Duplex Doppler and Spectral Flow Analysis of Racial Differences in Cerebrovascular Atherosclerosis

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We compared carotid artery disease in 99 black and 106 white patients using duplex ultrasonography (B-mode imaging and Doppler spectral analysis). Blacks had significantly less stenosis of the extracranial internal carotid artery than whites. Among the risk factors investigated, hypertension alone, ischemic heart disease, diabetes mellitus, and smoking failed to explain the racial difference. Although carotid stenosis of $\geq 40\%$ correlated significantly with age in both races ($p=0.001$ in whites and $p=0.005$ in blacks), blacks had significantly less carotid stenosis of any degree even when age was taken into account. Multivariate analysis showed that race is a significant and independent risk factor for carotid stenosis ($p<0.0001$). Hypertension interacting with race was also significant. Our results require verification in population-based studies. Carotid duplex ultrasonography offers a noninvasive method for carrying out such studies. (Stroke 1990;21:740–744)

Racial differences in pathology of the intracranial and extracranial arteries have been reported among patients with ischemic stroke.1–9 The importance of disease of the extracranial internal carotid artery as a cause of ischemic stroke was appreciated early in whites.10 Later, blacks were shown to have less extracranial internal carotid artery disease, more lesions of the supraclinoid internal carotid artery and middle cerebellar artery stem, and more symptomatic lesions in the middle cerebral artery stem than whites.5 A study11 of 25 black and 50 white patients with transient ischemic attacks (TIAs) using B-mode ultrasonography revealed no significant difference in the degree of internal carotid artery stenosis, but whites had significant stenosis in the carotid artery ipsilateral to the symptoms more often than blacks. In an autopsy study,7 blacks who suffered from diseases associated with atherosclerosis or who died of other causes had more advanced intracranial atherosclerotic lesions than whites. However, there were only small and inconsistent differences between races in the extent and frequency of fibrous plaques, of plaques with hemorrhage, necrosis, or thrombosis, and of calcified lesions.

Clinical series comparing carotid atherosclerosis in blacks and whites have not always controlled for age, hypertension, diabetes mellitus, or other risk factors that, if different between the races, might account for the observations. Autopsy data also have some shortcomings for racial comparisons because such information is subject to considerable selection bias. Clearly, additional comparisons of carotid disease in blacks and whites are of interest.

We used carotid duplex ultrasonography, which combines Doppler spectral analysis and real-time B-mode images, as a noninvasive method to examine differences in the frequency of atherosclerotic lesions of the extracranial internal carotid artery in blacks and whites.

Subjects and Methods

Between 1988 and 1989, 214 patients had complete noninvasive evaluation of their extracranial vessels in the vascular laboratory at Temple University Hospital. Data including reason for referral; age; sex; presence/absence of ischemic heart disease, diabetes mellitus, hypertension, peripheral vascular disease, and smoking; and race were collected on each patient from the medical record. Age was treated as a continuous variable in the logistic regression analysis and as a categorical variable when comparing various degrees of carotid stenosis by race. Sex was categorical (either male or female). Ischemic heart disease, diabetes mellitus, hypertension, peripheral vascular
disease, and smoking were treated as dichotomous variables, that is, they were considered to be present or absent. Ischemic heart disease was deemed present in patients with a history of myocardial infarction or angina. Diabetes was considered present in those receiving insulin or an oral hypoglycemic agent. Hypertension was deemed present in patients with a positive history or using antihypertensive agents. Peripheral vascular disease was considered present in patients with a mention in their records. Similarly, smoking was deemed present in those currently smoking or with such a history. Nine patients were excluded from our study, as their race could not be definitively ascertained. This retrospective analysis is based on the remaining 205 patients.

Carotid duplex ultrasonography was performed using the Biosound 2000IIsa system (Indianapolis, Indiana) with the patient supine. The head was turned away from the side being scanned, and the neck was extended. The internal and external carotid arteries were individually followed from the clavicle to the angle of the mandible. Anterior, lateral, and posterior longitudinal views as well as a transverse view were obtained in each patient. Doppler spectral waveforms were obtained from the proximal and distal common carotid artery, the proximal and distal internal carotid artery, and the external carotid artery. If the image revealed a stenosis, a Doppler signal was also obtained in the area of the smallest residual lumen. Percent reduction of the diameter of the vessel was estimated according to previously established criteria using information from the various views and the Doppler spectral waveforms interpreted according to the guidelines of Roederer et al.

