International Journal of Medical Science and Clinical Inventions 4(9): 3206-3212, 2017
DOI:10.18535/ijmsci/v4i9.06 **ICV 2015: 52.82**
e-ISSN:2348-991X, p-ISSN: 2454-9576

Original Article

Electrocardiographic Changes and Its Correlation with Three Months Outcome in Patients of Stroke

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Abstract:

Background Stroke is on the rise in India with great impact on morbidity and mortality. One of the factors associated with poor outcome among stroke patients are some electrocardiographic (ECG) changes resulting from massive autonomic discharge that interferes with cardiac autonomic control.

Objective To determine ECG changes and three months outcomes of patients admitted with new onset stroke at a tertiary care teaching hospital in western India.

Methodology 160 patients with new onset stroke regardless of its type were enrolled in the study. All eligible patients underwent 12 lead resting ECGs. These patients were then followed up at one and three months from the day of enrollment for determination of their survival/morbidity and mortality outcomes.

Results Nine ECG patterns were identified out of which left ventricular hypertrophy (LVH), ischemic changes and QT Prolongation were dominant (83.1%, 63.1% and 50.6% respectively). QT prolongation and Ischemic changes were found to be statistically significant in predicting outcomes at 1-month and at 3-months ($p < 0.001$ and 0.036 respectively). Patients with haemorrhagic stroke were more likely to present with multiple ECG changes. Those with QT prolongation and Ischemic changes had poorer outcomes than those without these changes. Patients with more than three changes had poorer outcomes as compared to those with less than three (p 0.018) with risk of three times likely-hood of mortality at three months.

Conclusion Bed side ECG was a significant tool in predicting poor outcomes. ECG patterns such as QT-prolongation and Ischemic changes were associated with poor outcomes at three months, irrespective of co-morbid conditions. Some ECG changes such as QT-prolongation were highly predictive of haemorrhagic stroke.

Keywords: STROKE, HAEMORRHAGIC, ISCHEMIC, ECG, PROGNOSIS.

INTRODUCTION

Stroke is the second commonest cause of death worldwide,[1] with two-thirds of these deaths occurring in developing countries. The incidence of stroke in developing countries is also expected to rise in the future as the populations undergo what has been referred to as the health transition.[2] Stroke may produce ECG changes and arrhythmia. Byre and colleagues, for the first time in 1944, described the ECG changes in sufferers of subarachnoid haemorrhage.[3] ECG changes have been reported in 60-90% of patients with intra-parenchymal or subarachnoid bleed and in about 5-20% of patients with acute ischemic stroke.[4] The underlying cause has been postulated to be disordered depolarization process.[5] There is also a relationship between these changes and sudden death in sufferers of stroke.[6] Abnormalities such as ischemic-like ECG changes and/or QT prolongation, were found in 76% (95% CI 73–90) of patients with subarachnoid hemorrhage, irrespective of whether they had preexisting heart disease or not. In the same study, it was found out that of 555 consecutive patients

with acute stroke, 72% had cerebral infarction and 28% had intracranial hemorrhage (ICH).[7]

In patients with stroke the ECG abnormalities most frequently noted are ischemic changes (35%), prolongation of QT interval (45%) and disturbances in rate and rhythm (25%), which include atrial fibrillation, premature atrial and ventricular complexes, supra-ventricular tachycardia (SVT) and ventricular tachycardia (VT), *Torsades de pointes* or polymorphic ventricular tachycardia's.[8]

Stroke induced ECG changes are transient (temporary,) resolving over a period of days to months. The frequency and severity of ECG changes is highest within 48 hours of the onset of stroke which explains the importance of continuous ECG monitoring for these patients**.**[9]

The ECG abnormalities and part of mortality in stroke patients have been found to be attributable to cardiac autonomic imbalance generated by acute cerebral lesion.[10] Massive autonomic discharge along the sympathetic outflow tracts of the nervous system produces tachyarrhythmias.[11] Muhammad A.A *et al* reported repolarization abnormalities, manifesting as prolonged QTc to be one of the most frequent ECG abnormalities irrespective of the stroke type (63.63% vs. 68.29%).The two varieties of stroke (ischemic and hemorrhagic stroke) manifest more or less similar patterns of ECG changes.[12] In some studies in patients with ischemic stroke, the prognostic importance of these ECG parameters, particularly ST-segment changes and prolonged QT interval has been demonstrated.[13,14] Corrected QT interval (QTc) has been found to be an independent indicator of arrhythmias and mortality in conditions such as long-QT syndrome, cardiomyopathy and chronic heart failure.[15,16] Stroke patients with prolonged QTc are at a higher risk of death within the next three months (highest for women with a QTc >440 milliseconds and for men >438 milliseconds).[17]

