

Original Article

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The Relationship Between QT Interval and Intra-Hospital Mortality in patients with Spontaneous Intracranial Hemorrhage

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Abstract

Introduction: Repolarization abnormalities such as prolongation of QT interval and changes in ST segment and T wave are the most usual electrocardiogram (ECG) changes in patients with intracranial hemorrhage (ICH). It has recently been recommended that prolonged QTc interval raises the risk of death due to malignant ventricular arrhythmias or sudden cardiac death.

Objective: The goal of this study was to evaluate the relationship between QT interval and death in patients with ICH.

Method: This cross-sectional study was performed on patients with ICH who referred during 2015-2017 to Poursina Hospital, Rasht, Iran. The QT interval was manually measured based on the BAZETT formula. Max QT and Max QTc and QT dispersion were the variables evaluated by the ECG of the patients. The outcome under the study was the death or survival of patients during hospitalization.

Results: Finally, 466 cases with the mean age of 69±12 years were studied of whom 68.7% were male. The average QT-Max interval was 350.4±56.5 milliseconds, and the average QTc-Max was 583.6±57.6 msec. Totally, 22.7% of the patients died. There was a significant statistical relationship between QTc-MAX and death ($p=0.001$). However, there was no statistically significant relationship between QT-MAX and the outcome ($p=0.593$).

Conclusion: It is likely that, prolonged QT interval is correlated with in-hospital mortality of patients with ICH. Therefore, it can be expected that assessing ECG abnormalities, especially prolonged QTc could be valuable in these patients.

Key words: Cerebral Hemorrhage; Electrocardiography; Hospital Mortality; Outcome

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INTRODUCTION

Spontaneous intracranial hemorrhage (ICH) is the main cause of 4 to 15% of acute stroke cases and also the most fatal form of this disease (1). The incidence of electrocardiogram (ECG) changes in patients with ICH is reported between 14 to 35% and repolarization abnormalities such as prolongation of QT interval and changes in ST segment and T wave are the most common ones (2-4).

The mechanism through which stroke and ICH results in ECG abnormalities is still unknown. However, there is evidence that reveals that the ECG changes related to stroke are somehow an indicator of the disordered autonomic system which is due to an increase in the sympathetic activity of the autonomic nervous system (5). It has been suggested that prolonged QT increases the

risk of death due to malignant ventricular arrhythmias or sudden cardiac death (6). The relationship between prolonged QT and mortality rates in ICH patients has been reported in a limited number of studies (4, 7).

Meanwhile, studies related to ECG findings associated with the central nervous system events mainly focus on subarachnoid hemorrhages (8). Unclear outcomes were reported in some studies, while some others showed that QT intervals in stroke victims were significantly longer than those who survived, which means the risk of death increases in presence of prolonged QT interval (9-11). Therefore, this research was performed to assess the possible relationship between prolonged QT and the outcome of death in ICH patients admitted in emergency department (ED).

Methods

Study design

This cross-sectional study was carried out on patients with ICH who referred from 2015 to 2017 to Poursina Hospital, Rasht, Iran. The study protocol was approved by ethics committee of Guilan University of Medical Sciences.

Study population

All patients who had trapped blood in their brain parenchyma, according to their brain computed tomography (CT) scan, were eligible. The exclusion criteria were patients with traumatic brain injury and those who were known by previous malignant diseases, organ dysfunction or heart disease (such as arrhythmia, coronary artery disease); and patients with recent ECG changes, atrial fibrillation, conduction disorder, or recent myocardial infarction.

Data gathering

Patients' demographic and baseline data (age, sex, comorbidities) were collected from their files. Disease severity was assessed based on National Institutes of Health Stroke scale (NIHSS) for each patient.

The patients' ECG were evaluated by the investigators. The QT interval was considered as the distance from the beginning of the QRS wave to the T wave return on the TP base in 12-lead ECG and corrected QT interval (QTc) was manually measured according to the BAZETT formula. If the U waves were present, the QT interval was measured on the curve side between T and U waves. Three consecutive cycles were measured and analyzed in each of the 12 leads. QTc dispersion which is defined as the difference between the maximum QTc interval and the minimum QTc interval in 12-lead ECG. Max QT, Max QTc and QT Dispersion variables were also calculated by reviewing the ECG of the patients. QTc-Max and QTc less than 430, 431-450 and more than 450 msec in men, and less than 450, 451-470 and more than 470 msec in women were considered as normal, borderline and prolonged respectively.

The outcome under the study was death or survival of patients during hospitalization.

Statistical Analysis

Descriptive indicators and univariate analytical tests like Fisher exact test and Mann Whitney's U test were used. Values are represented in frequency (%) and mean and standard deviations as applicable. T-test or its non-parametric version, i.e. Mann Whitney's U test, was used to compare continuous variables between the groups. All analyses were performed using Stata 13 software

and P-values <0.05 were considered as statistically significant.

RESULTS

Our study was performed on 466 cases with the mean age of 69±12 (range of 24-95) years. Baseline characteristics of the studied patients are reported in table 1. Based on the findings, the majority of our cases (68.7%) were male. Among studied patients, 315 (67.6%) had comorbidities, in which hypertension, diabetes and hyperlipidemia were the most frequent ones, respectively. Most of the patients (77.3%) recovered and discharged from the hospital, and the mortality rate was 22.7% of the patients.

