A study on the electrocardiographic findings in acute stroke, a case controlled study in a tertiary hospital in Eastern India

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Abstract

Context: In cerebrovascular accident (CVA) patients, electrocardiogram (ECG) changes may or may not be due to underlying cardiac illness. Aims: This study was done on CVA patients without underlying cardiac illness and diabetes, to evaluate the incidence and patterns of ECG changes in acute stroke. Settings and Design: Prospective nonrandomized case-control study in a tertiary hospital. Subjects and Methods: Ninety-seven CVA patients as case and 97 patients' age and sex matched, attending preanesthetic check-up without cardiac illness and diabetes were taken as control. ECG computed tomography brain, magnetic resonance imaging brain (in inconclusive situations) were done. Statistical Analysis Used: Chi-square test and Levine test using appropriate software IBM SPSS Version 22. Results: Among 97 CVA subjects, 80 had hemorrhage and 17 had infarcts. 55 lesions were situated in the right hemisphere and 42 in the left hemisphere. ECG changes were present in 89.6% patients (87 of 97). Among control 22.6% (22 of 97) had new ECG changes (P < 0.01). The most common ECG changes were prolonged QT interval (78/97) 80.4%, increased QT dispersion (QTd) (66/97) 71%, and ST-T changes (16/97) 16.5%. Hemorrhagic strokes had more QT prolongation (71/80) (81%) than ischemic CVA (7/17) (41%) (P < 0.001) QTd was more with hemorrhage (63/80 = 79%) than with ischemia (6/17 = 35.3%) (P < 0.001) QTd increase had increased mortality (29/69 = 42%) than with no QTd increase (1/28 = 3.5%) (P < 0.001). Ischemic CVA had more ST-T changes (8/17 = 47%) than hemorrhage (8/80 = 10%) (P < 0.01). Conclusions: This study showed increased incidence of ECG changes following CVA. QTd and QTd prolongation were more in hemorrhagic CVA while ST-T changes were more in ischemic CVA. Increased QTd were associated with increased short-term mortality.

Key words: Clinical significance, electrocardiographic changes, stroke

INTRODUCTION

Changes in electrocardiogram (ECG) in stroke may reflect deranged central nervous system (CNS) influences on cardiac autonomic function. There might also be an actual concomitant myocardial injury that may or may not be due to underlying cardiac disease.[1] Lateralization studies indicate that destruction of areas adjacent to the right insular cortex has specially marked cardiac effects.[2]

Several studies done on the development of stroke and new ECG changes, its relation with the type of stroke and prognosis with variable results.[3,4]

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This present study was done on CVA patients without underlying cardiac illness and diabetes, to evaluate the incidence & and patterns of ECG changes in acute stroke.

The present study aims at detecting new ECG changes such as QT dispersion, QT duration, ST-T changes, its relation with the type of stroke and prognosis.

SUBJECTS AND METHODS

Ninety-seven stroke patients admitted to General Medicine wards during February 2013–October 2014 were selected for the study. Patients with history of diabetes, Ischemic Heart disease, arrhythmias/previous ECGs showing arrhythmias, ingestion of drugs known to produce a QT prolongation or predispose to arrhythmias including antiarrhythmics, presence of dyselectrolytemia were excluded from the study. Ninety-seven patients’ age and sex matched, attending preanesthetic check-up for a disease other than cardiac illness and diabetes were taken as control. Detailed clinical history and examination and imaging with a noncontrast computed tomography (CT) scan of brain and magnetic resonance imaging brain (if CT brain inconclusive), ECG recording-12 lead with long lead II within 24 h of admission, laboratory tests like blood glucose, electrolytes, etc., were done. Outcome at the end of hospital stay was considered as short-term.

ECG – Paper speed was 25 mm/s. 1 mm = 1 mV. Following parameters were evaluated:

- QTc – Corrected QT calculated using Bazett formula$^{[5]}$
  \[ QTc = \frac{QT}{\sqrt{RR)} \]  
  A cut-off of 460 ms (females) and 440 ms (males) was used-values above considered increased for the purposes of this study

- QT dispersion (QTcD) – Corrected QT dispersion calculated first by calculating the longest QTc in each lead and then calculating the difference between the highest and lowest among the 12 QTc calculated thus. A lot of variabilities exist regarding normal values of QTcD. However, values ranging from 10 to 71 ms have been noted.$^{[6]}$ A QTcD value >80 ms have been used to define “increased QT dispersion” for this study

- ST-T changes – following changes were considered:
  - ST elevation
  - ST depression
  - Tall T waves (>10 mV)
  - T wave inversion
  - Nonspecific ST-T changes.

