SUPPLEMENTAL MATERIAL

Materials and Methods

Subjects

MESA is a longitudinal study of the prevalence, risk factors, and progression of subclinical CVD. The multi-ethnic cohort was composed of a population-based sample of individuals from six communities within the United States. All 6,814 study participants were 45 to 84 years old and free of clinically apparent CVD at baseline. A description of study design and objectives was described previously.[1,2] Participants included in this analysis represent a subset with valid carotid distensibility measurements at examination 1 (baseline) and examination 5 who were not missing pertinent examination 1 covariates (n=2650; see Data Supplement I: Flow diagram).[1] The baseline examination occurred between July 2000 and August 2002 and included blood sample analysis as well as demographic and medical history assessments. The final and 5th examination occurred between April 2010 and February 2012. Participants with SBP ≥140 mmHg, DBP ≥90 mmHg, or who used antihypertensive medication were classified as having hypertension. Participants with fasting glucose ≥126 mg/dL or who used antiglycemic medications were classified as having diabetes mellitus. Impaired fasting glucose was defined as blood glucose from ≥100 but <126 mg/dL. Following a 12-hour fast, total and high-density lipoprotein (HDL) cholesterol levels were measured.

B-Mode Ultrasound and Brachial Artery Blood Pressure Measurements

These methods have been described previously.[1] For exam 1, B-mode ultrasound video loops of a longitudinal section of the distal right common carotid artery were recorded on videotape using a Logiq 700 ultrasound system (General Electric Medical Systems, transducer frequency 13 MHz). Video images were digitized at high resolution and frame rates (30 frames/second) using a Medical Digital Recording device (PACSGEAR, Pleasanton, CA) and converted into DICOM compatible digital records. At exam 5, a similar protocol was performed using the same ultrasound and digitizing equipment; however, the video output was directly digitized using the same MDR settings without use of videotape. Certified sonographers used pre-selected reference images from exam 1 to match the scanning conditions of the initial study.[1] After 10 minutes of resting supine and immediately before the ultrasound image acquisition, repeated measures of brachial blood pressures were obtained using a standardized protocol with an automated upper arm sphygmomanometer (DINAMAP, GE Medical Systems, Milwaukee, WI). Ultrasound images were reviewed and interpreted by the MESA Carotid Ultrasound Reading Center (University of Wisconsin Atherosclerosis Imaging Research Program, Madison, WI). Systolic and diastolic diameters were determined as the largest and smallest diameters during the cardiac cycle. All measurements were performed in triplicate from 2-3 consecutive cardiac cycles to derive mean internal diameter at peak systole. Internal and external diameters were measured at end-diastole using Access Point Web version 3.0 (Freeland Systems, LLC). Carotid artery diameters and wall thickness were measured non-invasively with B-mode ultrasound of the right common carotid artery as described previously.[1,3,4] The carotid artery distensibility coefficient (DC, (10-3 mmHg-1)) and Young's Elastic modulus (YEM, mmHg) were calculated using standard formulae (see Data Supplement II). Reproducibility data are in Data Supplement III.

Statistical Analysis

Descriptive statistics are reported as means (standard deviations) for continuous variables or percentages for categorical variables. Student's t-tests for continuous variables and chi-squared tests for categorical variables were used to compare baseline descriptive statistics between males and females. We used multivariable linear regression models stratified

by sex to investigate the primary aim of defining the independent predictors of changes in DC and YEM progression by sex. Two models were examined for each sex. The predictors assessed in the first model included: age, ethnicity, education, diabetes mellitus, smoking, total and HDL cholesterol, body-mass index, systolic blood pressure, use of lipid-lowering medication at baseline, use of antihypertensive treatment at baseline, and menopausal status in models restricted to females. The second model was the same as the first except that the variable for baseline use of antihypertensive medication was replaced with a four category variable defined by antihypertensive medication use at baseline and exam 5: antihypertensive medication use at (1) neither baseline nor exam 5, (2) both baseline and exam 5, (3) baseline but not exam 5, and (4) not at baseline but at exam 5. To confirm these findings in parsimonious models, we performed backwards elimination on the full models presented in Tables 2 and 3 with $P<0.10$.

Tests for interaction of each predictor with sex were performed individually by pooling the data for men and women and including the product of the predictor variable with the sex variable in the models. Also, in models restricted to women, the interactions of menopausal status with antihypertensive medication in model 1 and with antihypertensive medication category in model 2 were tested. A two-sided P value of 0.05 was considered statistically significant; however P values up to 0.10 are reported for the interaction analyses because they are potentially underpowered.

Given the important relationship between age and arterial stiffening,[1] we treated age as both a continuous and categorical variable, the latter classified into 4 decades (ages 45-54, 55-64, 65-74, and 75-84 year). Analysis of variance was used to compare sex differences in baseline DC and YEM, progression of DC and YEM. As in our previous report,[1] we adjusted for baseline carotid stiffness measures to account for the possibility that in subjects with the most stiff arteries at baseline, the independent variables may have less of an effect on progression of YEM and DC. Similar results were found in models unadjusted for baseline, therefore only adjusted data are presented. Unadjusted models are presented in Data Supplement IV (Supplementary Tables IV-A and IV-B).[1]

References

1. Gepner AD, Korcarz CE, Colangelo LA, Hom EK, Tattersall MC, Astor BC, Kaufman JD, Liu K, Stein JH. Longitudinal effects of a decade of aging on carotid artery stiffness: the multiethnic study of atherosclerosis. Stroke. 2014;45:48-53.
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