The Pattern and Prognostic Features of QT Intervals and Dispersion in Patients with Acute Ischemic Stroke

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Background: Ischemic stroke, which is perhaps the commonest subtype of stroke, is associated with electrocardiographic (ECG) changes. Some of these changes have been thought to be due either to the stroke state itself or pre-existing heart disease. Some, particularly QT intervals, have been associated with increased mortality.

Objective: The aim is to investigate the pattern of QTcmax, QTd and QTcd in patients with ischemic stroke and to compare these changes in patients without pre-existing heart disease in order to determine their prognostic importance.

Methods: Sixty-four patients with acute ischemic stroke were compared with 60 controls observing the various ECG changes. Patients without pre-existing heart disease were isolated and compared with the total cohort.

Results: Thirty-five (54.7%) of the patients had ischemic-like ECG changes made up of ST depression (29.7%), T-wave inversion (21.8%) and U wave (9.3%). Twenty-eight (43.8%) had QTcmax prolongation. Twenty-four (37.5%) of the patients had no pre-existing heart disease. The QT was similar when compared with the total cohort except in QTcmax, where there was significant difference (447.3 ± 72.2 vs. 408.6 ± 40.3 msecs). Mortality rate of the total cohort at 28.1% was significantly higher than in those without pre-existing heart disease at 8.3%, suggesting that presence of pre-existing heart disease contributed to mortality. QTcmax (r=0.293 p=0.045) and days on admission (r=-0.543 p=0.001) were the other variables that correlated with mortality in the total cohorts.

Conclusion: Ischemic-like and repolarisation ECG changes are common in our patients with acute ischemic stroke. These changes tend to be due to pre-existing heart disease rather than the stroke state.

Key words: ischemic stroke ■ QT intervals ■ QT dispersion ■ prognosis

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INTRODUCTION

Stroke is defined as rapidly developing clinical signs of focal or global disturbance of cerebral function lasting ≥24 hours or leading to death with no apparent cause other than vascular origin.[1] Ischemic stroke, which could be thrombotic or embolic, is the commonest type of stroke. It occurs in about three-quarters of all strokes worldwide,[2] and it is said to be equally common in the black race,[3,4] though some studies claimed that cerebral hemorrhage might be commoner.[5] When compared with subarachnoid hemorrhage, it occurs in older patients[6] and causes less mortality,[2] though it is associated with considerable disability and morbidity. In developing countries, the morbidity adduced to ischemic stroke adds significantly to the burden of communicable diseases already being carried by these communities. This has considerable socioeconomic implications.

The commonest risk factor for ischemic stroke includes hypertension, whose prevalence has been put at 11.2% in Nigeria and noted to be the commonest noncommunicable disease in the country.[7] Other risk factors include obesity, dyslipidemia and diabetes mellitus.[8]

Over the years, various electrocardiographic (ECG) parameters in stroke have been studied. In some studies and in ischemic stroke, the prognostic importance of these ECG parameters—particularly ST-segment changes and prolonged QT interval—has been demonstrated.[9,10] However, studies of QT dispersion (QTd) and corrected QT dispersion (QTcd) are few.

QTd is defined as the difference between the maximum and minimum QT intervals. QTcd is this measurement when the QT intervals have been corrected for heart rate.[11] It is a measure of ventricular repolarisation across the 12-lead ECG, and it represents ventricular inhomogeneity within the myocardium.[12] It has been found to be an independent indicator of arrhythmias and mortality in such conditions as the long-QT syndrome, cardiomyopathy and chronic heart failure.[12,13] In some studies, prolonged QT interval has been associated with higher mortality in stroke patients,[14] while in some—

particularly in ischemic stroke—this has not been so.[10]

Studies of the prognostic importance of the QTd and QTcd with mortality in stroke patients are very few, and they have not been previously reported in ischemic stroke patients in our environment. We thus decided to investigate the pattern and prognostic importance of these intervals in our patients with acute ischemic stroke. We also sought to compare the effects of the intervals in those without pre-existing heart disease and the total cohort.