- Conduction disturbances – following conduction disturbances were considered:
  - 1°/2°/Complete heart block

  - Right bundle branch block/left bundle branch block
  - Bi-fascicular block
  - Stroke volume assessment.

The ABC/2 formula$^{[7]}$ was used for calculating approximate stroke volume in “ml.” It was used for both infarction and hemorrhage.

\[ A = \text{longest diameter in X-axis (cm)} \]
\[ B = \text{longest diameter in Y-axis (cm)} \]
\[ C = \text{(number of slices \times slice thickness in cm) (cm)} \]

Slices with lesion volume <25% of the maximum volume slice were excluded from the calculation.

The volume was approximated to the nearest whole no.

RESULTS

This study was completed with a sample $n = 97$ with 65 males and 32 females. Most patients (86) belong to 40–79 years age group. Ninety-seven patients’ age and sex matched, attending preanesthetic check-up for a disease other than cardiac illness and diabetes were taken as control. Regarding hemispheric localization, there was slight right hemispherical predominance over left hemisphere (55 vs. 42).

Regarding nature, there was overwhelmingly larger number of hemorrhagic cerebrovascular accident (CVA) as opposed to ischemic CVA (80 vs. 17). Among the specific lesions basal ganglia lesions topped the list (30%) closely followed by thalamic (18%). In them also hemorrhage was the predominant lesion.

ECG changes were found in (87/97) 89.6% of subjects – only 10.4% did not have any ECG changes. Among control 22 out of 97 (22.6%) had ECG changes. Regarding the ECG changes the two most predominant ECG changes were prolonged QTc and increased QTcD. (78/97) 80.4% of the sample had increased QTc while nearly (66/97) 71% had increased QTcD. ST-T changes were found to be (16/97) 16.5%. The ECG changes are given in [Table 1].

Levine’s test for equality of variances showed no increase in QTc with increase of stroke volume but the increase in QTcD with an increase of stroke volume ($P = 0.001$). There is no significant increase in ST-T with increased stroke size.
### Table 1: Frequency of electrocardiographic changes

<table>
<thead>
<tr>
<th>ECG changes</th>
<th>Percentage of sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus tach</td>
<td>10</td>
</tr>
<tr>
<td>Sinus brad</td>
<td>5</td>
</tr>
<tr>
<td>RAD</td>
<td>4</td>
</tr>
<tr>
<td>LAD</td>
<td>15</td>
</tr>
<tr>
<td>↑QTc</td>
<td>80.4</td>
</tr>
<tr>
<td>↑QT dispersion</td>
<td>71</td>
</tr>
<tr>
<td>ST-T</td>
<td>16.5</td>
</tr>
</tbody>
</table>

ECG: Electrocardiographic, RAD: Right axis deviation, LAD: Left axis deviation, QTc: QT dispersion

### Table 2: Increased QTc and QT dispersion values and ST-T change in patients of right and left hemispheric cerebrovascular accident and their statistical significance

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Right hemisphere %</th>
<th>Left hemisphere %</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased QTc</td>
<td>80.3 (45/56)</td>
<td>80.4 (33/41)</td>
<td>0.599</td>
</tr>
<tr>
<td>Increased QT dispersion</td>
<td>64.2 (36/56)</td>
<td>80.5 (33/41)</td>
<td>0.09</td>
</tr>
<tr>
<td>ST-T changes</td>
<td>21.4 (12/56)</td>
<td>9.7 (4/41)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

### Table 3: Increased QTc and QT dispersion values and ST-T change in patients of hemorrhagic and ischemic cerebrovascular accident and their statistical significance

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hemorrhagic stroke %</th>
<th>Ischemic stroke %</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTc prolongation</td>
<td>81 (71/80)</td>
<td>41 (7/17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Increased QT dispersion</td>
<td>79 (63/80)</td>
<td>35.3 (6/17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST-T changes</td>
<td>10 (8/80)</td>
<td>47 (8/17)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

In our study, mortality was calculated using Fisher’s exact test. QTc prolongation associated mortality (28/78 = 36%) was not significantly more than in no QTc prolongation (2/19 = 11%) (P = 0.045). It was found that QT dispersion increase was associated with significantly increased mortality (29/69 = 42%) than with no QT dispersion increase (1/28 = 3.5% mortality) (P < 0.001). Differences in mortality in ST-T change (4/16 = 25%) and no ST-T change (26/55 = 47%) (P = 0.4) were not significant.

