Racial Differences in Thoracic Aorta Atherosclerosis Among Ischemic Stroke Patients

Vishal Gupta, MD, MPH; Navin C. Nanda, MD; Dilek Yesilbursa, MD; Wen Ying Huang, MD; Vijaya Gupta, MS; Qing Li, MD, PhD; Camilo R. Gomez, MD

Background and Purpose—Atherosclerosis of the thoracic aorta is an independent risk factor for stroke. There is little information on the impact of race in the prevalence of thoracic aorta atherosclerotic plaques among ischemic stroke patients. This study was an attempt to objectively assess the prevalence, thickness, and burden of thoracic aorta atherosclerotic plaques in a large population of ischemic stroke patients and to compare the differences between American blacks and whites.

Methods—This is a retrospective study of clinical data and transesophageal echocardiography (TEE) of 1553 ischemic stroke patients (664 blacks, 889 whites) over a period of 4.5 years. Atherosclerotic plaque prevalence, thickness, morphology, and burden (sum of maximum thickness in ascending aorta [AA], aortic arch [AO], and descending aorta [DA]) were assessed with TEE. Charts were reviewed for clinical information.

Results—Age and sex were similar among blacks and whites. Analyses of clinical data found that blacks had significantly higher hypertension (odds ratio [OR], 2.61; P<0.0001) and diabetes mellitus (OR, 1.99; P<0.0001) and significantly lower coronary artery disease (OR, 0.75; P=0.017) and carotid artery disease (OR, 0.62; P=0.0008) compared with whites. TEE showed that whites had significantly greater plaque prevalence (AA: OR, 1.37; P=0.04; AO: OR, 1.26; P=0.03; DA: OR, 1.39; P=0.002) and plaque burden (blacks, 4.28 mm; whites, 4.97 mm; P=0.007). Whites also had a trend of increased complex plaques and plaques >4 mm thick in all regions of the thoracic aorta.

Conclusions—Among ischemic stroke patients, blacks had a lower prevalence of extra cranial atherosclerotic disease even though they had significantly higher hypertension and diabetes mellitus compared with whites. This difference cannot be explained by the existing risk factors in ischemic stroke patients. (Stroke. 2003;34:408-412.)

Key Words: atherosclerosis ■ cerebrovascular disorders ■ echocardiography ■ echocardiography, transesophageal ■ stroke
Carotid artery disease was defined as significant stenosis (≥50% lumen narrowing) of a carotid artery on an angiogram or a carotid Doppler ultrasound study.

Transesophageal Echocardiogram
Commercially available imaging systems were used in the hospital while the TEE was performed. Biplane mode was used in 682 cases; multiplanar mode, in 871 cases. All TEEs were done in a standard manner by 2 cardiologists at the UAB hospital.13,14 The cardiac structures and thoracic aorta were examined as previously described.13–15 Each region of the aorta was reviewed for the presence of atherosclerotic plaques. Plaque thickness was assessed as the thickness of the intimal and medial layers of the walls measured perpendicularly during systole on a freeze frame.16,17 Maximum thickness of the plaque in each aortic region was recorded regardless of the number of lesions.

Statistical Analysis
We performed χ² tests to compare the proportions and analysis of variance to compare the means. The odds ratio (OR) for the ischemic stroke risk factors was calculated with both a 2×2 contingency table and multivariate logistic regression, adjusting for age, sex, diabetes, hypertension, smoking, transient ischemic attacks, coronary artery disease, carotid artery disease, peripheral vascular disease, transient ischemic attack, alcohol abuse, and personal and family history of stroke. While comparing the age between the different groups, we calculated the total means of all ages and compared them after stratifying them into different age groups. A κ index of interobserver agreement was used in randomly assigned 100 cases for assessment of comparability of plaque thickness measurements. The entire analysis was done with the SAS software package.18

Results
American blacks constituted 42.8% (664 cases) and whites 57.2% (889 cases) of the total study population. Of the total, 45.65% (709 cases) were men and 54.35% (844 cases) were women. The age of the cases ranged from 19 to 97 years. The mean age of the total population was 61.8 years, and there was no statistical difference between blacks (61.7 years) and whites (62.0 years) and between men (61.2 years) and women (62.5 years). Table 1 shows the prevalence of different clinical risk factors of ischemic stroke in our study population. Hypertension was present in 64.65% (1004 cases) of the total population, making it the most common risk factor for ischemic strokes in the study group. Diabetes was present in 29.8% of the cases (n=463), followed by smoking (26.3%; 408 cases), coronary artery disease (26.3%; 408 cases), transient ischemic attacks (21%; 326 cases), and

