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CORRELATES OF CAROTID ARTERY INTIMA-MEDIA THICKNESS IN RECENTLY MENOPAUSAL WOMEN SCREENED FOR THE KRONOS EARLY ESTROGEN PREVENTION STUDY

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Background: The timing of initiation of menopausal hormone therapy (MHT) may be critical to its effects upon atherosclerosis and vascular disease. The Kronos Early Estrogen Prevention Study (KEEPS) is a placebo-controlled trial of 4 years of oral or transdermal estrogen in recently menopausal (<36 months) healthy women aged 42-58. Common carotid artery intima-media thickness (CIMT), a validated measure of atherosclerosis, is the primary endpoint. There is only limited information on links to subclinical atherosclerosis in this population. We correlated CIMT with a variety of conventional risk markers in 691 women screened to date for the KEEPS.

Design and Methods: CIMT was read centrally at USC by computer image-processed B-mode ultrasound. Values were tested against elements of the Framingham Risk Score (FRS), including age, systolic BP, total and HDL cholesterol (C), hypertension, and smoking status; and also with other risk markers, including components of the metabolic syndrome (MS: diastolic BP, LDL-C, triglycerides (TG), BMI, waist circumference, and fasting glucose); and with MS diagnosis as defined by 2001 NCEP ATP-III criteria.

Results: CIMT ranged from 0.532 to 1.168 mm (mean 0.724 ± 0.091 SD). Systolic BP ($r^2=0.044$, $p<0.0001$), age ($r^2=0.015$, $p=0.0008$), and hypertension diagnosis ($p=0.038$) correlated significantly with CIMT. Smoking/nonsmoking status, which is strongly linked to coronary artery calcification (CAC; Newman AB et al., Am J Cardiol 2008; 101: 186-192.), was not significantly linked to CIMT in this population ($p=0.06$). Lipid measures also lacked significance as CIMT correlates.



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Overall FRS correlated with CIMT ($p < 0.0001$) but with wide scatter ($r^2 = 0.057$). Groupwise, the lowest FRS tertile had lower CIMT than the middle or highest tertiles (L vs. H, 0.706 ± 0.087 vs. 0.737 ± 0.088 mm, $p = 0.05$). CIMT values were similar in women with ($n = 53$, 0.728 ± 0.074) and without ($n = 620$, 0.723 ± 0.074) the metabolic syndrome ($p = 0.3$). A multivariate model showed age and systolic blood pressure as the only significant predictors of CIMT.

Conclusions: CIMT measurements are heterogeneous in clinically healthy early postmenopausal women. Consistent with studies in other populations, systolic BP and age correlate with higher CIMT, while lipids and smoking status are not significantly linked. Although the FRS is significantly correlated with CIMT, the high variability makes FRS of minimal utility as a predictor of individual values.