The patients were separated into two groups; the first included patients with a referral diagnosis of stroke/TIA, and the second comprised those with all other referral diagnoses. Within each group the relation between race and stenosis caused by the most severe extracranial internal carotid artery lesion was analyzed using the Mantel-Haenszel $\chi^2$ test. Using various criteria of stenosis from no discernible lesion to occlusion, the results of racial comparisons were consistent, but the comparison of $\geq 40\%$ stenosis was used for some statistical analyses because this cut point yielded sufficient numbers. Within each group, the relation between age class (<45, 45–64, 65–74, or >75 years) and stenosis of $\geq 40\%$ by race was tested using Pearson’s correlation. The distributions of risk factors for carotid atherosclerosis were compared between races using the $\chi^2$ test (or the corrected $\chi^2$ when numbers were small).

Stepwise logistic regression (backward elimination) was used to identify potential risk factors associated with $\geq 40\%$ stenosis for all patients. BMDP statistical software was used. Their (PLR) program for logistic regression estimates regression coefficients by the maximum-likelihood method and proceeds in a stepwise fashion, removing one variable from the regression equation at each step. Selection of variables to be removed is based on the magnitude of their probability values (largest logarithmic likelihood).

### Results

Of the 205 patients, 106 (52\%) were white and the other 99 (48\%) were black. The stroke/TIA group included 106 patients, 45 whites (42\%) and 61 blacks (58\%) (Table 1). Among the whites the referral diagnosis of TIA was more common than that of stroke, but among the blacks the referral diagnosis of stroke was more common. The second group included 99 patients, 61 white (62\%) and 38 black (38\%). The racial distribution of each referral diagnosis is shown in Table 1.

In the stroke/TIA group, whites had at least some degree of carotid artery disease more often than blacks (82\% and 62\%, respectively; Table 2, Mantel-Haenszel $\chi^2=7.522, p<0.006$). Also, whites had bilateral lesions more often than blacks (62\% and 38\%, respectively, $p=0.01$). The predominance of lesions

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**Table 1. Racial Distribution by Referral Diagnosis**

<table>
<thead>
<tr>
<th>Referral diagnosis</th>
<th>Whites No.</th>
<th>%</th>
<th>Blacks No.</th>
<th>%</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Stroke/TIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stroke</td>
<td>20</td>
<td>44</td>
<td>42</td>
<td>69</td>
<td>62</td>
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<tr>
<td>TIA</td>
<td>25</td>
<td>56</td>
<td>19</td>
<td>31</td>
<td>44</td>
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<tr>
<td>Total</td>
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<td>2</td>
<td>4</td>
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<td>5</td>
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<tr>
<td>Asymptomatic carotid bruit</td>
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<td>26</td>
<td>7</td>
<td>18</td>
<td>23</td>
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<tr>
<td>Dizziness and vertigo</td>
<td>19</td>
<td>31</td>
<td>11</td>
<td>29</td>
<td>30</td>
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<tr>
<td>Peripheral vascular disease</td>
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<td>5</td>
<td>3</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Cardiovascular surgery</td>
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<td>16</td>
<td>1</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
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<td>4</td>
<td>7</td>
<td>3</td>
<td>8</td>
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<tr>
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<tr>
<td>Total</td>
<td>61</td>
<td>100</td>
<td>38</td>
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</tbody>
</table>

TIA, transient ischemic attack. Percent of column total.

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Haenszel $\chi^2=7.522, p<0.006$). Also, whites had bilateral lesions more often than blacks (62\% and 38\%, respectively, $p=0.01$). The predominance of lesions...
in the right extracranial internal carotid artery in whites was significantly greater than in blacks (78% and 49%, respectively; \( p < 0.01 \)), while in the left extracranial internal carotid artery the difference between races was not significant (67% and 51%, respectively; \( p = 0.1 \)). Whites were more likely to have severe (40–64% and 65–95%) stenosis than blacks (Table 2).

In the second group, carotid lesions of any degree were also significantly more common in whites than in blacks (69% and 55%, respectively; Table 2, Mantel-Haenszel \( \chi^2 = 7.797, p < 0.005 \)). Again, the difference between races was more striking in the right carotid artery (64% and 39%, respectively) than in the left (54% and 53%, respectively). No black patient had an occlusion of the carotid artery while three white patients did (Table 2).

