Electrocardiographic Assessment of Coronary Artery Disease and Stroke Risk Factors in Rural and Urban Tanzania: A Case–control Study

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Background: Although the association between cerebrovascular and coronary artery disease (CAD) is well known in high-income countries, this association is not well documented in black Africans. *Aims:* The aim of this study was to document electrocardiographic (ECG) evidence of CAD in stroke cases and controls and to identify other common ECG abnormalities related to known stroke risk factors in a community-based population of incident stroke cases in Tanzania, East Africa. *Methods:* This was a case–control study. Incident stroke cases were identified by the Tanzanian Stroke Incidence Project. Age- and sex-matched controls were randomly selected from the background population. Electrocardiograms were manually analyzed using the Minnesota Coding System, looking for evidence of previous myocardial infarction (MI), atrial fibrillation (AF) or atrial flutter (AFl), and left ventricular hypertrophy (LVH). *Results:* In Hai, there were 93 cases and 241 controls with codable electrocardiograms, and in Dar-es-Salaam, there were 39 cases and 72 controls with codable electrocardiograms. Comparing cases and controls, there was a higher prevalence of MI and AF or AFl (but not LVH) in cases compared with controls. *Conclusions:* This is the first published study of ECG assessment of CAD and other stroke risk factors in an incident population of stroke cases in sub-Saharan Africa. It suggests that concomitant CAD in black African stroke cases is more common than previously suggested. **Key Words:** Electrocardiography—stroke—Tanzania—coronary artery disease—sub-Saharan Africa.
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Introduction

Coronary artery disease (CAD) is commonly found in conjunction with cerebrovascular disease in high-income countries.[1] A person may be asymptomatic of their CAD but several studies have shown a relationship between computed tomography evidence of cerebrovascular disease and abnormal myocardial perfusion defects indicative of CAD.[1-3] However, the association between CAD

and cerebrovascular disease is more tenuous in the black population in sub-Saharan Africa (SSA), with the frequency of myocardial infarction (MI) in the general black population in South Africa less than 1/10th that in whites,[4] and a similarly low prevalence of CAD recorded in black African stroke cases.[5]

The INTERSTROKE study of stroke risk factors across 22 countries worldwide reported that hypertension and cardiac causes (such as ischemic heart disease [IHD], atrial fibrillation [AF] and atrial flutter [AFl]) were the 2 strongest independent predictors of stroke risk.[6] However, few of those countries studied were from SSA. The aim of this study was to use electrocardiographic (ECG) findings to evaluate the prevalence of CAD and arrhythmias in an urban and a rural population of incident black stroke cases in Tanzania.

Participants and Methods

Favorable ethical opinions were obtained from the National Institute of Medical Research in Tanzania and from the Newcastle and Northumberland Joint Ethics Committee, UK.

Setting and Recruitment

Cases

The study described here was part of the Tanzanian Stroke Incidence Project (TSIP).[7] The study prospectively identified people who had survived the initial stroke event and aimed to assess them as soon after stroke onset as possible. Details of the study have been published and they are described briefly here.[7] Cases were recruited from June 15, 2003, until June 15, 2006, in 2 demographic surveillance sites (DSSs): 52 villages in the Hai district of northern Tanzania and 8 geographical divisions of the city of Dar-es-Salaam. Both the urban and rural site chosen for the study were set up in the 1990s as DSSs for use in the Adult Morbidity and Mortality Project (AMMP), the key results of which have been published.[8] The Hai district, in northern Tanzania, is a rural area, with an economy based on cash crops, mainly coffee. Dar-es-Salaam is Tanzania's largest city and its commercial capital; the DSS within Dar-es-Salaam was selected to cover a range of socioeconomic conditions. The DSS in Hai had a population of 159,814 and the DSS in Dar-es-Salaam a population of 56,517, at the midpoint of the study, on December 15, 2004.[7] Both sites have previously been described as part of the AMMP.[8]

Controls

Controls were recruited from the background census population of the DSSs in Hai and Dar-es-Salaam. They were identified from the census list, and were frequency matched to cases for age (±3 years) and sex. A list of possible controls was produced using a random number gen-erator. The controls were randomly assigned a preference and visited in order. If a control was unavailable or refused to participate, the next person on the list was visited, and so forth, until sufficient controls had been recruited.

