHg were 3.6 (95%CI, 1.3–5.5) and 4.5 (1.9–8.7). Similar ORs were found for diastolic BP (DBP)<70 and >105 mmHg. Antihypertensive treatment was administered in the ED in 16.7% of patients (in 8% [65/810] with SBP<180, in 45% [86/190] with SBP 180–220, and in 83% [19/23] with SBP>220). Treatment was associated with SBP reduction at admission in the stroke unit >40 mmHg in 36% of patients and with DBP reduction >20 mmHg in 42%. The ORs of poor outcome for reductions of SBP>40 or of DBP>20 mmHg were 10.6 (5.0–22.0) and 2.1 (1.2–3.5) after adjustment for stroke severity, BP in the ED and use of antihypertensive drugs. CONCLUSIONS: Levels of SBP>180 and DBP>105 mmHg, as well as a relevant drop in BP, are associated with poor functional outcome in patients with ischemic stroke. These results replicate previous findings in a larger multicenter population.

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Clinical and Radiographic Predictors of Herniation in Malignant MCA Stroke

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Background: The reported incidence of cerebral herniation in complete Middle Cerebral Artery (MCA) territory ranges as high as 50–78%. The few studies of complete MCA territory infarction have identified "risk factor profiles" for herniation. The study reported here examined risk-factors identified in earlier studies in the patient population of the Hennepin County Medical Center Stroke Database. Methods: All cases from the HCMC Stroke database of patients admitted for acute stroke from 1997–2001 were reviewed to identify a study sample of patients with potential total MCA territory stroke. Of 626 potential cases, 31 patients were identified as having proximal MCA occlusion using convergent clinical and imaging inclusion parameters. Demographic, clinical and radiographic data from these patients were then recorded and analyzed. The following previously reported predictors of herniation were examined: Age; Baseline NIHSS score; Decreased level of consciousness (LOC) from baseline; Development of pupillary asymmetry; Hyper-acute changes on initial CT. Where available, percentage area of involvement on MRI/DWI was also assessed. Results: Herniation occurred in 7 (22.6%) of patients and was the confirmed cause of death in 6 (Mean time 52.9 h). The single survivor underwent surgical decompression. Mean age in the herniated group was 47.7 compared to 65.79 in the non-herniated group (p= 0.056.OR= 0.95). Baseline NIHSS was not a predictor of herniation, but deterioration in LOC from baseline was (Mean time 35.2 h; OR= 10, p= 0.001, CI 95%:1.7- 53). All patients with documented pupillary asymmetry (Mean time 44 h) herniated. The presence of ≥ 2 hyper-acute signs of stroke on CT trended towards increased risk of herniation (OR=6, p= .058, CI 95%:0.94–39) and percentage area of arterial territory involvement on MRI DWI showed a strong association (all patients with values of ≥80% herniated; p= 0.028). Conclusions: Baseline NIHSS did not predict risk of herniation however; a decrease in LOC from baseline is an important clinical parameter predictive of herniation. Age may be a negative predictor for herniation. CT and MRI imaging may allow early prediction of herniation however follow up studies of larger sample size are required.

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Correlation Between Corticospinal Injury and Prognosis of Stroke Indicated by Diffusion Tensor MRI

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Diffusion tensor MRI (DTI) could track corticospinal tract (CST) and identify relationship between CST and infarction. We assessed the hypothesis that extent of CST injury directly relates to dysfunction and prognosis of stroke. **Methods:** Images of 34 stroke patients (1~14days from symptoms) were obtained with a whole-body 3.0 T MR system (Siemens). The routine stroke protocol of T1,T2, diffusion -weighted images, MR angiogram and DTI were performed. DTI was performed using a single-shot echo-planar technique (b=0, 1000, 1500, TR/TE=8000/70.9ms,1NEX,flip angle =90, acquisition matrix= 128×128, FOV=240×240mm², slice thickness/ interslice =2 /3.2 mm). The CST trajectories was achieved by the Fiber Assignment by Continuous Tracking method. Tracking stop criterion was FA <0.3 or inner product <0.85. CSTs were classified into no (0), partial (1), total (2) involvement within the infarcts and its voxel numbers involved within infarcts in the largest injury cross section was recorded. Scores of

NIHSS on the MRI examination day and NIHSS and MRS scores in 2 week and 3 months indicated degree of dysfunction. Spearman correlation coefficient was analyzed to testify relationship between CST injury extent and neurological function scores. Tractography was successfully performed in 34 patients. no, partial, total injury of CST were in 4,27,3 patients with the biggest injuries voxel numbers of 0,22.7,65.3 respectively. NIHSS mean scores were 2.44±1.232 (0~6) in 2nd week and 1.65±1.012 (0~4) in 3rd month. MRS scores were 2.85±0.702 in 2nd week, 1.41± 0.500 in 3rd month. FA value varied from 0.139~0.352(0.244±0.318), voxel number varied from 0~98(46.59±11.793), the degree of CST was 0~2(1.265±0.646). The spearman correlation coefficients were seen in table. **Conclusions:** Degree of CST involved within the infarcts would directly relate to stroke severity and functional recovery.

The correlation between neurologic function and extent of corticospinal tract injury

Spearman r P value	MRS		NIHSS	
	2 week	3 month	2 week	3 month
Degrees	0.698,p=0.026	0.790,p=0.019	0.605p=0.032	0.712,p=0.020
Voxel numbers	0.728,p=0.021	0.820,p=0.013	0.667,p=0.024	0.734,p=0.017
FA value	0.540,p=0.043	0.597,p=0.038	0.569,p=0.046	0.534,p=0.041

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Atherosclerotic Burden and Early Mortality in Ischemic Stroke Patients

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Objective: To analyze the impact of previous atherosclerotic burden, assessed by the past history of heart ischemic disease and peripheral arterial disease, on the early mortality in patients with first ever acute ischemic stroke. **Methods**: clinical data from 1450 patients admitted to hospital with a first-ever acute ischemic stroke were prospectively evaluated from 1997 to 2005. A composite atherosclerotic burden score (ABS), from 0 to 2, was created using the past history of ischemic heart disease and peripheral arterial disease. We analyze the impact of this score on the in-hospital mortality by Cox proportional hadzard model adjusted by age, gender, stroke severity and vascular risk factors. **Results:** 172 patients (11.9%) died during acute hospitalization. Cox proportional hazards model showed an association between the ABS and the early mortality (p<0.0001). Comparing with patients having no previous atherosclerotic burden to patients with an ABS 1 or 2, the risk for in-hospital death increased from 1.83 (95% CI 1.27–2.64) for patients having an ABS of 1 to 2.54 (95% CI 1.31– 4.90) for those having an ABS of 2. Age ≥75 years, HR 2.49 (95%CI 1.68–3.70); gender male, HR 1.55 (95% CI 1.13–2.12), atrial fibrillation HR 1.39 (95% CI 1.02–1.90), hyperlipidemia, HR 0.48 (95% CI 0.31–0.76), and Canadian Score Scale (≥7) , HR 9.01 (95% CI: 5.07–15.99) were also predictors of in-hospital death. **Conclusions:** Previous atherosclerotic burden is an independent predictor of early mortality in patients with first ever ischemis stroke in a dose-dependent manner.

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Long-Term Outcome of North American Adult Moyamoya Disease

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Background and Significance: The purpose of this study was to better define the epidemiology and outcome in a large cohort of North American patients with moyamoya disease. Methods: 45 adult (≥ 18 years of age) patients with moyamoya disease were retrospectively identified by review of an angiographic database. Baseline imaging, clinical and epidemiologic stroke risk factors were recorded. Clinical outcome was determined by review of hospital and clinic charts as well as by telephone interview. Comparisons of baseline factors and outcome was done for clinical presentation (ischemic event, hemorrhagic event, or asymptomatic) and treatment group(medical versus surgical revascularization). Risks of subsequent stroke or death were determined with Kaplan-Meier analysis. Results: Most (34) patients were women and the median age was 42 years. 34 presented with an ischemic event, 8 with hemorrhage, and three as asymptomatic findings. There were no significant differences in baseline epidemiologic or angiographic factors between these groups. Over a mean period of 4.5 years, the risk for subsequent stroke or death in symptomatic medically-treated patients was 54%. 19 of the 45 patients underwent surgical revascularization procedures for one or both cerebral hemispheres. Similarly, there were no significant baseline differences between patients treated medically or surgically. A non-significant trend for a better outcome was seen with surgery (Figures 1 and 2). Conclusions: The epidemiology of North American Moyamoya disease is different from the Asian form. The risk for future stroke in medically-treated patients is high. The optimal treatment remains undefined.
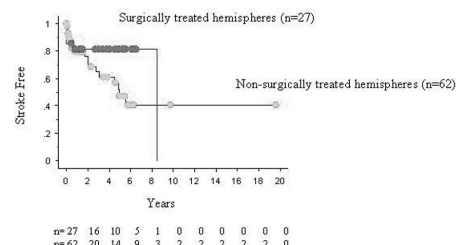

Figure 1. Kaplan-Meier estimates of stroke-free status between patients surgically treated (surgery date to perioperative or subsequent ipsilateral stroke) and non-surgically treated (**symptom onset** to subsequent ipsilateral stroke) hemispheres. The number of hemispheres at risk is listed below the x-axis at 2 year intervals. Circles represent censored hemispheres.

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Gender Differences in the Clinical Presentation and Outcome of Acute Stroke

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Introduction. The possibility of gender differences in the clinical presentation and outcome of stroke has been suggested. Hypothesis. In order to assess the clinical impact of stroke in women and men, we evaluated the degree of neurological impairment and that of disability at hospital discharge and at 1 year in 296 consecutive patients admitted to our Stroke Unit. Methods. Neurological impairment was expressed with the NIH Stroke Scale and disability with the Barthel Index at hospital discharge and the modified Rankin Scale at 1 year. Results. Among 269 stroke patients, 120 were women. NIH Stroke Scale score was 4.2 ± 5.3 in men and 6.6 ± 7.9 in women ($p=0.001$), indicating a higher neurological impairment in females. The degree of disability at hospital discharge was higher in women than in men, as indicated by a lower Barthel Index score (65 ± 35 vs 82 ± 30; $p=0.002$). At 1 year severe disability (Rankin scale >4) was more frequent in women (24%) than in men (10%) ($p=0.01$) while no differences in mortality were observed. The gender differences in disability are only partially explained by the older age of women at the time of stroke (76 ± 12 vs 69 ± 12; $p<0.001$), since they persist in patients older than 75 years. Women differed from men for a higher prevalence of atrial fibrillation (41% vs 22%; $p=0.001$). Conclusions. After acute stroke women have a higher degree of neurological impairment and a greater degree of disability at hospital discharge and at 1 year when compared to men. The higher prevalence of atrial fibrillation which is associated with a more severe stroke, may contribute to explain the higher disability in women.

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Cognitive Performance Following Angioplasty and Stenting in High-Grade Carotid Stenosis

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Background and Purpose Cognitive outcomes after carotid endarterectomy (CEA) have been extensively studied. Impacts of carotid angioplasty and stenting (CAS), a less invasive alternative for CEA, on cognitive functions have not been investigated. Present study was designed to determine degree and pattern of cognitive change, if any, after CAS among patients with high-grade carotid stenosis. **Methods** Fifty-four patients with high-grade carotid artery stenosis undergoing elective CAS and 66 patients with similar medical conditions requiring carotid angiography (CAG) were enrolled. Cognitive functions among patients in both groups were evaluated before and after procedures utilizing a battery of neuropsychometric tests. Results were analyzed by inter-group and within-group comparisons. **Results** There were no statistically significant differences between CAS and CAG patient groups regarding demographic characteristics, risk factors for stroke and baseline cognitive performance. CAS patients performed significantly better than CAG patients in Rey Auditory Verbal Learning Tests at both 1- and 12-week follow-ups ($p<0.001$). CAS patients, however, performed significantly worse than CAG patients in Boston Naming Tests at 1-week follow-up ($p<0.05$) but not at 12-weeks. Comparison of z-score changes before and after procedures indicated that, CAS patients improved significantly less than CAG patients in Trail Making Test B at 12-weeks but not at 1-week follow-up. **Conclusions** CAS patients demonstrated improvement in verbal memory but decline in executive function. It is postulated that improved cognitive performance is due to correction of cerebral hypoperfusion and reduction of artery-to-artery embolisation; and decreased executive function may be a result of procedure related embolisation or post-procedure luxury perfusion.