There is strong clinical evidence of cerebrogenic cardiac arrhythmias and myocardial changes during ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage. Clinical and experimental studies suggest that cortical and subcortical structures such as the insular cortex and amygdala play a pathogenic role. The peripheral mechanisms involve abnormal sympathetic activity, altered parasympathetic activity, and raised levels of circulating catecholamine's, whereas the central mechanisms are largely unknown.[18] Insular damage may cause activation of the sympathico–adrenal system because of decreased inhibitory insular activity.[19]

ECG findings may also have prognostic significance in stroke patients. Ventricular arrhythmias, concurrent MI, and a prolonged QTc interval have all been associated with increased mortality in stroke patients.[20] In India, there have been few studies to associate ECG changes in stroke patients with morbidity/mortality outcome.

AIM & OBJECTIVES: This study was aimed at identifying ECG patterns in patients presenting with acute stroke and determine their significance in relation to outcome at three months.

METHODOLOGY:

This was a descriptive follow up study. Patients with new onset stroke were seen at admission, investigated and followed up at one and three month's intervals for their outcome in terms of mortality. Patients with new onset stroke clinically were included in the study.

Inclusion criteria:

1. All patients, 18 years or older, presenting with symptoms and detectable neurological signs of stroke

Exclusion criteria:

1. Patients with previous history of stroke.
2. Patients with history of Ischemic Heart Disease.
3. Patients with known ECG abnormality, prior to onset of Stroke.

An informed consent was obtained from all patients with stroke (or their relatives on their behalf if the patients had altered sensorium). Follow up of the patients was done at one month and three months after discharge. The collected information also included date of death. A structured questionnaire was used to collect the data and a standard 12 lead ECG was recorded to all the recruited patients. Where possible, the diagnosis was confirmed by a Non-contrast CT Scan (NCCT) of head.

The following ECG indices and patterns were identified and analysed.

1. **CORRECTED QT INTERVAL (QTc)** was calculated for each ECG using Bazetts formula $QTc = {}^{QT}/_{\sqrt{RR}}$
2. **ISCHEMIC CHANGES-** ST segment elevation or T- wave inversion in two consecutive leads of > 2mm, and T wave inversion in corresponding leads or presence of Q-waves in two consecutive leads, suggesting of old myocardial infarct.
3. **ARRYTHMMIAS**- Sinus Arrhythmias, Atrial Fibrillation, Ventricular Premature Contraction (VPC) and Left Ventricular hypertrophy (LVH) as per Sokolow-Lyon criteria

RESULTS

During the study period from August 2015 to mid-October 2016, a total of 160 patients were recruited into the study. Out of 160 patients recruited, 82 (51.25%) were males and 78 (48.75%) were females. At one month of follow-up a total of 8 (5%) patients and at 3 months total of 27 (16.8%) patients were lost to follow up. Of 160 patients, 151 (95%) patients had CT-scan of the brain and the type of the stroke could therefore be identified. The rest 5% of patients CT scan could not be done because of various reasons.

CO-MORBIDITIES IN NEW STROKE PATIENTS

The majority of the patients (87.5%) were hypertensive. Diabetes mellitus was seen in 41.3% of the patients while co-existence of hypertension and diabetes mellitus was seen in

39.4% of the study population. Only 1.3% of the patients had dyslipidemia at baseline. Females and males were similarly affected by these co-morbidities as all the p-values were not statistically significant (Table 1).

TABLE 1: CO-MORBIDITIES IN NEW STROKE PATIENTS (N=160)

Co-morbidity	Total	Males (N = 82)	Females (N = 78)	MVSF (P value)
	Number (%)	Number (%)	Number (%)	
Hypertension (HTN)	140 (87.5)	71 (86.6)	69 (88.5)	0.720
Diabetes Mellitus (DM)	67 (41.3)	35 (42.7)	32 (39.7)	0.706
Dyslipidaemia	2 (1.3)	2 (2.4)	0 (0.0)	0.169
HTN and DM	63 (39.4)	33 (40.2)	30 (38.5)	0.659
Smokers	91 (100)	82 (90.1)	9 (9.9)	0.01
Alcohol use	109 (100)	71 (65.1)	38(34.9)	0.03
Chewing Tobacco Users	9 (100)	8 (88.8)	1 (11.1)	0.68

Smokers comprised of 91 (56.9%) of the total new onset stroke patients, of which 82 (90.1%) were males. Alcohol consumption, whether past or current, was also found to be statistically significant in males (p values 0.04 and 0.03 respectively) compared to females. There was no statistical difference in tobacco consumption among males and females. However, statistical difference was found among current tobacco users (p 0.048).

