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Using MRI to Assess Aortic Wall Thickness in the Multiethnic Study of Atherosclerosis: Distribution by Race, Sex, and Age

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OBJECTIVE. Understanding the determinants of subclinical atherosclerosis may aid in elucidating the pathogenesis of atherosclerosis and guide prevention strategies. In this pilot study, we investigated the role of aortic wall thickness as a measure of subclinical atherosclerosis, assessed a method by which to measure aortic wall thickness using MRI, and attempted to define differences in aortic wall thickness by patient race, sex, and age.

SUBJECTS AND METHODS. In this prospective study, 196 participants (99 black, 97 white; 98 men, 98 women) were selected from the Multiethnic Study of Atherosclerosis, which consists of participants 45–84 years old without clinical cardiovascular disease, who were recruited from six study centers in the United States. We performed fast spin-echo double inversion recovery MRI to measure thoracic aortic wall thickness. We tested interobserver agreement using the intraclass correlation coefficient, for sex and race differences in wall thickness using the Mann-Whitney test, and for associations between age and wall thickness using linear regression.

RESULTS. Reproducibility was excellent for measurements of average and maximal wall thickness on MRI. Average and maximal wall thickness increased with age ($p < 0.001$ and $p = 0.002$, respectively). Men had greater mean average wall thickness (2.32 vs 2.11 mm, $p = 0.028$) and mean maximal wall thickness (3.85 vs 3.31 mm, $p = 0.010$) than women. Blacks had greater mean maximal wall thickness than whites (3.74 vs 3.42 mm, $p = 0.023$).

CONCLUSION. MRI is a feasible method to measure aortic wall thickness with high interobserver agreement. Aortic wall thickness increases with age and also varies by race and sex.

Measurements of arterial wall thickness have proven useful in predicting cardiovascular disease risk. This correlation has been most extensively studied in several large prospective studies that showed increased medial thickness of the carotid intima as an independent risk factor for overt coronary artery disease and stroke [1–5]. It is hypothesized that increased carotid arterial wall thickness in asymptomatic participants represents subclinical cardiovascular disease and that conventional atherosclerotic risk factors would contribute to progressive thickening. Indeed, conventional risk factors have been shown to positively correlate with carotid wall thickness in multiple previous studies [6–9]. Many of these studies, as well as the recently initiated Multiethnic Study of Atherosclerosis [10], were in part designed to evaluate objective measurements of subclinical cardiovascular disease, given that such measurements may increase power to detect risk associations and may also provide a relatively undistorted picture of the early pathogenesis of clinical disease.

Relative to the medial thickness of the carotid intima, the thickness of the aortic wall has not been as extensively investigated, and normal values have not been established. In particular, aortic wall thickness distribution by age, sex, and race has not been studied in a population-based multiethnic cohort without clinical cardiovascular disease. MRI is a noninvasive imaging technique that has been shown to provide accurate arterial wall measurements and reproducible assessments of aortic anatomy [11–16]. In this prospective pilot study of 196 participants selected from the Multiethnic Study of Atherosclerosis cohort, we describe an MRI protocol to measure the thoracic aortic wall and explore the relationship between aortic wall thickness and patient race, sex, and age.

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Subjects and Methods

Subjects

The Multiethnic Study of Atherosclerosis is a population-based sample of 6,814 men and women who are 45–84 years old. These participants, who showed no clinical evidence of cardiovascular disease, were recruited from six communities in the United States (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; New York, NY; and St. Paul, MN). Approximately 40% of the cohort is white, 30% black, 20% hispanic, and 10% Asian. The study's primary objective was to determine the characteristics related to progression of subclinical cardiovascular disease.

For this prospective study, 196 consecutive subjects—who were selected until the study cohort consisted of approximately 25% white women, 25% black women, 25% white men, and 25% black men—were enrolled after July 2000. Subjects were selected from all six of the participating field centers (Johns Hopkins University, Northwestern University, Wake Forest University, University of California at Los Angeles, Columbia University, and University of Minnesota). The institutional review boards at each of the six field centers approved the study. Informed consent was obtained from all study subjects.

