Cerebral Atherosclerosis and Its Relationship to Selected Diseases in Nigerians: A Pathological Study

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Abstract:
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Factors which are known to be associated with cerebral atherosclerosis were evaluated in Nigerian Africans. Of 465 autopsied adult Nigerians, 62 (13%) had cerebral atherosclerosis. The frequency and severity of atherosclerosis among Nigerians with hypertension, particularly male subjects, were higher than in normotensives. Although there was a similar frequency of hypertension among autopsied Nigerian and Minnesota Caucasian populations, the severity and extent of atherosclerosis were greater in the Minnesota population. The relatively short duration of hypertension in the Nigerian before death might be an important factor which did not permit progressive development of cerebral atherosclerosis. Other factors which predisposed the Nigerian to increased frequency and severity of atherosclerosis included increased heart weight and diabetes mellitus. The relatively low frequency of cerebrovascular disease in the Nigerian may be explained on the basis of a low degree of cerebral atherosclerosis and relatively short duration of hypertension.

Additional Key Words
- autopsy study
- heart weight
- cancer
- diabetes mellitus
- subarachnoid hemorrhage
- cerebrovascular disease
- intracerebral hemorrhage
- berry aneurysm
- hypertension

Cerebrovascular disease in the African has been the subject of a few recent clinical studies but these have presented minimal pathological correlation and confirmation.1-4 Morphological studies of arteries, including cerebral arteries in different population groups in Africa, have been carried out to evaluate the extent and severity of atherosclerosis5-10 and of certain conditions associated with atherosclerosis.11-14 These studies have shown that cerebral or coronary atherosclerosis is less in the different African population groups living in Nigeria, Uganda or Senegal6,15 when compared with American Caucasians and Negroes. There is, however, little information on the potential factors which predispose the African to the relatively low observed amounts of atherosclerosis.16 Even though the observed amounts of atherosclerosis are low in Africans, there may be risk factors which influence the degree of atherosclerosis. The present study, therefore, attempts to evaluate the role of certain recognized factors which are known either to predispose to, or are associated with, cerebral atherosclerosis. Nigerian Africans over the age of 16 years form the basis of this autopsy study.

Patients and Methods
The severity and extent of atherosclerosis of the circle of Willis were estimated on 804 unselected consecutive autopsies carried out at the University College Hospital (UCH), Ibadan, Nigeria. Of these, 465 were adults over the age of 16 years. The autopsy rate for both sexes in the hospital was approximately 70% during the period of study (1967-1968). The method of grading the amount of cerebral atherosclerosis was based on a scoring system devised by Resch and Baker.17 In order to determine the severity and extent of the atherosclerotic process, 22 predetermined sites in the circle of Willis were examined and graded according to the degree of atherosclerotic changes. Each of these 22 areas was graded from 0 to 4, the highest possible score being 88. Reliability studies on the scoring method were carried out between JAR and AOW on two occasions under the supervision of a biostatistician (RBL). The details of these studies have been published elsewhere.18 The possible association between the observed vessel scores and the following features was evaluated: (1) hypertension, (2) heart weight, (3) diabetes mellitus, (4) cancer, (5) cerebrovascular disease, and (6) cause of death.

The mean vessel scores of the circle of Willis were computed by sex in ten-year age groups up to the age of 69. The curves connecting these mean vessel scores gave an indica-
TABLE 1

| Age Distribution of Nigerian Subjects by Presence or Absence of Hypertension |
|---------------------------------|-----------------|-----------------|-----------------|
| Age    | Hypertensive Males | Hypertensive Females | Total Males | Total Females | Total | Normotensive Males | Normotensive Females | Total Males | Total Females | Total |
| 17 – 19 | 1                | 1                | 2              | 8              | 7    | 15               |
| 20 – 29 | 4                | 12               | 16             | 25             | 55   | 80               |
| 30 – 39 | 16               | 5                | 21             | 38             | 49   | 87               |
| 40 – 49 | 14               | 10               | 24             | 33             | 17   | 50               |
| 50 – 59 | 8                | 14               | 15             | 21             | 12   | 45               |
| 60 – 69 | 8                | 7                | 15             | 9              | 1    | 5                |
| 70 +    | 1                | 0                | 1              | 4              | 1    | 5                |
| Total   | 52               | 41               | 93             | 162            | 150  | 312              |