ECG PATTERN IN ACUTE STROKE

FIGURE 1: ECG PATTERNS IN PATIENTS WITH NEW STROKE (N=160)

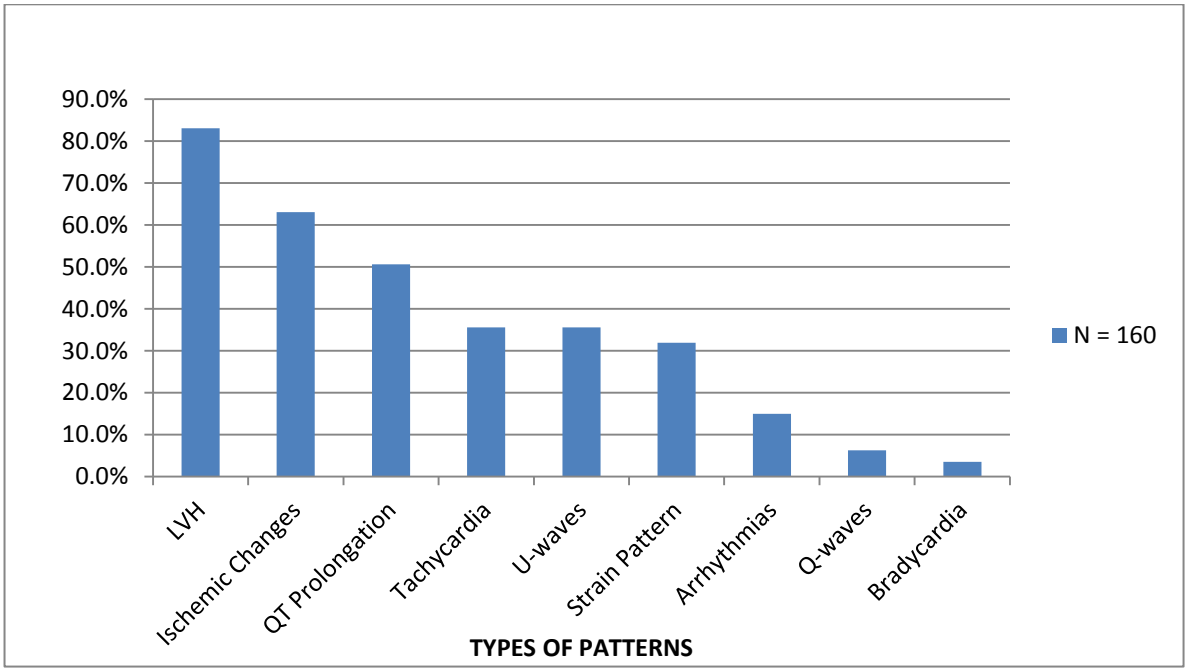
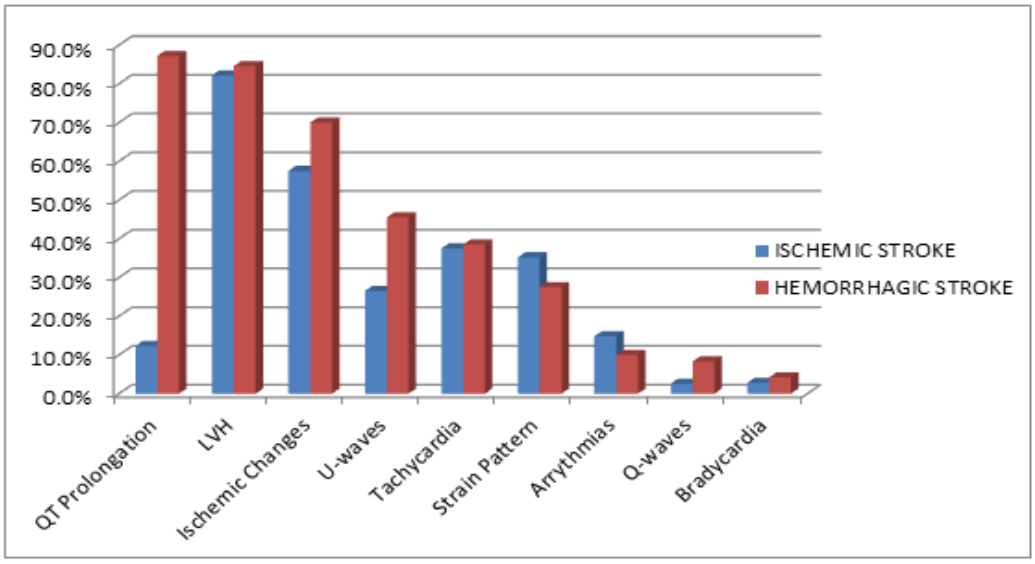


