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Relationship between QTc interval prolongation and mortality of acute ischaemic stroke patients during treatment and three months after treatment at Adam Malik Hospital

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ABSTRACT

Introduction: QTc interval prolongation is associated with an increased risk of mortality and incident cardiocerebrovascular disease in high-risk individuals and the general population. In addition, QTc interval prolongation in patients with acute stroke is associated with a significantly greater risk of death within 3 months. Based on the description in the background above, this study aims to determine how the relationship of QTc interval prolongation to mortality in acute ischaemic stroke patients during treatment and three months post-treatment at H. Adam Malik Hospital Medan.

Method: This study was an analytical study with a case control research design to determine the relationship of QTc interval prolongation to mortality in acute ischaemic stroke patients during treatment and three months post-treatment at Adam Malik Hospital Medan. The research time was carried out in March 2023 by taking a sample of cases from January 2021 to December 2022. The association of QTc interval prolongation with mortality of acute ischaemic stroke patients during treatment and three months post-treatment was analysed by Chi-square test. The statistical significance threshold used was $p < 0.05$.

Results: In patients who died, the mean QTc interval was 490 ms (453.0 - 547.0 ms). Comorbidities in this study included 27 (32.9%) patients with Type 2 DM, 42 (51.2%) patients with hypertension, 7 (16.6%) patients with chronic kidney disease, 13 (15.8%) patients with atrial fibrillation, 1 (1.21%) with pneumonia, and 1 (1.21%) with upper feeding tract bleeding (PSMBA).

Conclusion: QTc interval prolongation is associated with mortality in acute ischaemic stroke patients during treatment and three months post-treatment at Haji Adam Malik Hospital Medan

Keywords

QTc interval prolongation, Mortality, Acute ischaemic stroke

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INTRODUCTION

Ischaemic stroke specifically refers to central nervous system infarction accompanied by obvious symptoms. Ischaemic stroke is the most common type of stroke.[1] Stroke is the leading cause of serious long-term disability and the fifth leading cause of death in the American population. The average person in the United States has a stroke every 40 seconds, resulting in approximately 795,000 cases of stroke per year. Ischaemic stroke accounts for 87% of cases, while 10% is intracerebral haemorrhage and 3% is subarachnoid haemorrhage. Data in Indonesia shows stroke as the leading cause of death with a mortality rate of 131.8 deaths per 100,000 population.[2]

QTc interval prolongation is found in +25% of stroke patients, both haemorrhagic and ischaemic stroke, and has been reported in 23-45% of patients with acute ischaemic stroke (AIS) which is the single most

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frequently associated ECG abnormality.[3] Daniele et al. found that cardiac arrhythmias were found in 21.9% of patients with ischaemic stroke, including 26.8% of patients with right hemispheric lesions and 14.3% of patients with left hemispheric lesions.[1]

The pathology of QTc interval prolongation in patients with acute stroke is potentially related to cardiac dysautonomia.[4] Autonomic and ECG changes after acute stroke in patients without underlying heart disease result from dysautonomic activity or impaired autonomic regulation of the cardiovascular system.[5] In addition to nerve-mediated autonomic dysregulation causing QTc interval prolongation, other factors commonly found in patients with stroke that contribute to QTc interval prolongation are atherosclerotic, cardiac disease, electrolyte imbalance, and certain medications.[6] QTc interval prolongation is the electrophysiological basis for the onset of serious ventricular arrhythmias. Various experimental studies have found a significant relationship between the spread of myocardial repolarisation and the development of ventricular arrhythmias.[7]

METHOD

This study is an analytical study with a case control research design to determine the relationship of QTc interval prolongation to mortality in acute ischaemic stroke patients during treatment and three months post-treatment at Haji Adam Malik Hospital Medan. The study will be conducted at H.Adam Malik Hospital Medan. The study will be conducted in March 2023 by taking case samples from January 2021 to December 2022.