The mean vessel scores for hypertensives and normotensives are presented in figure 1. It is evident that hypertensives have a much higher degree of cerebral atherosclerosis than normotensives. The highest mean score for Nigerian hypertensives occurred between 50 and 59 years, but this did not exceed a value of 10 points; the corresponding mean score for normotensives was below 1 point. In females the maximum difference in vessel scores between hypertensives and normotensives was also found in the 50 to 59 year age group, whereas in the males it occurred in the 40 to 49 year age group. The average amount of cerebral atherosclerosis was relatively small for all subjects under the age of 40 years, and the proportion of hypertensives with cerebral atherosclerosis in the age group 30 to 39 years was 10% compared with 4% in the normotensives (fig. 2). With increase in age the difference in frequency of atherosclerosis between the two groups also increased and reached a maximum in the 50 to 59 year age group; this difference was more striking among males than females (fig. 3).

Results

HYPERTENSION

For identification of hypertensive individuals we adopted one or more of the following criteria: (1) recorded clinical diagnosis of the disease; (2) blood pressure reading over 160 mm Hg systolic or over 95 mm Hg diastolic, or both;19 and (3) the presence of hypertensive arteriolar changes in the kidneys. Subjects without clinical or pathological diagnosis of hypertension either were considered normotensive, if their recorded blood pressure reading was below 140 mm Hg systolic and below 90 mm Hg diastolic, or were grouped under the category of borderline hypertensives.19 The age distribution of subjects belonging to the group of hypertensives (93) and normotensives (312) are presented in figure 1; the borderline hypertensives (51) were excluded from this analysis.

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Percent of male and female Nigerian subjects with cerebral atherosclerosis in the presence or absence of hypertension.

Previous reports had shown that the Minnesota subjects had considerably higher average vessel scores and a greater frequency of cerebral atherosclerosis than the Nigerian subjects. When the criteria for hypertensives and normotensives used for the Nigerian data were applied to the Minnesota subjects, the percentages of patients with the disease were similar. Between the ages of 20 and 69 years, 21% of the Nigerian subjects and 22% of Minnesota subjects were hypertensive. However, in the age group of 40 to 49 years, 29% of Nigerians were hypertensive compared with only 17% in the Minnesota sample. In any other given age group the percentages did not differ by more than 4%, with relative frequencies less than 20% in the younger age groups and greater than 20% in the older age groups.

Mean vessel scores for the two autopsy series are presented in figure 4. The average amount of cerebral atherosclerosis was consistently less in the Nigerian hypertensive than in the Minnesota hypertensive. The smallest difference between the mean scores was 2 points in the age group of 40 to 49 years. However, in the older age groups the Nigerian mean scores for hypertensives did not follow the upward trend of the mean scores for the Minnesota hypertensives (fig. 4).

A comparison of the prevalence of cerebral atherosclerosis between the two geographic groups showed higher percentages of cases with atherosclerotic involvement in the Minnesota subjects than in the Nigerian subjects for both hypertensives and normotensives (fig. 5). As early as in the 30 to 39 year age group, 49% of Minnesota hypertensives had cerebral atherosclerosis compared with only 10% of Nigerians. In the normotensive groups the corresponding values were 22% and 2% in Minnesotans and Nigerians, respectively. In the subsequent two decades (40 to 59 years), the percentages of Minnesota hypertensives with atherosclerosis increased considerably and approached corresponding percentages for Minnesota hypertensives. The difference of percentages between Nigerian and Minnesota normotensives was much larger than those for the hypertensives (fig. 5).

HEART WEIGHT

The heart weight had often been used as evidence of

Percent of Nigerian and Minnesota subjects with cerebral atherosclerosis in the presence or absence of hypertension. Note the similarity in percent of Nigerian hypertensive and normotensive Minnesota subjects.
hypertension and arbitrary values for heavy hearts, depending on sex, have been selected in previous studies. It was decided to use weights over 300 gm as indicating a heavy heart because the estimated median heart weight of adult Nigerians, over 16 years of age, based on an analysis of approximately 6,000 autopsies carried out in UCH, Ibadan, over a 12-year period, was between 200 and 225 gm for females and males.

The mean vessel scores for all subjects with heavy heart weights (over 300 gm) were higher for all age groups over the age of 30 years when compared with those with light hearts (fig. 6). The vessel scores were higher in subjects of both sexes with an increased heart weight, but this was most marked in females between 50 and 59 years. The percentage of subjects with cerebral atherosclerosis was larger in the group with heart weights exceeding 300 gm than in the group with heart weights less than 300 gm. This observed difference was most marked between 50 and 70 years (fig. 7).

