

E2051 JACC March 12, 2013 Volume 61, Issue 10



## CAROTID ADVENTITIAL NEOVASCULARIZATION AND INTIMA-MEDIA THICKNESS AS MARKERS OF ATHEROGENESIS: EVIDENCE FROM TWO RANDOMIZED CONTROLLED TRIALS

Moderated Poster Contributions Poster Sessions, Expo North Saturday, March 09, 2013, 3:45 p.m.-4:30 p.m.

Session Title: Classic and Novel Cardiovascular Risk Predictors and Impact Abstract Category: 35. Vascular Medicine: Non Coronary Arterial Disease Presentation Number: 1167M-170

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**Background:** Arterial adventitial vasa vasorum (W) constitute an index of neovascularization, a critical process in atherogenesis. Therefore, we sought to determine factors associated with quantitative measures of carotid W.

**Method:** We analyzed data from 324 diabetics and 141 non-diabetics who prospectively underwent in vivo contrast enhanced ultrasonography (CEUS) imaging for the assessment of carotid adventitial neovascularization (W) ratio and intima-media thickness (CIMT). Adjusted multivariable linear models were used to evaluate the relationship between baseline covariates and W ratio and CIMT.

**Results:** There was no difference in age between non-diabetics and diabetics (59.8 vs 59.3, p = 0.525). The diabetics had mean hemoglobin A1C of 7.44 ± 0.99. The median CIMT (in mm) was 0.82 ± 0.22 among non-diabetics and 1.06 ± 0.19 among diabetics (p < 0.0001). The median W ratio was higher in diabetics than non-diabetics ( $1.21 \pm 0.26$  vs. 0.80 ± 0.19, p<0.0001). The mean LDL cholesterol was higher among non-diabetics than diabetics ( $139 \pm 30$  vs.  $107 \pm 31$ , p<0.0001), likely because statin use was higher among diabetics (55% vs. 15%, p<0.0001). Diabetic status was associated with almost 40% higher W ratio (95% Cl 0.243 to 0.480, p < 0.001) whereas a unit increase in body mass index was associated with a 0.9% higher W ratio (95% Cl 0.0014, p<0.001). A ten-year increase in age was associated with 4% higher CIMT (95% Cl 0.001 to 0.007, p = 0.005). A ten-unit increase in systolic blood pressure was associated with 2% higher CIMT (95% Cl 0.001, p<0.003) whereas diabetic status increased CIMT by 31% (95% Cl 0.191 to 0.421, p<0.001). Female sex was associated with 9% (95% Cl -0.129 to -0.041, p<0.001) lower CIMT. Lipids, blood pressure, and CIMT were not significantly associated with W ratio in this population.

**Conclusions:** Both neovascularization and CIMT were strongly associated with diabetes. W ratio and CIMT were not associated with each other in this cohort of patients with minimal carotid atherosclerosis mostly driven by diabetes. The data suggest that the W ratio is a distinct and strong marker of atherogenesis in cardiovascular patients, and has potential application for risk stratification.