

QT INTERVAL PROLONGATION AND VENTRICULAR ARRHYTHMIAS IN PATIENTS WITH CHRONIC HEART FAILURE

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ABSTRACT

Objective: To determine the association of QTc interval prolongation with ventricular arrhythmias in patients with chronic heart failure.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi, Pakistan from April 2013 to August 2013.

Patients and Methods: Fifty three heart failure patients were monitored for 48 hours using ambulatory holter electrocardiography recorders. Digital ECG data was analyzed for QTc interval along with frequency and severity of arrhythmias. Association of prolonged QTc interval with ventricular arrhythmias and severity of arrhythmias was analyzed.

Results: Cardiac arrhythmias were observed in 79.2% patients. QT analysis revealed that 69.8% patients had prolonged QTc interval, 86.4% patients with prolonged QTc had ventricular arrhythmias. Of these 66% patients were found to have severe ventricular arrhythmias. Comparison of mean QTc interval of our study population with a reference value showed significantly higher QTc interval of our study group than the test value.

Conclusion: Arrhythmia frequency and severity significantly increases with an increase in QTc interval in heart failure demonstrating association of prolonged QTc interval with high risk of severe ventricular arrhythmias and sudden cardiac death in chronic heart failure.

Keywords: Ambulatory ECG recording, Arrhythmias, Holter monitoring, QT interval

INTRODUCTION

Heart failure is a clinical condition resulting from any structural or functional cardiac disorder consequently leading to failure of heart to deliver oxygen at a rate adequate to meet the requirements of the metabolizing tissues. The structural and functional changes of ventricular tissue, cause alterations in the electrophysiological properties of heart resulting in abnormal impulse generation and propagation thus, causing arrhythmias¹. In animal model of heart failure it has been observed that mechanical stretch of cardiac tissue results in significant prolongation of action potential duration and membrane recovery². In congestive heart failure, main underlying mechanism responsible for

arrhythmogenesis is altered myocardial repolarization due to down regulation of outward potassium current or a late sodium current of cardiac myocytes³. It manifests as variation in QT interval and is associated with increased incidence of ventricular tachycardia and fibrillation⁴.

On surface ECG, QT interval represents sum of ventricular depolarization and repolarization time. It begins from start of the Q wave of the QRS complex and ends where the T wave returns to the isoelectric baseline. Since 1920, Bazett's formula is used to calculate heart rate-corrected QT (QTc) taking into consideration changes in RR interval (heart rate)⁵. Corrected QT (QTc) interval has been widely used in pharmacology for drug development as a standard method to assess impaired ventricular repolarization⁶. It has been observed that ventricular repolarization behavior is a critical step in cardiac electrical activity as it corresponds to a recovery period before next

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systole. Altered conduction and repolarization is the basis of the reentrant arrhythmias thus indicating association of prolonged QT interval with arrhythmogenesis^{7,8}. QT prolongation is considered as a risk marker for increased cardiac mortality and complex ventricular arrhythmias such as polymorphic ventricular tachycardia in patients with structural cardiac diseases^{5,9}. Small changes in QT interval increase the likelihood to detect electrophysiological abnormalities due to impaired conduction or altered repolarization and can predispose cardiac tissue to lethal arrhythmias. Two-thirds of the cases of sudden cardiac death are associated with an abnormal prolongation of the QTc interval^{7,10}. In heart failure myocardial stress due to enlargement of ventricular chamber along with electrolyte imbalance results in repolarization abnormalities evident by prolongation of QT interval. Cardiac repolarization analysis provides valuable information for stratifying patients at high risk of developing arrhythmic events that could lead to sudden cardiac death, as well as for assessing efficacy of antiarrhythmic drugs¹¹. Early detection and timely management of these changes will improve overall outcome in heart failure¹². In clinical practice, Holter ECG has proved to be one of the most cost-effective, noninvasive clinical tools employed to calculate QT interval, QT interval dispersion and adjustment of QT for heart rate i.e. QTc interval¹³. It provides useful information about autonomic nervous system imbalance and myocardial repolarization abnormalities thus, help to predict mortality and progression of heart failure^{14,15}.