**HYPERTENSION AND HEART WEIGHT**

An attempt was made to assess the association between heart weight and cerebral atherosclerosis on the one hand and the presence or absence of hypertension on the other. Figure 8 presents the percentages of Nigerian patients with atherosclerosis by heart weight and hypertension. The sample sizes in some of the age groups were too small to provide reliable estimates of the mean vessel scores, but the observed percentages in the different age groups gave an indication of trends. Hypertensive subjects with heavy hearts seemed to have a much higher percentage of cerebral atherosclerosis than normotensives with heavy hearts. Above the age of 40 years, the percentages of subjects with atherosclerosis for all normotensives, irrespective of heart weight, and for hypertensives with light hearts were approximately in the same range of 5% to 30%. The percentage of patients who were hypertensive and had heavy hearts was between 55% and 90%. It is of interest to note that 59% of hypertensives had heart weights above 300 gm in comparison to only 23% of normotensives with heavy hearts.

**CANCER**

Malignant neoplastic disease was present in 113 (24%) of the adult subjects. There was a slight increase of
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mean vessel scores among those without cancer under the age of 50 when compared with those with cancer. However, this trend was reversed in the older age groups (fig. 9).

DIABETES MELLITUS
Seven of the adult subjects studied had diabetes mellitus, and three of these had cerebral atherosclerosis. The numbers were therefore too few to analyze the relationship between this disease and cerebral atherosclerosis. However, the individual vessel scores of the three diabetic subjects with atherosclerosis were relatively high. A larger series is required to evaluate this factor further in the African even though this small set of data showed a trend of increased atherosclerosis in patients with diabetes mellitus.

CEREBROVASCULAR DISEASE
Of the 465 autopsied adult subjects, 22 (5%) had morphological evidence of central nervous system tissue damage, including those secondary to cerebrovascular disease. Among the patients without cerebrovascular atherosclerotic lesions of the central nervous system were subarachnoid hemorrhage (three cases), intracerebral hemorrhage (seven cases), pyogenic meningitis (one case), embolic softening (two cases) and softening due to internal carotid occlusion (one case). Of the seven patients with intracerebral hemorrhage, four had hypertension using the adopted criteria for this study and one had increased heart weight. The remaining two patients had cirrhosis of the liver and miliary tuberculosis. The two patients with cerebral softening due to emboli had bacterial endocarditis and endomyocardial fibrosis. Only three instances of subarachnoid hemorrhage occurred in the entire group. This low frequency is in keeping with previous observations of relative rarity of congenital berry aneurysms in the African.22

Among the patients with cerebral tissue damage and atherosclerosis, five subjects had intracerebral hemorrhage with or without secondary subarachnoid extension. The remaining three patients had cerebral infarcts. The vessel scores for the subjects with cerebral hemorrhage ranged between 2 and 46 and for the cerebral infarcts, between 4 and 57. The highest score of 57 observed in the study was in a 56-year-old woman with a two-year history of malignant hypertension.

Of the 22 subjects with cerebrovascular disease, only 8 (36%) had morphological evidence of cerebral atherosclerosis. It would appear, therefore, that cerebral atherosclerosis, although encountered as a cause of cerebrovascular disease, is relatively uncommon as a cause of neurological morbidity or mortality in the Nigerian population.

CAUSE OF DEATH
The main causes of death for the 465 patients in relation to presence or absence of cerebral atherosclerosis are summarized in table 2. Among the specified causes of death, cancer (23%) showed by far the highest frequency in the present study.

### TABLE 2

<table>
<thead>
<tr>
<th>Selected causes of death</th>
<th>Atherosclerosis</th>
<th></th>
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<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>No.</td>
<td>%</td>
<td>Males</td>
<td>Females</td>
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<tr>
<td>Occlusive</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cancer</td>
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<td>7</td>
<td>16</td>
<td>25.8</td>
<td>52</td>
<td>38</td>
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<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>3</td>
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<tr>
<td>Coronary atherosclerosis</td>
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<td>1</td>
<td>9</td>
<td>14.5</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Other*</td>
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<td>53.2</td>
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<td>156</td>
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<tr>
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<td>0</td>
<td>1</td>
<td>1.6</td>
<td>7</td>
<td>3</td>
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<td>Total</td>
<td>43</td>
<td>19</td>
<td>62</td>
<td>69.7</td>
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</table>