Assessment

Blood pressure (BP) was recorded at least 7 days poststroke to allow for the fact that BP rises during the first few days after stroke. BP was recorded while sitting using an A&D UA-767 (A&D Instruments Ltd, Abingdon, Oxfordshire, United Kingdom) BP monitor.[9] Three measurements were taken 1 minute apart after 5 minutes resting quietly. An average of the last 2 readings was taken.[10] Nonfasting blood samples were taken from those who consented. The collected blood samples were frozen on dry ice and subsequently transported back to the United Kingdom before being analyzed at North Tyneside General Hospital.

During assessment, resting 12-lead ECGs for cases and controls were recorded using a GE MAC 1200 machine (GE Healthcare, Chalfont St Giles, Buckinghamshire, United Kingdom) and interpreted by the study cardiologist (M.D.).[11] Every 10th ECG was then reviewed by a second independent cardiologist (P.C.A.). The Minnesota Coding System (MCS) was developed for population-based studies to analyze ECGs for the prevalence of prognostically significant abnormalities.[12] In order that the evaluation was standardized, we used the MCS as a guideline to analyze the ECGs manually. Manual evaluation has previously been shown to be reliable when reporting ECG abnormalities by the MCS.[13] We paid particular attention to pathological Q waves (Q waves in 2 contiguous leads, Q/R ratio >1/3 and Q duration >30 ms) and ST–T wave changes, in particular ST elevation in presence of reciprocal ST depression/T-wave inversion (TWI) when looking for potential MI or ischemia. We defined subjects as having evidence of previous MI, using the MCS, if their ECG revealed pathological Q waves. In addition, according to MCS classification, we looked for evidence of arrhythmias, particularly AF and AFl, and left ventricular hypertrophy (LVH).

Statistics

Frequency matching for age and sex was employed, and data were analyzed as for an unmatched case–control study. The data were quantitative in nature and collected at a nominal, ordinal, and interval/ratio level. Data were analyzed using standard statistical software, PASW (version 18; PASW, Chicago, IL) and SAS (version 9.2; SAS Institute, Cary, NC). Confidence intervals (CIs) were calculated for odds ratios (ORs; categorical data), with a 95% CI not containing 1.0 signifying significance. For differences between means (continuous, normally distributed data), 95% CI not crossing zero signifies significance.

Two-tailed tests were used throughout, and the significance level was set at 5%. Missing values were treated as being missing completely at random.

Results

Study Population Characteristics

The TSIP system identified 132 cases of stroke in the DSS in Hai and 69 in the DSS in Dar-es-Salaam. We attempted to interview cases as soon after incident stroke as possible, but a few cases were not identified as having had a stroke until visited by a health care worker or key informant some months later. Nevertheless, only 17 cases (11 Hai and 6 Dar-es-Salaam) were interviewed at greater than 6 months poststroke; the median time from incident stroke to assessment interview was 19 days (range 0-252 days). One case of subarachnoid hemorrhage from Hai was excluded from further analysis because of the different etiology of this stroke type.

Cases were matched to 260 (1:1.98) controls in Hai and 138 (1:2) controls in Dar-es-Salaam. The study aimed to capture all persons having a stroke within the study period. Twenty-eight cases were identified shortly after death had occurred (20 in Hai and 8 in Dar-es-Salaam) and a further 2 (both in Hai) died before a full interview could take place. In addition, in 35 cases (14 in Hai and 21 in Dar-es-Salaam), an ECG was not recorded because of lack of equipment or personnel at the time. In 2 cases (1 in Hai and 1 in Dar-es-Salaam), the ECG recorded was uninterpretable because of the poor quality of the recording and could not be coded. Therefore, a codable ECG was recorded on the remaining 94 cases (71.8%) in Hai and 39 cases (56.5%) in Dar-es-Salaam. In Hai, 241 of 260 controls (92.7%) had codable ECGs, whereas in Dar-es-Salaam 71 of 138 controls (51.4%) had codable ECGs. In Dar-es-Salaam, the lower rate of codable ECGs was mainly because of the lack of equipment for a part of the study.