Our study found significant mortality associated with QT dispersion in much shorter term.

### DISCUSSION

The study was done with the aim of grossly exploring ECG findings in acute stroke with special reference to QT dispersion, QT duration, and ST-T changes and its relation with the type of stroke, hemispheric localization and size with short-term prognosis.

This study was completed with a sample n = 97 with 65 males and 32 females. Regarding hemispheric localization of CVA, there was slight right hemispherical predominance over left hemisphere (55 vs. 42). Regarding nature, there was overwhelmingly larger number of hemorrhages as opposed to infarction (80 vs. 17). As the study was done in a tertiary care hospital, may be, hemorrhagic CVA with more overt clinical manifestations were admitted more. Among the specific lesions basal ganglia lesions topped the list (30%) followed by thalamic (18%). In them also, hemorrhage was the predominant lesion.

Regarding the distribution of ECG findings, ECG changes were found in 89.6% of subjects – only 10.4% did not have any ECG changes. Among control 22.6% (22 of 97) had new ECG changes. ECG changes were significantly higher in CVA patients (P < 0.01). This is also reflected in other studies like Bozluolcay et al., where the frequency of the ECG changes observed in patients with cerebral infarct was 62.1% while it was 29.9% in the control group (P < 0.0001). Ebrahim et al. found similar figures in his study of electrocardiographic changes in acute ischemic stroke where he found ECG changes in 68% of the subjects as compared to 30% of control. Goldstein noted in his study with 150 patients 138 (92%) showed ECG abnormalities which is quite high.

Changes in ECG in acute stroke may reflect deranged CNS influences on cardiac autonomic function in the form of autonomic neural stimulation from the hypothalamus or elevated circulating catecholamines. There might also be an actual concomitant myocardial injury that may or may not be due to underlying cardiac disease. In our study, assessment for correlation between new ECG change and catecholamine level could not be done.

Regarding the ECG changes the two most predominant ECG changes were prolonged QTc and increased QT dispersion. 80.4% of the sample had increased QT while nearly 71% had increased QT dispersion. Goldstein noted in his study of 180 patients, QT prolongation (68 patients, 45%), ischemic changes (59, 35%) found similar figures. Fure et al. found the most frequent ECG changes were: Prolonged QTc 36.0%, quite less compared to our study. A huge body of contemporary work has been done on exploring the importance of an increased QT dispersion in acute stroke – its presence, correlation to stroke size, stroke site and relation to mortality. The importance of QT dispersion stems from the fact that QT-dispersion represents inter-lead variability of QT interval and reflects the heterogeneity of myocardial repolarization. QT dispersion was originally proposed as an index of the spatial dispersion of ventricular recovery times. Attempts to characterize and quantify the nonhomogeneity of ventricular repolarization from...
the surface ECG using precise mathematical methods, such as principal component analysis of the T wave, can be traced back to the 1960s.[10] In our study, mortality was calculated using Fisher's Exact Test. It was found in our study that QTc prolongation was not associated with significantly increased mortality (36%) compared with no QTc prolongation (11%) \((P = 0.045)\).

Wong et al.,[11] showed in his study that the increased QTc measured from any lead of the ECG (except aVR) was associated with increased death from any cause. A prolonged QTc in limb lead III and chest lead V6 carried the highest relative risk of cardiac death (a 3.1-fold increase). After adjusting for overt ischemic heart disease, pulse pressure, glucose, and cholesterol, a prolonged QTc in lead V6 was associated with a relative risk of cardiac death of 2.8 (95% confidence interval [CI] 1.1–7.3) \((P = 0.028)\). If the QTc in V6 exceeded 480 ms, then the specificity of predicting cardiac death within 5 years after the stroke was 94%.[11] In our study, we did not compare the magnitude of QTc prolongation with mortality, but patients with prolonged QTc did not have higher mortality in short-term.