Figure 1 shows the different ECG patterns found in patient with acute stroke. The majority were found to have left ventricular hypertrophy (LVH) (83.1%), followed by ischemic changes (63.1%) and QTc prolongation (50.6%). Other patterns which were found were tachycardia (35.6%), U-waves (35.6%), arrhythmias (15%), and Q-waves (6.3%). It was also found that (31.9%) of study participants had strain pattern on their ECGs. On univariate analysis, QT prolongation was seen more in patients with hemorrhagic stroke compared to ischemic stroke (87.2% vs. 12.3%) which is statistically significant (p <0.001). Similarly, significantly more patients with hemorrhagic stroke exhibited ischemic changes than the patients with ischemic stroke (70.5% vs. 57.5%) (p=0.096). Other patterns were statistically insignificant (Figure 2).

FIGURE 2: ECG PATTERN ACCORDING TO TYPE OF STROKE (N=151)

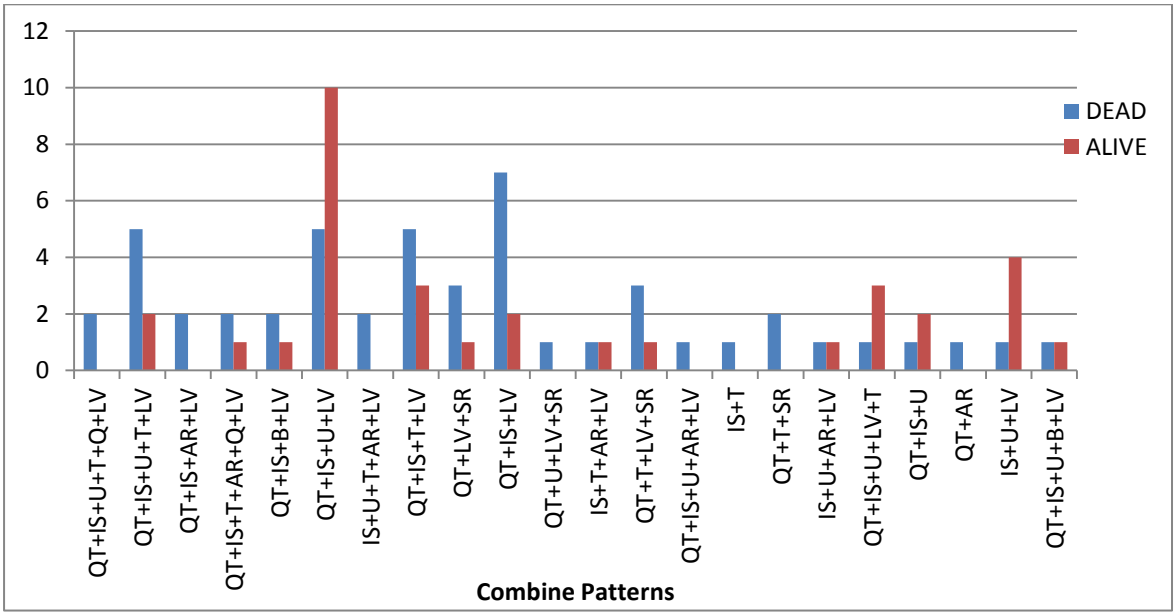


The patients with QT prolongation and ischemic changes as a pattern had highest mortality with p-values of < 0.001 and 0.039 respectively. Other patterns were statistically not significant (Table 2).