MRI

MRI was performed with one of four 1.5-T whole-body MRI systems: Signa CV/i (General Electric Medical Systems, Waukesha, WI), Signa LX (General Electric Medical Systems), Vision (Siemens, Munich, Germany), or Symphony (Siemens). A four-element phased array torso coil was placed anteriorly and posteriorly. Images were obtained using a double inversion recovery black blood fast spin-echo sequence [12] with ECG gating. Axial images of the descending thoracic aorta were obtained at the level of the right pulmonary artery. Imaging parameters were TR, 2 R-R intervals; TE, 42; field of view, 40 cm; slice thickness, 4 mm; echo-train length, 32; and receiver bandwidth, 62.5 kHz.

TABLE 1 Descriptive Statistics from 100 Subjects of Aortic Wall Thickness as Measured by Two Observers

Wall Thickness	Mean	SD	Minimum	Maximal
Average (mm)				
Observer 1	2.23	0.48	1.50	4.76
Observer 2	2.22	0.49	1.52	4.79
Maximal (mm)				
Observer 1	3.82	1.10	2.23	8.94
Observer 2	3.82	1.14	2.14	9.97

Wall Thickness Analysis of MRI Data

Wall measurements were performed by a radiologist (observer 1) using the Magnetic Resonance Analytical Software System (MASS) version 4.1 beta (Medis, Leiden, The Netherlands). Images were magnified to 450%. The gray scale was inverted to suppress periaortic fat. Window width was between 350 and 400; image contrast was 40–55; image brightness was 25–35 (arbitrary units set by software manufacturer). These settings optimized wall visualization. Aortic wall measurements were taken perpendicular to the center of the vessel lumen using electronic calipers at four standard positions: 12, 3, 6, and 9 o'clock. The average value of these four measurements was then calculated. In addition, the maximal wall thickness was measured three times for each slice, and the average of these three measurements was used. For interobserver variability analysis, wall measurements were performed on a subset of 100 subjects by a second radiologist (observer 2) who was unaware of the results of wall thickness measurements taken by observer 1 for these same subjects. In addition, both observers were blinded to the race, sex, and age of the study subjects. Both observers also attended an observer training session on 15 cases not included in the study before reviewing the study cases.

Statistical Analysis

The reproducibility of the average and maximum aortic wall thickness measurements is summarized by the intraclass correlation coefficient. Sex, race, and scanner platform differences in the distribution of aortic wall thickness measurements were tested for statistical significance with the Mann-Whitney test, which is a nonparametric equivalent to the independent sample *t* test. Simple linear regression was used to assess the association between age and aortic wall thickness. Average and maximal wall thicknesses were adjusted for height and weight by fitting multiple linear regression models predicting wall thicknesses with height, weight, and one of the demographic variables (race, sex, or age). Finally, multiple linear regression models were used to test for interactions between wall thickness and race, sex, age, or scanner platform.

Results

We prospectively analyzed the reproducibility of aortic wall thickness measurements in a subset of 100 subjects whose aortic MR images were interpreted independently by two observers. Table 1 provides descriptive statistics for the measurements by observer. The wall thickness measurements from observer 1 are plotted against those from observer 2 in Figures 1 and 2. A high degree of agreement is apparent for both the average and maximal aortic wall thickness. The intraclass correlation coefficient is 0.980 (95% confidence interval

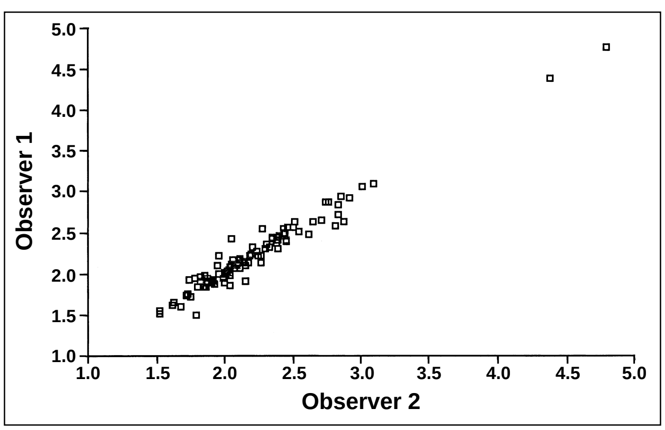

Fig. 1.—Scatterplot shows average wall thickness (in millimeters) as measured by observer 1 plotted against measurements by observer 2. Subset of 100 subjects was used for analysis. Note excellent agreement between two observers.