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Effects of Tobacco Dose and Length of Exposure on Vasospasm and Clinical Outcome After Aneurysmal Subarachnoid Hemorrhage

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Introduction The association between smoking and intracranial aneurysms is now well recognized. However, the relationship between tobacco use and outcome after aneurysmal SAH is less well understood. In addition, the degree to which the amount of tobacco exposure/dose impacts vasospasm and outcome is not known. Methods We reviewed of our retrospective database of patients with aneurysmal SAH. We assessed the impact of four tobacco variables, tobacco use, current smoker, long-term smoker (>20 pk-yrs) and tobacco dose on three outcome variables, clinical vasospasm, new deficit from vasospasm and categorized Glasgow Outcome Score. Covariates included in the analysis included, age, gender, Hunt & Hess grade, Fisher grade and medical co-morbidities. Stepwise elimination with logistic regression was used to arrive at a final multivariate model for each of the three outcomes. Results A total of 320 patients were analyzed. As expected Hunt & Hess grade was a significant predictor for all three outcome variables. Tobacco use, current smoker and tobacco dose, showed no independent association with vasospasm. However, long-term smoker was an independent risk factor for vasospasm ($p=0.046$, OR 1.73 95%CI 1.01–2.97). Likewise, long-term smoker was the only "tobacco" variable independently associated with new deficit from vasospasm ($p=0.019$, OR 1.84 95%CI 1.11–3.07). There was no significant association between any tobacco variable and final GOS category. Conclusions Tobacco use does not appear to influence clinical outcome after aneurysmal SAH. However, the duration of tobacco use, rather than the dose of tobacco per se, appears to be a risk factor for the development of vasospasm and subsequent delayed neurological deficits.

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Neuronal Reactivity in Cerebral Cortex Is Influenced by Carotid Endarterectomy in Patients with Symptomatic High-Grade Internal Carotid Artery Stenosis

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Introduction: The guidelines for performing carotid endarterectomy (CEA) have been set by clinical randomized studies (NASCET, ECST, ACAS). Hypothesis: Neuronal function depends on regional cerebral blood flow (rCBF) and on vascular reactivity. Animal experiments (dogs) provided evidence of neuronal reactivity depending on vascular reactivity. Restoration of blood flow values in the cerebral vascular system may be another benefit of CEA in a specific group of patients. There are no reports on neuronal reactivity changes related to altered perfusion parameters in humans yet. Material and methods: The cohort under study was made up of 40 patients after TIA or RIND, whose neurological findings were normal (group 1) and 15 patients after minor stroke with mild-degree hemiparesis or hemihypaesthesia (mRS ≤ 2) (group 2). All were examined at 0–2 days before CEA, on post-operative days 3–7, and at 3 months after CEA. The tests included median nerve SEPs and TCD at rest, during hypercapnia (et-CO_2 = 7 - 7.5 kPa), and at rest after hypercapnia. The following values were examined and monitored: N20 latency, N20/P25 amplitude, area under curve (AUC) 15 - 100 ms, V_{sys} and V_{mean} in both median cerebral arteries, and Gosling's pulsatility index (PI). Results: The results were processed for statistical values, with the level of statistical significance set at $p = 0.05$. Group 1 was found to have significantly increased V_{sys}, V_{mean} and PI in response to hypercapnia ($p < 0.0001$) in all periods, N20/P25 amplitude increased only preoperatively ($p = 0.03$). Changes in other SEPs parametres prior to and after hypercapnia were non-significant. Group 2 showed significant differences resulting from hypercapnia before and after CEA both in vasoreactivity (V_{sys}, V_{mean}, PI) ($p < 0.03$) and in neuronal reactivity (N20/P25 amplitude) ($p = 0.05$). In conclusion, carotid endarterectomy improves impaired neuronal activity in cerebral cortex. Impairment of vascular reactivity is not detected. Restoration of neuronal activity set in immediately after CEA in group 1 (TIAs). Restoration in group 2 (minor stroke) takes longer (up to 3 months). Such a function restoration may be considered as another benefit of CEA.

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Lesion in the Posterior Putament Predicts a Poor Recovery of Hemiparesis After Stroke

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Functional imaging and outcome studies demonstrate that lesion location affects motor impairment in stroke patients. Thus far, investigations in motor recovery are predominantly lesion-based outcome studies. Here we use a voxel-based statistical analysis to identify lesion sites associated with poorer motor outcomes in stroke patients with moderate to severe hemiparesis (Fugl-Meyer motor score ≤ 80). Forty-four patients were divided into either severe (score ≤ 36) or mild to moderate (score >36) groups based on their Fugl-Meyer motor scores three months post-stroke onset. Lesions were traced on 3D T1-weighted MRI images and co-registered to a template brain approximately matching Talairach space. Overlay of lesions in the severe motor deficit group (n=13) showed overlapping areas in the putamen and the posterior limb of the internal capsule (arrows in Fig1). Voxel-based statistical analysis showed that the posterior putamen was damaged significantly more often in those with severe persisting motor deficits than in the mild to moderate motor deficit group ($\chi2 > 28.24$ after Bonferroni correction to $P<0.05$, Fig. 1). Importantly, tracts from the posterior putamen project somatotopically to the posterior pre-motor cortex and primary motor cortex. Damage to the posterior putamen, therefore, appears to be critical for motor outcome after stroke, predicting poorer recovery of moderate to severe initial hemiparesis.

1. Severe vs. mild to moderate hemiparesis
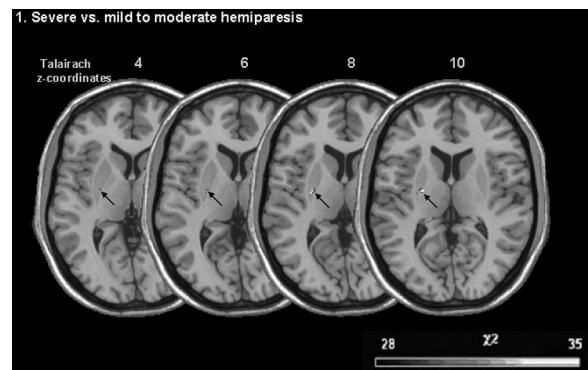
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Medical and Endovascular Therapy for Cervicocephalic Dissecting Pseudoaneurysms: The Cleveland Clinic Experience

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Objectives: We describe our experience with dissecting pseudoaneurysms to clarify the natural history and the impact of medical and endovascular treatments upon outcomes. **Methods:** The Cleveland Clinic radiology database from 1993–2003 was queried for patients with imaging confirmed cervicocephalic dissection. Patients with pseudoaneurysms and at least one follow-up imaging study were then identified by chart review. **Results:** There were 124 patients, 54% women, with a mean age of 45.6 years (range 4 - 80) followed for an average of 16 months. One hundred and fifty dissected vessels (87 internal carotid arteries and 63 vertebral arteries) were analyzed and 104 vessels had at least 1 follow-up study. At baseline, 35 patients had a pseudoaneurysm; 26 received medical treatment alone and 9 underwent endovascular therapy. Pseudoaneurysm healing (complete or near complete resolution) at 6 and 12 months occurred in 33% and 50% of patients with antiplatelet therapy (n=18) and 25% and 38% with anticoagulant therapy (n=8) (NS). Medically treated patients had a median time to healing of 325 days. Indications for endovascular treatment included: SAH at presentation (n=3), intradural vertebral location without SAH (n=3), and enlarging extracranial aneurysm with (n=1) and without (n=2) recurrent ischemia. At baseline, endovascular patients were more disabled than medical patients. At 3 months, all medical patients were functionally independent compared to 60% of endovascular patients. Complications included: recurrent TIA (n=2) in medical patients on antiplatelet therapy, delayed ICH (n=1) and life-threatening systemic bleeding (n=1) in medical patients on anticoagulation, and death due to rupture (n=1) in endovascular patients. **Conclusions:** Healing of pseudoaneurysms has a delayed course, with 38% to 50% healing within the first 12 months. There was no significant difference in outcomes in patients treated with antiplatelet or anticoagulant therapy. The risk of recurrent hemorrhagic or ischemic events from a pseudoaneurysm was low. The indications for endovascular therapy are not standardized and require further investigation.

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rtPA Treatment of Acute Ischemic Stroke Is Associated with Lower Mortality and Better Functional Outcome in a Biracial Population

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Background and Purpose: Treatment of acute ischemic stroke (AIS) with rt-PA within three hours of symptom onset has been shown to improve patient outcomes at three months. There are little population-based data that characterize how patients treated with rt-PA differ in terms of short-term outcome and disposition from the hospital compared to those not treated with rt-PA. We examined the outcomes of AIS patients treated with rt-PA compared with those who were excluded from treatment. Methods: We identified all adult ischemic stroke patients in 1999 at all local hospitals in the Greater Cincinnati/Northern Kentucky region by screening ICD-9 codes 430–436. Comparison of outcome for patients treated and those not treated with rt-PA was made by using multivariate logistic regression models adjusting for age, race, gender, pre-stroke disability and stroke severity. Outcomes were death at thirty days, modified Rankin score (mRS) at discharge, and discharge disposition. Results: Of 2379 ischemic strokes identified, 73 were treated with rt-PA (3.1%). Thrombolytic use did not vary significantly by age, gender, or race. The median baseline NIHSS for patients treated with rt-PA was 15, as opposed to 6 in those not treated (p <0.0001). After adjustment for stroke severity, baseline disability, age, gender, and race, patients treated with rt-PA were more likely to survive beyond 30 days of stroke (OR 5.2, 95% CI 2.2 - 12.1), more likely to have a good functional outcome at discharge (mRS of 0–1, OR 2.9, 95% CI 1.2 - 7.0) and more likely to be discharged to home than to a long-term care facility (OR 4.3, 95% CI 1.6 - 11.8). Conclusions: Within our population, patients treated with rt-PA for AIS had greater severity of neurologic deficit upon admission. After adjusting for greater stroke severity, patients treated with rt-PA were more likely to survive beyond 30 days of stroke, more likely to have a favorable functional outcome at discharge, and more likely to be discharged home, as compared to all stroke patients who were not treated with rt-PA.

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Impact of Diabetes on Long-Term Mortality After Stroke: First-Ever vs Recurrent Ischemic Stroke

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Background: While there have been reports suggesting that diabetes is associated with poor long-term mortality after ischemic stroke, it is not clear whether this effect is different for patients with first-ever ischemic stroke (FIS) vs. those with recurrent ischemic stroke (RIS). **Methods:** All patients age ≥ 35 hospitalized with ischemic stroke in the Greater Cincinnati/Northern Kentucky region during 7/93–6/94 were identified retrospectively using ICD-9 codes. All cases were verified by physician review. Diabetes had been diagnosed before stroke. Patients who had one or more prior strokes were classified as RIS. Vital status information for the study population was obtained through 12/31/01 by querying Ohio and Kentucky death records and the Social Security Death Index. Kaplan-Meier survival curves were constructed, and comparison of cumulative survival was performed by log-rank test. Cox proportional-hazard modeling was used for identifying factors associated with long-term mortality. **Results:** Among 2,065 patients with ischemic stroke, FIS was identified in 1,518 (73.5%). The proportion of diabetes was higher in patients with RIS than FIS (36.8% vs. 31.2%, p=0.03). Comparison

of cumulative survival rates is presented in Table 1. Significant factors associated with long-term mortality for FIS were diabetes, male gender, increased age, atrial fibrillation, myocardial infarction, current smoking, prior disability, and stroke severity. Increased age, prior disability and stroke severity were associated with long-term mortality for patients with RIS. **Conclusion:** Our study reveals that the impact of diabetes on long-term mortality is significant for patients with FIS but not for RIS. Further study is required to determine the cause of death in patients with RIS as well as those with FIS.

COMPARISON OF CUMULATIVE SURVIVAL RATES ACCORDING TO DIABETES BETWEEN SUBJECTS WITH FIS AND RIS

Follow-up duration	Cumulative survival rate					
	First-ever ischemic stroke (n=1518)			Recurrent ischemic stroke (n=547)		
	Diabetics (n=473)	Non-Diabetics (n=1045)	p-value	Diabetics (n=199)	Non-Diabetics (n=348)	p-value
30 days	0.8795	0.8756	0.84	0.8643	0.8592	0.89
1 year	0.7442	0.7474	0.92	0.6985	0.6753	0.60
3 years	0.5941	0.6067	0.70	0.5025	0.4713	0.53
5 years	0.4334	0.5139	0.02	0.3317	0.3276	0.73
7 years	0.3277	0.4144	0.006	0.2312	0.2471	0.97

*P-values were calculated from Log-rank test.

