Peripheral Artery Disease and Aortic Disease

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ABSTRACT

We reviewed published MESA (Multi-Ethnic Study of Atherosclerosis) study articles concerning peripheral arterial disease, subclavian stenosis (SS), abdominal aortic calcium (AAC), and thoracic artery calcium (TAC). Important findings include, compared to non-Hispanic whites, lower ankle-brachial index (ABI) and more SS in African Americans, and higher ABI and less SS in Hispanic and Chinese Americans. Abnormal ABI and brachial pressure differences were associated with other subclinical cardiovascular disease (CVD) measures. Both very high and low ABI independently predicted increased CVD events. Looking at aortic measures, TAC and AAC were significantly associated with other subclinical CVD measures. Comparisons of AAC with coronary artery calcium (CAC) showed that both were less common in ethnic minority groups. However, although CAC was much more common in men than in women in multivariable analysis, this was not true of AAC. Also, when AAC and CAC were adjusted for each other in multivariable analysis, there was a stronger association for AAC than for CAC with CVD and total mortality.

The MESA (Multi-Ethnic Study of Atherosclerosis) study is a large prospective cohort study designed to include 4 major race or ethnicity groups: non-Hispanic White, Hispanic, African American, and Chinese. Participants at baseline were 6,814 men and women 45 to 84 years of age without clinical cardiovascular disease (CVD). The objective was to study the epidemiology and prognosis of several different measures of subclinical CVD, as well as the progression of subclinical CVD, and their predictive role in clinical CVD. The ankle-brachial index (ABI) was 1 of the measures studied, and indicates whether one has lower extremity peripheral arterial disease (PAD). Using MESA study data, many aspects of PAD have been explored, including the role of race or ethnicity, the influence of different methods of calculating the ABI on PAD prevalence, standard and novel risk factors, genetics, the association of PAD with other subclinical CVDs, and the ABI as a predictor of incident CVD. The interarm blood pressure difference was used to assess the prevalence of subclavian stenosis.

Thoracic aortic calcium (TAC) was measured in the MESA study using the computed tomography (CT) scans for coronary artery calcium (CAC). Measurement of abdominal aortic calcium (AAC) by CT scan was done on a random subset of approximately 2,000 participants. Within the MESA study many aspects of TAC and AAC have been explored, including aortic lengthening and dilation, standard and novel risk factors, associations with other subclinical CVDs, and the utility of TAC and AAC as predictors of incident CVD.

PERIPHERAL ARTERIAL DISEASE

Race or ethnicity and PAD in the MESA study

Using data from the baseline the MESA study visit, an analysis found significant differences in prevalence rates of PAD by race or ethnicity [1]. Specifically, African Americans had a substantially higher unadjusted prevalence of PAD (7.2%) compared with non-Hispanic Whites (3.6%), Hispanics (2.4%), and Chinese (2.0%; $p < 0.01$). In a multivariable logistic regression model consisting of age and sex, and compared with non-Hispanic Whites, African Americans were found to have over twice the odds of an ABI <0.90 (odds ratio [OR]: 2.28; $p < 0.01$) whereas Chinese had significantly lower odds (OR: 0.56; $p = 0.03$). The odds for Hispanics were also lower (OR: 0.74), but this result was not statistically significant ($p = 0.14$). The addition of body mass index, diabetes, pack-years of cigarette smoking, hypertension, dyslipidemia, education level, and annual income changed the ORs for all 3 race-ethnic groups (African American OR: 1.67; Chinese OR: 0.39; Hispanic OR: 0.49; $p < 0.05$ for all). Additional adjustment for interleukin-6, fibrinogen, D-dimer, and homocysteine modestly changed the magnitudes of these associations: African Americans 1.47 (95% confidence interval [CI]: 1.07 to 2.02), Hispanics 0.45 (95% CI: 0.29 to 0.70) and Chinese 0.44 (95% CI: 0.24 to 0.78). These results are summarized in Figure 1.

Among the MESA study participants without any of the traditional CVD risk factors or the presence of abnormalities for different measures of subclinical atherosclerosis, an analysis of the MESA study data found that African Americans had an ABI 0.02 lower than

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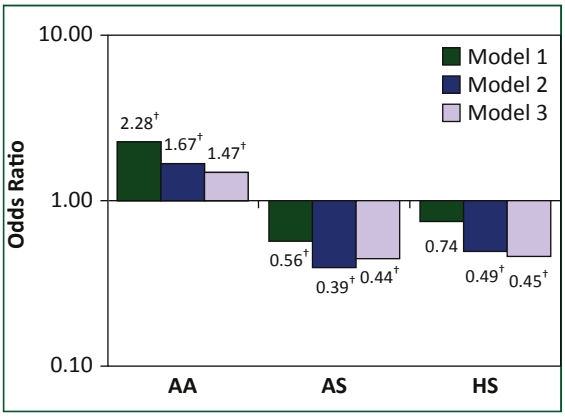

