Stiffening of the central elastic arteries is one of the earliest detectable manifestations of adverse change within the vessel wall. Although an association between carotid artery stiffness and adverse events has been demonstrated, little is known about the relationship between stiffness and atherosclerosis. Even less is known about the impact of age, sex, and race on this association. To elucidate this question, we used baseline data from the Multi-Ethnic Study of Atherosclerosis (2000–2002). Carotid artery distensibility coefficient was calculated after visualization of the instantaneous waveform of the common carotid diameter using a high-resolution B-mode ultrasound. Thoracic aorta calcification was identified using noncontrast cardiac computed tomography. We found a strong association between decreasing distensibility coefficient (increasing carotid stiffness) and increasing thoracic aorta calcification, as well as a graded increase in the thoracic aorta calcification score ($P<0.001$). After controlling for age, sex, race, and traditional and emerging cardiovascular risk factors, individuals in the stiffest quartile had a prevalence ratio of 1.52 (95% CI: 1.15 to 2.00) for thoracic aorta calcification compared with the least stiff quartile. In exploratory analysis, carotid stiffness was more highly correlated with calcification of the aorta than calcification of the coronary arteries ($\rho=0.32$ versus 0.22; $P<0.001$ for comparison). In conclusion, there is a strong independent association between carotid stiffness and thoracic aorta calcification. Carotid stiffness is more highly correlated with calcification of the aorta, a central elastic artery, than calcification of the coronary arteries. The prognostic significance of these findings requires longitudinal follow-up of the Multi-Ethnic Study of Atherosclerosis cohort. (Hypertension. 2009;54:1408-1415.)

Key Words: carotid stiffness ■ carotid compliance ■ subclinical atherosclerosis ■ thoracic aorta calcification ■ coronary calcification

S

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1408
To better describe the association between stiffness and atherosclerosis, we assessed the cross-sectional association between carotid DC measured with ultrasound and thoracic aortic calcification (TAC) measured by CT in a large, multiethnic cohort. In further analysis, we looked for regional variability in the association between carotid stiffness and calcification in the aorta (an elastic central artery) and the coronary arteries (peripheral arteries).

Methods

Study Design and Patient Population

We used baseline data from the Multi-Ethnic Study of Atherosclerosis (MESA; 2000–2002). The MESA study design, patient recruitment, and selection have been described previously. In summary, MESA enrolled 6814 asymptomatic men and women of 4 different ethnic groups (white, Chinese, black, and Hispanic), aged 45 to 84 years, into a population-based, prospective cohort study aimed at describing the prevalence, progression, and significance of subclinical atherosclerosis. Patients were drawn from 6 geographically distinct population centers in the United States. All of the patients were free of known cardiovascular disease at enrollment.

Each MESA participant underwent 2 baseline cardiac CT scans for the evaluation of coronary and extracoronary calcification. In 6529 participants (96%), baseline carotid ultrasound imaging was sufficient to calculate DC. Patients without sufficient carotid imaging were more likely to be women and black but did not differ in age or any other measured covariate. All of the participants gave informed consent for the study protocol, which was approved by the institutional review boards of all 6 of the MESA field centers.

Carotid Imaging and DC

The right and left carotid arteries were imaged according to a common scanning protocol using high-resolution B-mode ultrasound with a Logiq 700 machine (General Electric Medical Systems). Carotid IMT was measured in the common carotid artery, and reported as the mean of the maximum intima-media thickness (IMT) measured in the right and left sides for both the near and far walls. Data necessary for calculating DC were obtained from a separate 20-second-long acquisition of longitudinal images of the right distal common carotid artery. All of the images were interpreted at a central MESA ultrasound reading center (Tufts Medical Center) by readers blinded to all of the clinical information.

For each participant, an edge detector was used to process the images and to extract carotid arterial diameter curves. Diastolic and systolic diameters were determined as the smallest and largest diameter values during a cardiac cycle. Blood pressure measurements were taken by upper arm sphygmomanometry (DINAMAP System; GE Medical Systems) at the time of the carotid artery ultrasound.