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2-Year Survival of Acute Ischemic Stroke Patients Aged 80 Years and Older

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Background & Purpose: The short life expectancy hampers secondary prevention (SP) or may influence decision making for active intervention such as carotid endarterectomy in very elderly stroke survivors. We investigated the 2-year survival rate and the predictors in very elderly acute ischemic stroke patients. **Methods:** Consecutive 134 acute ischemic stroke patients aged 80 years and old were recruited from Hallym Stroke Registry, a prospective multicenter-hospital base stroke data bank. We excluded fatal stroke patients who died during admission or who were discharged due to lethal prognosis (n=25). The information about 2-year survival was obtained from structured telephone inquiries, medical records, death certificates from the Korean National Statistical Office and social security data. Conventional risk factors, outcomes at discharge, and compliance with SP were analyzed as the predictors for 2-year survival. **Results:** Among 109 patients, 58 patients (53.2%) survived more than 2 years. In a multivariate logistic regression, outcomes at discharge (odds ratio 22.17, 95% CI=6.90 to 71.18, p=0.00), compliance with SP (OR 4.82 (1.64 to 14.12), p=0.004), and age (OR 0.82 (0.70 to 0.95), p=0.01) were independent predictors for 2-year survival. Among 80 to 84 year-old patients with favorable outcomes, 2-year survival rates were 94.1% in those with appropriate SP and 62.5 % in those without (p=.009). **Conclusion:** In contrast to high in-hospital mortality, most of very elderly patients with acute ischemic stroke showing favorable outcomes at discharge could survive more than 2 years with appropriate SP. A more active approach may be needed for selected patients having favorable predictors for survival.

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Prognosis of Perforating Artery Stroke After Intracranial Stent-Assisted Angioplasty

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Background: Angioplasty and stenting is currently an option for the treatment of patients with symptomatic intracranial stenosis refractory to medical management. An important challenge is to overcome the potential risk of infarction or ischemia resulting from the compromise of perforating branch arteries during procedure of intracranial angioplasty and stenting. The aim of the present study is to report the prognosis of perforating artery stroke after intracranial stent assisted angioplasty (ISSA). Methods: We retrospectively analysed the cases who developed perforating artery stroke after ISAA. 189 consecutive cases treated for intracranial stenosis by stent assisted angioplasty procedures in 175 symptomatic patients. Detail neurological examination, National Institute of Health Stoke score (NIHSS) and mRS (modified Rankin Scale score) were noticed at time of admission, just after ISAA procedure, at time of discharge, 3, 6 and 12 months after the procedure. Perforating artery stroke was considered 'recovered' if mRS was 0–1 within six months Results: Five patients developed perforating artery stroke i.e. 2.8% of patients (5 / 175); or 2.7% of attempted stenoses (5 / 189). They included 3 cases in vertebro-basilar territory and 2 cases in MCA territory. Four patients (80%) recovered within six months and rest was minor disable stroke within 12 months. Conclusion: Prognosis of perforating artery stroke after intracranial stent assisted angioplasty in our case series is good. It will require larger studies to prognosticate perforating artery stroke.

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Influence of Cognitive Impairment on Discharge and Institutionalization Within 3 Years After Stroke

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Background: post-stroke dementia is frequent and adversely influences vital outcome, but whether it influences discharge at home and institutionalization remains unsettled. **Objective:** to evaluate the influence of cognitive impairment present before stroke or occurring after, on

discharge at home and institutionalization within 3 years after stroke. **Method:** we prospectively evaluated (i) pre-existing dementia with the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), (ii) new-onset dementia, (iii) discharge at home, and (iv) institutionalization within 3 years, in 165 acute stroke patients living at home before stroke and followed-up over a 3-year period. **Results:** pre-existing cognitive decline or dementia did not significantly influence the proportion of patients discharged at home after the acute stage. Predictors of institutionalization within 3 years that were available at admission, were age (adjusted OR [adjOR] for 1 year increase: 1.08; 95% CI: 1.03 - 1.15), severity of the clinical deficit (adjOR for 1 point increase in Orgogozo score: 0.98; 95% CI: 0.96 - 0.99), and IQCODE score (adjOR for 1 point increase: 1.03; 95% CI: 1.0001 - 1.06). Age (adjOR for 1 year increase =1.17; CI 95%:1.07–1.27), and pre-existing or new dementia (adjOR = 5.85, CI 95%:1.59–21.59), were associated with institutionalization at year-3. **Conclusion:** pre-existing cognitive impairment and dementia (pre-existing or new), are associated with an increased rate of institutionalization within 3 years after stroke, but did not influence the proportion of patients discharged at home after the acute stage. This finding underlines that the evaluation of pre-existing cognitive functions, and their follow-up, are crucial in stroke patients.

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Impact of Atorvastatin on Cardiovascular Events in 2440 Men and Women Aged 65 Years and Above: Evidence from the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA)

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The results of the PROSPER trial raised doubts about the benefits of statin use on stroke events in the elderly population. Hence the ASCOT-LLA database was investigated to evaluate the effects of atorvastatin 10mg daily compared with placebo on various cardiovascular (CV) events among 4440 patients with hypertension who were aged 65 years and above and who had at least 2 other CV risk factors and a total cholesterol $\leq$ 6.5mmol/l at baseline. The effects of atorvastatin for the primary and all secondary endpoints of the trial for this elderly subgroup are shown in the table. As shown, too few CV related events occurred to allow a robust evaluation of the impact of active intervention for several of these endpoints. However in contrast to the PROSPER trial there was an 18% (albeit non-significant) reduction in fatal and non-fatal strokes associated with statin use. There were no significant differences between any of these results and those observed among younger trial participants (aged 40–64). There were no significant differences in the incidence of major elevations in CPK and ALT levels among those allocated atorvastatin and placebo nor any significant differences in reported serious adverse events in the atorvastatin and placebo groups (25.6% and 26.6% of patients respectively).

Endpoint	Atorvastatin		Placebo		Unadjusted hazard ratio	p-value
	n (%)	Rate *	n (%)	Rate *		
Non-fatal MI (inc silent) + fatal CHD [1° endpoint]	51(2.3%)	7.4	83(3.7%)	11.7	0.63(0.44–0.89)	0.009
Total CV events and procedures	223(10.2%)	33.6	283(12.6%)	41.9	0.80(0.67–0.96)	0.014
Total coronary endpoints	92(4.2%)	13.4	135(6.0%)	19.3	0.70(0.53–0.91)	0.007
Non-fatal MI (exc silent) + fatal CHD	43(2.0%)	6.2	71(3.2%)	10.0	0.62(0.43–0.91)	0.012
All cause mortality	135(6.2%)	19.3	143(6.3%)	19.9	0.97(0.77–1.23)	0.829
Cardiovascular mortality	51(2.3%)	7.3	51(2.3%)	7.1	1.03(0.70–1.52)	0.873
Fatal and non-fatal stroke	63(2.9%)	9.1	79(3.5%)	11.2	0.82(0.59–1.14)	0.238
Fatal and non-fatal heart failure	31(1.4%)	4.5	28(1.2%)	3.9	1.14(0.69–1.91)	0.606

* per 1000 patient years

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Baseline Malnutrition Predicts Subsequent Malnutrition, Poststroke Complications, and Poor Clinical Outcomes in Acute Ischemic Stroke Patients

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Background: Although previous studies indicate that malnutrition is associated with poor outcomes, nutrition has gained little attention in acute stroke management. With the serial nutritional assessments using more sensitive parameters, we sought to estimate whether nutritional status changes over the first week after stroke. The associations of malnutrition with post-stroke complications and functional outcomes were also evaluated. Methods: We included acute ischemic stroke patients who were evaluated for nutritional status within 24 hours and at 1 week after symptom onset. Malnutrition was diagnosed when at least one of 5 parameters showed moderate or severe undernutrition: 1) weight loss $\geq$10% for the past 3 months and $\geq$6% during 1 week after admission; 2) weight index <80%; 3) serum albumin <3.0mg/dL, 4) transferrin <150mg/dL, 5) prealbumin <10mg/dL. Multiple logistic regression analysis was performed to estimate the independent contribution of malnutrition to post-stroke complications and clinical outcome. Poor clinical outcome was defined as modified Rankin Scale $\geq$3 at 3 months. Demographics, risk factors, stroke severity, diet methods, and stroke subtypes were also considered for analysis. Results: Of 93 patients included in this study, malnutrition was observed in 15 (16.1%) at admission and in 21 (22.6%) at 1 week. Baseline malnutrition independently predicted 1-week malnutrition (odds ratio [OR], 10.9; 95% confidence interval [CI], 2.1–25.0; p=.004) and post-stroke complications (OR, 9.2; 95% CI, 1.1–81.0; p=.045). Both baseline (p=.033) and 1-week (p=.004) malnutrition were associated with poor 3month outcome by univariate analysis. Conclusions: These data suggest that acute ischemic stroke patients are being undernourished during hospitalization. Strategic nutritional support in acute ischemic stroke, particularly in patients with malnutrition at admission, may improve clinical outcomes.

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Risk of Subsequent Myocardial and Cerebral Ischemic Events Following Emergency Department Presentation for Ischemic Stroke

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OBJECTIVE To determine the risk of myocardial and cerebral infarction following Emergency Department (ED) presentation for acute ischemic stroke (AIS), and to study whether any clinical parameters are associated with a worse risk. **METHODS** The cohort consisted of 662 consecutive patients with AIS who provided research authorization and presented to our Emergency Department in the 27 month period of the study. All patients had laboratory, imaging and ECG evaluation per our acute stroke protocol. Stroke severity was assessed with the NIH Stroke Scale, administered by a physician certified in its use. Associations with survival were evaluated based on fitting univariate Cox proportional hazards models and summarized by calculating hazard ratios (HR) and 95% confidence intervals (CI). **RESULTS** There 311 women (47%) and 351 men (53%). Their mean age was 72.4 years (SD=14.4). The median follow up among those alive at last follow-up was 1.9 years , with an interquartile range of 7.4 to 29.5 months. The risk of subsequent myocardial or cerebral ischemic event (SMCIE) after AIS is summarized in table 1. In terms of ED clinical parameters that were associated with risk of SMCIE, after adjusting for age and stroke severity, patients elevated troponin were 3.1 times more likely to develop SMCIE than patients with normal glucose (HR= 3.1; 95% CI, 1.2–8.3; p=0.025); patients with thrombocytosis were 5.2 times more likely to develop ACS than patients with normal platelet counts (95% CI, 1.2–22.3; p=0.026). Patients with a low magnesium level (<2.1 mg/dl) were 4.8 times more likely to suffer a SCMIE compared to those with normal serum magnesium. **CONCLUSION** Preliminary results suggest that elevated troponin, thrombocytosis, and low serum magnesium appear to be associated with an increased risk of developing a subsequent myocardial or cerebrovascular ischemic event following ED presentation for AIS.

SURVIVAL-FREE OF EVENT ESTIMATES (SE) OF SUBSEQUENT ADVERSE EVENTS

Event	# within 1 yr	@ 7 days	@30 days	@90 days	@ 180 days	@ 365 days
MI	10	100.0%(0)	99.1%(0.004)	98.9%(0.005)	98.9%(0.005)	97.9%(0.007)
Stroke	16	99.8%(0.002)	99.8%(0.002)	99.0%(0.004)	98.4%(0.006)	96.4%(0.009)
TIA	8	99.7%(0.002)	99.5%(0.003)	99.3%(0.003)	99.1%(0.004)	98.3%(0.006)
Stroke/TIA	22	99.5% (0.003)	99.4% (0.003)	98.4% (0.005)	97.4% (0.007)	95.2% (0.01)
MI/Stroke/TIA	31	99.5% (0.003)	98.4% (0.005)	97.2% (0.007)	96.4% (0.008)	93.4% (0.012

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Persistent Hyperglycemia in Patients with Acute Ischemic Stroke Predicts Poor Outcome

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Objective Our objective was to examine the association between glucose values and hospital outcome across stroke severity categories.<br Methods This subgroup analysis of an ongoing medical record review included acute ischemic stroke patients admitted to two Connecticut hospitals (1998–2003). Two outcomes included: in-hospital mortality and the combined endpoint of death, discharge to hospice or a skilled nursing facility. Because the results for both outcomes were similar, we present only the results for the combined endpoint. We examined glucose values upon admission, during the first 24 hours, and from the 24th hour to the end of the hospital stay. Because the results were similar for the various time points, we present the data for glucose values from 24th hour to discharge. Glucose values were classified as "low" (10). Results Increasing glucose values were associated with increasing likelihood of poor outcome: <200 mg/dl, 7/120 (6%); 200<350 mg/dl, 7/28 (25%); $\geq$350 mg/dl, 2/5 (40%); p=0.001. Patients whose glucose changed to a high value had the worst outcomes: low-to-low, 6/101 (6%); high-to-low, 1/19 (5%); high-to-high, 4/19 (21%); and low-to-high, 5/14 (36%); p=0.002. Patients with higher glucose values were more likely to have an adverse event within stroke severity groups (mild-moderate: <200 mg/dl, 4/98 (4%); 200<350 mg/dl, 5/32 (23%); $\geq$350 mg/dl, 1/3 (33%); p=0.004; severe: <200 mg/dl, 3/22 (14%); 200<350 mg/dl, 2/6 (33%); $\geq$350 mg/dl, 1/2 (50%); p=0.31. Conclusions These findings demonstrate (1) the prognostic importance of hyperglycemic in predicting adverse events post-stroke; (2) that glucose beyond the first day is strongly associated with adverse events; and (3) that glucose is associated with outcomes independent of stroke severity. These findings support the hypothesis that glucose control throughout the hospital stay may improve outcomes for stroke patients.