FIGURE 1. Ethnic-specific odds ratios for peripheral arterial disease. Model 1 was adjusted for age and sex; Model 2 was adjusted for those in Model 1 + diabetes, smoking, hypertension, dyslipidemia, body mass index, education, and income; Model 3 was adjusted for those in Model 2 + interleukin-6, fibrinogen, D-dimer, and homocysteine. Non-Hispanic (HS) white = reference group. †$p < 0.05$. AA, African American; AS, Chinese. Reproduced with permission from Allison et al. [1].

non-Hispanic Whites, suggesting an intrinsic difference in the ABI [2]. These slight differences, although clinically negligible, could significantly impact the estimation of PAD prevalence in different sex- and race-ethnic- groups.

Using baseline data from the MESA study, an analysis was conducted to determine PAD prevalence within Dominican, Mexican, Puerto Rican, and other Hispanic Americans (n = 1,437), as well as the magnitude and significance of associations between CVD risk factors and PAD within each Hispanic subgroup [3]. In a multivariable logistic model containing the CVD risk factors, only Other Hispanic Americans had significantly lower odds of an ABI >1.0 (OR: 0.51; 95% CI: 0.28 to 0.93), compared with Mexican Americans. In separate Hispanic subgroup-specific multivariable logistic models including the CVD risk factors, increasing age was a significant risk factor for an ABI <1.0 among all Hispanic subgroups except Dominican Americans. In general, female sex was consistently associated with lower odds of PAD, whereas diabetes, current smoking, and hypertension were associated with higher odds of PAD (except for hypertension in Puerto Rican Americans).

Influence of ABI calculation method on PAD prevalence

Both the posterior tibial and dorsalis pedis arteries were used in calculating the ABI. The ABI could be calculated using the highest (ABI-HI), lowest (ABI-LO), or mean (ABI-MN) ankle systolic blood pressure (SBP) in a given leg. In clinical practice, the highest arm and leg SBPs are used to compute the ABI. However, the choice of which pressure to use may have implications for associations between ABI and the underlying burden of atherosclerosis. In an analysis differences were determined in the prevalence of PAD in the MESA study using 3 different methods of calculating the ABI [4].

The ABI was calculated separately in each leg with 3 distinct methods: specifically, for ABI-HI, the higher of the measurements in a given ankle was used; for ABI-LO, the lower of these 2 pressures was used; and for ABI-MN, the average of the 2 pressures was used. This resulted in each participant having 6 different ABI values (3 on the right and 3 on the left). From this, 3 index ABI values (ABI-HI, ABI-LO, and ABI-MN) were defined as the lower of the corresponding right and left values for each method. In all cases, the highest brachial artery pressure (right vs. left) was used for the denominator to account for the possible influence of subclavian stenosis.

The prevalence of PAD between men and women was compared by ABI method within each race-ethnic group. In general, the prevalence of PAD was higher among women than among men, regardless of race-ethnic group. When the ABI-LO method was used, a significantly higher prevalence of PAD was identified among women for non-Hispanic Whites, Chinese, and African Americans. When the ABI-MN method was used, a significantly higher prevalence of PAD was identified among non-Hispanic Whites and Chinese. When the ABI-HI method was used, there were no significant sex differences in PAD prevalence within any race-ethnic group.

Among all race-ethnic groups and in both sexes, the prevalence of PAD differed by the calculation method. Overall and compared with ABI-HI, the prevalence of PAD was 3.95 times higher among women when ABI-LO was used, whereas among men the prevalence was 2.74 times higher when this pressure was used. When the ABI-LO method was used, the corresponding (female and male) prevalence among non-Hispanic Whites, Chinese, African Americans, and Hispanics were 4.71 and 3.19, 3.44 and 3.15, 3.39 and 2.56, and 3.94 and 2.04 times higher, respectively. When ABI-MN was used, the prevalence of PAD was intermediate between the prevalence for the highest and lowest ankle pressures.

Standard and novel risk factors for PAD

Using data from the baseline the MESA study visit, the associations of several risk factors for CVD and the presence of PAD defined using the ABI have been examined. Among participants without traditional CVD risk factors or subclinical atherosclerosis, an analysis showed that male sex, weight, and high education level were positively correlated with ABI, whereas triglycerides, pack-years (in past smokers), and pulse pressure were negatively correlated [2].

From a separate analysis of all the MESA study participants using multivariable logistic regression, the associations between risk factors and PAD (ABI ≤0.90) are shown in Table 1. The results indicate that age, diabetes