The inclusion criteria in this study were patients with acute ischemic stroke, and patients with acute ischemic stroke who had a 12 lead ECG examination. Patients with bundle branch block, patients with pacemaker, haemorrhagic stroke, hypocalcaemia, use of drugs that can prolong QTc interval were included as exclusion criteria.

Before the study began, the researchers requested ethical clearance from the Standing Committee for Research Ethics Assessment of the Faculty of Medicine, University of Sumatera Utara. All samples of this study were patients with a diagnosis of ischaemic stroke based on clinical and radiological findings. The researcher checked the patient's medical record to see the history, physical examination, electrocardiography (ECG), blood laboratory, and Head CT Scan, then the researcher contacted patients who met the inclusion criteria to ensure the patient was still alive or had died. From the mortality data, the relationship between mortality and QTc interval prolongation was analysed. Data processing, analysis, and hypothesis testing that has been determined using SPSS edition 24. So that it will be known whether there is a significant difference in the value of the parameters tested in the two groups.

RESULT

Table 1. Basic Characteristics of Subjects

Variable	Interval QTc	
	Normal	Prolongation
Age, years	59.4±11.8	
Comorbid		
DM Type 2	12 (44.4)	15 (55.6)
Hypertension	20 (47.6)	(52.4)
Chronic kidney disease	1 (14.3)	6 (85.7)
Atrial fibrillation	6 (46.1)	7 (53.9)
Pneumonia	1 (100)	0
Upper gastrointestinal bleeding	1 (100)	0
Mortality		
Yes (during inpatients)	0	33 (100)
Yes (90-days inpatients)	0	8 (100)
No	37 (90.2)	4 (9.8)
NIHSS score	3 (2-8)	6 (4-13)

Table 2. Relationship between QTc and Mortality

QTc	Total (n = 82)	Mortalities				p
		Yes		No		
		n	%	n	%	
Prolongation	44	40	97.6%	4	9.8%	<0.001
No prolongation	38	1	2.4%	37	90.2%	

Based on the data obtained in this study, of the 41 patients who died, the QTc interval was prolonged in 40 patients (p value <0.001). In contrast, of the 41 patients who did not die, only 4 had QTc interval prolongation (Table 2). Of the 41 patients who died, 19 had multiple lesions based on head CT scan results. Of the 41 patients who died, 8 died within 90 days post-treatment.

Based on the mortality interval, 13 patients died within 7 days of treatment (QTc interval range 505 - 547 msec), 20 patients died within 7-14 days of treatment (QTc interval range 460 - 490 msec), and 8 patients died within 90 days post-treatment (QTc interval range 453 - 486 msec) (Fig. 1).

