Ischemic Heart Disease in Black South African Stroke Patients

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Background and Purpose—Stroke patients in western countries frequently have coronary artery disease (CAD). In black Africans, CAD has been reported as being rare in both stroke patients and the general population. In this study, an attempt has been made to determine the prevalence of CAD in a black South African stroke population.

Methods—The prevalence of CAD was determined by indicators identified through a series of 5 observational studies in black patients diagnosed with stroke. CAD indicators included (1) bedside diagnosis in 741 patients; (2) resting ECG in 555 consecutively admitted patients; (3) a combination of clinical examination, cardiac ultrasound, radionuclide scintigraphy, and multigated blood pool studies in 102 consecutively admitted patients; (4) thallium scintigraphy in 60 patients; and (5) necropsy in 23 patients.

Results—On bedside questioning, only 0.7% complained of previous angina. There was no history given of myocardial infarction (MI), but documentation of this was found in the clinical notes of 0.7% of the patients. In the resting ECG study, evidence of myocardial ischemia was present in 14.6% and MI in 2.1%. In the combined study, cardiac ischemia was documented on ECG in 12.7% of patients and evidence of previous MI in 5.8%. Cardiac scintigraphic studies revealed changes of myocardial ischemia in 31.7% and MI in 13.3% of the 60 patients studied. Four (17.4%) of 23 patients in the necropsy study had histological evidence of previous MI, and 50% of all patients had evidence of >50% atherosclerotic stenosis in 1, 2, or 3 coronary arteries.

Conclusions—The prevalence of CAD in black African stroke patients is significantly higher than has been documented in the general nonstroke black population as well as in stroke patients. Black stroke patients may have a risk for CAD similar to that of their white counterparts. (Stroke. 2000;31:1294-1298.)

Key Words: blacks ■ cerebrovascular disorders ■ coronary artery disease ■ South Africa

Coronary heart disease (CAD) is rare in black Africans,1–5 Japanese,6 and Melanesian Islanders.7 In a recent review,3 CAD accounted for only 6% of all forms of cardiovascular disease in black Africans. In South Africa (Soweto, population 3 to 4 million), CAD accounts for <1% of deaths.8 A similar low prevalence of CAD has been recorded in black African stroke patients.9 In recent years, major social and demographic changes have taken place in Africa, with large sections of rural black populations migrating to the cities, adopting a more western style of life, and being exposed to vascular risk factors with respect to diet, smoking habit, and level of physical activity, with the consequent emergence of a variety of degenerative “first-world” diseases.10 Recent hospital morbidity and intensive care unit statistics in South Africa indicate that the prevalence of CAD in urban blacks is increasing.11,12 However, the frequency of MI in the general black population is still considered to be less than one tenth that in whites.8

In western populations, there is accumulating evidence that asymptomatic CAD is common in patients with ischemic cerebrovascular disease.13–15 In fact, in one longitudinal study more than half the patients who survived an ischemic stroke subsequently died of MI.13

A significant association with asymptomatic CAD has been demonstrated in patients with both extracranial and intracranial carotid artery stenosis.16,17 A direct relationship has been reported between both the degree and the angiographic features of carotid artery disease and the severity of CAD and iliac stenosis in all age groups for men as well as older women.18 Atheroma of the carotid artery appears to be a marker for atherosclerosis in both coronary and peripheral limb vessels. Moreover, western patients with CT evidence of cerebral ischemia but who are asymptomatic for coronary heart disease have significantly more abnormal radionuclide myocardial perfusion defects than do nonstroke con-
It would therefore appear that in western populations, patients with ischemic cerebrovascular disease are at particular risk for CAD.20

The aim of the current study was to assess the prevalence of ischemic heart disease in South African black stroke patients through a variety of methods, ranging from bedside evaluation to cardiac scintigraphy and, finally, necropsy studies.