TABLE 2. ECG PATTERN AND 1 MONTH MORTALITY IN PATIENTS WITH NEW ONSET STROKE (N=152)

ECG CHNAGES	MORTALITY 1-MONTH (N = 152)		P- Value
	DEAD (57)	ALIVE (95)	
QT Prolongation	44 (77.2)	34(35.8)	< 0.001
Ischaemic Changes	43(75.4)	56(58.9)	0.039
Tachycardia	25(43.9)	36(37.9)	0.468
Bradycardia	3(5.3)	3(3.2)	0.519
U-Wave	22(38.6)	34(35.8)	0.728
Arrhythmias	10(17.5)	12(12.6)	0.405
Q-Wave	5(8.8)	5(5.3)	0.398
LVH	50(87.7)	77(81.1)	0.168
Strain Pattern	13(22.8)	33(34.7)	0.121

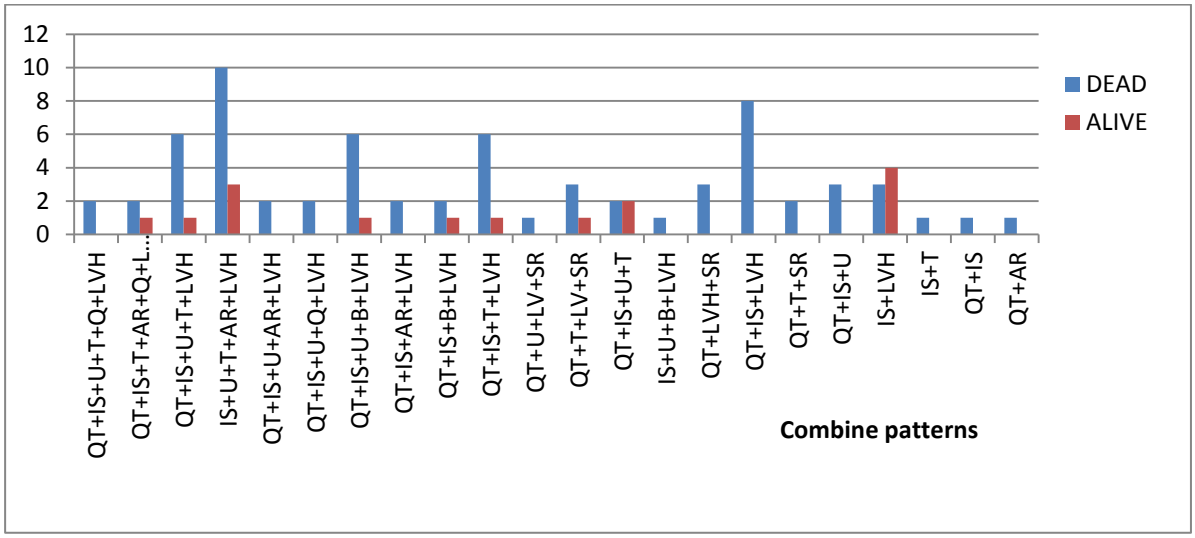
FIGURE 3. ASSOCIATION OF ECG CHANGES THAT WHICH CAUSE MOST MORTALITY AT 1 MONTH (N=152)



KEY: **QT**=Corrected QT**, IS**=Ischemic changes, **AR**=Arrythmias**, Q**= Q-waves,

U=U waves, **LV**=LVH **T**=Tachycardia, **B**=Bradycardia, **SR**=Strain pattern.

FIGURE 4: ASSOCIATION OF ECG CHANGES THAT CAUSE MOST MORTALITY AT 3 MONTHS (N=133)



KEY: **QT**=Corrected QT**, IS**=Ischemic changes, **AR**=Arrythmias**, Q**= Q-waves,

U=U waves, **T**=Tachycardia, **B**=Bradycardia, **SR**=Strain pattern.

A Total of 47 different combinations of patterns were identified. Figure 3 and Figure 4 show combined ECG patterns and mortality at 1-month and 3-months: all the patterns inclusive of QTc prolongation and Ischemic changes were statistically significant in causing mortality (p <0.001).

TABLE 3: ECG CHNAGES AND 3- MONTH MORTALITY IN PATIENTS WITH NEW ONSET STROKE (N=133)

ECG PATTERN	MORTALITY 3 MONTHS (N=133)		P- VALUE
	DEAD (79)	ALIVE (54)	
QT Prolongation	59 (74.7)	14(25.9)	<0.001
Ischaemic Changes	60(75.9)	26(48.1)	0.01
Tachycardia	32(40.5)	24(44.4)	0.651
Bradycardia	5(6.9)	1(1.9)	0.222
U-Waves	37(46.8)	15(27.8)	0.027
Arrythmias	12(15.2)	8 (14.8)	0.953
Q-Waves	7(8.9)	2(3.7)	0.245
LVH	68(86.1)	42(77.8)	0.214
Strain Pattern	18(22.8)	24(44.4)	0.008

Table 3 shows association of different ECG patterns with 3-months mortality. QTc prolongation and ischemic changes are associated with statistically significant mortality at 3-months (p <0.001 and <0.01 respectively). Other patterns showed no statistical significance.

