B-Mode-Detected Carotid Artery Plaque in a General Population

Rongling Li, MD; Bruce B. Duncan, MD, PhD; Patricia A. Metcalf, PhD; John R. Crouse III, MD; A. Richey Sharrett, MD, DrPH; H.A. Tyroler, MD; Ralph Barnes, PhD; Gerardo Heiss, MD, PhD; for the Atherosclerosis Risk in Communities (ARIC) Study Investigators

Background and Purpose There is little information on the distribution of atherosclerotic lesions of the extracranial carotid artery wall in free-living populations. The purpose of the present study was to describe the prevalence from 1987 through 1989 of extracranial carotid artery plaque and plaque with acoustic attenuation (shadowing) lesions in a general population of white and black adults from four US communities.

Methods B-mode ultrasound was used to characterize wall lesions in the common and internal carotid arteries and at the carotid artery bifurcation in 14,046 men and women 45 to 64 years old who participated in the Atherosclerosis Risk in Communities Study baseline survey.

Results Thirty-four percent of participants had plaque and 6.4% had plaque with acoustic shadowing. The prevalence of plaque with acoustic shadowing increased steadily with age from 2.5% at ages 45 to 49 to 12.4% at ages 60 to 64. Overall, whites had more plaque with acoustic shadowing lesions than blacks (odds ratio [OR], 1.22; 95% confidence interval [CI], 1.02 to 1.46), and men had more than women (OR, 1.42; 95% CI, 1.22 to 1.63). However, plaque lesions in the common carotid artery were less common among whites than among blacks, and no racial difference was observed in the prevalence of plaque with acoustic shadowing at this segment.

Conclusions Although these prevalence rates are likely to be underestimated because of the emphasis on arterial boundary visualization of the scanning protocol, they show a large, mostly asymptomatic burden of atherosclerosis in these populations, especially among older individuals. Site-specific frequency rates of plaque varied between blacks and whites. Among those with plaque, however, whites had more lesions with acoustic shadowing attenuation. (Stroke. 1994;25:2377-2383.)

Key Words • atherosclerosis • carotid arteries • epidemiology • racial differences • ultrasonics

B-mode ultrasound examination of the extracranial carotid artery permits a noninvasive characterization of atherosclerosis. Much of the current emphasis in population-based research has been on refining quantitatively the information obtainable from B-mode ultrasound. Yet, given the complex nature of the atherosclerotic process and its nonuniform nature throughout the arteries of a given individual, its qualitative characterization may provide information complementary to that of the more sophisticated quantitative measurements such as intimal-medial wall thickness and lumen diameter. Qualitatively, one may define the presence of a lesion ("plaque") by means of a threshold of wall thickness criterion, a lumen encroachment feature, irregular intimal surfaces, and/or image characteristics reflective of structural heterogeneity of the arterial wall. The presence of sono-opaque structures ("acoustic shadowing") in the arterial wall, which is indicative of mineral deposits,1 adds an element to the definition of arterial lesions detected by B-mode ultrasound imaging. Although not a requisite characteristic of an arterial lesion, the presence of acoustic shadowing can be taken as an indicator of the complexity or advanced nature of atherosclerotic involvement.

There is little information2-5 on the frequency and distribution of qualitatively defined carotid lesions in populations not referred for study on the basis of cardiovascular disease or its symptoms. Data from studies of community-based representative samples of adults6 are especially scarce. Data on the prevalence of these qualitative lesions in free-living populations not selected by disease may eventually be of use in clinical and public health decision making. Such information, for example, places a perspective on carotid artery findings seen in clinical settings, as well as contributes to our knowledge of the process of atherosclerosis.

The Atherosclerosis Risk in Communities (ARIC) Study performed B-mode ultrasound examination of the extracranial carotid artery system in more than 14,000 individuals 45 to 64 years old. The purpose of the present study was to describe the prevalence of ultrasoundographically detected carotid artery plaque and plaque with acoustic shadowing in a general population from four communities in the United States and to determine the distribution of these findings by age, sex, and race.