Subjects and Methods

Patients

The results reported in this study were derived from the Medical University of Southern Africa (Medunsa) Stroke Data Bank (MSDB),21 into which all black patients with the diagnosis of stroke admitted to Garankuwa Hospital (450 beds), the teaching hospital for the University of Southern Africa, were entered. Although the MSDB was not strictly a population-based registry, with very few exceptions, all stroke patients in the area are referred to Garankuwa Hospital, the only hospital in the district. We therefore considered the data bank a fair representation of cerebrovascular disease in the black community served by the hospital. The total black population of the area has been reported as 168 936 black adults (82 722 men and 86 214 women), who live in the townships of Garankuwa, Mabopane, and Shoshanguwe (1991 National Census Data).

Diagnosis of Stroke

Stroke was defined as rapidly developing signs of focal or global disturbance of cerebral function leading to death or lasting >24 hours with no apparent cause other than vascular. Transient ischemic attacks (TIAs) were defined as deficits lasting <24 hours. The primary diagnostic categories of stroke—TIAs, cerebral infarction, and parenchymal cerebral hemorrhage—were made on the basis of CT appearances, clinical guess, or autopsy evidence. In the stroke data bank as a whole, 73% of patients underwent CT scanning. For all patients, the final diagnosis of stroke and its subtype was made by the treating neurologist (J.J.).

Study Design

The study design was observational and consisted of a series of 5 separate sequential studies that evaluated the prevalence of CAD by a variety of different investigative modalities (see the Table). For the most part, the patients were consecutive admissions to the stroke database, but in the scintigraphic study patients were randomized according to a computer-generated randomization schedule. The necropsy study was on consecutive patients who had been admitted to the MSDB and who died while in hospital. Although it would have been ideal to have performed all the studies on the same groups of patients, this was not possible due to practical considerations. The groups were very similar with respect to age, sex, and stroke pathology.

Historical Data

In this prospective study, symptoms of chest pain suggestive of MI were assessed according to the London School of Hygiene Rose questionnaire22 in all patients who were entered into the MSDB. Two interviewers who were fluent in the local black languages (Pedi, Tswana, and Zulu) were trained to administer the questionnaire. They questioned the patients directly if they were able to give a history, or the patients’ relatives or friends if they were unable to do so. The clinical notes were studied for documentation of previous historical or ECG evidence of CAD. The historical data of all patients who had symptoms suggestive of myocardial ischemia were checked by the first author (J.J.), who is fluent in the local black languages.

ECG Study

An evaluation of the 12-lead resting ECGs of 555 stroke patients who were consecutively admitted to the MSDB was made by 2 readers blinded to both cardiovascular and stroke pathology of the patients. Using the Minnesota coding system,23 attention was given to the presence of poor R wave progression in the precordial leads, pathological Q waves (defined as Q waves present in 2 contiguous leads, ≥25% of the R wave in the same lead and of 0.04 seconds duration), and ST-T wave changes, such as flat depression ≥1 mm below the baseline.

Combined Clinical, ECG, Cardiac Ultrasound, and Nuclear Medicine Study

An additional 102 consecutively admitted stroke patients were examined clinically by a cardiologist and underwent a resting ECG, chest radiograph, cardiac ultrasound examination, and multigated blood pool scan (MUGA). A final diagnosis of ischemic heart disease was made by the cardiologist on the basis of all of the available data.

Scintigraphic Study

Myocardial perfusion studies (methoxyisobutylisonitrile or thallium) were performed on 60 randomly selected stroke patients admitted to the data bank. Exclusion criteria were age <20 years; moribund or very ill patients; and recognized contraindications for provocative tests for myocardial ischemia, such as asthma, severe hepatic dysfunction, and known allergy to dipyridamole. Each myocardial perfusion study was reviewed independently by 2 observers blinded as to the clinical details. If there was disagreement in the interpretation, arbitration was sought from a third observer. All of the studies were performed with and without dipyridamole stress testing, as

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### Study Group Demographic and Stroke Classifications for Black South African Stroke Patients in 5 Observational Studies Estimating the Prevalence of Ischemic Heart Disease