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Total (n=1553)</th>
<th>Black (n=664)</th>
<th>White (n=889)</th>
<th>OR* (95% CI)</th>
<th>P</th>
<th>Adjusted OR† (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1004 (64.65%)</td>
<td>509 (76.7%)</td>
<td>495 (55.7%)</td>
<td>2.61 (2.09–3.27)</td>
<td>&lt;0.0001</td>
<td>2.64 (2.05–3.47)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>463 (29.8%)</td>
<td>253 (38.1%)</td>
<td>210 (23.6%)</td>
<td>1.99 (1.60–2.48)</td>
<td>&lt;0.0001</td>
<td>1.70 (1.34–2.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>408 (26.3%)</td>
<td>190 (28.6%)</td>
<td>218 (24.5%)</td>
<td>1.23 (0.98–1.55)</td>
<td>0.07</td>
<td>1.24 (0.96–1.61)</td>
<td>0.09</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>408 (26.3%)</td>
<td>154 (23.2%)</td>
<td>254 (28.6%)</td>
<td>0.75 (0.60–0.95)</td>
<td>0.017</td>
<td>0.64 (0.49–0.82)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Carotid artery disease</td>
<td>253 (16.3%)</td>
<td>84 (12.6%)</td>
<td>169 (19.0%)</td>
<td>0.62 (0.46–0.82)</td>
<td>0.0008</td>
<td>0.58 (0.42–0.78)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>326 (21.0%)</td>
<td>125 (18.8%)</td>
<td>201 (22.6%)</td>
<td>0.79 (0.62–1.02)</td>
<td>0.07</td>
<td>0.83 (0.63–1.06)</td>
<td>0.16</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>114 (7.3%)</td>
<td>52 (7.8%)</td>
<td>62 (7.0%)</td>
<td>1.13 (0.77–1.66)</td>
<td>0.5</td>
<td>1.03 (0.68–1.57)</td>
<td>0.9</td>
</tr>
<tr>
<td>Family history of stroke</td>
<td>148 (9.5%)</td>
<td>69 (10.4%)</td>
<td>79 (8.9%)</td>
<td>1.19 (0.85–1.67)</td>
<td>0.3</td>
<td>1.09 (0.76–1.56)</td>
<td>0.6</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>287 (18.5%)</td>
<td>118 (17.8%)</td>
<td>169 (19.0%)</td>
<td>0.92 (0.71–1.19)</td>
<td>0.5</td>
<td>0.83 (0.60–1.07)</td>
<td>0.1</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>199 (12.8%)</td>
<td>98 (14.8%)</td>
<td>101 (11.4%)</td>
<td>1.35 (1.00–1.82)</td>
<td>0.05</td>
<td>1.36 (0.97–1.89)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*OR with whites as the base for comparison; †Adjusted OR obtained using multivariate logistic regression analysis.

Methods
This was a retrospective study of ischemic stroke patients who were admitted to the University of Alabama at Birmingham (UAB) Hospital. The prevalence of ischemic stroke risk factors and objective evaluation of atherosclerotic disease of thoracic aorta were studied and compared between American blacks and whites.

Study Population
All patients had been hospitalized with the diagnosis of recent ischemic stroke at the UAB Hospital between July 1995 and December 1999. The diagnosis of stroke was based on clinical presentation of new-onset neurological deficit beyond 24 hours and neurological imaging such as cranial CT imaging, MRI of the brain, or both. All patients had a history and physical examination and underwent a TEE to evaluate any cardiac cause of ischemic stroke within 10 days of initial presentation.

Data Collection
An experienced physician using standardized data collection forms abstracted medical records of all participants. During the review, the following stroke risk factors were noted: age, sex, race, hypertension, smoking, diabetes mellitus, hyperlipidemia, alcohol abuse, transient ischemic attack, personal and family history of stroke, and documented peripheral vascular, coronary artery, and carotid artery disease.