Subjects and Methods

The ARIC Study is an investigation of atherosclerosis and clinical atherosclerotic disease in four US communities: For-
system County, NC; Jackson, Miss; the northwestern suburbs of Minneapolis, Minn; and Washington County, Md. One aspect of the study involves examination and follow-up of 15,800 individuals 45 to 64 years old. The cohort was selected by probability sampling from each community. To ensure that estimates could be made by race, blacks were oversampled in Forsyth County and exclusively sampled in Jackson, whereas sampling was conducted without consideration of race in the other two communities. Details of the complete study design, sampling strategy, and examination techniques have been published. Overall response rates were 66%, 46%, 67%, and 65% in Forsyth County and Jackson, respectively. Institutional review board approval was obtained, and renewed yearly, for the study at all collaborating institutions. Informed consent was obtained from all study participants before their participation.

Of the 15,800 individuals enrolled in ARIC, 387 did not complete the ultrasound examination; 1313 had unread scans at the time of these analyses; 46 were Native American, Asian, or of unknown race; 4 were of an age that was outside the stated range; and 4 had missing ultrasound reader information. Therefore, these analyses are based on information related to 14,046 individuals.

Analyses of the presence of plaque or plaque with acoustic shadowing lesions at any site were performed only on the 13,766 individuals for whom there were complete information for plaque and acoustic shadowing readings for all segments of the left carotid artery, the right carotid artery, or both. Carotid artery atherosclerosis was determined by high-resolution B-mode ultrasound following a uniform protocol standardized across the four field centers and processed at a central reading center according to a standardized protocol.

The extracranial carotid arteries were divided into three segments: the distal 1.0-cm straight portion of the common carotid artery, the carotid bifurcation, and the proximal 1.0 cm of the internal carotid artery, and they were scanned bilaterally using standardized angles. To provide equal representation of readings across sites, only the lateral scans ("optimal angle" views) were used for the common carotid artery.

All ultrasound scans were obtained by sonographers trained and certified in the ARIC protocol, which outlines a series of scanning steps standardized for angle of interrogation, arterial segment, and optimization of the leading edge of the intimal-medial boundaries. The presence of arterial lesions did not lead to a deviation from the scanning protocol and was addressed by the sonographer only for participant safety considerations (on a separate copy of the videotape). All scans were processed at the ARIC Ultrasound Reading Center by readers trained to achieve a high degree of proficiency and repeatability in reading arterial intimal-medial wall thickness measurements. Reader training usually required 3 months and was followed by certification, and reader performance was monitored through the use of a comprehensive quality assurance program.

Although readings were primarily aimed at the measurement of the intimal-medial thickness in each segment, readers also indicated the presence of a lesion (plaque) and acoustic shadowing if located in any of the 1-cm segments read for each participant (common carotid, area of bifurcation, and internal carotid, bilaterally). Readers recorded the presence of a lesion if two of the following three conditions were met: (1) wall shape (protrusion into the lumen, loss of alignment with adjacent arterial boundary, roughness of the arterial boundary), (2) wall texture (brighter echoes than adjacent boundaries), and (3) wall thickness (intimal-medial thickness ≥1.5 mm, ie, approximately 22 pixels). Because it is not uncommon to observe a lack of definition of the arterial boundary echoes required for measurement of the intimal-medial space in the area of an arterial lesion, the latter criterion (thickness ≥1.5 mm) could be based on an estimate.

Readers were not clinically trained or prepared to recognize special qualitative features of arterial plaque lesions visualized by B-mode ultrasound such as heterogeneity or intraplaque hemorrhage. The recognition of acoustic shadowing, defined as the reduction in amplitude of echoes caused by intervening structures with high attenuation, was an element of the reading protocol included in the reader's training and was recorded independently. Acoustic shadowing is indicative of mineral deposits within the plaque and clinically is assumed to be suggestive of prior intraplaque hemorrhage. Unless otherwise stated, the category "plaque" includes lesions with acoustic shadowing.

Prevalent coronary heart disease was defined as (1) the presence on ECG of major Q waves (Minnesota codes 1.1.1 through 1.1.7) or minor Q waves with ST or T-wave changes (codes 1.2.1 through 1.2.8 with 4.1.1, 4.1.2, 4.2, 5.1, or 5.2) in the absence of intraventricular conduction disturbances interfering with the Q-wave readings (codes 7.1.1, 7.1.2, or 7.4) or (2) a self-report of physician-diagnosed myocardial infarction or of coronary artery bypass graft surgery or balloon angioplasty.