Pediatric Stroke

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Transfusion Lowers Plasma-Free Hemoglobin in Children with Sickle Cell Disease at Risk for Stroke

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Background: Plasma free hemoglobin (PFH) is released by intravascular hemolysis in Sickle Cell Disease (SCD). PFH has been linked to pulmonary hypertension in SCD and has deleterious endothelial actions by scavenging nitric oxide. We used stored samples from the Stroke Prevention Trial in Sickle Cell Anemia (STOP) to determine if regular transfusion, shown in that

trial to reduce stroke by 90%, was associated with reduction in PFH. Methods: Follow-up (F) serum samples were chosen at approximately a year (6–18 months) from baseline (B). STOP children at high stroke risk, by transcranial Doppler ultrasound, were randomized to regular red cell transfusion or no transfusion. PFH in children on transfusion was compared to PFH in those not on transfusions using the t-test. Subjects were considered to be on transfusion if they received at least 0.75 transfusions per month and had a transfusion no more than 8 weeks prior to the blood sample. Subjects were not on transfusion if they had no more than 0.17 transfusions per month. Serum samples were analyzed for PFH (Catachem's Plasma Hemoglobin Kit). This colorimetric assay is based on the peroxidase activity of Hb. Results: PFH in serum from 50 children 8.0 ± 3.6 (mean $\pm$ sd) years old at (B) who were placed on transfusion was compared to PFH in 62 children 8.1 ± 3.0 years old with no transfusion. Average separation between samples was 13.3 ± 4.8 months (transfusion) and 13.4 ± 4.4 months (no transfusion). PFH in the two groups did not differ at baseline (p=0.8). PFH declined with transfusion from 78.7 ± 8.2 mg/dl to 34.4 ± 3.4 mg/dl (mean $\pm$ se) (p<0.001); without transfusion there was a smaller drop from 80.9 ± 7.5 to 62.8 ± 5.0 (p=0.019). When the follow-up samples were compared, the transfusion group showed a significantly greater decrease in PFH versus no transfused group (p<0.001). Conclusion: Regular transfusion is associated with a pronounced drop in PFH and this may in part explain its protective effect. Further exploration of this mechanism is warranted.

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The Cerebral Protective Effect of Graded Reoxygenation and PH-Stat Strategy During Cardiopulmonary Bypass in Infants with Cyanotic Congenital Heart Disease

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Introduction: Cerebral complication remains a major morbidity in patients undergoing operation for cyanotic congenital heart diseases (CHD). Our previous study has demonstrated that oxygen pressure is an important determinant of cerebral integrity during cardiopulmonary bypass (CPB) in these children. However, acid-base strategy, another important determinant in terms of cerebral oxygenation and metabolic integrity, remains to be determined with modified oxygenation strategy. **Hypothesis:** Graded (i.e., normoxic-to-hyperoxic reoxygenation with ph-stat strategy could provide further protective effects. **Methods:** Thirty-two cyanotic patients (6 to12 months of age) with CHD were prospectively randomized into 2 groups. Group 1 (n = 15, 6.3 +/- 3.5 kg) underwent CPB with graded reoxygenation (i.e, FiO_2 from 0.21 to 1.0 within 15 minutes after initiation of CPB) and alpha-stat strategy. Group 2 (n = 17, 6.8 +/- 2.9 kg) underwent the same reoxygenation strategy during CPB with ph-stat strategy. Cerebral oxygenation was assessed continuously by near-infrared spectroscopy (NIRS). Serum S100beta was measured preoperatively, during CPB, and 24 hours postoperatively. Cerebral lactate production was measured during CPB as an index of cerebral anaerobic metabolism. **Results:** There were no significant differences in preoperative hematocrit, oxygen saturation, CPB duration, minimal temperatures, perfusion flow and pressure between the groups. Tissue oxygenation were significantly lower in group 1 compared with group 2 (P < 0.01), suggesting better provision of oxygen with ph-stat strategy. Before CPB, S100beta and lactate were similar between both groups. After CPB, S100beta increased in both groups with significant delay of and reduced extent of increment in group 2 (p<0.05). Serum lactate was significantly lower in group 2 till the end of cardiopulmonary bypass (P <0.01). **Conclusions:** The ph-stat strategy combined with graded reoxygenation provided better cerebral protection during CPB in infants with cyanotic CHD, as reflected by better cerebral oxygenation and metabolism.

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Evolution of Cerebral Arteriopathies in Childhood Arterial Ischemic Stroke

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Objective: 80% of children with arterial ischemic stroke (AIS) have cerebral arteriopathy. Our aim was to investigate the relationship between natural history of arteriopathy and AIS recurrence. Methods: Serial magnetic resonance angiograms from children with first AIS were evaluated. Severity of arteriopathy was graded on initial and follow-up imaging. Diagnostic categories were assigned using a recently proposed classification. Results: Fifty children identified from a tertiary center pediatric cerebrovascular clinic were included (30 male, median age at AIS 49 months). Other risk factors for childhood AIS were identified in 40 (1 other risk factor in 28 and 2 other risk factors in 12). All had middle cerebral artery (MCA) territory infarction. Arteriopathy affected 72 arteries (most commonly MCA) in 43 of the 50 children. Arteriopathy was categorised as transient cerebral arteriopathy in 24 cases, chronic cerebral arteriopathy in 11, arterial dissection in 3, primary moyamoya in 1, possible moyamoya in 2, dysplastic arteriopathy in 1 and cerebral vasculitis in 1. The median duration of clinical follow-up was 38 months (range 1 - 120 months) and to final re-imaging was 22 months (0.5 - 105 months). Five children had recurrent clinical TIA or AIS, with re-infarction in 4; a further child had clinically silent re-infarction. Twelve children (24%), including 4 of those with recurrence, had progressive arteriopathy. Arteriopathy improved in 24 cases (of whom one had recurrent TIAs) and was stable in 7. MRA remained normal in all seven patients with initially normal MRA; one had recurrent AIS. In univariate logistic regression analyses, only progression of arteriopathy (compared with stable or improved) was significantly associated with recurrence (odds ratio (OR) 9, 95% confidence intervals (CI) 1.4, 58, p = 0.02). This association remained significant in a multivariate model (OR 53.9, 95% CI 1.5, 2010, p = 0.03). Conclusion: Progressive cerebral arteriopathy is significantly associated with recurrence of childhood AIS; a causal link between the two remains to be established. Identification of patients with progressive arteriopathy as a high-risk group has important implications for impending clinical trials of secondary prevention in pediatric AIS.

Diagnosis

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Influence of Early MRI-Based Diagnosis on Functional Outcome and Costs in Management of Patients with Acute Ischemic Stroke

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Objective To compare functional outcome, associated direct costs, and diagnostic confidence of two diagnostic strategies based on MRI or CT as the first radiological test in patients with acute ischemic stroke (AIS). Methods Prospective observational study of patients with AIS of less than 12 hours' evolution. CT or multiparametric MRI allocation was decided according to the time of hospital arrival and technique availability. Good clinical outcome was defined as a Rankin score ≤ 2 measured according to a structured interview at discharge and 90 days after stroke. The expenses of hospital resources (diagnostic tests, treatment and hospital stay) were included in the costs. The radiological diagnostic confidence was evaluated by using an analogical scale. Results 130 patients were included in the study (60% men, mean age 69y). CT was the first radiological test in 87 patients and MRI in 43 patients. The two groups were comparable regarding baseline variables such as cardiovascular risk factors, stroke severity (NIHSS score) and stroke subtype. Good outcome at discharge was 26% and 35% in the CT and MRI groups; the median (range) length of stay (LOS) was of 6.0 (4–11) and 6.0 (4–7) days, and the mean costs of LOS were €2864.50(1938.44) and €2448.70(1289.84) (all p=NS). The mean direct cost of hospital resources were €3536.85(2196.29) and €3165.25(1446.63) (all p=NS). Follow-up at 3 months was recorded in 127 patients. Good outcome was present in 51% of the CT group and in 43% of the MRI group. Approximately 52% of the patients in both groups required a caregiver. 13 patients died, 7 of CT group and 6 of MRI group. In the assessment of radiological diagnostic confidence both, radiologists and neurologists, showed a higher degree of confidence by using MRI in the detection of early signs of infarction (91% vs. 21%), location (91% vs. 8%) and vascular occlusion (72% vs. 6%), and similar results than CT in the exclusion of intracranial haemorrhage (95% vs. 98%). Conclusion The acute radiological diagnostic confidence is much greater by using MRI, without increase in the costs of hospital resources. However our results do not suggest a significant effect on clinical outcome.

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Studies of Acute Ischemic Stroke with Proton Magnetic Resonance Spectroscopy

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Objective: Proton magnetic resonance spectroscopy (MRS) can be used to study metabolite abnormalities in the brains of stroke patients. We have used it to examine the relations between the metabolites in the infarct, the presenting neurological deficit and clinical outcome Methods: Between February 2004 and February 2005,70 in-patients in the Neurology Ward of Beijing Tiantan Hospital, who had been diagnosed with cerebral embolism by CT and 48 hours of symptom onset were selected for this study. We sought to measure the temporal evolution and spatial distribution of lesion macromolecules and small molecules, such as N-acetylaspartate (NAA), choline (Cho), creatine (Cr) and lactate (Lac), and compared the results with that of the mirror hemisphere. Clinical features and baseline demographic data were collected independently by a stroke physician and the changes of MRS values were correlated with National Institutes of Health Stroke Scale (NIHSS) score on admission and after 60 days. Results: Of 70 cases, there were 43 male and 27 female. The average was 57.9 ± 4.23 years. The results of MRS showed that there were statistically significant differences in the amount of NAA and Cho between lesions and the mirror hemisphere (P =0.038 and P =0.020 respectively), but there were no significant differences in Cr (P = 0.327). Lactate peak appeared in lesions, but not appeared in the mirror hemisphere, with significant differences between them (P = 0.000). Reduced NAA and Cho in the infarct within the first 48 hours was related to the clinical stroke syndrome. Clinical outcome was most closely related to the extent of the infarct, the larger the infarct, the worse the outcome. Conclusions: The lesions of acute stroke patients exhibit hypometabolism, The reduction in NAA and Cho in a infarct lesion was related to infarct extent and clinical outcome. Key words: Acute Ischemic Stroke, MRS, Hypometabolism, Clinical outcome

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Lesion Visibility in Blood-Oxygen Level Dependent Imaging Is Related to NIH SSS in Acute Stroke Patients

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Introduction Delineation of tissue at risk is a major challenge for acute stroke imaging. Metabolic characterization of the penumbra might be achieved by the application of blood-oxygen-level-dependent (BOLD) imaging. **Patients and Methods** We analyzed MRI data from 29 I.V. tPA treated patients within the first 6 hours after stroke onset and after 5–8 days. The MRI protocol consisted of FLAIR, diffusion-weighted- (DWI/ADC=apparent diffusion coefficient) and perfusion-imaging with cerebral blood flow and -volume maps (CBF and CBV) and the time-to-peak (TTP), as well as quantitative T2- and T2*-imaging (qT2, qT2*). BOLD-images (T2') were calculated using $1/T2'=1/qT2*-1/qT2$. BOLD lesions were rated by two blinded observers. **Results** Lesion side was rated correctly by observers 1 and 2 in 72/55%, wrong in 14/38% and rated not visible in 14/7%. After unblinding, the visibility was

rated 43/43% good, 30/43% reasonable, and 27/13% poor. Good lesion visibility was associated with a NIH-SSS of >10 (p=0.001, Fisher's Exact Test) but not with initial ADC lesion volume or with time after symptom onset (p=0.713 and 0.885, Kruskal-Wallis Test). BOLD-lesions exceeded ADC lesions in 60/58% of the patients, were smaller in 17/25% and equal in 17/13% (Figure). TTP/CBF lesions exceeded BOLD-lesions in 87/70% of the patients, where equal in 0/27%, and were smaller in 13/3%. **Discussion** Lesions in BOLD images were observed in the majority of patients. BOLD-lesion might be a correlate of the penumbra since lesion visibility is strongly related to the severity of neurological symptoms. Artefacts may make lesion detection complicated or even impossible. Improvement of the sequences is under way.