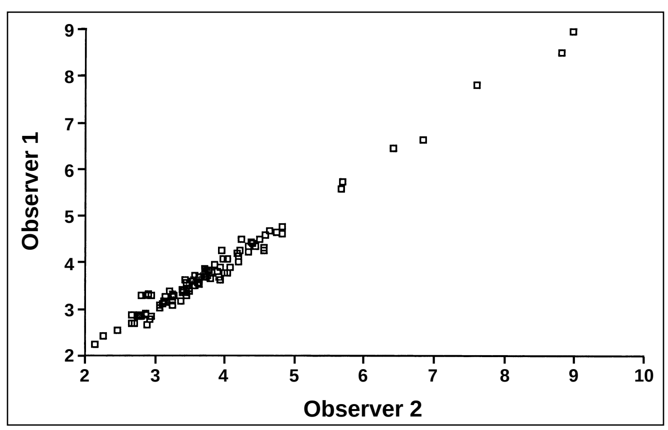

Fig. 2.—Scatterplot shows maximal wall thickness (in millimeters) as measured by observer 1 plotted against measurements by observer 2. Subset of 100 subjects was used for analysis. Note excellent interobserver agreement between two observers.

[CI]: 0.970–0.986) for average wall thickness and 0.991 (95% CI: 0.987–0.994) for maximal wall thickness, indicating that the variability in measurements due to the observer is very small relative to the overall variability. For each pair of interpretations, the arithmetic difference (observer 1 – observer 2) and the absolute difference (absolute value of the arithmetic difference) were computed. These differences are summarized in Table 2. The mean absolute differences in measurements of average and maximal wall thicknesses were 0.07 and 0.11 mm, respectively.

The distributions of average and maximal aortic wall thickness measurements are summarized in Table 3 by sex, race, and 10-year age groups. Men tended to have higher average wall thickness measurements (2.32 mm) than women (2.11 mm) ($p = 0.028$). Men also had higher mean maximal wall thickness (3.85 mm) than women (3.31 mm) ($p = 0.010$). Blacks tended to have higher mean maximal wall thickness (3.74 mm) relative to whites (3.42 mm) ($p = 0.023$).

When wall thickness was plotted against age, with a line fitted by linear regression for both average and maximal wall thicknesses, linear regression analysis suggested that age is positively associated with both average ($p < 0.001$) and maximal ($p = 0.002$) wall thickness (Figs. 3 and 4). A 5-year increase in age is associated with a 0.07-mm increase in average wall thickness and a 0.10-mm increase in maximal wall thickness.

Multivariate linear regression was used to test for interactions between the race, sex, age, and scanner platform effects on wall thickness. No interactions were found to be statistically significant. There was no significant difference in average wall thickness by scanner platform between subjects scanned on a General Electric Medical Systems (2.24 mm) versus a Siemens (2.16 mm) scanner ($p = 0.25$).

Discussion

Our MRI-based method of measuring aortic wall thickness achieved high interobserver agreement. In a multiethnic population-based cohort, we also presented the distribution of aortic wall thickness by race, sex, and age. Both average and maximal wall thickness increased with age. This finding is consistent with multiple previous studies of carotid and aortic plaque burden [1, 13, 17–19], as well as electron beam CT studies of coronary calcifications [20], which established age as a powerful predictor of subclinical atherosclerotic disease.