Intrarreader and interreader evaluations of B-mode ultrasound scans were assessed by randomly selecting 483 and 671 scans, respectively, for rereading. These scans were returned to the same reader or given to another reader in a blinded fashion. Concordance of information was evaluated with the κ statistic, which reflects the extent to which the observed agreement between the two readings is in excess of that expected by chance. Statistical differences in sample distributions of wall thickness among those without lesions, those presenting with plaque, and those with plaque with acoustic shadowing were evaluated through \( \chi^2 \) testing.

Multivariable adjusted odds ratios (OR) were estimated through logistic regression with SAS. All models included variables for age, race, sex, ultrasound reader, and date of ultrasound reading.

Results

Intrarreader and interreader agreement regarding the presence of plaque with and without acoustic shadowing in individual segments was fair to excellent, as expressed by κ, which varied from .59 to .82 and from .33 to .69, respectively. For intrarreader agreement for the presence or absence of plaque in any of the six artery segments, κ was .76; for interreader agreement, κ was .56. According to the criteria of Landis and Koch, \( \kappa \) values in our study generally fell in the range of good agreement beyond chance (\( 0.40 \leq \kappa \leq 0.75 \)).

The lower prevalence of plaque with acoustic shadowing limited the ability to assess agreement at individual sites. At the carotid bifurcation, where prevalence rates were higher, intrarreader agreement was .78 and .68 for the left and right sides, respectively, and interreader agreement was .41 and .45, respectively. κ for intrarreader agreement on the presence or absence of plaque with acoustic shadowing in any of the six segments was .76, and for interreader agreement, κ was .45.

Of the individuals studied, 7735 (55%) were women and 6311 (45%) were men; 10,276 (73%) were white and 3770 (27%) were black; and 3771 (27%) were between 45 and 49 years old, 3658 (26%) were between 50 and 54, 3408 (24%) were between 55 and 59 years old, and 3209 (23%) were between 60 and 65 years old. Approximately 7% (919 of 13,376) of the individuals studied had prevalent coronary heart disease as defined in "Methods."

Overall, 4491 of the 13,376 individuals (33.6%) with complete readings for at least one of the two carotid arteries had plaque in at least one segment, and 858...
(6.4%) had plaque with acoustic shadowing in at least one segment.

Table 1 presents the sex and race group-specific prevalence rates of plaque for each of the six carotid artery segments that were studied. Plaque lesions were most prevalent in the bifurcation, being approximately twice as frequent there as in the internal carotid artery and approximately four times as frequent there as in the common carotid artery. Overall, men had plaque lesions more frequently than did women—40.1% (2406 of 5998) versus 28.3% (2086 of 7382). Whites had slightly more lesions than did blacks—34.4% (3376 of 9820) versus 31.4% (1116 of 3560).

Similarly, Table 2 shows sex and race group-specific prevalence rates of plaque with acoustic shadowing in each of the six carotid artery segments that were studied. Plaque with acoustic shadowing lesions were, again, approximately twice as frequent in the bifurcation as in the internal carotid artery; they were extremely rare in the common carotid artery. Overall, 5.1% (382 of 7378) of women and 7.7% (476 of 5998) of men had plaque with acoustic shadowing lesions in at least one of the six segments assessed. Five percent (177 of 3558) of blacks and 6.9% (681 of 9818) of whites had plaque with acoustic shadowing lesions.

The prevalence of plaque increased sharply with age, rising from 21.5% (776 of 3621) of individuals 45 to 49 years old to 47.1% (1434 of 3042) of individuals 60 to 64 years old. Table 3 shows these frequency rates for each sex and race.

The prevalence rate of plaque with acoustic shadowing also increased significantly with age. Only 2.5% of individuals 45 to 49 years old presented with plaque with acoustic shadowing in any segment compared with 4.1% of individuals 50 to 54 years old, 7.7% of individuals 55 to 59 years old, and 12.4% of individuals 60 to 64 years old. Table 4 presents the frequency rate of ultrasonographically detected plaque with acoustic shadowing at different ages for black and white men and women.

The adjusted associations of age, race, and sex with plaque with acoustic shadowing were evaluated through logistic regression models controlling for the effects of ultrasound reader and date of reading. The odds (plus 95% confidence interval [CI]) of whites presenting with plaque with acoustic shadowing in any of the segments
studied were 1.22 (CI, 1.02 to 1.46) times those of blacks, and the odds of men were 1.42 (CI, 1.22 to 1.63) times those of women. The odds of having plaque with acoustic shadowing for individuals 50 to 54, 55 to 59, and 60 to 64 years old compared with individuals 45 to 49 years old were 1.65 (CI, 1.26 to 2.16), 3.18 (CI, 2.48 to 4.07), and 5.39 (CI, 4.24 to 6.84), respectively.

Not only did whites have more plaque with acoustic shadowing lesions overall than blacks, but they also had important differences in the localization of these lesions. These differences appear to result from racial differences in the frequency of plaque at specific segments. The frequency of plaque in the common carotid artery was lower in whites (OR, 0.70; CI, 0.51 to 0.98), whereas the frequency in the internal carotid artery was higher in whites (OR, 1.68; CI, 1.48 to 1.91). No substantial difference in plaque frequency was noted at the bifurcation (OR, 1.11; CI, 0.89 to 1.39). Among those with plaque, independent of location, whites had more acoustic shadowing (OR, 1.25; CI, 1.03 to 1.50). As a result of these two effects, whites presented more frequently than blacks with plaque with acoustic shadowing at the internal carotid artery (OR, 1.62; CI, 1.22 to 2.16) and tended to have more at the bifurcation (OR, 1.18; CI, 0.98 to 1.43) but not at the common carotid artery (OR, 0.58; CI, 0.31 to 1.07).

The overall prevalence rates of plaque with acoustic shadowing on each side were essentially equal, with 521 individuals (4.2%) presenting with plaque with acoustic shadowing in at least one left carotid artery segment and 504 (3.9%) with plaque with acoustic shadowing in at least one right carotid artery segment.

Of the 10,894 individuals with complete reader interpretation of plaque with or without acoustic shadowing for all three artery segments on both sides, 758 (7%) had plaque with acoustic shadowing lesions. Of these 758 individuals with plaque with acoustic shadowing, 250 (33%) had lesions in more than one segment, and 167 (26%) had lesions on both sides.

To examine the relationship of plaque and plaque with acoustic shadowing to several quantitative measures of atherosclerosis in the carotid artery, several comparisons were undertaken. Fig 1 shows the sample distribution of intimal-medial wall thickness in each of the three segments of the left carotid artery for individuals classified by the presence or absence of plaque within these same segments. The right carotid artery segments showed a virtually identical pattern. The distribution of those with plaque in relation to those found to be without a lesion was shifted to higher wall thicknesses. The distribution of those with plaque with acoustic shadowing was shifted to an even greater extent. Compared with those without lesions, these

### Table 3. Age-Specific Frequencies of Plaque for 13,376 Black and White Men and Women 45 to 65 Years Old With Complete Readings of Either the Left or the Right Carotid Artery Who Were Examined During the ARIC Baseline Survey, 1987 Through 1989

<table>
<thead>
<tr>
<th>Age, y</th>
<th>45 to 49</th>
<th>50 to 54</th>
<th>55 to 59</th>
<th>60 to 64</th>
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<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
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<tr>
<td>White</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
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<td>23.2</td>
<td>442</td>
</tr>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>109</td>
<td>25.8</td>
<td>108</td>
<td>32.6</td>
<td>137</td>
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<tr>
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<td>125</td>
<td>18.0</td>
<td>160</td>
<td>26.3</td>
<td>144</td>
</tr>
<tr>
<td>Total</td>
<td>776</td>
<td>21.5</td>
<td>1002</td>
<td>28.7</td>
<td>1279</td>
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</tbody>
</table>

### Table 4. Age-Specific Frequencies of Plaque With Acoustic Shadowing for 13,376 Black and White Men and Women 45 to 65 Years Old With Complete Readings of Either the Left or the Right Carotid Artery Who Were Examined During the ARIC Baseline Survey, 1987 Through 1989

<table>
<thead>
<tr>
<th>Age, y</th>
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<th>55 to 59</th>
<th>60 to 64</th>
<th>Total</th>
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<td>n</td>
<td>%</td>
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<tr>
<td>Women</td>
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<td>Black</td>
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<td></td>
</tr>
<tr>
<td>Men</td>
<td>17</td>
<td>4.0</td>
<td>15</td>
<td>4.5</td>
<td>20</td>
</tr>
<tr>
<td>Women</td>
<td>15</td>
<td>2.2</td>
<td>17</td>
<td>2.8</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>2.5</td>
<td>143</td>
<td>4.1</td>
<td>249</td>
</tr>
</tbody>
</table>
rightward shifts in the distribution of individuals with plaque or with plaque accompanied by acoustic shadowing were statistically significant \( (P < .001) \) in all three arterial segments. Nevertheless, there was a large overlap of these three distributions in all arterial segments, particularly between those of individuals presenting with plaque and those of individuals presenting with plaque with acoustic shadowing.

Fig 2 examines the frequency of plaque (with or without accompanying acoustic shadowing) and plaque with acoustic shadowing at various levels of wall thickness in the same segments as shown in Fig 1. Although, as seen in Fig 1, sample wall thickness distributions of individuals with plaque and with plaque with acoustic shadowing were quite similar, the larger overall prevalence of plaque becomes clear (Fig 2). A small percentage of individuals were noted to have plaque lesions at low wall thicknesses. This fraction increased rapidly at wall thicknesses of >0.8 mm, frequencies at a given wall thickness being slightly higher at the bifurcation than in the common carotid or internal carotid artery segments. At a wall thickness of 1.0 mm, approximately 30% were considered to have plaque. At a wall thickness of 1.5, this percentage increased to >90%. In contrast, the proportion of individuals with plaque with acoustic shadowing was never large, being >10% only at the extreme upper range of wall thickness.

**Discussion**

Qualitative lesions attributed to atherosclerosis were detected in a large fraction of the ARIC subjects—33.6% had plaque and 6.4% had plaque with acoustic shadowing. The adjusted prevalence rate of plaque with acoustic shadowing was approximately 40% higher in men than in women and 20% higher in whites than in blacks and increased more than fivefold in those 60 to 64 years old compared with those 45 to 49 years old.

These findings are important in that they derive from the study of more than 13,000 free-living men and women of a relatively broad age range who were selected through a probability sample of four US communities. There were more than 3,700 blacks in the study sample. No other study of carotid artery lesions approaches ARIC in size or generalizability.

Limitations of this study, however, must be acknowledged. ARIC ultrasound readers were intentionally instructed to not follow a clinical algorithm for plaque definition. The clinical and public health significance of these prevalence findings thus is more difficult to interpret. However, the relative distribution of lesions by artery segment and demographic characteristics is affected considerably less by this aspect of the study design.

Another limitation of the present study derives from its overall response rate of only 60% for those invited to take part in the field center examination. This introduces the possibility of selection bias. If those with cardiovascular disease or its risk factors were more...
likely to enter the study than were those without disease or risk factors, the reported prevalence rates would be artificially high. If those participating in the examination were predominantly individuals who were healthy and had a lower frequency of cardiovascular risk factors, ie, the "worried well" as reported by Criqui and colleagues,46 our prevalence estimates of carotid artery plaque might be artificially low. The field center examination was preceded by a home visit to all eligible participants, with a response rate of >85% at all sites. Results from the interview conducted at the home indicate that nonrespondents had a more adverse pattern of cardiovascular risk factors (data not shown), making it likely that the number of individuals with plaque and plaque with acoustic shadowing were underestimated in the study sample.

Another possible source of error was misclassification by the ultrasound reader. The quality assurance program at the ARIC Ultrasound Reading Center included repeat readings by the same reader and by a different reader in a blinded fashion, as described in "Methods." Examination of the reader statistics over the course of the 3 years of data collection and processing indicated a stable reader-specific pattern of reading practices and of the frequency with which carotid artery lesions and acoustic shadowing were reported. The latter is supported by the randomly selected induction cycles of study participants, which contribute to producing a uniform pattern of distribution of study participant attributes over time. The relatively low κ scores for interreader agreement (.33 to .69) indicate that some observations were misclassified, presumably at random. Therefore, it is likely that some of the observations presented in this report were underestimates of the association between individual characteristics and the presence of carotid artery lesion and/or acoustic shadowing. The magnitude of such a bias, however, is unknown but not likely to be large.

The 1313 scans performed but not yet read would contribute little if any additional bias, as chronologically they were the first scans performed, and ARIC participants were scheduled to begin the study in a random fashion.