ADC · BOLD · FLAIR (day 6)
TTP · CBV · CBF
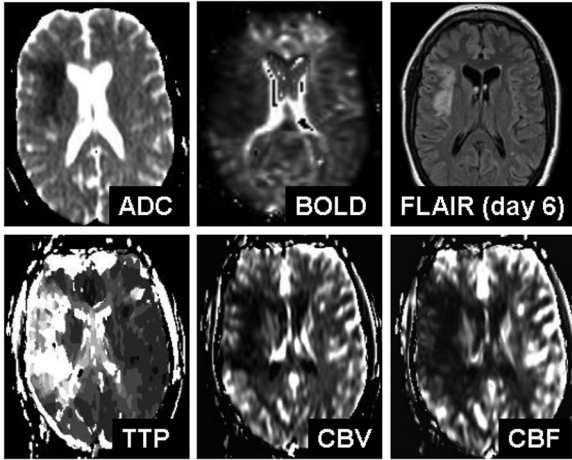
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Recurrent Ischemic Lesions Outside the Territory of Initial Perfusion Deficit Are Caused by Cardioembolism

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Introduction. One third of stroke survivors have a stroke-prone state with frequent recurrent lesions on MRI early after initial stroke. Although often asymptomatic, recurrent ischemic lesions (RIL) are associated with an increased risk of clinical stroke and are easily detectable with diffusion-weighted imaging (DWI). RIL within initial perfusion deficit can be attributed to the index cause, while those outside can be considered to be new events. Risk factors for RIL are still not completely elucidated. **Methods.** To test the hypothesis that patients with RIL might be predicted by their risk factor profile, serial MRI scanning with both DWI and PWI (perfusion imaging) was performed in 85 consecutive, ischemic stroke patients on Day 1, Days 2–7 (early RIL), and Day 90 (late RIL). RIL were defined using image co-registration, as new ischemic lesions outside the initial perfusion deficit. Differences in risk factors and stroke mechanism, using the TOAST classification, were compared between patients with and without RIL. **Results.** RIL were detected in 14/85 (16.5%, 95%CI [9%, 26%]) patients. Early and late RIL were identified in 7 patients each. None of the patients had both early and late RIL. Only one patient with late RIL was symptomatic. There was a trend for patients with RIL to have a cardioembolic mechanism (p=0.16), while none of the patients with RIL had large artery atherosclerosis (p=0.05). Multiple acute DWI lesions on initial MRI scans were not associated with RIL occurrence (p=0.90). There were no significant differences in other variables. **Conclusions.** Both early and late RIL are relatively common and usually asymptomatic. There is some evidence for a higher risk in patients with cardioembolic pathogenesis. MRI-defined RIL are a potential marker of stroke recurrence and surrogate endpoint in clinical trials.

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Cerebrovascular Reactivity and Microalbuminuria in Patients with Diabetes Mellitus Type II

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Microalbuminuria (MAO) is an independent predictor of renal insufficiency, stroke and death. This study examines whether the systemic microvascular alteration reflected by the presence of MAO in patients with diabetes mellitus type II (DM-II) is associated with cerebral microangiopathy as evaluated through cerebrovascular reactivity (CVR) study. **Materials and methods** 49 patients consecutively visited in the nephrology surgery affected by DM-II with creatinine <3 mg/dL and without history of stroke were included. Mean velocity was continuously monitored in the two MCA's both at rest (breathing room air) and during CO_2 inhalation (carbogen 5%), used as a vasodilatory stimulus. The Bishop method was used to calculate CVR. Normal values were obtained from 100 healthy controls evaluated in our neurosonology unit. Albuminuria was quantified using the nephelometric method: normal (<30 mg/L), MAO (30–300 mg/L) and macroalbuminuria (>300 mg/L). **Results** The mean age was 63 years, with a median evolution of diabetes of 9.5 years [4,15]. 14 (28.6%) patients had normal albuminuria, 14 (28.6%) had MAO and 21 (42.8%) macroalbuminuria. Mean CVR was similar in patients and healthy controls (4.36±1.48 vs. 4.82±1.85). However, a negative correlation was found between CVR and the level of albuminuria, (r=-0.34, p=0.01) and lower CVR tended to correlate with longer duration of the DM-II (r=-0.249, p=0.08), higher systolic blood pressure (p=0.08), non-dipper pattern (p=0.09) and treatment with calcium antagonists

(p=0.08). **Conclusions** In patients with DM-II there is a negative association between systemic microvascular lesion, measured by albuminuria, and CVR, which has not previously been described. This finding may prove to be useful in the identification of patients at greater risk of cerebrovascular complications.

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Aortic Plaque Detection and Time-Resolved 3D Velocity Mapping in Stroke Patients at 3T MRI

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Objective: To develop an MRI protocol for the non-invasive localization and description of aortic plaques in order to replace TEE. Furthermore, to perform 3D MRI flow visualization to advance understanding of development of aortic atheroma. Methods: For 3 volunteers and 6 patients the entire thoracic aorta was examined with both TEE and 3T MRI (TRIO, Siemens, Germany). MRI plaque localization was based on multi-slice, fat saturated, and ECG gated diastolic data acquisition using T1 contrast dark blood 2D multi-slice Turbo-Flash and bright blood 3D gradient echo imaging consisting of four slices packages (figure 1 A). Furthermore, localized 20 s breath-hold and high resolution multi-contrast (dark and bright blood) imaging (0.7 x 0.8 x 4 mm) was used to analyze plaque morphology (figure 1 B: white arrow indicating 3 mm thick plaque in the descending aorta). Time resolved 3D blood flow visualization data were acquired using an ECG and respiration controlled phase contrast sequence. Results: MRI detected 3 plaques in the aortic arch (mean thickness 3.5 mm) and 2 in the descending aorta (mean 3.3 mm) correlating closely with TEE data. Concordance regarding plaque calcification was moderate. Figure 1 C shows an example of normal 3D systolic blood flow characteristics in the aorta and supra-aortic vessels. Conclusions: Our results demonstrate the feasibility and accuracy of plaque localization and description as well as flow visualization in the aorta by high resolution MRI as a potential alternative for TEE. Combined with blood flow velocities and derived wall stress parameters this may provide insight into development of aortic atheroma.
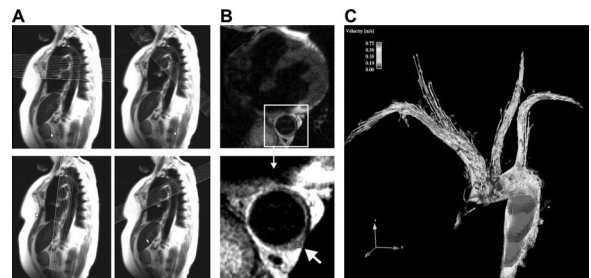
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Changes in Superficial Temporal Artery Blood Flow and Cerebral Hemodynamics of Moyamoya Disease After Extracranial-Intracranial Bypass Surgery

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Purpose: The purpose of the present study is compare changes in STA blood flow and cerebral hemodynamics after the extracranial-intracranial (EC-IC) bypass between patients with atherothrombotic carotid occlusive disease and moyamoya disease. Methods: This study included 40 consecutive patients with athrothrombotic carotid occlusive disease (Athero-Group) and 13 consecutive patients with moyamoya disease (Moya-Group) who underwent EC-IC bypass. We adopted the inclusion criteria using single photon emission computed tomography (SPECT) as follows: rCBF <32ml/100g/min (80% of the mean value in the normal control subjects) and acetazolamide (ACZ) reactivity <10% in the ipsilateral middle cerebral artery (MCA) territory. STA duplex ultrasonography (STDU) was performed to measure the flow velocity and diameter of the operated STA before and 14 days and 3 months after EC-IC bypass surgery. Results: STA mean flow velocity (MFV) was correlated with the rCBF in the ipsilateral MCA territory 14 days after EC-IC bypass surgery (R=0.57, p<0.0001) 14 days after EC-IC bypass. There was no significant difference in any baseline STDU and SPECT parameters between Athero-Group and Moya-Group. Two patients in Moya-Group showed a hemispheric hyperperfusion syndrome within 14 days after EC-IC bypass. Between Moya-Group and Athero-Group, there was a significant difference in STA MFV 14 days after EC-IC bypass (76.0±21.5 vs 55.2±16.5 cm/sec, p<0.001). The rCBF of the ipsilateral MCA territory was also higher in Moya-Group than Athero-Group 14 days after EC-IC bypass (40.0±8.0 vs 34.2±5.9 ml/100g/min, p<0.01). These differences were not observed 3 months after EC-IC bypass. Changes in STA MFV (42.6±25.4 vs 30.5±15.7 cm/sec, p<0.05) and rCBF (10.4±5.8 vs 5.1±4.3 ml/100g/min, p<0.01) before and 14 days after EC-IC bypass were also higher in Moya-Group than Athero-Group. Conclusions: In patients with severe cerebral hemodynamic failure, STA MFV is a highly sensitive parameter for predicting rCBF in the ipsilateral MCA territory after EC-IC bypass. In moyamoya disease, changes in STA MFV as well as rCBF were higher than those in atherothrombotic carotid occlusive disease after EC-IC bypass. Hyperperfusion syndrome was observed only in patients with moyamoya disease.

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A New Category of MRA Estimates the Regional Severity of Moyamoya Disease: Comparison with 15O-Gas PET

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Stage 0   Stage 1   Stage 2
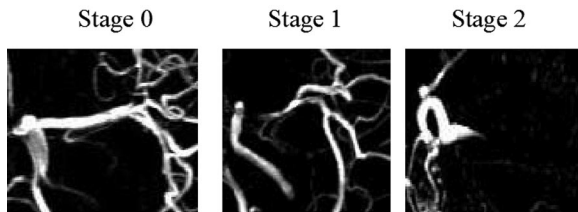
PET FINDINGS

MRA stage	0	1	2
Cortex			
CBF ml/100g/min	47.8 ±7.3	39.6 ±9.3	30.0 ±8.3
OEF	0.38±0.06	0.42±0.09	0.48±0.10
CMRO$_2$ ml/100g/min	3.1 ±0.9	2.7 ±0.9	2.1 ±0.6
CBV ml/100g	3.0 ±0.6	3.8 ±1.4	5.1 ±1.5
White matter			
CBF ml/100g/min	28.5 ±4.8	25.2 ±2.9	20.6 ±3.8
OEF	0.38±0.05	0.47±0.07	0.51±0.07
CMRO$_2$ ml/100g/min	2.5 ±0.5	2.2 ±0.4	1.7 ±0.4
CBV ml/100g	2.4 ±0.9	2.5 ±1.1	3.2 ±1.6
Basal ganglia			
CBF ml/100g/min	49.9 ±4.4	47.7 ±4.2	38.1 ±9.4
OEF	0.37±0.06	0.46±0.04	0.49±0.06
CMRO$_2$ ml/100g/min	4.0 ±0.7	3.5 ±0.6	2.9 ±0.9
CBV ml/100g	2.8 ±0.7	3.4 ±1.6	4.4 ±1.3
Cerebellum			
CBF ml/100g/min	55.3 ±6.3	47.2 ±8.9	51.5 ±8.7
OEF	0.41±0.03	0.44±0.09	0.42±0.09
CMRO$_2$ ml/100g/min	3.4 ±0.8	3.6 ±0.9	3.2 ±0.9
CBV ml/100g	4.6 ±0.9	4.0 ±1.1	4.1 ±1.1

Introduction: Moyamoya disease (MMD) is characterized by stenosis or occlusion around the circle of Willis. In this study, we contrived a new MRA category for MMD to evaluate its regional severity. Method: We enrolled 20 patients with MMD. All patients underwent MRI, MRA and 15O-gas PET. MRA was obtained with 3-D FISP (TR = 35ms, TE = 7.2 ms, flip angle = 20°, FOV = 193×220 mm, matrix = 235×512, slab thickness = 36 mm, 32 partitions). We graded each of the major cerebral arteries into 3 stages (Total: 120 arteries)(Ex. See Graphic). Stage 0 was defined as normal appearance (22/120). Stage 1 was defined as stenosis or occlusion limited from distal ICA or basilar BA to proximal ACA, MCA or PCA and normal appearance of its distal portion (32/120). Stage 2 was defined as occlusion from distal ICA or BA to proximal ACA, MCA or PCA and no or faint appearance of its distal portion (66/120). We compared the stage of each cerebral artery with PET findings at the ischemic core in cortex, white matter, and basal ganglia. Results: As the MRA stage increases, CBF and CMRO2 decreased and OEF, CBV increased in cortex, white matter, and basal ganglia (See Table). Conclusion: Our new MRA category enables estimation of regional severity in MMD. Proximal stenosis or occlusion alone causes a serious ischemia in white matter and basal ganglia. Distal occlusion causes a serious ischemia in cortex. Cerebellum is intact in MMD.