PATIENTS AND METHODS

Sixty-four patients who suffered ischemic stroke, which was confirmed by World Health Organization (WHO) criteria and the Siriraj stroke score, were recruited for the study after obtaining informed consent from the patient or accompanying relative. The diagnosis was confirmed by CT scan in a proportion of the patients where affordable. They had ECG recorded within 24 hours, which was analyzed and compared with ECG of 60 sex- and age-matched controls by a cardiologist who was blinded to the clinical history of the patients.

Detailed clinical history was taken from the patient or accompanying relative and the patient was examined particularly to detect whether there was evidence of pre-existing heart disease. Patients with history of angina pectoris, myocardial infarction and heart surgery, use of cardiotonic drugs or ECG features of left ventricular hypertrophy (LVH), chamber enlargement, bundle branch block or myocardial infarction were classified as having pre-existing heart disease.[10] Hypertension without clinical and ECG evidence of LVH or ischemic heart disease was not accepted as pre-existing heart disease.

Ischemic-like ECG features include downsloping ST-segment depression or its flat depression of 1 mm or elevation of 1 mm in extremity and precordial leads (but ≥2 mm of elevation in V1 and V2)[10] Other significant ischemic-like changes include T-wave abnormalities of peaked, flat or inverted wave, U wave when negative or a positivity >25% of the preceding T wave.[9] QT interval was measured from the beginning of the QRS complex to the end of the T wave, defined as the return to the TP baseline. If U wave was present, the end of the measurement was taken as the nadir between the T and U wave.[12] The QT interval was rejected if the T wave was not clearly discerned. Three consecutive QT intervals were measured and the mean taken. The QT was corrected for heart rate (QTc) using the Bazzett's formula.[15] The intervals were manually measured, a method which has been shown to compare favorably with the existing automated methods.[16]

LVH was estimated using the Araoye criteria,[17] which have been validated to correlate well with echocardiogram in Nigerian patients particularly over 30 years of age.[18]

Death within four weeks of onset was taken as early mortality.

Exclusion criteria included use of drugs known to prolong QT intervals, including antimalarials such as halofantrine, antiarrhythmic and psychotropic drugs.

STATISTICAL ANALYSIS

Statistical analysis was performed using the SPSS® 11.0 Windows® data editor. All data were reported as mean ± SD and frequencies expressed as percent. Continuous variables were compared by the Student's t test. Frequencies were compared by Chi square. Pearson's coefficient (r) was used to test correlation between relevant variables, and the 95% confidence interval (CI) was determined. Level of significance was put at $p<0.05$.

Table 1. The basic characteristics and qt intervals of all stroke patients and controls

	Patients	Control	p Value
n (%)	n=64	n=60	
Age (years)	63.2 ± 11.6	62.0 ± 12.8	0.86
Sex (male)	34/64 (53.1)	30/60(50.0)	0.78
SBP (mmHg)	170.8 ± 27.6	128.2 ± 12.3	0.01
DBP (mmHg)	103.6 ± 17.7	82.5 ± 11.6	0.02
QTmax (secs)	377.5 ± 33.9	356.2 ± 42.9	0.04
QTcmax (secs)	447.5 ± 72.2	418.5 ± 36.8	0.04
QTd (msecs)	60.6 ± 25.1	48.8 ± 13.2	0.03
QTcd (msecs)	72.3 ± 32.8	51.7 ± 15.4	0.02
Arrhythmia	22 (34.4)	2 (3.3)	0.001
Prolonged QT	28 (43.8)	2 (3.3)	0.001
T-wave inversion	14 (21.8)	3 (5.0)	0.01
ST changes	19 (29.7)	1 (1.7)	0.001
U wave	6 (9.3)	0 (0.0)	0.001
Hospital stay (days)	15.6 ± 9.3	not relevant	
Mortality	18 (28.1)	not relevant	