These data were used to calculate a simplified DC via the following equation described by Gamble:

$$DC = \frac{2AD}{\Delta PD}$$

where $\Delta D$ is the change in systolic/diastolic diameter, $\Delta P$ is the brachial pulse pressure, $D_s$ is the systolic diameter, $D$ is the average common carotid artery diameter, and $h$ is the mean wall thickness (IMT) measured 10 mm proximal to the carotid bulb.

Reproducibility studies were performed in 221 participants; 211 were intraobserver repeated-image analyses, and 10 were interobserver correlations. For DC and YM, the intraobserver class correlation coefficients were 0.71 and 0.69, respectively. The interobserver intraobserver class correlation coefficients were 0.85 and 0.84, respectively. The intraobserver variability in reading exams was assessed in 204 patients, revealing an intraobserver class correlation coefficients of 0.68 for DC and 0.80 for YM. This reflects good-to-excellent agreement.

Cardiac CT Protocol

Cardiac CT was performed at 3 sites using a cardiac-gated, electron-beam CT scanner (Imatron C-150XL; GE-Imatron) and at 3 sites using a 4-section multidetector CT. All of the participants were scanned over phantoms of known physical calcium concentration. Images were read at the MESA CT reading center (Harbor-University of California Los Angeles).

The MESA scanning protocol has been described previously. Image sections were obtained with the participant supine, with no couch angulation, during a single breath hold. A minimum of 35 contiguous images was obtained, beginning above the left main coronary artery and proceeding below both ventricles. Section thickness of 3 mm, field of view of 35 cm, and matrix 512×512 were used to reconstruct the raw data. Nominal section thickness was 3.0 mm for electron beam CT and 2.5 mm for 4-detector row CT. Spatial resolution, expressed as the smallest voxel able to be discriminated, was 1.38 mm$^3$ (0.68×0.68×3.00 mm) for electron beam CT and 1.15 mm$^3$ (0.68×0.68×2.50 mm) for 4-detector row CT.

The ascending and descending thoracic aortas were visualized from the lower edge of the pulmonary artery bifurcation to the cardiac apex on each cardiac CT. TAC is defined as total calcification in the ascending plus the descending portions. For this study, TAC was considered both as a binary measure (present versus not present) and a continuous measure (Agatston score).

The reproducibility of extracoronary measures of calcification within MESA has been discussed in detail previously. To summarize for TAC, among 1729 randomly chosen participants undergoing rescanning on dual scanners, the intrascan $\kappa$ statistic for agreement on presence of TAC was 0.95 (95% CI: 0.94 to 0.97). This varied slightly by scanner type, with multidetector CT outperforming electron beam computed tomography (0.97 versus 0.94). The mean rescan percentage of absolute difference in Agatston score for measurement of TAC $>0$ was 10.2%. This variability is most likely attributed to slightly different starting points for the 2 scans, such that that slightly different anatomy may be examined in scan 1 and scan 2. The reproducibility of coronary artery calcium (CAC) within MESA has also been thoroughly described. The $\kappa$ statistic for agreement on the presence of CAC was 0.92, and the mean rescan percentage absolute difference in CAC $>0$ was 20.1%.

Study Covariates

Hypertension, smoking, diabetes mellitus, and family history of heart attack are presented as binary variables. Hypertension was defined as the use of antihypertensive medication or baseline sphygmomanometric measurements of blood pressure fulfilling the Joint National Committee guidelines (≥140/90 mm Hg identifying hypertension). Smoking was defined as previous or present use of tobacco cigarettes. Diabetes mellitus was defined according to American Diabetes Association guidelines (fasting blood sugar ≥126 mg/dL) or the use of hypoglycemic medications. Replacement of hypertension, smoking, and diabetes mellitus with absolute systolic and diastolic blood pressures, pack-years of smoking, and fasting blood glucose in the study models resulted in minimal change with no overall impact on study conclusions. Medication use was defined as the present use of prescription medications for the treatment of hypertension or hypercholesterolemia. Family history was positive if an immediate family member (parents, siblings, or children) had suffered a heart attack.

Statistical Analysis

Baseline characteristics of the study participants are presented over decreasing quartiles of DC (increasing carotid stiffness). The fourth quartile (most distensible) is used as the reference group for subsequent analyses. Frequencies and proportions are reported for categorical variables, and either means with SDs or medians with interquartile ranges are reported for continuous variables on the basis of the normality of distribution. $\chi^2$ tests, Fisher exact tests, 1-way ANOVA, or Kruskal–Wallis tests were used for the comparison of variables between groups.
Because the prevalence of CAC in our cohort was >10%, odds ratios overestimate the relative risk. Therefore, prevalence ratio estimates are presented from the regression model $y = \exp(X^T\beta)$, with the exponentiated parameter $\beta$ interpreted as the relative risk or prevalence ratio. Using this method, we assessed the relationship between DC and the presence of TAC in a hierarchal fashion. Model 1 adjusts for key demographic variables: age, sex, and race. Model 2 adds traditional and emerging cardiovascular risk factors: body mass index, heart rate, low-density lipoprotein cholesterol, hypertension, diabetes mellitus, cigarette smoking, family history of heart attack, and lipid-lowering medication use. Model 3 adds the inflammatory variable C-reactive protein and baseline measures of subclinical vascular disease: CAC and carotid IMT.

To better discern the influence of important study covariates, additional stratified analyses were conducted, with results expressed as the prevalence ratio of having TAC per 1-SD increase in DC. Finally, to explore differential correlations between DC and calcification of the thoracic aorta and coronary arteries, we constructed a Spearman correlation coefficient matrix among DC, TAC, and CAC. We used logarithmically transformed values of TAC and CAC (log-normal [score +1]) to normalize their distributions.

All of the analyses used a 5% 2-sided significance level. Calculations were performed using Stata software, version 8.2 (Stata Corp).

## Results

**Baseline Characteristics of the MESA Participants**

The mean age of the 6526 study participants was 62±10 years. Approximately 53% were men, with mean calculated 10-year Framingham risk for the entire cohort of 8.2±7.0%. Mean DC for the study cohort was 2.51 mm Hg, with a SD of 1.1×10⁻³ mm Hg. Median DC was 2.36×10⁻³ mm Hg reflecting a slight rightward skew. The mean and median DC values are similar to those reported in other studies after adjusting for differences in calculation.

Patients were divided into 4 categories on the basis of their values for DC (see Table 1). Across decreasing DC quartiles (increasing carotid stiffness), patients were, on average older, more likely to be women, and enriched in the black and Hispanic ethnicities. Most traditional and emerging cardiac risk factors were associated with decreasing DC, including body mass index, blood pressure, diabetes mellitus, smoking, and C-reactive protein. In addition, decreasing DC was associated with a higher prevalence of CAC, a higher CAC score, and higher carotid IMT (all $P<0.001$).
Prevalence of TAC by DC Quartile

The prevalence of TAC was 28% for the study cohort. Across all 4 of the ethnicities, there was a graded association between increasing DC quartile and decreasing prevalence of TAC ($P<0.001$; see Figure 1). The prevalence of TAC reached 61% among whites for quartile 1, the group with the stiffest arteries. The association between DC and TAC remained strong among blacks, the ethnicity known to have the lowest incidence of TAC.

Association Between DC and TAC Score

Considering only patients with a prevalent TAC (score $>0$), there remains a “dose-response” relationship between the DC quartile and TAC score (see Figure 2). From the least to the most distensible carotid artery quartile, the median TAC scores were 367, 275, 187, and 133, respectively ($P<0.001$). To better demonstrate this graded relationship, we examined median DC over quartiles of TAC score, retaining the large TAC=0 group as a distinct category (see Figure 3). Across all of the races, mean DC was higher among patients with no TAC ($P<0.001$), with a modest threshold effect for lower DC among individuals in the highest TAC score quartile. In linear regression analysis adjusting for age, race, and sex, 1 SD decrease in DC corresponded with a 12% relative increase in log-transformed TAC score ($P=0.008$).

Multivariable Regression Models

The results from 3 different regression models are presented in Table 2. Adjusted for demographic variables, the prevalence ratio for having TAC among the least distensible compared with the most distensible quartile was 1.79 (95% CI: 1.41 to 2.26). Adding cardiovascular risk factors to the model, the prevalence ratio was slightly attenuated to 1.52 (95% CI: 1.19 to 1.96). Adding measures of subclinical vascular disease resulted in little change, with a prevalence ratio of 1.52 (95% CI: 1.15 to 2.00). Further analyses including creatinine and fasting glucose in the model did not change these results.

Table 3 shows the results of stratified multivariable analyses examining the prevalence ratio for TAC with 1-SD change in DC (see Table 3). For the entire cohort, a 1-SD decrease in DC resulted in a 25% increase in TAC prevalence (95% CI: 1.12 to 1.41). In stratified analyses, individual risk factors did not have a major impact on this association, with numerous statistically significant associations and overlapping CIs. Associations between DC and TAC remained strong in middle-aged participants and individuals in the lower Framingham risk categories.

Correlation Between DC and Regional Calcification

Table 4 displays a stratified Spearman correlation matrix among DC, TAC, and CAC. All of the individual correlation coefficients were statistically significant at $P<0.001$. In general, the correlation between DC and calcification was the...
least strong among men and blacks. There was a tighter correlation between DC and TAC than between DC and CAC (0.315 versus 0.221; \( P < 0.001 \) for comparison of coefficients across the entire study population). This difference remained statistically significant in both sexes (women: \( P < 0.001 \); men: \( P < 0.01 \)) and all races (white: \( P < 0.001 \); Chinese: \( P < 0.03 \); black: \( P < 0.03 \); Hispanic: \( P < 0.008 \)).

**Supplementary Analysis**

To facilitate comparison with existing literature, we subsequently conducted exploratory analyses using YM, a measure of arterial elasticity, as well as a parameter indicating “distension” that was achieved by adjusting our primary analysis for pulse pressure. Results were similar to those seen with the analysis using DC. For YM quartile 4 (most elastic), there was a statistically significant 35% increase in TAC prevalence (95% CI: 1.02 to 1.80). After adjusting for pulse pressure, there remained a strong association between carotid distention and TAC. Point estimates of the association were slightly attenuated but remained statistically significant (Figures S1 and S2, please see the online Data Supplement, available athttp://hyper.ahajournals.org).

**Discussion**

In this large multiethnic cohort, we demonstrate a strong association between decreasing carotid distensibility (increasing carotid stiffness) and increasing prevalence of TAC, as well as a graded increase in TAC score. This association is independent of age, sex, race, and traditional and emerging cardiovascular risk factors, and importantly remains broadly applicable to low and intermediate Framingham risk groups. In addition, we demonstrate regional variability in the association with calcific atherosclerosis, with carotid DC more highly correlated with TAC than CAC.

**Distensibility Coefficient**

We chose the DC as a measure of stiffness because of its intuitive calculation, its common use in the epidemiological literature, and its use in the Rotterdam studies enabling a direct comparison of results. Prespecified analysis with a single index also avoids problems with “multiple looks” seen in studies that test every index of stiffness. We did subsequently conduct an exploratory analysis using YM, a measure of arterial elasticity, which revealed similar associations although less strong point estimates of risk (please see http://hyper.ahajournals.org). This pattern is consistent with previous studies relating these 2 indices.

Indices such as DC that rely on blood pressure have been criticized because of their reliance on pulse pressure, which is itself an independent predictor of cardiovascular risk. To adjust for the influence of pulse pressure, we repeated our analyses adjusting for this variable, resulting in attenuated but continued statistically significant associations (see http://hyper.ahajournals.org). After adjustments for pulse

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**Table 2. Multivariable-Adjusted Prevalence Ratio (95% CI) for TAC by Decreasing Quartile of DC**

<table>
<thead>
<tr>
<th>DC, Decreasing Quartiles, in 1/mm Hg x 10^3</th>
<th>Quartile 4 (( \geq 3.02 ))</th>
<th>Quartile 3 (2.36 to 3.01)</th>
<th>Quartile 2 (1.78 to 2.35)</th>
<th>Quartile 1 (( \leq 1.77 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>1 (ref group)</td>
<td>1.15 (0.90 to 1.47)</td>
<td>1.50 (1.19 to 1.89)</td>
<td>1.79 (1.41 to 2.26)</td>
</tr>
<tr>
<td>Model 2</td>
<td>1 (ref group)</td>
<td>1.17 (0.91 to 1.50)</td>
<td>1.43 (1.13 to 1.83)</td>
<td>1.52 (1.19 to 1.96)</td>
</tr>
<tr>
<td>Model 3</td>
<td>1 (ref group)</td>
<td>1.24 (0.95 to 1.64)</td>
<td>1.43 (1.09 to 1.87)</td>
<td>1.52 (1.15 to 2.00)</td>
</tr>
</tbody>
</table>

Model 1 was adjusted for age, sex, and race. Model 2 was model 1 + body mass index, heart rate, low-density lipoprotein cholesterol, hypertension, diabetes mellitus, cigarette smoking, family history of heart attack, and cholesterol-lowering medications. Model 3 was model 2 + log-transformed C-reactive protein, log-transformed CAC+1, and carotid IMT. ref indicates reference.
pressure, the stiffness parameter becomes more similar to a measure of carotid distention.\textsuperscript{20}

Although inversely correlated ($\rho < 0.25$), our study demonstrates that DC provides information that is independent of carotid IMT (see Table 2, model 3). This is consistent with previous studies.\textsuperscript{18,20} Both DC and carotid IMT can be calculated from the same longitudinal scanning sequence using a high-resolution ultrasound. This raises the possibility of combining these noninvasive measures for a more comprehensive evaluation of vascular disease.\textsuperscript{29}

Carotid Distensibility and Arterial Calcification

Why is DC more highly correlated with TAC than CAC?

There is increasing evidence that the determinants of calcification and atherosclerosis are different for different vascular beds.\textsuperscript{30} For example, studies by Nasir et al\textsuperscript{31} within MESA have shown that, whereas whites have more CAC than Chinese subjects, their burden of TAC is similar. Sex associations are reversed: although men have more CAC than women, women appear to have more TAC than men.\textsuperscript{31} This observation has been corroborated by Post et al\textsuperscript{32} with data from the Pennsylvania Amish, showing that male sex is associated with CAC and not TAC. In the Amish population, aging is more highly associated with TAC. CAC and TAC are in fact loosely correlated before the age of 50 years ($\rho=0.135$).

### Table 3. Prevalence Ratio (95% CI) for TAC With 1-SD Decrease in DC

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>No. With TAC $&gt;0$</th>
<th>Relative Risk (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Tertile 1 (45 to 56 y)</td>
<td>2239</td>
<td>107</td>
<td>1.58 (0.70 to 3.57)</td>
<td>0.27</td>
</tr>
<tr>
<td>Tertile 2 (57 to 67 y)</td>
<td>2125</td>
<td>480</td>
<td>1.15 (0.97 to 1.36)</td>
<td>0.10</td>
</tr>
<tr>
<td>Tertile 3 (68 to 84 y)</td>
<td>2162</td>
<td>1239</td>
<td>1.33 (1.14 to 1.55)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex Women</td>
<td>3427</td>
<td>992</td>
<td>1.30 (1.10 to 1.54)*</td>
<td>0.002</td>
</tr>
<tr>
<td>Men</td>
<td>3099</td>
<td>834</td>
<td>1.21 (1.03 to 1.41)*</td>
<td>0.017</td>
</tr>
<tr>
<td>Race White</td>
<td>2517</td>
<td>814</td>
<td>1.27 (1.10 to 1.47)*</td>
<td>0.001</td>
</tr>
<tr>
<td>Chinese</td>
<td>783</td>
<td>252</td>
<td>1.24 (0.89 to 1.73)</td>
<td>0.21</td>
</tr>
<tr>
<td>Black</td>
<td>1779</td>
<td>401</td>
<td>1.17 (0.85 to 1.61)</td>
<td>0.34</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1447</td>
<td>359</td>
<td>1.32 (0.96 to 1.82)</td>
<td>0.09</td>
</tr>
<tr>
<td>Risk factor status Normotensive</td>
<td>3613</td>
<td>651</td>
<td>1.34 (1.14 to 1.58)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2913</td>
<td>1175</td>
<td>1.21 (1.02 to 1.43)*</td>
<td>0.03</td>
</tr>
<tr>
<td>Nondiabetic</td>
<td>5605</td>
<td>1482</td>
<td>1.23 (1.09 to 1.39)*</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>921</td>
<td>334</td>
<td>1.46 (1.10 to 1.94)*</td>
<td>0.008</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>5681</td>
<td>1602</td>
<td>1.27 (1.12 to 1.45)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>845</td>
<td>224</td>
<td>1.22 (0.97 to 1.54)</td>
<td>0.09</td>
</tr>
<tr>
<td>Framingham risk score† Low (0% to 6%)</td>
<td>2890</td>
<td>414</td>
<td>1.30 (1.05 to 1.63)*</td>
<td>0.02</td>
</tr>
<tr>
<td>Intermediate (6% to 20%)</td>
<td>2570</td>
<td>806</td>
<td>1.21 (1.03 to 1.44)*</td>
<td>0.03</td>
</tr>
<tr>
<td>High ($&gt;20%$)</td>
<td>1066</td>
<td>606</td>
<td>1.12 (0.85 to 1.47)</td>
<td>0.42</td>
</tr>
<tr>
<td>Total</td>
<td>6526</td>
<td>1826</td>
<td>1.25 (1.12 to 1.41)*</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

$SD=1.1 \times 10^{-3}$ mm Hg. Data were adjusted for age tertile, sex, race, body mass index, heart rate, low-density lipoprotein cholesterol, hypertension, diabetes mellitus, smoking, family history of heart attack, cholesterol-lowering medications, transformed C-reactive protein, log-transformed CAC, and carotid IMT when not first stratifying by these variables.

*Association was statistically significant ($P<0.05$).

†Data were adjusted for age tertile, sex, race, body mass index, heart rate, diabetes mellitus, family history of heart attack, cholesterol-lowering medications, transformed C-reactive protein, log-transformed CAC, and carotid IMT.

### Table 4. Correlation Among DC, CAC, and TAC

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>$\rho$ DC, TAC</th>
<th>$\rho$ DC, CAC</th>
<th>$\rho$ TAC, CAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>$-0.349$</td>
<td>$-0.271$</td>
<td>0.487</td>
</tr>
<tr>
<td>Men</td>
<td>$-0.275$</td>
<td>$-0.214$</td>
<td>0.441</td>
</tr>
<tr>
<td>White</td>
<td>$-0.374$</td>
<td>$-0.279$</td>
<td>0.450</td>
</tr>
<tr>
<td>Chinese</td>
<td>$-0.361$</td>
<td>$-0.261$</td>
<td>0.441</td>
</tr>
<tr>
<td>Black</td>
<td>$-0.243$</td>
<td>$-0.172$</td>
<td>0.387</td>
</tr>
<tr>
<td>Hispanic</td>
<td>$-0.358$</td>
<td>$-0.269$</td>
<td>0.454</td>
</tr>
</tbody>
</table>

CAC and TAC are defined as continuous variables by the following equation: natural log (calcification score +1). All of the individual correlations are significant at $P<0.001$. $P<0.001$ for $\rho$ DC, TAC vs $\rho$ DC, CAC for the entire population ($\rho=0.315$ vs $-0.221$). Difference remains significant across both sexes ($P<0.01$) and all races: whites ($P<0.001$), Chinese ($P=0.03$), black ($P=0.03$), and Hispanic ($P=0.008$).
There are likely distinct features characterizing the pathophysiology of calcification within the thoracic aorta versus the coronary arteries. Histological studies demonstrate that calcification of the coronary arteries is largely confined to the intimal layer. However, within the large arteries, including the aorta, calcification can be present both in the intima and tunica media. Medial calcification is more strongly associated with aging, diabetes mellitus, and severe renal disease. Structural features of different vascular beds likely also play a role. The elastic carotid artery can be considered structurally more similar to central arteries (such as the aorta) than the nonelastic predominantly conduit coronary arteries, perhaps contributing to the tighter correlation.