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Patients, n</th>
<th>Mean Age, y</th>
<th>Men/Women, %</th>
<th>Cerebral Hemorrhage, %</th>
<th>Cerebral Infarction, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of angina, and/or previous myocardial infarction</td>
<td>741</td>
<td>55—M</td>
<td>44:56</td>
<td>29</td>
<td>71</td>
</tr>
<tr>
<td>Resting ECG</td>
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<td>55—M</td>
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<tr>
<td>Clinical examination, chest radiograph, cardiac ultrasound, and MUGA</td>
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<td>Cardiac scintigraphy</td>
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<td>Necropsy study</td>
<td>23</td>
<td>68—M</td>
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opposed to exercise stress testing. Images were documented as either (1) normal, with no perfusion defect before or after dipyridamole stressing; (2) ischemic, demonstrating a perfusion defect after dipyridamole stressing, with the defect spontaneously reversing after a 4-hour delay, or (3) infarction, ie, demonstrating an irreversible perfusion defect present both before and after dipyridamole stressing. In abnormal scans, the location of the perfusion defects (inferior wall, anterior wall, apex, and septum) and an arbitrary estimation of size according to the number of segments involved (small: involving 1 segment; moderate: 2 or 3 segments; and large: involving ≥4 segments) was documented.

Necropsy Study
We performed macroscopic and microscopic pathological examinations of the hearts, coronary vessels, and kidneys of 23 consecutive stroke patients dying in hospital after being admitted to the MSDB. The hearts were examined for evidence of infarction, with fibrosis being considered significant for MI at a measurement of ≥1 mm in diameter. The entire dissected length of each major coronary artery was transsected and the maximum area of stenosis determined. The number of vessels showing >50% stenosis was recorded, as were evidence of renal hypertensive changes and left ventricular hypertrophy.

Consent and Institutional Review Procedures
The data for the historical and ECG studies were obtained as part of the general medical workup of all stroke patients admitted to the hospital. Therefore, consent was not sought from each patient individually. Institutional review was obtained, however, for the ongoing Medunsa Stroke Data Base, a project that began in 1983 and ended in 1993. Ethics approval was obtained for all the other studies (combined clinical, ECG, echocardiographic, and MUGA study; the scintigraphic study; and the autopsy study). Individual patient approval was obtained for the combined clinical, ECG, echocardiographic, and MUGA study, and for the scintigraphic study. Consent for the autopsy study was obtained from the relatives of the deceased.

Results
Age, sex and stroke classifications of subjects participating in all 5 observational studies are shown in the Table. The estimates of prevalence of CAD derived from the 5 observational studies are shown in the Figure.

History of Angina or Previous Myocardial Infarction
Of the total of 984 patients entered into the MSDB between 1984 and 1993, the historical data of 741 were considered adequate for the evaluation in mind. There were 526 patients (71%) with cerebral infarction and 215 (29%) with parenchymal cerebral hemorrhage. There were no patients with a history of TIA. A history compatible with angina was present in 0.7% of the patients. No patient was aware of having had a previous myocardial infarction (MI). However, according to the medical records, 5 patients (0.7%) had previously documented MI. No patient was aware of the distinction between cardiac ischemia and other cardiac disease.

Electrocardiographic (ECG) Study
In the group of 555 consecutive stroke patients admitted to the MSDB who were studied with resting ECGs, 72% had CT-confirmed cerebral infarction, 28% had CT-confirmed parenchymal hemorrhage, and 3 had TIAs. All of the patients had a resting ECG performed between the 3rd and the 5th day after the stroke. In the 555 patients, ECG changes compatible with myocardial ischemia were present in 81 patients (14.6%). In this group there were 56 patients with cerebral infarction and 25 with parenchymal cerebral hemorrhage. Pathological Q waves compatible with previous MI were present in 8 patients (1.4%), 3 of whom had cerebral infarction and 5 parenchymal cerebral hemorrhage. ECG changes of acute MI were present in 4 patients (0.7%); all of these patients had CT evidence of cerebral infarction. Of the 555 ECGs evaluated, changes considered to be indicative of CAD were present in 16.8%.