Chi-squared test: 5.11, $p<0.05$

RESULTS

There were 64 patients with ischemic stroke who met the inclusion criteria, 34 (53.1%) of which were male. The mean age of the patients at 63.2 ± 11.6 years was not different from the 60 controls at 62.0 ± 12.8 years. Thirty-three (51.6%) of the patients had diagnosis confirmed by CT scan. There were 40 (62.5%) patients who had some form of pre-existing heart disease made up of 34/40 (85%) with LVH, two (5%) with right bundle branch block (RBBB) and two with rheumatic heart disease manifested as mitral regurgitation confirmed by echocardiography. There were two patients who had ischemic heart disease manifested as old inferior myocardial infarction; they also had LVH. Six patients had diabetes mellitus. The mean hospital stay was 15.6 ± 9.3 days. Ten (15.6%) of the patients died within four weeks of the onset of stroke (Table 1).

Thirty-five (54.7%) of the patients had some form of ischemic-like ECG change, the commonest of which was ST depression occurring in 29.7% of the patients. The mean QTcmax was prolonged at 447.5 ± 72.2 msecs. Twenty eight (43.8%) of the patients had QTcmax prolonged beyond 440 msec. The QTd interval was significantly longer in patients than control (60.6 ± 25.1 vs. 48.8 ± 13.2; $p<0.05$) just as the QTcd interval (72.3 ± 32.8 vs. 51.7 ± 15.4).

Arrhythmia occurred in 22 (34.4%) of all the patients made up of 13/22 (59.1%) with ventricular extra systoles, four (18.2%) with atrial fibrillation and two (9.1%) with supraventricular tachycardia. Five patients had sinus bradycardia, while two had RBBB.

When the 24 patients who had no pre-existing heart disease were compared with the total cohort (Table 2), there was no difference in the mean age of the two groups. Though the repolarization intervals were longer in the total cohort, it was only in QTcmax that this reached statistical significance. The percentage of patients with absolutely prolonged QTcmax was significantly more in the total patients when compared with those without heart disorder. A total of six (25.0%) patients in the group without pre-existing heart disease had some form of ischemic-like change on ECG compared with 54.7% of the total cohort ($p<0.05$).

Seven (29.2%) of the patients in the group without pre-existing heart disorder had arrhythmias made up of five with ventricular extra systole and two with sinus tachycardia.

The mortality rate of the total cohort at 28.1% was significantly more than the group without pre-existing heart disorder at 8.3%, suggesting that presence of pre-existing heart disease contributed to mortality. None of the deaths were sudden or associated with malignant arrhythmias.

The only other variables that correlated with mortality were QTcmax ($r=0.293$, 95% CI 0.01–0.78; $p=0.045$) and the days of admission ($r=-0.543$, 95% CI 0.32–1.10; $p=0.001$).

DISCUSSION

This study of ischemic stroke in our wholly black population revealed similar trends in age group among Caucasian patients,[10] though about a decade less than a wide review of patients usually in the seventh decade.[6] The generally low life expectancy in our population might account for this. However, African Americans are known generally to have higher risks when compared with their Caucasian counterparts.

When the total cohort group was considered, the repolarization indices were significantly longer in patients than controls. The ischemic-like changes at 54.7% were higher than that of Goldstein at 35%.[9] In this study, the commonest ischemic-like change was ST-

Table 2. Comparison in the ecg changes between the total cohort (unselected) and those without pre-existing heart disease (selected)

Unselected	Selected	p Value	
n (%)	64 (100)	24 (37.5)	0.02
Age (years)	63.2 ± 11.6	64.8 ± 12.8	0.64
QTmax (msec)	377.5 ± 33.9	363.3 ± 39.9	0.23
QTcmax (msec)	447.5 ± 72.2	408.6 ± 40.3	0.04
QTd (msec)	60.6 ± 25.1	51.7 ± 32.4	0.40
QTcd (msec)	72.3 ± 32.8	58.9 ± 34.4	0.26
SBP (mm Hg)	170.8 ± 27.6	172.5 ± 32.2	0.86
DBP (mmHg)	103.6 ± 17.7	101.7 ± 19.9	0.78
Hospital stay (days)	15.6 ± 9.3	17.5 ± 11.1	0.61
Arrhythmia	22(34.4)	7(29.2)	0.07
Prolonged QT	28(43.8)	5 (20.8)	0.03
T-wave inversion	14(21.8)	3 (12.5)	0.05
ST changes	19 (29.7)	4(16.7)	0.05
U wave	6 (9.3)	2 (8.3)	0.73
Mortality	18 (28.1)	2 (8.3)	0.02