This was in contrast to the study of Wong et al.[11] The frequency of QTc prolongation in our study was to the tune of 72%. It was the predominant finding in both hemorrhagic and ischemic strokes, but it was significantly more in hemorrhagic CVA (79%) than ischemic strokes (35.3%) \((P < 0.001)\). Although, left hemispheric CVA had more QTc prolongation than right hemispheric CVA (80.5% vs. 64.2%), it was not statistically significant \((P = 0.09)\).

In our study, it was found that QTc prolongation was associated with increased mortality (42%) than with no QTc increase (3.5% mortality) \((P < 0.001)\).

Bicakci et al. also conducted mortality studies related to QTc prolongation in acute stroke patients. She involved two groups of patients—one with death (Group II) at end of hospital stay and the other with survival (Group I) and ventured to find the relative prevalence of ECG changes in both. It was found that corrected QT and QTc were prolonged in both groups; but particularly Group II had relatively higher QTc compared to Group I.[12]

Lazar et al. found QTc prolongation was higher in patients with intracerebral hemorrhage as compared to ischemic CVA and transient ischemic attack (70 ms vs. 53 ms vs. 48 ms, respectively; \(P = 0.03\)). Increasing QTc prolongation was associated with lower functional outcomes on all 3 scales (all \(P < 0.05\)) and with higher mortality \((P = 0.02)\). On multivariate analysis, other independent predictors of worse outcome were QTc prolongation \((\text{odds ratio, 1.35; 95\% CI, 1.08–1.68})\) and a trend toward age \((\text{odds ratio, 1.07; 95\% CI, 0.99–1.16})\). On age-adjusted logistic regression, mortality increased by odds ratio of 1.28 and 95% CI of 1.02–1.61 for every 10 ms increase in QTc. QTc is an independent predictor of functional outcome and mortality following acute neurological events. In this setting, QTc reflects neurological injury as well as underlying heart disease.[13] The findings on QTc sit very well with the findings of our study. However, in our study, the exact cause of death could not be determined. Further well-randomized control studies are required in this field.

Few studies have been done with a view to have an approximation of the particular cortical areas associated with ECG anomalies namely QTc and QTc in view of its importance as electrocardiological substrate for fatal ventricular arrhythmias. Eckardt et al.[14] attempted to localize cortical areas where cerebrovascular damage was associated with prolonged QTc. In his study with 40 subjects, he found that patients with involvement of the insular cortex, the QT dispersion is significantly longer than in those without insular involvement. In our study, localization could not be done to that extent. But in our study, there was no significant hemispheric predilection for ECG changes.

New onset QTc prolongation found at the time of stroke may be an indicator of underlying ischemic heart disease. Mortality in those subset of stroke patients with prolongation of QTc may thus be a composite marker of underlying cardiac disease compounded by the prospect of developing fatal arrhythmias due to the prolonged QTc. Findings of such sort were revealed in the study by Familoni et al.[15]

Total ST-T changes were seen in 16.5% of patients but it was quite high in ischemic CVA group -8 of 17 (47%). This is similar to Ebrahim et al.[9] who found ischemic changes, ST-T changes and abnormal T waves to be the predominant findings in his series of ischemic CVA with changes in 98 (37.4%) patients and 16 (15.7%) controls. Our study was close with. Fure et al. where he found the most frequent ECG changes were: ST depression 24.5%, T wave inversion 17.8%.[4] Higher incidence of ST-T changes in ischemic CVA may be due to some underlying ischemic heart disease which we could not study.

ST-T changes in our study have no predilection for particular hemisphere. It has no significant association with the stroke size. ST-T changes were not associated with increased mortality outcomes–mortality in ST-T change (25%) and no ST-T change mortality (47%) \((P = 0.4)\).
CONCLUSION

ECG changes of some nature were found in majority of stroke patients with majority being increased QT Dispersion (QT\textsubscript{c,d}) and increased QTc. While statistically significant correlation with ↑QT\textsubscript{c,d} and mortality was found (in consonance with contemporary studies related to neurological outcomes with QT\textsubscript{c,d} changes), the same couldn’t be found for ↑QTc and mortality (in contrast to similar contemporary studies). Inability to quantitatively correlate QT\textsubscript{c,d} with mortality remains a limitation; further studies might illuminate this point as well as identify subsets of stroke patients with high risk ECG changes who might need more intensive cardiologic monitoring.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES