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ABSTRACTS

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We-W31:3 VASA VASORUM NEOVASCULARIZATION VISUALIZED WITHIN THE HUMAN CAROTID ATHEROSCLEROTIC PLAQUE: CONTRAST-ENHANCED ULTRASOUND IMAGING AND HISTO-PATHOLOGIC CORRELATES

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Background: Previous studies have demonstrated the existence of neovascularization in the human atherosclerotic plaque, a far greater incidence of neovascularization from the adventitia relative to the lumen, and a correlation between plaque instability and carotid occlusive disease. Using contrast-enhanced ultrasound examinations, the vasa vasorum and the plaque neovascularization in the adventitial/media/intima region of the carotid arteries can be visualized.

Objectives: To correlate the degree of neovascularization observed in carotid plaque during contrast-enhanced, ultrasound imaging to the pathology specimens obtained from carotid endarterectomy surgery.

Methods: Patients underwent a contrast-enhanced, carotid ultrasound exam with a GE VIVID7 Dimension or a Philips/ATL HDI 5000 using an intravenous ultrasound contrast agent (Optison). Twenty-one (21) patient carotid examinations were included in this review based on the entry criteria that a >50% stenosis was present. Fifteen (15) patients underwent surgical carotid endarterectomies (17 carotid specimens). The degree of neovascularization was visually based on standard criteria.

Results: A visual grading system for the presence of neovascularization was applied (3=extensive, 1=minimal, and 2=moderate). Of the 20 patients observed with plaque neovascularization, extensive neovascularization was observed in the plaque of 4 patients, moderate neovascularization was observed in the plaque of 5 patients, and minimal, sporadic vasculature was observed in the plaque of 11 patients. The correlation between the contrast-enhanced ultrasound imaging and tissue neovascularization was $r=0.68$.

Conclusion: The ultrasound contrast-enhanced visualization of the neovascularization correlated with the presence and degree of neovascularization in the human atherosclerotic carotid plaque. The use of contrast-enhanced, carotid imaging may be used to detect the systemic atherosclerosis in at-risk populations.

We-W31:4 ULTRASOUND PHENOTYPES OF CAROTID ATHEROSCLEROSIS ARE BIOLOGICALLY AND GENETICALLY DISTINCT

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Background: Determinations of carotid intima-media thickness (IMT), plaque size and stenosis are commonly used to predictor risk, as phenotypes for genetic research and as surrogate outcomes.

Purpose: To compare biological and genetic characteristics of ultrasound phenotypes, and response to therapy.

Methods: we studied correlation of these phenotypes and their association with risk factors and genetic markers, in several populations: patients with stroke or TIA, diabetic nephropathy, in vascular prevention clinics and in aboriginal people with diabetes and their rate of progression/regression with therapy.

Results: IMT was only modestly correlated (~ 0.5) with both total plaque area (TPA) and total plaque volume (TPV), while TPA and TPV were highly correlated ($R \sim 0.9$) with each other. Multiple regression analysis showed that the proportion of explained variance (R^2) from traditional risk factors was 0.52 for TPA, but only 0.15 for IMT and 0.13 for stenosis. Furthermore, IMT was most strongly associated with hypertension, while TPA was most strongly associated with cholesterol and smoking and TPV was most strongly associated with diabetes. Marked differences in genetic associations were seen: the PPARG A12 allele was associated with reduced IMT but not TPV, while the PPARG c.1431T allele was associated with increased TPV but not IMT, while the PCK1-232G/G allele had more IMT and less TPV. TPV regressed significantly in 3 months on atorvastatin vs placebo in only 20 per group, much less than IMT.

Conclusion: Investigators using ultrasound phenotypes of atherosclerosis should recognize that various traits are distinct.

We-W31:5 HOMOCYSTEINE AND FOLIC ACID LEVELS AND RELATION TO CAROTID ATHEROSCLEROSIS IN HIGH-RISK INDIVIDUALS

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Objective: Epidemiological studies suggest that mild/moderate elevation in plasma homocysteine (Hcy) is associated with atherothrombotic cardiovascular (CV) disease. The association of Hcy and atherosclerosis is not clear in populations with high CV risk. We evaluated the relationships between Hcy, folic acid and atherosclerosis in 921 patients with known CV disease or diabetes enrolled in the Homocysteine and Atherosclerosis Reduction Trial (HART).

Methods: Atherosclerosis was assessed by high resolution B-mode ultrasound measurements of carotid intima-media thickness (IMT) and plaque calcification.

Results: Mean and single max IMT was 1.27 ± 0.34 and 2.41 ± 0.83 mm, respectively and plaque calcification was found in 27.7%. Hcy correlated with mean ($r=0.13$; $p<0.001$) and single max ($r=0.12$; $p<0.001$) carotid IMT. There was a progressively gradual increase across quartiles of Hcy of both mean max (Q1: 1.17 to Q4: 1.28 mm; $p<0.001$ for trend) and single max IMT (Q1: 2.14 to Q4: 2.44 mm; $p<0.001$ for trend). The associations were no longer significant after adjustments for age and sex and in multivariate analyses. For folate, a weak trend towards an inverse relation was found (NS). Both Hcy ($p=0.02$) and low folic acid ($p=0.01$) were independent predictors of plaque calcification, even after adjustments for age and sex.

Conclusions: In high risk individuals Hcy and folate concentrations are associated with carotid IMT in univariate analyses but not after adjustments for age, sex and other risk factors. The associations with plaque calcification appear stronger.

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We-W31:6 CAROTID INTIMA-MEDIA THICKNESS BY B-MODE ULTRASOUND AS A NEW TOOL TO RECOGNIZE CAD IN PATIENTS WITH NO EVIDENCES OF ANGIOGRAPHIC NARROWINGS

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Objective: to evaluate the ability of external carotid ultrasound (ECU) and quantitative coronary angiography (QCA) to classify patients with coronary atherosclerosis documented by intravascular ultrasound (IVUS).

Methods: ECU, IVUS and QCA were performed in 48 patients. The potential of ECU and QCA variables to identify patients with a positive IVUS test (IVUS(+)) was analyzed.

Results: The whole group was stratified according to a QCA diagnosis of normality [maximal %coronary stenosis (%CSmax) $\leq 40\%$; $n=16$, group A]; intermediate (%CSmax from 40% to $\leq 70\%$; $n=19$, group B) or overt atherosclerosis (%CSmax $> 70\%$; $n=13$, group C). The lowest group C IVUS-determined coronary-IMTmax was used as threshold to define subjects in group A and B as IVUS(+) or IVUS(-). Five (31.2%) subjects of group A and 16 (84.2%) of Group B were classifiable as IVUS(+) despite their QCA diagnosis of normal or intermediate atherosclerosis. Pooling data from groups A and B, the area under the ROC curve increased from 0.730 to 0.798 to 0.885 when calculated on the basis of %CSmax, carotid-IMTmax, carotid-IMTmean, respectively. Using a 1 mm cut-off value for carotid-IMTmean, no IVUS false negatives were identified neither in group A nor in Group B, and 2/16 patients in Group A and 2/19 in Group B were classifiable as IVUS false positives. Sensitivity, specificity, positive and negative predictive values were 1, 0.75, 1, 0.57 for Group-A and 1, 0.25, 1, 0.83 for Group-B.

Conclusions: ECU variables have a higher capacity than QCA variables in recognizing patients with a positive IVUS test.

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