The large overall prevalence of lesions should not be unexpected. Pathology findings from the International Atherosclerosis Project, the largest autopsy study of carotid artery lesions,17 found that in Oslo, Norway, for example, raised fibrotic atherosclerotic lesions were present in 100% of examinees over the age of 45. They covered, on average, 25% of the intimal surface of arteries from individuals who were 45 to 54 years old who died of noncardiovascular causes and 32% of the surfaces of arteries of similar individuals who were 55 to 64 years old. That only far wall lesions were evaluated by ultrasound here may explain part of the discrepancy in prevalence rates between that study and the present one. Differences in the extent of the carotid system examined, demographic characteristics of the population sample, and the definition of plaque used make it impossible to directly compare the prevalence rates obtained in the ARIC Study with those of other ultrasound studies. Gostomzyk and colleagues,3 using similar methods, found plaque in 27.8% of free-living German male subjects 45 to 54 years old. Josse and colleagues,4 studying the internal carotid artery in French patients who were not referred for cardiovascular disease or symptoms, found prevalence rates for plaque of 34% and 37% in men 45 to 54 and 55 to 64 years old and respective rates of 14% and 18% in women. Other studies used more stringent criteria. Salonen and colleagues,6 scanning the common carotid and carotid bifurcation in free-living middle-aged Finnish men, found considerably lower plaque frequency rates, ranging from 4.1% in 48-year-olds to 27.7% in 60-year-olds, when using a definition of plaque resulting in cases usually having intimal-medial wall thicknesses of >2 mm. Bonithon-Kopp and colleagues,2 studying the common carotid artery only in 45- to 54-year-old French women without cardiovascular disease, found plaque, defined as an intimal-medial wall thickness of ≥1.75 mm, in 8.7%. A discrete category of plaque with acoustic shadowing was not reported in these studies.

The Cardiovascular Health Study, characterizing B-mode–detected ultrasound lesions as percent stenosis in 5201 men and women >65 years old, detected lesions with some degree of stenosis in 75% of men and 62% of women. In the age range of 65 to 69 years, 68% of men and 54% of women had detectable lesions, with 28% of men and 23% of women having stenoses of ≥25% of the lumen diameter.18

The variation in the anatomic distribution of lesions within the extracranial carotid artery system found here is quite similar to those reported previously in the literature for more selected populations.5,19 as is the higher prevalence of lesions among men than women,2,19,20 and the marked rise in the prevalence of lesions with age.2

The complex finding of race-specific localization of plaque lesions, ie, the relatively increased frequency of lesions in the common carotid artery for blacks and in the internal carotid artery for whites, combined with a generalized increased propensity among whites who had plaque with acoustic shadowing, has not been previously reported. An angiographic study of a small, select clinical sample has suggested that there is an increased propensity to lesions at the origin of the internal carotid artery among whites and in the intracranial arteries among blacks.21 Angiographic22 and ultrasound23 studies of symptomatic patients have also demonstrated more carotid artery lesions in whites than in blacks with similar clinical presentations, and a review of findings in 1428 whites and 153 blacks19 who underwent clinical ultrasound examination, performed usually because of the presence of cerebrovascular disease or symptoms, suggested that blacks had relatively more plaque in the common carotid artery and that whites had relatively more plaque in the bifurcation and internal carotid artery.

The cause of these apparent differences is unclear. There are known differences in the profile of cardiovascular disease risk factors between blacks and whites. In addition to major differences in various indicators of socioeconomic status, blacks generally have higher rates of hypertension and diabetes mellitus and are less adequately treated, are more likely to be obese, primarily women, and have higher levels of lipoprotein(a), high-density lipoprotein cholesterol, and fibrinogen and lower levels of triglycerides.24–26 The role of these and other risk factors in the differences in carotid artery lesions, as well as the relative importance of genetics
and the environment in their determination, are important areas for future investigation.

Discrete, qualitatively defined lesions become common only at high intimal-medial wall thicknesses (Fig 2). However, the large overlap in the quantitatively defined distributions of intimal-medial thickness of those with and without these plaque lesions (Fig 1) suggests that the qualitative measures may provide information in some ways different from that gained from the quantitative data.

In conclusion, the present study of plaque and plaque with acoustic shadowing measured by B-mode ultrasound in a population-based sample provides estimates of the prevalence of carotid atherosclerotic disease, which varies by demographic factors, in men and women 45 to 64 years old.

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