In our study, men had greater average and maximal wall thickness than women. An excess of coronary death rates among men in all age groups has been documented [21, 22]; hence, it is expected that measurements of subclinical atherosclerotic disease would be higher among men. Previous investigations of carotid wall thickness and plaque burden, including those of Howard et al. [17] and Joakimsen et al. [18], found increased wall thickness and plaque burden among men. In the study of Joakimsen et al., the male predominance in atherosclerotic burden declined after age 50. A similar trend was seen in aortic plaque burden in the study of Jaffer et al. [13], in which atherosclerotic lesions in women over 70 years old exceeded those of men over 70 years old. Although we did not find this latter trend among our participants (data unpublished), subjects in the highest age group were disproportionately underrepresented in our cohort.

Our study also showed that blacks had greater maximal wall thickness than did whites, although there was no statistically significant difference between blacks and whites in average wall thickness. Maximal wall thickness is a reflection of plaque formation, which is nonuniform. Similarly, O'Leary et al. [4] found that maximal rather than average wall thickness was the key variable that was directly associated with cardiovascular events. Other researchers have found that blacks have a higher incidence of stroke [23] and higher mortality rates from cardiovascular disease [24] than whites. Hence, our finding that maximal aortic wall thickness is higher among blacks would suggest that maximal aortic wall thickness potentially might correlate with cardiovascular events, although testing of this hypothesis awaits longitudinal follow-up studies.

To our knowledge, no previous study has described differences in aortic wall thickness by race. However, racial differences in carotid plaque burden and wall thickness have been investigated. In the study by Li et al. [25] of 15,124 participants, whites were found to have significantly more carotid plaque lesions with acoustic shadowing than blacks. Similarly, Schreiner et al. [26] found that white men have greater carotid wall thickness than black men, although this relationship was reversed among women. However, in a smaller study of 526

TABLE 2 Descriptive Statistics of Differences Between Observer Measurements

Wall Thickness	Mean	SD	Minimum	Maximal
Average (mm)				
Arithmetic difference	0.01	0.10	–0.29	0.36
Absolute difference	0.07	0.07	0.00	0.36
Maximal (mm)				
Arithmetic difference	0.003	0.15	–0.32	0.50
Absolute difference	0.11	0.10	0.00	0.50

Note.—Arithmetic difference = observer 1 measurement – observer 2 measurement, absolute difference = absolute value (arithmetic difference).

TABLE 3 Descriptive Statistics of Wall Thickness Measurements by Sex, Race, and Age

Patient Demographics	No. of Subjects	Average Wall Thickness (mm)		Maximal Wall Thickness (mm)	
		Mean (SE)	*p*	Mean (SE)	*p*
Sex			0.028		0.010
Men	98	2.32 (0.06)		3.85 (0.13)	
Women	98	2.11 (0.06)		3.31 (0.13)	
Race			0.061		0.023
Black	99	2.15 (0.05)		3.74 (0.10)	
White	97	2.27 (0.05)		3.42 (0.10)	
Age range (yr)			< 0.001		0.002
45–54	66	2.03 (0.05)		3.33 (0.12)	
55–64	52	2.18 (0.06)		3.61 (0.13)	
65–74	39	2.26 (0.07)		3.56 (0.15)	
74–84	39	2.51 (0.07)		3.98 (0.16)	

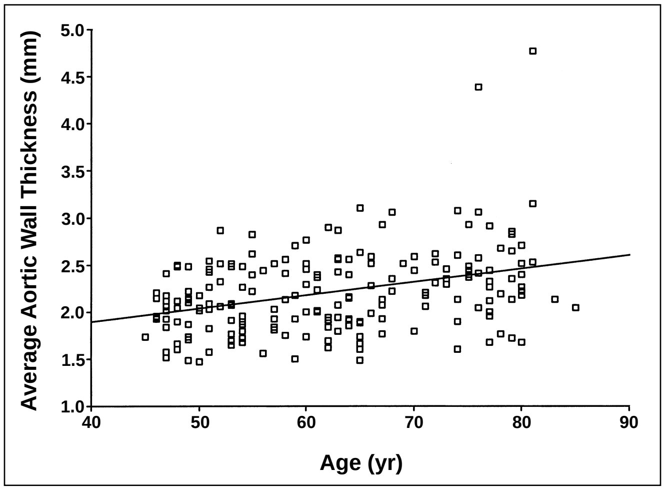

Fig. 3.—Scatterplot shows average wall thickness (in millimeters) for 196 subjects plotted against age. Line fitted by linear regression is also plotted. Note that average aortic wall thickness increases with age. Five-year increase in age is associated with 0.07-mm increase in average wall thickness.