Combined Study of 102 Patients (Clinical Assessment, Radiographic, ECG, Cardiac Ultrasound Examination, and MUGA)
There were 45 men and 57 women. The mean age of the male patients was 55 years and that of the females 60 years (range 18 to 100 years). All patients had CT scans of the brain. Cerebral hemorrhage was observed in 22 patients, and the diagnosis of cerebral infarction was made in 80.

In this group, 13 (12.7%) patients had T-wave or ST-segment changes on the ECG compatible with myocardial ischemia. Four patients had ECG evidence of old transmural MI. In 2 additional patients the ECG was negative, but the cardiac ultrasound revealed focal dyskinetic segments compatible with previous MI. A final diagnosis of previous MI was therefore made in 6 patients (5.8%). When the echocardiogram contributed to the diagnosis of previous MI by demonstrating segmental hypokinesia, the MUGA confirmed
these findings. The average age of patients with evidence of MI was 68 years (range 56 to 82 years). No patient had evidence of recent MI, and none had a history of previous MI or of chest pain.

Scintigraphic Study
Of the 60 patients (30 men and 30 women), the average time between stroke and scintigraphic study was 4 weeks. Their mean age was 53 years (range 24 to 94 years). Cerebral infarction was diagnosed on CT scan in 53 patients (88.3%) and parenchymal intracerebral hemorrhage in 7 (11.7%). There were no patients with TIAs. Thirty-four patients (56.7%) had normal myocardial perfusion imaging before and after dipyridamole. Reversible perfusion defects (ischemia) were present in 19 (31.7%), and fixed perfusion defects (MI) were recorded in 8 (13.3%). CAD was therefore diagnosed scintigraphically in a total of 27 patients (45%).

The mean age of the patients with MI was 53 years, compared with that of the patients with myocardial ischemia (52 years) and those with normal scintigrams (46 years).

Six patients with evidence of MI had perfusion defects of the inferior wall. This was taken into account in the assessment of the scintigraphs to differentiate between true perfusion defects and the "normal" attenuation seen in the proximity of the diaphragm. The majority of the abnormal scintigrams had only small perfusion defects; only 8 had "moderate" sized defects (3 in patients with MI), and none had "large" defects.

ECG evidence of ischemia was present in only half of the patients with myocardial ischemia on scintigraphy and in 1 patient with MI, the latter possibly because the majority of fixed perfusion defects observed on scintigraphy were inferiorly located.

Necropsy Study
The stroke pathology in the 23 patients was cerebral infarction (in 16 patients) and parenchymal cerebral hemorrhage (in 7 patients). Although no patient had a history of previous MI, necropsy evidence of previous MI was observed in 4 patients (17.4%). Fifty percent of all of the patients had stenosis of >50% in 1, 2, or 3 coronary vessels. Of all the patients (n=23), 21.7% had stenosis of >70% in 1 vessel, 4.3% had 2-vessel stenosis >70%, and 4.3% had 3 vessels with stenosis >70%. The most frequently involved vessels were the left main coronary artery (n=5) and the left anterior descending coronary artery (n=7). Pathological findings consistent with systemic hypertension were found in 52% of the patient group as a whole, slightly less than those with a known documented history of hypertension (71%). All 4 patients with MI were diabetic.

Discussion
Clearly, the prevalence of CAD in black African stroke patients referred to Garankuwa Hospital is much higher than that reported previously. The hospital is typically large, well-equipped, and serves an almost exclusively urban and semirural population. Previous community research (J.J.) indicated that the great majority of black African stroke patients are not treated initially by traditional methods (herbalist/traditional healer) and, if they survive the first hours, are taken to the nearest hospital. Where road transport and ambulance service is adequate, as in the area described, only the minority of patients dying within a short while would not be admitted to hospital. Thus, stroke patients admitted to the hospital may be regarded as a true reflection of the condition. Limitations include possible selection bias, as in the scintigraphic study, in which patients who were too ill were excluded; and in the autopsy study, in which only the severely ill patients were investigated. However, there was unequivocal evidence of CAD in a substantial proportion of the necropsy material, a finding supported by the results of 3 of the other substudies. Coronary vessel stenosis of >50% was observed in ≥1 of the coronary arteries in over half of all necropsy patients examined, and 17.4% had histological evidence of previous MI. There was good correlation between the necropsy findings and those of the scintigraphic study group, with 13.3% of the latter having evidence of previous MI in the form of irreversible perfusion defects.