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Vertebrobasilar Dolichoectasia as a Risk Factor for Cerebral Microbleeds on Gradient Echo MRI

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Background & Objective: Vertebrobasilar dolichoectasia (VBD) has been reported to increase not only the risk of the ischemic stroke but also the hemorrhagic stroke, especially in posterior circulation territory. This study was aimed to determine the role of VBD for cerebral microbleeds (CMBs) on gradient-echo T2*-weighted MRI (GE-MRI) according to the locations of CMBs. **Methods**: GE-MRI of brain was performed in a consecutive series of 268 participants. Locations of CMBs were divided into anterior and posterior circulation. Ectasia was defined as basilar artery (BA) diameter over 4.5 mm in any location along its course and dolichosis as either bifurcation of BA above the suprasellar cistern or evidence of any portion of BA lateral to the margin of the clivus or dorsum sellae. Associations of VBD with CMBs in any regions of brain, and in the territory of anterior or posterior circulation were investigated. **Results**: CMBs were detected in any regions of brain in 60 subjects (22.4%), in only anterior circulation in 10 (3.7%), in only posterior circulation in 15 (5.6%), and in both locations in 35 (13.1%). VBD was observed in 32 subjects (11.2%), in whom CMBs were more abundant than subjects without VBD (4.06±6.45 vs. 0.96±3.05, p<0.05). The proportion of subjects with VBD according to the location of CMBs were as followed: 12 of 208 subjects without CMBs (5.8%), 2 of 10 with CMBs in anterior circulation only (20.0%), 5 of 15 with CMBs in posterior circulation only (33.3%), and 13 of 35 with CMBs in both (37.1%). With respect to the presence of CMB, the crude odds ratio (OR) of VBD was 8.17 (95% confidence interval, 3.70 to 18.04). After adjusting age, hypertension, history of stroke, and the use of antiplatelets or anticoagulants, the OR of VBD was 6.37 (2.78 to 14.60). For the presence of CMBs in anterior circulation, the crude and

adjusted ORs were 6.06 (2.74 to 13.39) and 4.69 (2.06 to 10.66); whereas for the presence of CMBs in posterior circulation, the crude and adjusted ORs were 8.20 (3.71 to 14.09) and 6.34 (2.75 to 14.62). **Conclusion**: These results suggest that VBD increases the risk for CMBs on GE-MRI. The association between CMBs in posterior circulation and VBD remains to be clarified in larger population.

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Diffusion-Weighted Imaging Findings After Endovascular Stent Employment in Cerebral Artery Stenosis

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Background and Purpose: Cerebral emboli are major concerns during endovascular stent employment in cerebral arteries, and sometimes could be a cause of post-stent morbidity and mortality. We investigated the patterns and associating factors of cerebral emboli using diffusion weighted-MRI (DWI) in the extra and intracranial artery stent employment. **Methods**: Forty three patients undergoing endovascular stent placement with pre- and post-stent DW imaging were retrospectively studied. There were patients with five MCA stent, 8 intracranial (IC) internal carotid arteries (ICAs), 21 extracranial (EC) ICAs, 6 IC vertebral arteries (VA) and 3 EC VAs. DWI was done within 5 days (mean 2.5 days) in post-stent state. Symptomatic patients including transient ischemic attack were 33 (77%). We compared the clinical and radiological characteristics between positive and negative DWI group. High signal intensities (HSI) on DWI were analyzed the according to the size; small (<1 cm) or large (>1 cm). **Results**: Twenty six (60%) of 43 patients with stent placement showed new HSI in post-stent DWI. Symptomatic complications after stent employment occurred in 10 patients (23%). Large HSI in DWI (n = 10) were correlated with the in-procedural complications and new neurologic symptoms after stent employment. Between positive and negative DWI group, there were no differences in age, sex, conventional risk factor for stroke, symptom at pre-stent state, time interval from symptom onset to day of stent, site of stent employment, distal circulation state of stenosis, length of stenotic segment, degree of stenosis and use of protection device. The positive DWI group is correlated with neurologic symptoms after stent placement, in-procedural complications and morphology of stenosis at angiography. **Conclusion**: New DWI abnormalities after stent employment which means embolic signals are common phenomenon with or without symptom. The in-procedural complications and morphology of stenosis are correlated with the new-onset DWI abnormalities.

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Eustachian Valve May Be Part of the Paradoxical Embolism Mechanism Through a Patent Foramen Ovale in Adult Patients

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Background : The eustachian valve (EV) is a remnant embryonic right valve of the sinus venosus. Embryologically, the EV directs oxygenated blood from the inferior vena cava across the patent foramen ovale (PFO) into the systemic circulation. Inter-atrial septal aneurysm (IASA) is frequently associated with PFO. **Aim of the study :** To assess the prevalence of persistent EV in an adult population undergoing transesophageal echocardiography (TEE), and its correlation with inter-atrial septal abnormalities. **Methods :** 204 patients underwent TEE for different diagnoses including valvular disease, stroke and endocarditis. The presence of EV, PFO and IASA was evaluated with two-dimensional transesophageal echocardiography, color Doppler and contrast echocardiographic studies. **Results :** In a first step 103 patients were retrospectively analysed on videotape recorders. EV was found in 34 % of the patients and it correlated with septal abnormalities (PFO + IASA) p < 0.02. In a second step 101 consecutive patients underwent TEE and studied prospectively. EV was found in 50 patients (49%). Septal abnormalities in 26 Patients (25%), PFO in 18 patients (17%) and IASA in 15 patients (15%). EV was found in 88% patients with septal abnormalities (p<0.0001)), in 67% patients with PFO (p<0.02) and in 53% patients with IASA (NS). Clinical assessments did not significantly influence these relationships. **Conclusion** : Persistent EV is frequently found in adult patients with septal abnormalities and mainly PFO. A persistent EV may participate in the mechanism of a paradoxical embolism by directing the inflow blood from the inferior caval vein towards the interatrial septum.

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Added Benefit of Enhanced Versus Unenhanced MR Angiography in Determining Greater than 70% Internal Carotid Artery Stenosis? Not!

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Background: Internal carotid artery (ICA) atheromatous disease is an important cause of ischemic stroke; endarterectomy is generally indicated for symptomatic patients with ≥ 70% stenosis. Few studies have directly compared the accuracy of contrast enhanced (CE) MRA to that of non-contrast enhanced (nCE) MRA in the detection of hemodynamically significant ICA stenosis. In this study, we tested whether CE-MRA significantly improves sensitivity, specificity, and accuracy for detection of a ≥ 70% ICA stenosis, versus nCE-MRA, relative to a CT angiography (CTA) gold standard. **Methods:** We identified 177 patients (354 ICA's) who received correlative CE-MRA, nCE-MRA, and CTA within 3 months of one another (from 2001–2004). Two blinded neuroradiologists graded the degree of ICA stenosis for each vessel, on each modality, in random order, according to the following 5-point scale: 0=normal, 1=mild (<50%), 2=moderate (50–70%), 3=severe (>70%), and 4=critical (hairline or occluded). In making this assessment, special attention was paid to the degree of: (1) signal dropout, (2) distal vessel narrowing, & (3) distal vessel signal decrease, which were rated using the same 5-point scale. MRA results were correlated with those of CTA, and receiver-operating-

characteristic (ROC) curves were constructed from the CE- and nCE-MRA datasets. **Results:** On CTA, there were 55 ICA's with, and 299 without, $\geq$70% stenosis. CE-MRA was 84% sensitive and 96% specific for detecting a $\geq$70% stenosis; nCE-MRA was 80% sensitive and 96% specific. The area under the ROC curve for CE-MRA was 0.97; the area for nCE-MRA was 0.95 (p=0.51, NS). Each of the three components of stenosis grading (signal dropout, distal narrowing, and distal signal decrease), for both CE-MRA and nCE-MRA, had high specificity (>98.4%), but only moderate sensitivity (35–65%), for the detection of surgically relevant stenosis. There was a trend towards improved accuracy when the results of both CE- and nCE-MRA agreed. **Conclusions:** Although it is clear that CE-MRA more accurately delineates neurovascular anatomy than does nCE-MRA, *the administration of gadolinium did not offer significant advantage in distinguishing surgically treatable, 70% or greater, ICA stenosis*, in the highly selected patient cohort we studied.

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The Need for Performance Protocols for TCD and TEE in Detection of Right to Left Shunt

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Objective: To evaluate reasons for discrepancy between TCD and TEE for shunt detection in community use. Background: TEE is the gold standard for detection of right to left shunt (RLS). In our center, we observed informally that TCD was more sensitive than TEE. We sought an explanation for this discrepancy. **Methods:** We retrospectively reviewed TCD and TEE on pts eval for RLS over 2 yrs. TCD was done by 2 techs per literature-based performance protocol (PP): 2 MHz transducer; insonate mca; contrast= 9.5 cc saline + 0.5 cc air agitated between 2 syringes; inject via #18 antecub I.V w/ pts supine and rt lat.decub w/o, during, and after valsava (x2 each); recording time =20 sec; pos study=1 bubble artifact on > 1 inject. TEE was performed by 5 cardiologists: omniplane multihertz probe and mech index of 0.7; conscious sedation in left anterolat semi-upright position w/ long and short 4 chamber views. No PP specifications for size/location of I.V. line, prep of contrast, timing of injection, # of injections, use of valsava, recording time, criteria for positivity. **Results:** 138 pts had both studies w/in 24 hours of each other. Agreement: of 34 + on TCD, 12 were + on TEE (0.35); of 18 + on TEE, 17 were + on TCD (0.94). Overall agreement: 29/52=0.56. The lower yield of TEE and low interstudy agreement are unexplained by false pos TCD, and likely reflect the lack of uniform PP for TEE. This is supported by our observation that the likelihood of agreement between TCD and TEE correlated w/ the cardiologist doing the TEE. Analysis of 16 pub studies (861 patients) disclosed higher yields w/ TEE in 8; higher w/ TCD in 4; equal in 4. We found one consensus PP for RLS detection w/ TCD. No PP for either TCD or TEE was found at websites for: AAN, ACC, ACR, AIUM, ASE, ASN, SVU. **Conclusions:** The higher yield for TCD and low level of agreement between TCD and TEE appear to reflect operator differences in TEE. The results engender concern about the possibility of false negatives in community use of TEE. Given the operator-dependency of both modalities, either may be prone to false negatives. Consensus protocols and accreditation criteria for performance of TCD and TEE could have an important impact on accuracy of shunt detection.

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Long-Term Outcome in Patients with Misery Perfusion in Chronic Carotid Artery Occlusion

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BACKGROUND: In a prospective randomized study, the Carotid Occlusion Surgery Study (COSS), which is ongoing now, patients with elevated oxygen extraction fraction (OEF) on PET are subjected to clarify beneficial effects of EC-IC bypass surgery. However, the relationship between the degree of elevated OEF and subsequent ischemic stroke occurrence has been rather scarcely studied. We prospectively studied whether the elevated OEF is an independent risk factor of subsequent ischemic stroke. **METHODS:** We enrolled 102 patients (73 males, mean 66.2 yrs) with complete occlusion of the unilateral ICA or the trunk of MCA. Patients with severe stenosis were excluded to exclude embolic stroke in the following period. PET with O-15 inhalation method was performed at least 4 weeks after the last clinical episode. Patients were divided into two groups according to mean OEF values in the affected MCA area: Group A (n=67) with normal OEF (<0.52), and Group B (n=35) with elevated OEF (>/=0.52). Following the PET studies, patients were followed up under medical treatment for more than 1 year to observe the occurrence of stroke. **RESULTS:** During an average follow-up period of 4.2 years, ipsilateral ischemic stroke occurred in 2 of 67 patients (3%) in Group A and 10 of 35 patients (29%) in Group B. The frequency of stroke in Group B was significantly higher than in Group A (p<0.01). In 4 patients in Group B who had ipsilateral stroke within 1 year after PET studies, mean OEF values were enormously high showing 0.73, 0.70, 0.69 and 0.64, respectively. In the other 5 of 6 patients in Group B who had ipsilateral stroke more than 1 year after PET studies, the occurrence of stroke was related to the deterioration of hemodynamic status, such as reduction in blood pressure or further development of occlusive changes. **CONCLUSION:** Our study confirmed the current view that the misery perfusion in ICA or MCA occlusion indicates high risk of subsequent ischemic stroke. Patient with highly elevated OEF was particularly in danger of stroke in the near future, and surgical intervention may be indicated to avoid subsequence ischemic stroke. In patients with moderate OEF elevations, longitudinal follow-up of vascular lesions and careful blood pressure management are considered important for preventing stroke.