A trained cardiologist reviewed the TEEs of 1642 cases according to a standardized protocol. Of these, 89 were excluded because of poor-quality imaging, insufficient clinical data, or ethnicity other than American black or white, leaving us with 1553 cases. One hundred cases were randomly selected from this group and reviewed by another trained cardiologist to determine the comparability between the objective findings. These 1553 cases were grouped as blacks or whites.

Definitions
An atherosclerotic plaque was defined as discrete protrusion of the intimal surface of the vessel with different morphology and echogenicity.3 Plaque burden was defined as the sum of the maximum thickness of plaques in each region of the thoracic aorta, namely the ascending aorta, aortic arch, and descending aorta. The presence of any complex lesion (complex plaque) was recorded regardless of maximum thickness and position. Complex plaques comprised protruding, ulcerated, calcified, and mobile plaques. Ulcerated plaques were defined as discrete indentations of the luminal surface of the atheroma with a base width and minimum depth of at least 2 mm.3 Coronary artery disease was defined as history of documented acute myocardial infarction or angiographic evidence of significant stenosis (≥50% lumen narrowing) of coronary arteries. Carotid artery disease was defined as significant stenosis (≥50%
hyperlipidemia (18.5%; 287 cases). Analyzing the clinical risk factors, we found that hypertension and diabetes mellitus were significantly higher among the American blacks (hypertension: OR, 2.61; 95% CI, 2.09 to 3.27; \( P<0.0001 \); diabetes: OR, 1.99; 95% CI, 1.60 to 2.48; \( P<0.0001 \)). Whereas coronary artery disease and carotid artery disease were significantly lower among the American blacks (coronary artery disease: OR, 0.75; 95% CI, 0.60 to 0.95; \( P=0.017 \); carotid artery disease: OR, 0.62; 95% CI, 0.46 to 0.82; \( P=0.0008 \)). Alcohol abuse, which is considered to have some stroke protective effects, was just a little higher among blacks (OR, 1.35; 95% CI, 1.0 to 1.82; \( P=0.05 \)). The other clinical risk factors for ischemic stroke—sex, smoking, transient ischemic attacks, peripheral vascular disease, and personal and family history of stroke—were not significantly different between the 2 groups (see Table 1).

Table 2 shows the prevalence of plaques in different regions of the thoracic aorta among ischemic stroke patients in the study population. Atherosclerotic plaques were common in the aortic arch (65.5%), followed by the descending aorta (54.9%), but relatively less frequent in the ascending aorta (13.2%). Comparing the prevalence of plaques between the races, we found that whites had a significantly higher prevalence in all regions of thoracic aorta compared with blacks (ascending aorta: OR, 1.37; \( P=0.04 \); aortic arch: OR, 1.26; \( P=0.03 \); descending aorta: OR, 1.39; \( P=0.002 \)). Plaque burden was calculated by taking the sum of the maximum thickness in each of the regions of thoracic aorta. The mean plaque burden of the total population was 4.67 mm. Whites had a significantly greater plaque burden compared with blacks (whites, 4.97 mm; blacks, 4.28 mm; \( P=0.007 \); see Table 3). There was no difference in the atherosclerotic plaque burden between men and women. Comparing the prevalence of the complex plaques, we found that whites had a greater prevalence in all regions of thoracic aorta, but it was significant only in the aortic arch (OR, 1.52; \( P=0.0007 \); see Table 4). The results were similar for plaque thickness \( \geq 4 \) mm; whites had a higher prevalence in all regions with statistical significance only in the aortic arch (OR, 1.52; \( P=0.0008 \); see Table 5). The \( \kappa \) index of interobserver agreement for comparability of plaque thickness in 100 randomly selected patients showed 0.76 correlations.

### Discussion

The list of clinical risk factors for ischemic stroke continues to grow; while some factors are considered to have major association, others are assumed to have minor association. Traditionally, the risk factors of ischemic stroke are classified as nonmodifiable or modifiable. Age, sex, race, and heredity are nonmodifiable risk factors, whereas hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking, and asymptomatic carotid stenosis have been implicated as modifiable risk factors.\(^{19-23}\) Recently, newer risk factors such as patent foramen ovale, atrial septal aneurysm, chlamydia infections, hyperhomocysteinemia, and atherosclerotic disease of thoracic aorta have been named. The Northern Manhattan Stroke Study and other studies have shown that moderate consumption of alcohol, increased levels of high-density lipoproteins in the serum, and physical exercise provide protection from ischemic strokes.\(^{19,20,24}\) The risk factors, however, overweight protective factors, making stroke the leading cause of disability and the third-leading cause of death in the United States.

The search for atherosclerotic disease as a risk factor for ischemic stroke began with the Fisher et al\(^{26}\) angiography and serial autopsies in the 1950s, showing the link between carotid artery disease and ischemic strokes. Blackwood et al\(^{25}\) confirmed this in the 1960s. The Harvard Cooperative Stroke Registry was among the first few prospective studies directly linking cardiac disease and extracranial atherosclerotic disease to \( \approx 40\% \) of ischemic strokes.\(^{7}\) This was confirmed by the Solberg and Strong\(^ {27}\) postmortem studies. Intracranial atherosclerotic disease was also linked to ischemic stroke by Solberg and coworkers.\(^{28,29}\) Since then, Caplan et al,\(^ {30}\) Lynch and Gorelick,\(^ {31}\) and others\(^ {28,29}\) have clearly established these findings. This prompted the search for racial difference in the extra cranial distribution of atherosclerotic disease, especially the thoracic aorta.

Atherosclerotic disease of the thoracic aorta is a strong and independent risk factor of ischemic stroke, as demonstrated by the Amarenco et al\(^ {35}\) study, the Cohen et al\(^ {31}\) study in the multicentric French Study of Aortic Plaque in Stroke, and many other studies.\(^ {1,31,32}\) The association is particularly strong when the plaques are thick and complex in nature.\(^ {1,2,4}\) Recently, the Stroke Prevention: Assessment of Risk in a Community (SPARC) study with 581 subjects looked at the

### TABLE 2. Prevalence of Atherosclerosis in Different Regions of the Thoracic Aorta, Comparing American Whites and Blacks

<table>
<thead>
<tr>
<th>Location of Plaque</th>
<th>Total (n=1553)</th>
<th>Blacks (n=664)</th>
<th>Whites (n=889)</th>
<th>OR* (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>205 (13.2%)</td>
<td>74 (11.1%)</td>
<td>131 (14.7%)</td>
<td>1.37 (1.01–1.86)</td>
<td>0.04</td>
</tr>
<tr>
<td>Arch of aorta</td>
<td>1017 (65.5%)</td>
<td>415 (62.5%)</td>
<td>602 (67.7%)</td>
<td>1.26 (1.02–1.55)</td>
<td>0.03</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>853 (54.9%)</td>
<td>334 (50.3%)</td>
<td>519 (58.4%)</td>
<td>1.39 (1.13–1.70)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*OR with blacks as the base.

### TABLE 3. Plaque Burden, Comparing Race and Sex

<table>
<thead>
<tr>
<th>Category</th>
<th>Plaque Burden, mm*</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blacks</td>
<td>4.28±5.2</td>
<td>0.007†</td>
</tr>
<tr>
<td>Whites</td>
<td>4.97±4.8</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>4.60±5.1</td>
<td>0.5‡</td>
</tr>
<tr>
<td>Women</td>
<td>4.76±4.8</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>4.67±5.0</td>
<td></td>
</tr>
</tbody>
</table>

*Plaque burden is defined as sum of the maximum thickness of the plaques in ascending aorta, arch of aorta, and descending aorta; †\( P \) value for plaque burden comparison between blacks and whites; and ‡\( P \) value for plaque burden comparison between men and women.
distribution of atherosclerosis in different regions of the thoracic aorta and demonstrated a higher prevalence in the arch (27.6%) and descending aorta (38.2%), especially with increasing age. Looking for racial differences in atherosclerotic disease, Di Tullio et al. suggested previously that the risk of ischemic stroke with aortic atherosclerosis might be similar across different ethnic groups. That study had only 106 ischemic stroke patients and may not be the true representation of the ethnic distribution. They also found that whites had a higher incidence of complex plaques. Data from the Northern Manhattan Stroke Study (688 cases) also showed an equal proportion of extracranial disease among 3 ethnic races: blacks, 8%; whites, 9%; and Hispanics, 11%. This extracranial disease was based on carotid Doppler ultrasound and did not represent the atherosclerotic disease of the aorta. No prior study has been done to objectively measure and compare atherosclerotic disease of the thoracic aorta between blacks and whites with ischemic stroke.