Chi-squared test: 2.73, $p>0.05$

segment changes (29.7%) followed closely by T-wave inversion (21.8%).The mean QTcmax of the total cohort was prolonged at 447.5 msecs. A QTcmax prolongation of >440 msecs has been associated with dangerous ventricular arrhythmia and increased mortality particularly after myocardial infarction[19] and also in stroke patients.[14] The QTcmax was absolutely prolonged in almost half of the total cohort, and this correlated with increased mortality. The QTc dispersion did not reach the generally acceptable critical value of 80 msecs[13] and did not correlate with mortality in this study, just like the QTd.

When the patients without pre-existing heart disease (selected) were sorted out of the total cohort, the age was not different from the total unselected group. A total of 25% of the selected group had ischemic-like changes compared with 54.7% of the total cohort, suggesting that the ECG changes were due to heart conditions rather than the stroke state. This is the general trend in patients with ischemic stroke[6,9-10] as distinct from observation in subarachnoid hemorrhage.[6] The prevalence of 25% ischemic-like changes in our selected group is <65% observed by Dogan et al. and 54% by Lindgren et al[10,20] despite the fact that we did not also include patients who had hypertension without LVH in our group with pre-existing heart disease. Usually, ischemic-like changes are expected to decrease between 8–40% when patients with pre-existing heart disease are removed from the total cohort.[6,21] This is the trend in this present study.

ST change was the commonest ischemic-like change in selected patients in this study just like in other works.[6,20] It did not correlate with mortality. This is the same finding in the work of Lindgren et al.[20] However, Dogan et al. found ST as an independent indicator of mortality.[10]

Other changes include T-wave inversion and presence of U wave when compared with the total cohort. The generally observed lower prevalence of ischemic-like changes in those without heart disease suggests that these changes are due to the pre- existing heart disease rather than the stroke itself. However, none of these parameters correlated with mortality. This is the same observation in a large scale study by Goldstein.[9] The QTcmax correlated with mortality as in other works,[20] though some other workers did not observe this trend.[22]

Mortality rate in the selected group was 8.3%, which was significantly <28.1% in the total cohort. Presence of pre-existing heart disease seems to be a predictor of mortality in these patients. This is the same observation in some other studies.[9,20]

Ischemic-like and repolarization ECG changes that occur in patients with acute stroke have been thought to be due to neural myocardial stunning, changes in autonomic nervous system and catecholamine-mediated injuries.[6,10] Some have attributed these to lesions in the insular cortex, which can lead to cardiac abnormalities such as ischemic-like changes, arrhythmias and even myocytolysis.[23] This sometimes makes it difficult to make a diagnosis of heart disease in the presence of acute stroke.

The conclusion of this study is that ischemic-like and repolarization changes are common in our patients with ischemic stroke. The changes tend to be due to pre-existing heart disease rather than the stroke state. Only in QTcmax did this correlate with mortality. Other parameters that correlated with mortality include the days on admission and presence of pre-existing heart disease.

The limitations of this study include the fact that not all the patients had CT scan, and this could lead to misdiagnosis and misclassification,[24,25] although a good and detailed clinical assessment as in this study is expected to decrease the magnitude of this error.[26] Also, the Siriraj Stroke Score, when combined with the WHO score, as used in this study, has been validated as a useful tool in diagnosis and classification of stroke in our environment.[27] Only a percentage of the patients had echocardiography. We did not carry out a stress test or coronary angiograms to absolutely exclude patients with coronary artery disease, although this entity has been said to be rare as a risk factor for stroke in our environment.[2] Autopsy was not performed on the patients who died.

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