Because the incidence of carotid atherosclerosis increases with age, the proportion in each group with stenosis of ≥40% was calculated for each of four age classes by race. In both groups, the same trend was observed (higher proportions with ≥40% stenosis in whites than in blacks for each age class, Table 3). In Figure 1, the two groups are combined. Clearly, whites were more likely to have carotid stenosis than blacks in all age classes. The correlation between age and stenosis of ≥40% for whites was 0.43 in the stroke/TIA group \( (p = 0.002) \) and 0.36 in the second group \( (p = 0.002) \). Among blacks, the correlation was 0.20 \( (p = 0.057) \) in the stroke/TIA group and 0.48 \( (p = 0.001) \) in the second group. When both groups were combined, the correlation between age and stenosis of ≥40% was 0.40 \( (p = 0.001) \) in whites and 0.26 \( (p = 0.005) \) in blacks.

The distributions of risk factors for atherosclerosis besides age differed between races. In the stroke/TIA group, whites included a higher percentage of males but lower percentages of hypertensives and smokers than blacks (69% and 46%, 47% and 67%, and 27% and 51%, respectively). These differences were all significant \( (p < 0.03, 0.05, \) and \( 0.01, \) respectively).

Frequencies of the other risk factors (ischemic heart disease, diabetes mellitus, and peripheral vascular disease) did not differ significantly between races. In the second group, whites included a higher proportion of males than blacks (62% and 34%, respectively, \( p < 0.01 \)), while the frequencies of smoking and peripheral vascular disease (18% and 26%, 23% and 16%, respectively, \( p < 0.01 \)) were similar in the races. However, ischemic heart disease was significantly more frequent and diabetes mellitus and hypertension significantly less frequent in whites than in blacks (39% and 24%, \( p = 0.02 \); 18% and 39%, \( p = 0.02 \); and 39% and 61%, \( p = 0.04 \), respectively).

Because the racial difference in carotid atherosclerosis could be confounded by racial differences in

<table>
<thead>
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<tr>
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<td>Total</td>
<td>No. with stenosis of ≥40%</td>
<td>%</td>
<td>Total</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td></td>
<td></td>
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<td>73</td>
<td>31</td>
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<td>65–74</td>
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<td>10</td>
<td>83</td>
<td>16</td>
</tr>
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<td>&gt;75</td>
<td>15</td>
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<td>9</td>
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<tr>
<td>&lt;45</td>
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<tr>
<td>&gt;75</td>
<td>12</td>
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TIA, transient ischemic attack. Percent of total.
these other risk factors, stepwise logistic regression analysis (backward elimination) was carried out to determine whether any of these variables accounted for the observed racial difference in atherosclerosis or whether race contributed to it independently. Peripheral vascular disease was not included in the regression analysis. Among the remaining risk factors, ischemic heart disease, diabetes mellitus, and smoking proved to be nonsignificantly associated with carotid stenosis. However, age and hypertension were significantly associated with stenosis. To predict the probability of having \( \geq 40\% \) stenosis \((Y)\), the following regression model was formulated:

\[
Y = (e^{-4.2 - 0.86 \times \text{race} - 0.43 \times \text{hypertension} + 0.056 \times \text{age}}) + (1 - e^{-4.2 - 0.86 \times \text{race} - 0.43 \times \text{hypertension} + 0.056 \times \text{age}}).
\]

The regression coefficient for race was more significant (approximate \( p<0.001 \)) than that for hypertension (approximate \( p<0.02 \)), suggesting that race contributed more than hypertension to the likelihood of \( \geq 40\% \) carotid stenosis. The regression coefficient for age gave an approximate \( t \) of 3.8 (\( p<0.001 \)), indicating that age was strongly associated with \( \geq 40\% \) carotid stenosis. However, whites tended to have carotid stenosis more often and to a greater degree than blacks, even when hypertension and age were taken into account.

**Discussion**

Real-time B-mode imaging and Doppler spectral techniques can also be adopted for largescale, prospective, population-based epidemiologic studies to investigate reasons for racial differences in atherosclerosis. Carotid duplex ultrasonographic studies would minimize the bias inherent in autopsy series, in angiographic studies, and in case series. Our results, while consistent with some racial comparisons of carotid atherosclerosis,\(^1,5,6,8\) are not consistent with those reported by Ryu et al.\(^1\)

Using B-mode Doppler ultrasonography, Ryu et al\(^1\) compared carotid stenosis in 25 black and 50 white patients with TIAs. The authors concluded that blacks had "no less" overall carotid stenosis than whites. However, whites did have more stenosis on the side ipsilateral to the symptomatic cerebral hemisphere (66% in whites, 43% in blacks). This series cannot be compared directly with ours for several reasons: the numbers were small, only patients with TIA were compared, and the side of the stenosis was not taken into account. Moreover, only hospitalized subjects were compared, and hospitalized blacks may have more advanced disease than hospitalized whites.