*The majority were inflammatory or infectious diseases.
Discussion

Of 465 adult Nigerian subjects, 62 (13%) had detectable cerebral atherosclerosis. Ninety-three of the 465 subjects were classified as hypertensive and of this number 30 (32%) had detectable cerebral atherosclerosis. Among the hypertensive group, there was a consistently higher frequency of cerebral atherosclerosis in subjects between the ages of 30 and 69 years (fig. 2), particularly in males (fig. 3). The severity of cerebral atherosclerosis, using vessel scores, was also greater in hypertensive subjects when compared with normotensives (fig. 1). This confirms previous observations in other population groups that hypertension is frequently associated with cerebral atherosclerosis.26, 27

When similar criteria were used for the selection or identification of hypertensive groups among Nigerian and Minnesota subjects, there was a similarity in the frequencies of hypertension in both population groups. Despite the similarity in prevalence of hypertension in the two autopsy populations, cerebral atherosclerosis was evidently less in severity and frequency in the Nigerians than in the Minnesotans. It is noteworthy, however, that the observed difference in the amount and frequency of atherosclerosis was greater between the hypertensive and normotensive Nigerian subjects than in comparable Minnesota subjects (figs. 4 and 5). This difference was maximum in the fifth and sixth decades. The mean vessel scores and frequency of cerebral atherosclerosis decreased in Nigerians between the ages of 60 and 69 years but increased in Minnesota subjects during a comparable decade (fig. 4). A similar trend has been reported with the frequency or incidence of certain types of malignant disease in the elderly African.24

The difference in extent and severity of cerebral atherosclerosis between the Nigerian and Minnesota hypertensive subjects may be attributed to differing age distributions of both populations at death. The average life span of the Nigerian is shorter than that of the American Caucasian in general, and the late presentation of the Nigerian hypertensive for medical care predisposes him to development of complications and early death. The relatively short duration of hypertension in the Nigerian therefore may not permit progressive development of cerebral atherosclerosis. Of pertinence is the fact that symptoms and signs of cardiac failure are not uncommon as initial presentations of hypertension in several parts of Africa.25 In such situations, blood pressure readings of patients in cardiac failure may not be true reflections of the patients' clinical status.

For this study, it was therefore decided to investigate the possible association between cerebral atherosclerosis and cardiomegaly, particularly left ventricular hypertrophy due to hypertension. The results showed that the frequency and average amount of atherosclerosis among those with increased heart weights were higher than those with normal or low heart weights. However, the observed differences in mean vessel scores and frequencies of atherosclerosis between the two heart weight groups were not as large as those observed when hypertensives were compared with normotensives (figs. 6 and 7).

The subjects, classified by heart weights, were further subdivided into two categories, namely those with or without hypertension. Although the sample sizes were small in some categories, it was evident that subjects with cardiomegaly and hypertension showed the highest increase of percentages of cases with atherosclerosis (fig. 8). The corresponding percentages for normotensives with cardiomegaly were relatively low compared with those for subjects with light or normal hearts. Cardiomegaly due to hypertension appeared to be an indication of prolonged duration of the disease which in turn predisposed to the development of more extensive cerebral atherosclerosis. However, 41% of subjects diagnosed as hypertensives had relatively normal heart weights. This would tend to support the suggestion that the natural history of hypertension in the Nigerian has a relatively short duration.

There were no consistent differences in the severity of cerebral atherosclerosis between subjects with cancer and those without cancer. In previous studies of the Minnesota autopsy series it had been shown that atherosclerosis was less severe in patients with malignant neoplastic diseases than in patients without malignancies.26 The lack of a consistent trend in the observed differences in the Nigerian series did not permit us to draw any conclusions about a possible relationship between cancer and degree of cerebral atherosclerosis (fig. 9).

Diabetes mellitus and cerebrovascular disease were associated with an increase in cerebral atherosclerosis. These findings agree with results previously reported for Minnesota subjects.28 The relatively rare occurrence of cerebrovascular disease in the Nigerian sample may be partially explained on the basis of the relatively short duration of hypertension and a relatively low degree of cerebral atherosclerosis. A recent epidemiological study of Ugandan Africans also reported low rates of cerebrovascular disease,29 thus supporting our findings.

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