The prevalence of CAD (myocardial ischemic changes and/or frank infarction) in the 555 consecutive patients whose resting ECGs were analyzed was higher than that previously reported in studies on stroke and nonstroke populations of black Africans.2,3,9,11,24–26 The prevalence was similar to that found in a white nonstroke population in Durban, South Africa,27 and is comparable to the prevalence of CAD documented in stroke registries in Western populations.21,28,29

The ECG diagnosis of CAD in African blacks has been controversial since 1954, when Grusin30 reported that “ischemic” ECG variants were not indicative of CAD in this population. Later studies in both South African and Caribbean blacks confirmed these findings31,32 and led to certain local workers ignoring the ECG findings of “ischemia” in South African blacks and relying solely on a history of chest pain for the diagnosis of CAD.11 The danger of ascribing such ECG changes to a “normal variant pattern” in black Africans has been noted.33 In the nested study assessing clinical, ECG, ultrasound, MUGA evidence of CAD in 102 patients, the ECG prevalence of ischemic changes was found to be similar to that of the ECG study of 555 subjects; however, the adjunctive use of cardiac ultrasound and MUGA resulted in a 2-fold increase in detection of previous MI.

There is a significant difference between the prevalence of CAD in both the scintigraphic and necropsy studies of the stroke patients and the reported clinical experience reported in equatorial and Southern African countries, where evidence of CAD in the form of angina, or “events” such as MI, is still rare in the general black population as well as in stroke patients.1–5,11,24–26 For example, in King Edward VIII Hospital (250 beds) in Durban, between 1955 and 1980 the diagnosis of CAD was made only in 2.7% of all Zulu patients admitted with cardiovascular disease compared with 30% in the case of Indian patients. In the same hospital, between 1980 and 1986, MI as the cause of death was documented in only 2.7% in 5000 consecutive nonstroke adult black necropsies.11 These data are in agreement with those of a general necropsy study of black (nonstroke) Africans made in Ghana, where the coronary vessels of the majority of patients, both normotensive and hypertensive, were found to be either normal or only minimally affected by atherosclerosis.34

In a comparison of age- and sex-specific mortality rates from CAD in interethic populations in 1978 to 1989, a low mortality rate for ischemic heart disease in African blacks was reported.24
Similarly, in 1992, in an urban sample of 458 blacks (age range 16 to 69 years) the prevalence of CAD, assessed on the basis of anginal chest pain, was found to be only 2.4%. Clinical CAD is very uncommon in urban South African blacks and “nearly absent” in their rural counterparts. In Soweto (population 3 to 4 million), at the Chris Hani Baragwanath Hospital (with 3200 beds, the largest hospital in the southern hemisphere), which caters almost exclusively to blacks, on average only about 70 patients with CAD are admitted annually. In the present study, a history of angina and/or a past history of MI were very uncommon, being present in <1% of patients. However, the historical evidence of CAD in the stroke patient may be misleading because of factors associated with the stroke itself. There was a relatively high prevalence of diabetes in our study in the patients with MI, as is also the case in the general population, so silent MI may be common.

This low prevalence of clinical CAD in African blacks prevails despite relatively major changes in both lifestyle and environmental exposure. Indeed, in a recent study of 1611 adult South African blacks, it was found that all the risk factors necessary for an “epidemic” of CAD were present. In sharp contrast to the foregoing, mortality rates for CAD among South African whites, Indians, and coloreds (European–African–Malay South Africans of mixed ancestry) are among the highest in the western world. Furthermore, among African-Americans, CAD not only develops earlier but also, in the case of black women, carries a higher mortality rate than in white American women. Interestingly, blacks from both Africa and the Caribbean who migrate to the United Kingdom maintain a persistently low mortality rate from CAD compared with that of other migrant groups, for instance those from South Asia, which indicates a more complex multifactorial genesis for atherosclerosis than is apparent from known risk factors.

References


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