Although CAC is a well-established predictor of cardiovascular events, TAC has been less thoroughly studied with regard to cardiovascular outcomes. TAC measured by plain radiography and transesophageal echocardiography has a well-established correlation with obstructive coronary disease. TAC measured by CT is highly correlated with CAC and predicts the incidence and progression of CAC. Among patients with stable angina pectoris, TAC is an independent predictor of adverse cardiovascular events. However, among 2304 asymptomatic self-referred adults, TAC failed to predict events beyond the Framingham risk score and beyond CAC. A total of 31% of patients (724 total patients) had measurable TAC in this study, likely limiting its clinical application.

The second major limitation is the use of brachial pulse pressure rather than a direct measurement of carotid pulse pressure. Peripherally, such as the brachial artery, have pressure wave reflection sites that are closer than for central arteries. Reflected waves travel faster on peripheral arteries, which are stiffer, than on the elastic central arteries, which, in asymptomatic patients, are more elastic. Because of this “amplification phenomenon,” the pulse pressure in the brachial artery will be higher than in the carotid artery, which may lead to systematic underestimation of the association between stiffness and adverse events.

Perspectives
The results of this study suggest that noninvasive ultrasound measurements of carotid artery stiffness demonstrate a dose-response association with calcification of the thoracic aorta. The independence of this relationship from carotid IMT, in addition to the greater association with TAC compared with CAC, raises important mechanistic questions and highlights the complexity of the interplay among stiffening, calcinosis, and atherosclerosis. In the future, a combination of these measurements may provide the most comprehensive evaluation of subclinical vascular disease. To evaluate the prognostic significance of these relationships, we have planned longitudinal studies within MESA.

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Relationship of Carotid Distensibility and Thoracic Aorta Calcification: Multi-Ethnic Study of Atherosclerosis
Michael J. Blaha, Matthew J. Budoff, Juan J. Rivera, Ronit Katz, Daniel H. O'Leary, Joseph F. Polak, Junichiro Takasu, Roger S. Blumenthal and Khurram Nasir

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The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/54/6/1408

Data Supplement (unedited) at:
http://hyper.ahajournals.org/content/suppl/2009/10/05/HYPERTENSIONAHA.109.138396.DC1
Supplemental data for online publication
SUPPLEMENTAL TABLES

S1.

<table>
<thead>
<tr>
<th>Prevalence Ratio for TAC</th>
<th>Young’s Modulus (increasing quartiles)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quartile 1 (≤897)</td>
</tr>
<tr>
<td>Model</td>
<td>1 (ref group)</td>
</tr>
<tr>
<td></td>
<td>Quartile 3 (1176-1532)</td>
</tr>
<tr>
<td></td>
<td>1.13 (0.90-1.42)</td>
</tr>
</tbody>
</table>

**Model:** Adjusted for age, gender, and race, body mass index, heart rate, LDL cholesterol, hypertension, diabetes mellitus, cigarette smoking, family history of heart attack, cholesterol-lowering medications, log transformed C-reactive protein, log transformed CAC+1, carotid IMT.

Young's modulus: \[ \frac{D \Delta P}{\Delta D h} \]

S2.

<table>
<thead>
<tr>
<th>Prevalence Ratio for TAC</th>
<th>Distensibility Coefficient (decreasing quartiles, in 1/mmHg x 10^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quartile 4 (≥3.02)</td>
</tr>
<tr>
<td>Model</td>
<td>1 (ref group)</td>
</tr>
</tbody>
</table>

**Model 1:** Adjusted for pulse pressure, age, gender, race, body mass index, heart rate, LDL cholesterol, hypertension, diabetes mellitus, cigarette smoking, family history of heart attack, cholesterol-lowering medications, log transformed C-reactive protein, log transformed CAC+1, carotid IMT.