Based on CT scan findings, 661 different sites of bleeding were observed. Meanwhile, the highest percentage of bleeding was observed as ICH-Potamen (32.9%), followed by subarachnoid hemorrhage (SAH) (30.9%) and intra-ventricular hemorrhage (IVH) (29.3%).

In assessing the distribution of the frequency of disease severity based on NIHSS, the highest percentage of subjects (52.4%) had a moderate stroke scale and those with minor stroke scale,

Table 1: Baseline characteristics of the studied patients (n=466)

Variable	Number (%)
Sex	
Male	320 (68.7)
Female	126 (31.3)
Comorbidity	
Hypertension	225 (48.3)
Diabetes mellitus	144 (30.9)
Hyperlipidemia	66 (14.2)
NIHSS	
21-24 (severe)	75 (16.1)
16-20 (moderate to severe)	96 (20.6)
5-15 (moderate)	244 (52.4)
1-4 (minor)	51 (10.9)
CT scan findings	
ICH-Potamen	153 (32.8)
SAH	144 (30.9)
IVH	136 (29.2)
QTc- Max	
Normal	369 (79.2)
Border Line	65 (13.9)
Prolonged	32 (6.9)
QT- Max	
Normal	461 (89.9)
Border Line	5 (1.1)
Prolonged	0 (0.0)
Outcome	
Recovered	360 (77.3)
Died	106 (22.7)

NIHSS: National Institutes of Health Stroke scale; SAH: subarachnoid hemorrhage; IVH: intra-ventricular hemorrhage

Table 2: Relationship of the studied ICH patients' outcome with their QTc-Max and QT-Max intervals

ECG findings	Outcome		p
	Recovery (n=360)	Death (n=106)	
	Number (%)		
QTc-Max			
Normal (n = 369)	301 (81.6)	68 (18.4)	0.001
Border Line (n = 65)	42 (46.6)	23 (35.4)	
Prolonged (n = 32)	17 (53.1)	15 (46.9)	
QT-Max			
Normal (n = 461)	355 (77.0)	106 (23.0)	0.593
Border Line (n = 5)	5 (100)	0 (0.0)	
Prolonged (n = 0)	0 (0.0)	0 (0.0)	

formed only 10.9% of the patients. The mean scores of NIHSS scale among the studied patients were 13.01 ± 6.59 , while the lowest score obtained was 2 and the highest was 24.

The average QT-Max interval was 350.4 ± 56.5 milliseconds and the average QTc-Max was 583.6 ± 57.6 msec. The frequency distribution of the time status of QTc-Max and QT-Max findings in patients' ECG are reported in table 1.

Table 2 shows the relationship of the studied ICH patients' outcome with their QTc-Max and QT-Max intervals. According to the findings, a statistically significant relationship was found between QTc-Max and the outcome of the patients with ICH ($p < 0.001$). However, there was no significant statistical relationship between QT-Max and the outcome ($p = 0.593$).

DISCUSSION

In our study, the mortality rate of ICH patients was 22.7%. Among 106 dead cases, 15 patients (46.9%) were those who had prolonged QTc-Max (32 patients); and it was found that there was a significant relationship between QTc-Max time status in patients and the outcome of treatment in patients with ICH.

In the same study conducted by Stead et al. (2009), a total of 64 patients died within 90 days. Patients with longer QT intervals were more likely to die within 90 days than those who did not have a long QT. Life expectancy in patients with long QT and without long QT was 70.5% and 87.1%, respectively. Fifty-one percent of those who died due to stroke had a long QT interval, and among those who died due to cardiac causes, 50% had a long QT interval; also, 32% of those who died due

to other disorders had a long QT interval (12).

It is well-known that a long QT interval increases the risk of ventricular tachyarrhythmia especially torsade de point (13). Polymorphic arrhythmia might quickly turn into ventricular fibrillation and lead to sudden death. Hence, accurate monitoring is critical when the QT interval is detected as a long QT interval (12). Prognosis seems to be worse with QT interval of greater than 440 msec in women and more than 438 msec in men. Findings related to the association between prolonged QT intervals and increase in the mortality risk have been inconsistent so far (12).

Limitations

Several factors can influence the results of this study. Although disease severity was assessed, but patients care, location and volume of hemorrhage, underline diseases, coagulopathy and many other factors could be considered. So, performing high quality surveys considering all possible factors that lead to proper multivariate regression analysis is still needed.

CONCLUSIONS

Based on the results obtained, QTc related with intra-hospital mortality of the patients with spontaneous ICH. Therefore, it can be expected that studying the ECG abnormalities, especially prolonged QTc in patients with ICH, may be helpful in the process of their management.

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AUTHORS' CONTRIBUTION

Study concept, design and supervision was performed by NA and SZ; Acquisition of data, statistical analysis, interpretation of data and drafting of the manuscript were done by MS. PK gathered the data. NA and PK did critical revision of the manuscript for important intellectual content. Administrative, technical, and material support was done by NA. All the authors confirmed final version of the accepted paper.

CONFLICT OF INTEREST

None declared.

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