Data for cases with codable ECGs, cases without codable ECGs, and controls with codable ECGs are presented in Table 1. In both Hai and Dar-es-Salaam, there was no significant difference in age between those cases who had a codable ECG and those who did not or between cases who had a codable ECG and controls. There were no significant differences in gender distribution between cases with codable ECGs and cases without codable ECGs in Hai (OR 1.16, 95% CI .55-2.47) or Dar-es-Salaam (OR 1.83, 95% CI .70-4.80) or between cases with codable ECGs and controls with codable ECGs (Hai: OR 1.08, 95% CI .67-1.74; Dar-es-Salaam: OR 1.47, 95% CI .66-3.26). Therefore, we have no reason to suspect that our sample was demographically biased.

Although both systolic and diastolic BP was generally lower in controls when compared with cases with a codable ECG, this difference was only significant for diastolic BP in Hai. Total cholesterol to high-density lipoprotein cholesterol ratios were significantly lower in controls than cases.

ECG Results

Details of the findings by ECG using the MCS are summarized in Table 2. LVH appeared to be significantly more common in Hai controls than in Dar-es-Salaam controls. The 95% CIs for percentages of MI, AF/AFl, and LVH overlapped for cases in Hai district and Dar-es-Salaam, suggesting no significant differences between the 2 sites. Therefore, for further analysis, the data for both sites were combined, see Table 3. Comparing cases and controls, the prevalence of MI and AF or AFl was significantly higher in cases than controls. There was no

Table 1. *Comparison of cases with codable electrocardiograms, cases without codable electrocardiograms, and controls with codable electrocardiograms*

	Cases with codable ECG	Cases without codable ECG	Controls with codable ECGs
Hai	n = 93	n = 38	n = 241
Mean age (y) (95% CI)	68.2 (65.1-71.3)	70.0 (65.3-74.8)	69.6 (67.8-71.4)
Sex	43 female, 50 male	19 female, 19 male	107 female, 134 male
Mean systolic BP (mm Hg) (95% CI)	148.0 (142.2-153.7)	153.8 (133.1-174.5)	151.4 (147.1-155.7)
Mean diastolic BP (mm Hg) (95% CI)	91.6 (88.6-94.7)	92.9 (79.9-105.9)	84.2 (82.0-86.3)
Total cholesterol/HDL cholesterol ratio (95% CI)	6.4 (5.9-6.9), 23 missing values	6.4 (5.0-7.8), 32 missing values	5.0 (4.7-5.3), 80 missing values
Dar-es-Salaam	n = 39	n = 30	n = 71
Mean age (y) (95% CI)	61.1 (56.1-66.8)	62.1 (57.3-66.9)	61.1 (57.8-64.5)
Sex	15 female, 24 male	16 female, 14 male	34 female, 37 male
Mean systolic BP (mm Hg) (95% CI)	155.3 (142.3-168.4)	155.1 (142.9-167.2)	144.7 (137.9-151.4)
Mean diastolic BP (mm Hg) (95% CI)	95.0 (88.0-101.2)	94.4 (86.8-102.0)	85.3 (82.2-88.5)
Total cholesterol/HDL cholesterol ratio (95% CI)	6.6 (5.8-7.3), 3 missing values	6.4 (5.4-7.4), 13 missing values	5.0 (4.5-5.6), 16 missing values

Abbreviations: BP, blood pressure; CI, confidence interval; ECG, electrocardiogram; HDL, high-density lipoprotein.

Table 2. *Electrocardiogram findings for cases and controls*

	Cases	Controls
Hai	n = 93	n = 241
Number with MI (%)	22 (23.7; 95% CI 15.0 to 32.3)	36 (14.9; 95% CI 10.4 to 19.4)
AF or AFl (%)	6 (6.5; 95% CI 1.5 to 11.4), 4 AF and 2 AFl	2 (.8; 95% CI 0 to 2.0), 1 AF and 1 AFl with variable block
LVH (%)	30 (32.3; 95% CI 22.8 to 41.8)	94 (39.0; 95% CI 32.8 to 45.2)
Dar-es-Salaam	n = 39	n = 71
Number with MI (%)	6 (15.4; 95% CI 4.1 to 26.7)	5 (7.0; 95% CI 1.1 to 13.0)
AF or AFl (%)	3 (7.7; 95% CI −.7 to 16.1), All AF	0
LVH (%)	11 (28.2, 95% CI 14.1 to 42.3)	14 (19.7, 95% CI 10.5 to 29.0)

Abbreviations: AF, atrial fibrillation; AFl, atrial flutter; CI, confidence interval; LVH, left ventricular hypertrophy; MI, myocardial infarction.

significant difference in LVH prevalence between cases and controls. When the analysis was conducted on men and women separately, there were no significant differences in rates of MI and AF, AFl, or LVH between cases and controls.

As shown in Table 4, there was no significant difference between cases with LVH and cases without LVH regarding systolic or diastolic BP or total cholesterol/high-density lipoprotein cholesterol ratio. Comparing cases with and without evidence of MI, although there is no significant difference in cholesterol values or BP, those with evidence of MI by MCS had noticeably higher systolic and diastolic BP than those with no evidence of MI.

Discussion

Myocardial Infarction

The strong relationship between MI, IHD, and stroke has been well studied in predominantly white populations living in high-income countries. In these populations, the risk of stroke after MI is higher than in the general population and may be as high as 1 of 40 in the elderly population.[14,15] Moreover, stroke and IHD appear to share common risk factors such as raised cholesterol, diabetes, and hypertension. However, the small amount of current data available in SSA has been used to make the generalization that IHD is not commonly associated with cerebrovascular disease and that hypertension is a much more important risk factor than atherosclerosis.[16]

The major finding in our study was that, by ECG coding, the prevalence of CAD in a population of incident stroke cases was higher than in age- and sex-matched controls (see Table 3). Furthermore, rates of CAD in both cases and controls were higher than previously reported for black African populations.[4,5] One potential reason for the higher rates reported here is that much of the previous data were collected in the 1980s and that patterns of stroke risk factors may be changing as countries in SSA undergo demographic transition.[5] Gillum[17] has suggested 6 stages of epidemiological transition of cardiovascular disease in black people of African origin. Earlier stages show hypertension as the main risk factor for stroke, while later stages suggest that atherosclerotic processes become more important. However, when carotid ultrasound was carried out on consecutive stroke cases recruited to TSIP, evidence of carotid stenosis was very rare and when present was minimal.[18] Given the lack of apparent evidence of carotid atherosclerosis or overt IHD symptoms, it is interesting that so many have evidence of IHD by ECG.

It has been previously noted that ischemic ECG changes in black Africans may not necessarily represent CAD in this population. The MCS categorizes ECGs "diagnostic" of ischemia/previous infarction in 2 ways. The first (D1) is an ECG with a diagnostic Q-wave code and the second (D2) is an ECG with an ST elevation of 1 mm or more in contiguous leads with corresponding reciprocal TWI. D1 is reliable, in that while stroke cases have been shown frequently (up to 20%) to have Q waves on their ECG, these Q waves represent previous evidence of CAD (ie, were

Table 3. *Combined electrocardiogram findings*

	Cases (n = 132)	Controls (n = 312)	Percentage difference (95% CI for difference)
Number with MI (%)	28 (21.2)	41 (13.1)	8.1 (.2 to 16.0)
AF or AFl (%)	9 (6.8)	2 (.6)	6.2 (1.8 to 10.6)
LVH (%)	41 (31.1)	108 (34.6)	3.5 (−13.1 to 5.9)

Abbreviations: AF, atrial fibrillation; AFl, atrial flutter; CI, confidence interval; LVH, left ventricular hypertrophy; MI, myocardial infarction.