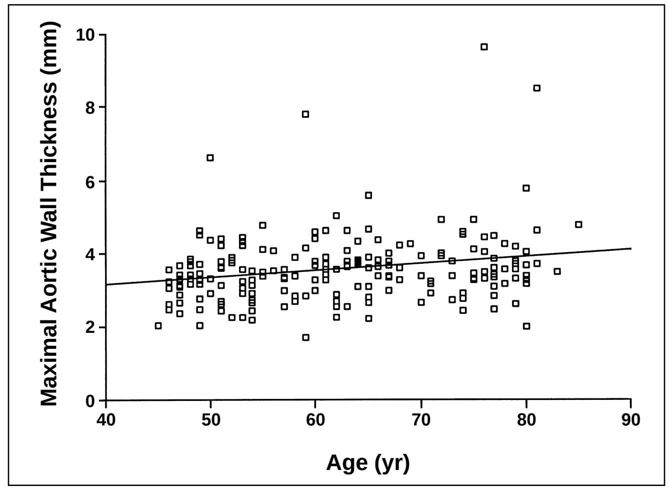

Fig. 4.—Scatterplot shows maximal wall thickness (in millimeters) for 196 subjects plotted against age. Line fitted by linear regression is also plotted. Note that maximal wall thickness increases with age. Five-year increase in age is associated with 0.10-mm increase in maximal wall thickness.

participants from New York, Sacco et al. [27] found no differences in carotid wall thickness for blacks and whites, although interestingly, hispanics had significantly decreased wall thickness. The reasons for these racial differences in wall thickness probably are the result of multiple genetic, acquired, and socioeconomic factors. For instance, other investigators have found that low income [28] and Medicaid status [27] are associated with increased carotid atherosclerosis, perhaps because of decreased access to adequate treatment. Overall, blacks have higher rates of hypertension and diabetes [29, 30]; hence, racial differences in cardiovascular risk factor burdens may also partially explain differences in arterial wall thickness. In our pilot study, we were unable to incorporate multivariate analysis to control for the effects of risk factors and socioeconomic status because unfortunately these items were not yet fully coded in the Multiethnic Study of Atherosclerosis database at the time of our analyses. However, if in future studies race is found to be an independent predictor of aortic wall thickness, it might be interesting to speculate on genetic explanations for racial differences in wall thickness. One group of researchers has suggested that genes account for 74.9% of phenotypic variation in internal carotid artery wall thickness [31]. Elucidating the factors behind the differences in subclinical disease among different racial groups remains an important area for future investigation.

Our study was designed as a pilot study to determine optimal methods, reproducibility, and potential areas of future investigation. Hence, the number of study subjects was small, and we were unable to conduct subgroup analyses stratifying by sex and race. This issue could be resolved in future studies with larger numbers of subjects. Also, we obtained only one slice of the midthoracic aorta, rather than a more representative sampling of both the thoracic and abdominal aorta. Our approach nevertheless yielded enough data to analyze basic trends that were inherent in our study population. As a final limitation, we did not use fat saturation to acquire images of the aortas. Subsequent to the design of our pilot study, fat saturation has been found useful when characterizing components of plaque in the arterial wall. Despite our not using fat saturation, image quality allowed excellent interobserver agreement.

In conclusion, in a prospective pilot study of 196 participants from the Multiethnic Study of Atherosclerosis cohort, we found that MRI can reliably reveal aortic wall thickness, and our data show that aortic wall thickness varies by race, sex, and age. Further investigations with more subjects are required to delineate the relationship between aortic wall thickness and subclinical disease (e.g., determining what constitutes "normal" vs "abnormal" aortic wall thickness) and the factors underlying the different associations of race and sex inherent to this relationship. In addition, longitudinal follow-up studies may help determine whether aortic wall thickness can be used to predict cardiovascular events.

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