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Paradoxical Brain Embolism May Not Be Uncommon: Prospective Study in Acute Ischemic Stroke

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Background and Purpose Paradoxical brain embolism (PBE) has been identified to be a potential risk factor for ischemic stroke especially in young adults. However, the frequency and clinical characteristics of PBE has been unclear. ***Methods*** We prospectively enrolled the consecutive patients with acute ischemic stroke within 7 days of onset. Transcranial Doppler (TCD) and/or transesophageal echocardiography (TEE) were performed in all patients to detect right-to-left shunt (RLS). If stroke patients have RLS, venous ultrasound and/or lung perfusion scintigraphy were carried out to detect embolic sources in venous system and pulmonary embolism. We identified diagnostic criteria for PBE as follows; 1) the presence of RLS; 2) brain imaging suggesting an embolic stroke; 3) the presence of thrombus in venous system and/or the coexistence of a pulmonary embolism; and 4) the absence of other emobolic sources. We divided the stroke patients into four groups according to the suggesting criteria: 1) meeting all four criteria (Definite group), 2) fulfilling 3 of the 4 criteria (Probable group), 3) fulfilling 1 or 2 of the 4 criteria (Possible group), and 4) meeting none of the criteria (Non-PBE group). ***Results*** 194 patients were enrolled into this study. 26/194 (13%) patients had positive RLS in TCD studies. 79 of 194 (41%) patients underwent TEE, and the positive RLS were found in 27 of 79 (34%) patients. In total, 36 patients (18.6%) had RLS in TCD and/or TEE studies. The frequency of Definite, Probable, Possible and Non-PBE group were 5%, 5%, 8%, and 82%, respectively. The frequency of young patients below 40 years old and females were 20% and 80% for Definite group, 10% and 30% for Probable group, 0% and 23% for Possible group, and 3% and 35% for Non-PBE group (Definite group versus Non PBE group, p=0.02 and 0.004, respectively). The patients with no any traditional risk factors such as hypertension, diabetes mellitus, and atrial fibrillation were also predominantly belong to Definite group rather than Non-PBE group (70% versus 15%, p<0.001). ***Conclusions*** The frequency of definite paradoxical brain embolism was 5% in all ischemic stroke patients, which is not uncommon. The clinical characteristics of PBE were a young age, female and the absence of traditional risk factors.

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Mobile Plaque: New Findings of Unstable Plaque in B-mode Images

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Background: Recently we found a patient (Case 1) showing a unique carotid plaque on ultrasound B-mode images. The part of plaque surface was moving with heartbeats and showed a jelly-like appearance beneath the moving surface. This patient had asymptomatic multiple lesions on magnetic resonance diffusion weighted images (DWI) and underwent carotid endarterectomy (CEA). Pathological findings of CEA specimen showed a large fresh hemorrhage inside of the plaque. The surface movement and jelly-like changes, thus, likely reflect a recent intra-plaque hemorrhage and may indicate the fragility of plaque. The aim of this study is to investigate the incidence of such mobile plaque and its relationship with clinical and pathological findings. Subjects and Methods: We investigated 127 patients (137 lesions) with 50–99% carotid artery stenosis by ultrasound examination during the last one year. Thirty lesions were symptomatic. CEA was performed in 27 lesions. The plaque movement on ultrasound B-mode images was carefully observed by one examiner and recorded as movie files. The movie files were later reviewed by another examiner independently to reconfirm the findings. Results: Fifteen plaques in 13 patients were found to move with heartbeats, and 9 of them had the jelly-like appearance partially. The echogenecity of these 15 plaques was heterogeneous but mainly echogenic. Four of 15 lesions were symptomatic. Three symptomatic lesions and one asymptomatic lesion with multiple DWI lesions (Case 1) underwent CEA. All these four CEA specimens obtained from mobile plaques showed the existence of fresh hemorrhage beneath the surface which consisted of thin fibrous cap. Such an intra-palque fresh hemorrhage was found only in 8 of 23 specimens obtained from non-mobile plaques. Conclusion: The mobile plaque on ultrasound B-mode images appears to reflect recent intra-plaque hemorrhage and indicate the instability of plaque. The careful attension should be paid to find the movement of plaque, since such a mobile plaque is likely unstable in spite of its echogenic nature.

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Advanced Imaging Techniques Reveal Detailed Angioarchitecture in Cerebral Cavernous Malformations

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Introduction: Cerebral cavernous malformations (CCMs) are a cause of hemorrhagic stroke and have generally been diagnosed by low field magnetic resonance (MR) imaging (1.5 T) and subsequent pathologic confirmation in resected lesions. CCMs consist of blood filled caverns lined by a single layer of endothelium, but little is known about their biologic behavior over time. *Hypothesis:* We assessed the hypothesis that advanced imaging techniques can reveal more details of the structure of CCMs than previous techniques. *Methods:* CCMs excised from three patients were fixed in formaldehyde and imaged by MR at 9.4 T, with histologic validation by confocal microscopy. The brains from six mice with the gene knockout (*CCM1+/-*) were imaged by MR at 4.7 T in vivo and ex vivo. *Results and Conclusions:* MR and confocal imaging of excised human CCMs revealed previously unsuspected small caverns appearing to arise

from larger caverns and more mature blood vessels in the lesion. The brains of transgenic mice revealed lesions similar to human CCMs. In conclusion, the high field MR imaging techniques manifest novel features of CCM genesis, visible at near histologic resolution. These offer new opportunities for further investigation of disease pathogenesis in vivo.
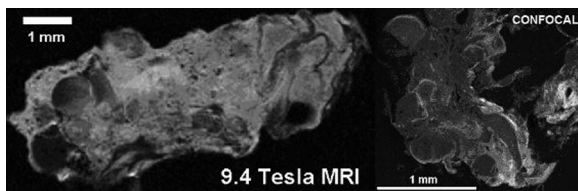
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Transcranial Doppler Is a Reliable Tool for Assessing Collateral Patterns in Patients with Carotid Artery Stenosis

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Introduction To determine the sensitivity and specificity of transcranial Doppler (TCD) on assessing the collateral flow patterns in patients with Carotid artery stenosis compared with digital subtraction angiography (DSA). Hypothesis -We assessed the hypothesis that TCD could accurately reflect the collateral patterns in patients with severe Carotid artery stenosis. **Methods** 150 patients with steno-occlusive ($\geq$70%) disease confirmed by DSA were enrolled. The presence of Anterior Communicating artery (ACoA),Posterior Communicating artery (PCoA) and ophthalmic artery (OA) collaterals were studied by TCD and compared with the data of DSA ; 43 patients with unilateral carotid artery occlusion were included and divided into two groups depend on the collateral degrees defined by DSA. Calculated the ratio of systolic flow velocity and pulsatility index of MCA in affected side (dV_{MCA}, dPI_{MCA}) with unaffected side (nV_{MCA}, nPI_{MCA}) and compared the ratios between the groups. The ROC analysis was used to define TCD criteria for distinct collateral degree. The ratios were also compared between the groups of different type and number of collaterals and between the carotid occlusion. The associations between the ratios and clinical outcomes were also investigated. **Results** Compared with DSA findings, the sensitivity of TCD was 94% and specificity was 99% for the presence of ACoA; 88% and 93% for the presence of PCoA; 98% and 94% for the presence of OA; The sensitivity was 76% and specificity was 75% for dV_{MCA} / nV_{MCA}>0.65 and 90% and 60% for dPI_{MCA} / nPI_{MCA} >0.60 to predict complete collateral flow in MCA region. The ratios of dV_{MCA} / nV_{MCA} and dPI_{MCA} / nPI_{MCA} correlated with cliniacal outcome and did not associate with the number of collaterals. The sensitivity was 83% and specificity was 84% for dPI_{MCA} / nPI_{MCA}<0.92 to predict carotid occlusion. **Conclusions** In conclusion, TCD was a reliable tool for evaluation of the presence of primary collaterals and ophthalmic collaterals, and its hemodynamic parameters could partly reflect the leptomeningial collateral patterns and the extent of collateral supply. Hemodynamic parameters of TCD can also reflect the perfusion status and the presence of carotid disease.

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Potential Benefits of Fibromuscular Dysplasia Diagnosis in Cervical Artery Dissections

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- # - Fibromuscular dysplasia (FMD) is a potential cause of cervical artery dissection (CAD). Moderate forms of FMD are undiagnosed by magnetic resonance angiography .The use of renal intra-arterial digital subtraction angiography (DSA) in identifying FMD in CAD has not yet been validated. Our objective was to determine the prevalence of combined cervical and renal artery FMD assessed by DSA in CAD. We also want to define the diagnostic impact of renal DSA in these patients. Methods: we prospectively included and followed one hundred and three patients consecutively admitted for a CAD between 1994 and 2004. CAD was diagnosed by cervical MRI or suggested by 2 concordant cervical imaging methods. A cohort was selected from this study, with retrospective inclusion of 54 patients (31 women and 23 men , mean age: 44 $\pm$ 9 years, 16 aged below 40 years and 38 over 40 years) , CAD being investigated by both cervical and renal artery DSA. FMD (21 patients , 17 women and 4 men) was defined as a string of beads image located in a non dissected vessel .The Chi square test and Fisher's exact test were used for assessing the association between renal FMD and vascular risk factors or age or head trauma. Results: according to the presence of FMD, 4 subgroups of patients were identified. I (4 patients) , showed renal FMD but no cervical FMD ; II (5 patients) , had cervical and renal FMD ; III (12 patients) , isolated cervical FMD ; IV (33 patients) without FMD. Renal FMD, bilateral in half of the cases, was significantly associated with an age over 40 years .Two out of patients with renal FMD had arterial hypertension . Conclusions: In patients with CAD, the prevalence of combined cervical and renal artery FMD is 9 %. More FMD cases are detected by cervical and renal DSA than by cervical DSA alone (7 %). The diagnosis of renal FMD could help to recognize patients at risk of renal artery dissection and reno-vascular hypertension. The presence of an arterial hypertension, other vascular risk factors or head trauma, are not predictive for renal FMD.

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Low CT Density of Carotid Bifurcation Atheroma Correlates with Symptomatic Plaque in Patients with High-Grade Stenosis

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Background: Current guidelines emphasize the degree of proximal internal carotid artery (ICA) stenosis as the most important determinant of future stroke, however there is much recent interest in further stratifying stroke risk according to other plaque imaging characteristics. These efforts have focused mainly on MRI, with relatively little attention paid to the more readily available modality of CT angiography (CTA). In this study, we assessed plaque density on axial CTA source images. We hypothesized that symptomatic patients would have lower density atheromatous lesions than did asymptomatic patients, owing to the greater likelihood of inflammatory cells in symptomatic patients, and calcification in asymptomatic patients, respectively. **Methods:** We identified 38 asymptomatic and 39 symptomatic patients from our neurovascular lab database who had > 70% stenosis on standard CTA. An experienced reader, blinded to the clinical symptoms, performed a region-of-interest (ROI) analysis of the area of maximal plaque abnormality for each case, using commercially available image segmentation software (Analyze 6.0, Mayo Clinic). Mean Hounsfield Unit (HU) attenuation was recorded for each plaque. Statistical analysis was by the t-test. **Results:** The asymptomatic group consisted of 16 females / 22 males, mean age 70.4 years, mean carotid stenosis 80.6%. The symptomatic group consisted of 14 females / 25 males, mean age 72.5 years, mean carotid stenosis 81.7%. The asymptomatic group had a mean plaque density of 201.8 $\pm$ 134.8 HU, compared to 155.6 $\pm$ 121.2 HU in the symptomatic group ($p = 0.03$, one-tailed t-test). **Conclusions:** As a group, patients with symptomatic high-grade carotid bifurcation stenosis are more likely to have low density, non-calcified atheromatous plaque on standard neck CTA than their asymptomatic counterparts. This observation, if further refined in combination with other imaging findings in symptomatic patients, such as vasa vasorum enhancement, has the potential to help more precisely stratify stroke risk for a given degree of ICA stenosis.