The diagnosis of 151 patients was confirmed by CT scan. 56 patients died at one month; 57.5% had hemorrhagic stroke compared to 15.5% with ischemic stroke (p <0.001). Similarly, there was higher mortality in patients of haemorrhagic stroke at three months (87.3%) compared to those with ischemic stroke (25.8%) (p<0.001) (Table 4).

TABLE: 4 MORTALITY BY TYPE OF STROKE AT ONE MONTH (N=151) AND THREE MONTHS (N=133) IN PATIENTS WITH STROKE

TYPE OF STROKE	OUTCOME ONE MONTH N=151 (%)		OUTCOME 3 MONTH N=133 (%)	
	DEAD	ALIVE	DEAD	ALIVE
ISCHEMIC	11(15.1)	62(84.9)	16(25.8)	46(74.2)
HEMORRHAGIC	45(57.5)	33(42.3)	62(87.3)	9(12.7)

DISCUSSION

Cardiac autonomic imbalance generated by acute cerebral insults plays an important role, not only in producing

electrocardiographic abnormalities, but also in predisposing the patients towards early mortality.

ECG PATTERNS AND CO-MORBIDITIES

In this study, it was found that patients with new onset of stroke had at least one ECG abnormalities at the time of ECG recording; some of these ECG abnormalities could be due to underlying co-morbidities. Majority of the patients had underlying co-morbidity such as hypertension (87.5 %), diabetes mellitus (41.3%) and 39.4% had both hypertension and diabetes mellitus.

ECG PATTERN AND MORTALITY

Among the 160 patients included in the study, 47 different ECG patterns were identified. A maximum of six types of ECG changes were recorded. The study result shows that those who had more than three changes had poorer outcomes within the next 3 months in terms of mortality. The results also indicate that those patients who had QTc prolongation and Ischemic changes had poorer outcomes at 3-months in terms of mortality. Thus, not all ECG pattern combination is associated with increased mortality at one and three months. The most common ECG patterns found among the study population were LVH (83.1%), followed by Ischemic changes (63.1%) and QT prolongation (50.6%). The findings of this study are consistent with some other studies done elsewhere, where Qt prolongation and Ischemic changes found in patients with new onset stroke were associated with poor outcomes in terms of mortality at 3-months.[14]

A study by Goldstein et al[14] found that 45% had QTc prolongation as compared to 50.6% noted in our study. The slight differences can be due to the difference in study design. In the same study, LVH was detected more frequently in sufferers of hemorrhagic stroke (69%) than cerebral infarction (15.5%). But in our study, we found out that suffers from hemorrhagic stroke and ischemic stroke had almost equal but high prevalence of LVH on ECG (84.6% and 82.2% respectively). This difference can be attributed to underlying high prevalence (87.1%) of hypertension. We also found that 31.9% of our patients had strain pattern on ECG and this had not been noted in previous studies. This could be in association to severe LVH and endocardial wall ischemia due to uncontrolled hypertension. However, this pattern had no statistical significance on overall outcomes.

ECG PATTERN AND STROKE

In this study, the three-month mortality in patients with ischemic stroke and ECG changes was 25.8%. Similarly, acute stroke patients had various ECG changes and overall mortality was similarly high.[6]

In terms of outcomes at 1-month this study revealed that there was a statistical significance in mortality in patients who had more than 3 ECG changes, especially if inclusive of QTc prolongation and ischemic changes as shown on univariate analysis. However, when multivariate analysis was done only QTc prolongation was found to be statistically significant on overall outcome ($p<0001$). Analysis of outcome at 3-months revealed that QTc prolongation and Ischemic changes, irrespective of underlying co-morbidities, predicted poor prognosis in stroke patients ($p<0.001$ and $=0.047$ respectively).

CONCLUSION

Bed side ECG is a useful tool in identifying certain ECG patterns associated with poor outcome. ECG changes such as QTc prolongation and Ischemic changes were associated with poorer outcomes at 3-months, irrespective of the co-existence of co-morbidities. QTc prolongation was seen more often in patients of haemorrhagic stroke but this change cannot be relied upon to make the diagnosis. Neuroimaging (CT/MRI) remains the definitive diagnostic tool for patients of stroke.

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