Table 4. *Association between presence of MI and left ventricular hypertrophy and BP and cholesterol measurements in stroke cases*

	Mean total cholesterol/HDL cholesterol ratio (95% CI)	Mean systolic BP in mmHg (95% CI)	Mean diastolic BP in mmHg (95% CI)
MI			
Present	6.3 (5.5-7.1)	155.9 (141.3-170.5)	94.7 (86.6-102.8)
Absent	6.3 (5.9-6.8)	148.6 (140.8-156.4)	91.7 (87.8-95.6)
LVH			
Present	6.2 (5.4-6.9)	151.4 (139.5-163.2)	90.6 (85.2-96.0)
Absent	6.4 (5.9-6.9)	149.6 (141.1-158.1)	93.4 (88.8-98.0)

Abbreviations: BP, blood pressure; CI, confidence interval; HDL, high-density lipoprotein; LVH, left ventricular hypertrophy; MI, myocardial infarction.

present on previous ECGs) rather than having been caused by an intracerebral event.[19] However, D2 is less reliable in this population, given that ECG–LVH (often giving TWI in "strain" pattern) in black adults is 2-4 times more prevalent than in white adults,[20-22] and "early repolarization" phenomenon, particularly in the anterolateral precordial leads (ie, ST elevation at the J point on the ECG), is significantly more common in African Americans.[23,24] In addition, in a stroke population, these matters are further confused by the fact that acute stroke cases often have acute ischemic ECG changes such as ST depression and T-wave inversion.[25] For these reasons, we have only reported MI as being present in those with pathological Q waves.

Atrial Fibrillation and Atrial Flutter

Across both sites, there were significantly more stroke cases with AF and AFl than controls. The attributable risk of AF is well established in high-income countries, accounting for almost one quarter of all strokes in persons older than 75 years.[26] However, its role in low-income countries is not well known. The incidence of AF was lower than reported in previous studies of black African stroke cohorts. We have recently shown the prevalence of AF to be low in elderly people in Tanzania and have suggested that one possible reason for this may be a high mortality rate in people with AF.[27] In a resource poor setting, with limited health care provision, lack of diagnosis and treatment of AF may well result in a much increased risk of morbidity and mortality. Prospective studies of younger cohorts investigating the effect of AF on the burden of disease in SSA should be conducted.

Left Ventricular Hypertrophy

LVH was slightly more common in controls than in stroke survivors, although not significantly so. Furthermore, it was not associated with the presence of known strong risk factors, such as high BP or high cholesterol. Whether this is because LVH, as identified by ECG coding, is a poor marker for the presence of clinical LVH in this population is not clear.

Limitations

The main limitation of this study has already been acknowledged; that ECG changes may not necessarily represent CAD in this population. This may have led to over-reporting, although our conservative diagnosis of MI only if pathological Q waves are present should help to reduce the impact of this potential bias. The diagnostic efficiency of abnormal Q waves alone has previously been shown to have a sensitivity of 61%, and specificity of 89%, with an averaged overall performance of 75%.[28] Transient ST elevation can occur in stroke cases but would not have increased false-positive rates in our study because we relied on pathological Q waves for diagnosis. Another limitation of this study is the nonblinding of the ECG observer as to whether the ECG was from a stroke case or control. Finally, there is likely to be under-reporting of the overall prevalence of AF in this group, as many may have had paroxysmal AF.

Conclusions

As in high-income countries, having had a stroke was associated with the presence of ECG CAD in our study population. Although we acknowledge that ECG is a crude instrument for the detection of CAD, our study suggests that the generalization that CAD and MI are not common in black African populations may require further investigation. If such risk factors are becoming more common in SSA as a whole, then this is a worrying trend.

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