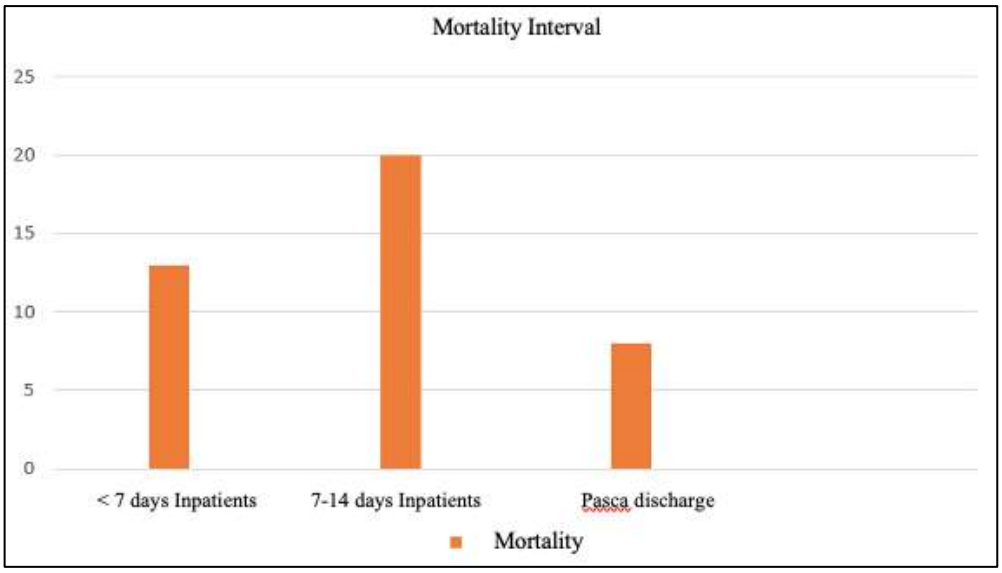

Figure 1. Patient Characteristics Based on Mortality

DISCUSSION

Acute ECG changes including ST segment elevation, ST segment depression, QT and QTc prolongation, T inversion, abnormal T wave morphology, pathological Q, and bundle branch block are often found in stroke patients.[8] In addition, cardiac arrhythmias, such as premature ventricular beats, or supraventricular ectopic beats, ventricular tachycardia and atrial flutter/fibrillation can also be found after stroke.[8] A prolonged QTc interval is found in 23% to 45% of patients with SIA; and is associated with cardiac arrhythmias and sudden death.[6] A prolonged QTc interval increases the occurrence of serious ventricular arrhythmias.[7] According to Moyakkis et al, a prolonged QTc interval is a predictor of early death in acute ischaemic stroke patients.[9] In addition, prolongation of the QTc interval in acute stroke patients is associated with a significantly greater risk of death within 3 months.[6] Impaired autonomic regulation of the cardiovascular system, or cardiac dysautonomia in acute stroke is thought to cause prolongation of the QTc interval.[4]

The QTc interval is the QT interval corrected for heart rate and sex. There is an increased mortality in patients with acute ischaemic stroke with prolongation of the QTc interval at presentation in the ED. A prolonged QTc interval is also associated with a worse prognosis, particularly at QTc intervals > 440 milliseconds in women and > 438 milliseconds in men.[6]

In this study, 48.8% of subjects were male, with a mean age of 59.4 years. More than half of the patients, or 53.7%, had a prolonged QTc interval. The mean QTc interval in patients who died was 490 msec (453.0 -

547.0). This result is consistent with the study of Ahn et al. who reported a mean QTc interval of > 460.5 ms.[6] In patients who did not die, the mean QTc interval was 413 msec (342.0 - 490.0) In both sex groups, about half of the subjects had a prolonged QTc interval with a similar mean QTc interval of 488.5 ms in men and 488.3 in women.

According to Zhang et al.'s meta-analysis study, QTc interval >450 ms is significantly associated with all-cause mortality and cardiovascular mortality in the general population.[10] In this study, the mean QTc interval was >488 ms which was significantly associated with mortality. A prolonged QTc interval may lead to an increased risk of fatal or non-fatal arrhythmias, as well as autonomic nervous system dysregulation that may contribute to mortality.[6]

Of the 41 patients who died, the QTc interval was prolonged in 40 patients (p value <0.001). This is consistent with the study of Stead et al. who found that patients with prolonged QTc interval were more likely to die within 90 days compared to patients without prolonged QTc interval.[11] Prolongation of QTc interval can cause ventricular arrhythmias, especially torsades de pointes, which can lead to sudden death.[12] Patients with acute ischaemic stroke have a high mortality, with various causes of death related to the stroke disease itself, cardiovascular disease and other causes. One of the most common ECG changes found in acute ischaemic stroke patients is QTc interval prolongation, which can cause fatal ventricular arrhythmias leading to death. In this study, the majority of patients with prolonged QTc interval died, which is consistent with previous studies.

CONCLUSION

QTc interval prolongation is associated with mortality in acute ischaemic stroke patients during treatment and three months post-treatment at Haji Adam Malik Hospital Medan.

DECLARATIONS

The research has received approval from the Universitas Sumatera Utara and RSUP Haji Adam Malik Health Research and Ethics Committee with Number. All participants were informed about subject of the study.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest in this research.

AUTHORS' CONTRIBUTIONS

All authors are responsible for conceptualization, manuscript preparation, manuscript editing, and manuscript assurance.

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