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Genomic Expression Profiles in Blood Change Rapidly Following Acute Ischemic Stroke

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Acute ischemic stroke activates and recruits peripheral leukocytes to brain. To assess gene expression in peripheral leukocytes, whole blood was examined using oligonucleotide microarrays in 15 patients at 3 hours, 5 hours and 24 hours after onset of ischemic stroke and compared to control blood samples. Genes involved in leukocyte activation, inflammation, interleukin 1β and calcium signaling were significantly up-regulated after stroke mainly in neutrophils and monocytes. A set of 18 genes correctly classified 10/15 patients at 3 hours and 13/15 patients at 5 hours after stroke. The genomic patterns of expression did not correlate with initial stroke severity or outcome of recanalization therapy. Patients on aspirin prior to entry into the study did have a different genomic expression pattern than those not on aspirin. Our data suggests that genomic profiling of leukocytes provides insights into the timing and nature of the inflammatory responses to acute stroke and may provide surrogate blood markers for stroke diagnosis.
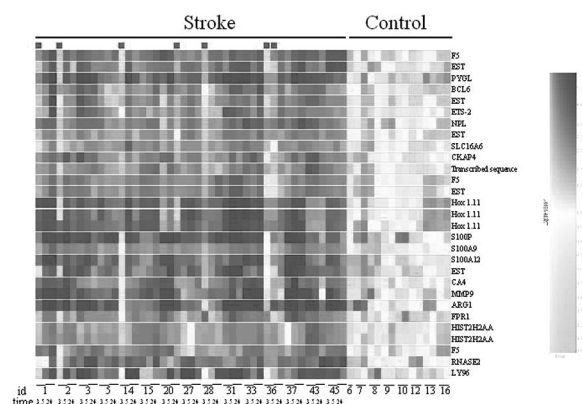
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The Topography and Pathogenesis of Subarachnoid FLAIR Hyperintensity in Acute Ischemic Stroke

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Background: Hyperintensity on FLAIR MRI sequences in the subarachnoid space has recently been described as a frequent finding in acute ischemic stroke patients associated with reperfusion, increased risk of hemorrhagic transformation, and poor functional outcome. The

pathogenesis of subarachnoid space FLAIR hyperintensities is not fully understood. We examined the topography, multisequence appearance, and angiographic correlations of this finding to further elucidate its biological substrate. **Methods:** Imaging review identified 29 consecutive acute anterior circulation ischemic stroke patients exhibiting FLAIR subarachnoid hyperintensity (FLASH) following perfusion imaging with Gd-DTPA bolus injection. Chemical and/or mechanical thrombolysis procedures were performed in 26. Angiographic findings were assessed with the ASITN/SIR collateral scale and the TIMI reperfusion scale. **Results:** Initial MRIs demonstrating FLAIR hyperintensity in CSF space were obtained a mean of 10.0 h (range 3.25 to 18.75h) after symptom onset. FLASH was most commonly observed in sulcal spaces remote from regions of DWI abnormality (76%), less often in regions near to DWI abnormality (48%), and least within regions of DWI abnormality (14%). Topographically, FLASH was most often identified in arterial convexity borderzones or in vascular territories adjacent to ischemic fields (e.g. PCA territory in MCA occlusion). In 3 cases, FLASH was observed in the hemisphere contralateral to the site of ischemia. On angiography, extensive collateral flow was frequently noted (65%). Sites of vigorous collateral recruitment on angiography frequently correlated with sites of FLASH. Recanalization and restoration of anterograde reperfusion was noted in 14 cases (54%). Among 10 patients undergoing repeat MR 24–72h after the MR exhibiting FLASH, new asymptomatic hemorrhagic transformation was observed in 2. FLASH had resolved in 30%, diminished in 40%, and increased in 30%. **Conclusions:** Early after symptom onset, FLASH is found preferentially in zones of abundant collateral flow in regions remote from the core ischemic zone. The disruption in blood-brain barrier that produces FLASH may be due as much or more to vascular remodeling than direct ischemic injury.

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Elevated Serum Levels of VEGF, bFGF, MMP-2, and MMP-9 in Patients with Moyamoya Disease

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Introduction - The induced angiogenic vessels seen on cerebral angiograms are the hallmark of Moyamoya disease. However characterization of its angiogenesis is poorly understood. While angiogenic proteins suchs as VEGF and bFGF have been assayed in the CSF and tissue of Moyamoya patients, serum levels of angiogenic proteins in these patients have not yet been described. **Methods** - After IRB consent was obtained, serum was collected preoperatively from 17 patients presenting to Stanford University for surgical treatment of their Moyamoya disease (STA-MCA bypass or EDAS). Serum was analyzed with ELISA studies for VEGF, bFGF, MMP-2, and MMP-9. Serum from 7 normal patients were processed in the same manner. **Results** - Average level of VEGF, bFGF, MMP-2, and MMP-9 in Moyamoya patients were 15.81 ng/ml, 381.6 ng/ml, 161.3 ng/ml, and 609.76 ng/ml respectively. In normals, the VEGF, bFGF, MMP-2, and MMP-9 levels were 0.54 ng/ml, 123.3 ng/ml, 194.4 ng/ml, and 228.3 ng/ml respectively. The difference observed between patients with Moyamoya and normals was significant for VEGF, bFGF, and MMP-9 but not for MMP-2. **Discussion** - Serum levels of the angiogenic proteins VEGF, bFGF, and MMP-9 were significantly elevated in patients with Moyamoya disease. Correlation to serum levels and density of angiogenesis as well as predictive value for surgical treatments for Moyamoya disease will be discussed.

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Clinical Use of Total/Free NR2 Peptide/Antibodies as Biomarkers of TIA/Acute Stroke

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Objectives: Transient ischemic attack (TIA) portends a significant future risk of stroke and its associated morbidity and mortality. Patients with TIA require further evaluation to assess for any potentially reversible cause. Despite the significant impact of stroke there remains a paucity of diagnostic tests to assist in the early evaluation of TIA patients presenting to the Emergency Department (ED). In this study, blood assays detecting unbound/bound NR2 peptide were obtained in patients presenting to the ED with symptoms suggestive of an acute cerebrovascular event. The feasibility of unbound/bound NR2 peptide assays in differentiating acute cerebrovascular ischemic events from stroke mimics was assessed. **Methods:** We prospectively enrolled patients presenting to the ED during a four month period that had symptoms suggestive of a transient ischemic attack (TIA) or stroke. Stroke was defined as having occurred if a patient developed a permanent neurologic deficit or demonstrated radiographic evidence of ischemic stroke (CT or MRI/DWI). Total/free NR2 peptide/antibodies in blood samples from 33 patients were assessed by ELISA. **Results:** Thirty-three patients were eligible, 25 (76%) of which were diagnosed with an acute cerebrovascular event. Fifteen (60%) patients had an ischemic stroke, and 10 (40%) had a TIA. Increased free NR2 peptide was detected in plasma of patients (n=23). The sensitivity of the free NR2 peptide assay was 96% and the specificity was 90% (9/10), resulting in a 10-fold increase in the risk of completed stroke. Elevated amounts of free NR2 peptide correlated with new lesion areas on DWI/MRI, while total NR2 peptide/antibodies associated with old areas of infarction. **Conclusions:** The risk of completed stroke in patients presenting with symptoms suggestive of acute cerebro-vascular ischemia increases 10 fold when free NR2 peptide levels exceed respective cut offs. The elevation of NR2 peptide significantly correlated with radiographic abnormalities as defined by MRI/DWI. The assays may have potential clinical utility in the diagnosis of patients with acute cerebral ischemia in the Emergency Department.

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Etiologic Diagnosis of Stroke Subtypes Using Plasma Biomarkers

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Since there is no biological marker offering precise information about stroke etiology, many patients receive a diagnosis of undetermined stroke even after all available diagnostic tests are done during their stay at the Stroke Unit. *Objective and methods-* To examine the value of a panel of blood-borne biochemical markers to differentiate stroke etiologies, consecutive patients with acute focal neurological deficit within the last 24 hours due to cerebral ischemia and attended by neurologists were evaluated. CT, ultrasonography, cardiac evaluations and other tests were done to make etiologic diagnosis following TOAST classification. Blood samples for biomarkers were drawn at emergency department arrival. Tested biomarkers were CRP, D-dimer, RAGE, MMP-9, s-100b, Brain Natriuretic Peptide (BNP), Neurotrophin-3, Caspase-3, Chimerin and Secretagogin (assayed by ELISA). *Results-* The study protocol was performed in 776 consecutive ischemic stroke patients. Regarding etiology 35.4% were cardioembolic, 21.8% aterothrombotic, 18.5% lacunars and 24.3% had an undetermined origin. The only identified biomarkers that were different regarding etiologies were high level of BNP (p<0.0001) and D-dimer (p<0.0001) among patients with cardioembolic strokes. In the logistic regression model, independent predictors of a cardioembolic stroke were: Atrial fibrillation OR 15.2 (8.4–27.7) p<0.001; other embolic cardiopathies OR 14.7 (4.7–46) p<0.001; TACI OR 3.9 (2.3–6.8) p<0.001; BNP >76 pg/ml OR 2.3 (1.4–3.7) p=0.001 and D-dimer >0.96 μg/mL OR 2.2 (1.4–3.6) p=0.001. Even among those with transient symptoms (n=153), high BNP level identified cardioembolic TIA [OR 15 (3.6–60) p<0.001]. The combination of D-dimer <0.96 and BNP <76 was present only in 10% of non-cardioembolic strokes and the opposite combination was present in 60% of cardioembolic strokes. Whether these biomarkers might help identifying etiologies among undetermined origin strokes will be discussed. *Conclusions-* Using a combination of biomarkers (including D-dimer and BNP) seem a promising strategy for making an etiologic diagnosis in the acute phase of stroke. These approaches will allow to rapidly guiding other diagnostic tests accelerating the onset of an optimal secondary prevention.

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Pretreatment Lesions or Mismatched Volumes Are Not Independent Predictors of Clinical Outcome After Standard Treatment with Tissue Plasminogen Activator

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Introduction: The volume of acute ischemic injury on diffusion weighted imaging (DWI) is an independent predictor of outcome in untreated patients. Prior work has shown that DWI lesions are partially reversible with early reperfusion, suggesting that tPA therapy may alter the association of baseline lesion volume to outcome. **Hypothesis**: We hypothesized that DWI lesion volume and diffusion-perfusion mismatch volume are not related to clinical outcome after tPA. **Methods**: The sample consisted of all consecutive patients treated with standard IV tPA who had interpretable pre-treatment DWI and a mean transit time (MTT) map. We calculated lesion volumes using a semi-automated technique. The outcome was the modified Rankin scale (mRS) at 3 months with last observation carried forward. **Results**: Over a 45 month study period we treated 134 patients with tPA , 76 of which met the inclusion criteria. The mean age was 74 (±16) years, the median baseline NIHSS was 10. The mean time from onset to baseline MRI was 89 (±33) min, and the mean DWI, MTT, and mismatch lesion volumes were 25.74 (±51) cm^2, 97.11 (±103) cm^2, and 73.38 (±86) cm^2, respectively; 56 patients (74%) had a perfusion-diffusion mismatch (MTT≥ 1.2 DWI). The median time to mRS was 91 days; in 27 patients the mRS score was 0 or 1 and in 31, 0–2. In the univariate analysis patients with mRS 0–1 were younger, had a lower pre-treatment NIHSS score (both at p<0.0001) and smaller pre-treatment DWI (p=0.01) and MTT (p=0.04) lesion volumes than patients with mRS 2–6, but the pre-treatment mismatch (considered both as absolute volume or dichotomous category) was similar for good and poor outcomes (p=0.46). There was a significant correlation between baseline NIHSS and each of the three volume measures (DWI, MTT, and mismatch). In the logistic regression model, the only significant independent predictors of good outcome were younger age (OR=0.91) and lower NIHSS score (OR for 0–8 vs. > 19 = 0.04). Results were similar for the outcome mRS 0–2. **Conclusion**: Baseline DWI and mismatch volumes are not independent predictors of outcome when patients are treated with tPA within 3 hours of onset of symptoms. Reversal of perfusion and diffusion abnormalities by tPA may explain this difference from natural history studies.

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Clinical Characteristics and Outcome in Transient Ischemic Attack Patients with Normal Versus Abnormal Diffusion-Weighted MRI

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Background and Purpose: The traditional notion of transient ischemic attack (TIA) has been proposed to be modified with the advent of diffusion-weighted imaging (DWI). We are to compare the clinical characteristics and outcome of patients with DWI positive TIA to those of DWI negative TIA**.** **Methods**: We identified 67 consecutive patients (mean age, 62 years; 50 men, 17 women) with TIA who visited our hospital from January 2003 to December 2004 and could undergo DWI within 48 hours of symptom onset. We reviewed the medical records to assess the clinical characteristics of TIA, the demographics and the subsequent vascular events. **Results:** DWI confirmed acute ischemic stroke in 24 patients (36%). Atrial fibrillation was significantly associated with positive DWI scan on univariate analysis of DWI abnormalities and clinical parameters including demographic data and clinical features of TIA (p=0.03). However, multiple logistic regression revealed no independent predictor of DWI abnormalities. During the mean follow-up period of 16 months, 21 patients (31%) experienced subsequent vascular events: acute ischemic stroke (7 of 67, 10%), TIA (13, 19%), spinal cord infarction (1, 2%), acute ischemic retinopathy (1, 2%), peripheral vascular claudication (1, 2%), and vascular surgery or intervention such as carotid artery endarterectomy, middle cerebral artery stenting, and common iliac artery stenting (9, 13%). All acute ischemic strokes (7, 100%), 11 of 13 TIAs (85%), and seven of nine vascular procedures (78%) occurred within three months of initial symptom. Only two TIAs (15%) and two vascular procedures (22%) happened after three months of initial TIA. No significant association of subsequent vascular events with DWI abnormalities was noted on univariate analysis. **Conclusions:** The clinical characteristics and outcome are not significantly different between patients with DWI positive versus negative TIA. Whether there are DWI lesions or not, the risk for subsequent vascular events is relatively high, especially in the early period after initial symptom.