Our study was not population-based and therefore may also be biased because patients evaluated in a vascular laboratory are already selected. For example, the patients must first be sufficiently concerned to seek medical advice, and then their physicians must be willing to refer them for additional studies. Reasons for referral differ by race (Table 1). Also, noninvasive carotid studies are costly, so economic factors may exclude some patients. These biases are minimized in population-based studies in which all individuals are equally likely to be evaluated. Retrospective classifications of risk factor status such that we used tend to underestimate the true frequency of the conditions because not all records are complete. Often, if one factor is listed others are omitted.\(^1\) In prospective assessments, a cohort of patients can be followed and evaluated regularly for the presence of all risk factors of interest.

Gorelick et al\(^5\) observed, as did we, a significantly higher frequency of right carotid artery stenosis in whites than in blacks, while the proportions with stenotic lesions in the left extracranial internal carotid artery were almost identical for the two races. Clearly, side cannot be ignored when comparing race and the significance of other stroke risk factors.

Racial differences can reflect genetic effects. However, culturally determined factors such as diet, occupation, and level of stress may differ between races and contribute to the risk of stroke.\(^2,3,7\) Since both races show atherosclerosis, the susceptibility is only relative. In any event, the susceptibility may be modified by proper treatment. Therefore, we examined the role of controllable factors such as hypertension, diabetes mellitus, smoking, and ischemic heart disease in extracranial internal carotid artery stenosis. Peripheral vascular disease was also considered, but not in the regression analysis.

Hypertension has been reported more often in blacks with ischemic stroke than in whites.\(^6,9,18,20\) In our series, too, hypertension was significantly more frequent in blacks. Yet, we found blacks to have less extracranial internal carotid artery disease. Hypertension appears to be more strongly associated with changes in the intracranial than in the extracranial arteries.\(^3\)
Diabetes mellitus has been reported more frequently in blacks with ischemic stroke than in whites,\textsuperscript{9,18} but the converse was also reported.\textsuperscript{5,6} Among active workers in another study, no racial difference in the relative frequency of diabetes was found.\textsuperscript{21} In our series, the frequency of diabetes did not differ significantly between races in patients referred for stroke/TIA, while in the second group blacks had a significantly higher proportion with diabetes. In both groups, extracranial internal carotid artery disease was less severe in blacks. The role of diabetes mellitus in atherosclerosis in each race needs clarification.\textsuperscript{22}

Myocardial infarction occurred more often in blacks than in whites in one series.\textsuperscript{9} The opposite occurred in another study,\textsuperscript{6} and there were no significant racial differences in a third.\textsuperscript{3} In our series, ischemic heart disease was slightly more common in whites with ischemic stroke than in blacks (data not shown); the opposite was found in the second group. Thus, ischemic heart disease is not clearly implicated in the racial difference in extracranial internal carotid artery atherosclerosis that we found. Although we did not examine the role of lipids, racial differences in this variable may account for variations in the sites of the atheromatous process.\textsuperscript{23}

In one study, serum cholesterol concentrations were higher in whites with ischemic stroke than in blacks,\textsuperscript{24} whereas in another study\textsuperscript{5} no racial difference was found. A significant racial difference in the distribution of lipoprotein fractions was shown when age, sex, and total serum cholesterol concentration were matched in yet another study.\textsuperscript{25} Lipids, like diabetes, myocardial infarction, and hypertension, need to be examined in future studies of racial differences in carotid artery disease.

Our multivariate analysis, which took interaction among the variables into account, showed that hypertension and age were more important than diabetes mellitus and ischemic heart disease but that race appeared to be even more important in determining the degree of atherosclerosis in the extracranial internal carotid artery.

Population-based studies are needed to confirm the existence of a racial difference in carotid stenosis. If the racial difference is confirmed, then epidemiologic and genetic investigations seeking an explanation can be undertaken. Modern ultrasonographic techniques offer a noninvasive method for conducting such studies.

References

Key Words • blacks • carotid artery diseases • ultrasonics
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