In this study, we have objectively measured the thoracic aorta atherosclerotic plaque prevalence, plaque thickness, plaque burden, and other clinical risk factors in a large group of white and black ischemic stroke patients. Ascending aorta was the most frequent site of atherosclerosis, followed by the descending aorta; this was different from the distribution seen in the SPARC study, in which the most frequent site was the descending aorta, followed by ascending aorta. This difference can be explained by the fact that the SPARC study had normal volunteers and our patients were ischemic stroke patients in whom embolization from the ascending aorta to the cerebral distribution was the most likely cause of stroke. Whites had a significantly higher prevalence of atherosclerotic plaques and greater plaque burden and complexity in the thoracic aorta, along with increased coronary artery disease and carotid artery disease, suggesting that they have increased extracranial atherosclerotic disease. This increase existed despite having lower incidence of hypertension and diabetes, which are both strong risk factors for ischemic stroke. In fact, the lower prevalence of hypertension and diabetes, which are also among the major risk factors for atherosclerosis, should have resulted in decreased atherosclerotic disease among the whites. One possible explanation could be the theory proposed by Caplan regarding hypertension and occlusive disease in blacks and whites. High-volume hypertension, which occurs mostly in blacks, predisposes them to intracranial occlusive disease, whereas high-resistance hypertension, which occurs mostly in whites, predisposes them to extracranial occlusive disease. Differences in histology of intracranial occlusive disease (predominantly media involvement) and extracranial occlusive disease (predominantly intima involvement) may support such a theory. This theory may also explain the increased complexity of the plaques among whites owing to shear force, leading to increased thromboembolic potential. These certainly may not be the only explanations; another possibility could be the effect of existing or still undiscovered risk factors, which could either predispose whites for increased atherosclerosis or decrease disease among blacks.

### Study Limitations
An important limitation of this study was determining the plaque burden in thoracic aorta. True plaque burden would be an average of the thickness of all the plaques in the aorta, but obtaining that is technically very difficult. Thus, we had to use the thickness of the largest single plaque as a representation for total plaque burden in each region of the thoracic aorta (ascending, arch and descending) and then take their sum as the total plaque burden. Another limitation was that the study represented a referral population to our institution, not all cases of ischemic stroke in the region, and thus may not be representative of the general population with ischemic strokes.

### Table 4. Prevalence of Simple and Complex Plaques, Comparing Blacks and Whites

<table>
<thead>
<tr>
<th>Plaque Location</th>
<th>Simple Plaques</th>
<th>Complex Plaques</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Black</td>
<td>White</td>
</tr>
<tr>
<td></td>
<td>(n=664)</td>
<td>(n=889)</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>42 (6.3%)</td>
<td>84 (9.45%)</td>
</tr>
<tr>
<td>Arch of aorta</td>
<td>289 (43.5%)</td>
<td>368 (41.4%)</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>252 (37.95%)</td>
<td>380 (42.7%)</td>
</tr>
</tbody>
</table>

*OR with blacks as the base.

### Table 5. Prevalence of Plaques of Different thicknesses, Comparing Blacks and Whites

<table>
<thead>
<tr>
<th>Location of Plaque</th>
<th>Absent or &lt;1-mm Plaque</th>
<th>1- to 3-mm Plaque</th>
<th>4-mm or Greater Plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Black (n=664)</td>
<td>White (n=889)</td>
<td>Black (n=664)</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>590</td>
<td>758</td>
<td>42</td>
</tr>
<tr>
<td>Arch of aorta</td>
<td>250</td>
<td>289</td>
<td>290</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>330</td>
<td>371</td>
<td>255</td>
</tr>
</tbody>
</table>

*OR with blacks as the base.
Conclusions
Among ischemic stroke patients, blacks had a significantly lower prevalence of extracranial atherosclerotic disease even though they had a significantly higher prevalence of hypertension and diabetes compared with whites. This difference in atherosclerotic disease cannot be explained by the existing risk factors in ischemic stroke patients.

References
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