In present study we aimed to find out the frequency of QTc prolongation in patients with worsening left ventricular dysfunction using 48 hours holter monitoring and study the effect of QTc interval prolongation on the frequency of arrhythmias in heart failure patients in our population. It is important not only to understand the manifestation and progression of heart failure but also facilitate in optimal management of heart failure patients.

PATIENTS AND METHODS

A descriptive, cross sectional study was conducted after taking a formal approval from Medical Ethics Committee of Army Medical College and Institutional Review Board of Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi (AFIC/NIHD), from April 2013 to August 2013. An informed written consent was acquired from all the patients.

Fifty three patients from either sex, having age more than 19 years with the diagnosis of chronic heart failure were recruited by convenience sampling. Patients with left ventricular ejection fraction $\leq 40\%$ were included and those who had acute myocardial infarction during the last six weeks were excluded from the study.

Patients fulfilling the inclusion criteria underwent ambulatory ECG recording for 48 hours using holter monitors. Three different types of holter recorders, Life Card CF, DMS 300-4A and DMS 300-7A, available at AFIC/NIHD were used in this study. After 48 hours of recording, the digital ECG data were transferred from holter recorder to the computer having compatible software. Out of three channels, the one which displayed best ECG recording and with least artifacts was selected. The first step was the editing of arrhythmia templates. The whole data was manually edited with extreme care using visual checks and manual correction of all QRS complexes (individual beats). All the erroneous beats were identified and edited from data. After editing, the Holter ECG data was analyzed for cardiac arrhythmias and QT analysis using 'Life card CF holter software (pathfinder 700)' and 'DMS serial Holter software premier 12' compatible with Life Card CF and DMS 300-4A/DMS 300-7A respectively. Different types and frequency of arrhythmias, QT interval and QTc interval were analyzed.

Statistical analysis was done by using IBM SPSS version 21. Frequency and percentages were calculated for qualitative variables. Mean and

standard deviation (SD) were calculated for quantitative variables. One sample t-test was applied to compare QTc value with internationally accepted reference value. Chi-square test was applied to study association between QTc interval and arrhythmias. A *p*-value of < 0.05 was considered as significant.

RESULTS

The mean age of patients was 57.68 ± 16.41 years and male to female ratio was 3.4:1. Ventricular arrhythmias were present in 42 (79.2%) patients. QTc interval was prolonged in 37 (69.8%) patients.

Mean QTc interval of our study population was compared with a value of 450 milliseconds as the reference value of QTc interval which is its internationally accepted upper limit. Mean QTc interval of our study group was 536.34 ± 125.08 milliseconds. The mean QTc interval of our study population was significantly higher than the test value (*p* < 0.001) (table-2).

Out of 37 patients with prolonged QTc interval, 32 had ventricular arrhythmias while 10 patients with normal QTc interval had ventricular arrhythmias. There was significant association between prolonged QTc interval and ventricular arrhythmias (*p* = 0.048) (table-1)

Severity of ventricular arrhythmias according to Lown grading system was cross tabulated with QTc interval. Out of 32 patients with prolonged QTc interval (n=32), 21 (66%) had severe ventricular arrhythmias (table 2).

DISCUSSION

Sudden cardiac death due to electrical and mechanical instability is the major cause of death among heart failure patients¹⁶. About one half of deaths in heart failure patients are sudden, mostly due to ventricular tachycardia degenerating to ventricular fibrillation¹⁷. Despite all the advancement in modern therapeutic measures the mortality and morbidity rate remains high in heart failure¹⁸.

In present study QT interval analysis was performed on 48 hours holter ECG recordings of

patients with heart failure. Results of the study showed that 37 patients (69.8%) had prolonged corrected QT intervals (QTc) whereas the QTc

Table-1: Association of prolonged QTc interval with ventricular arrhythmias in patients with chronic heart failure (n=53).

Ventricular arrhythmias	QTc interval		<i>p</i> value
	Normal (n=16)	Prolonged (n=37)	
Present	10 (62.5%)	32 (86.5%)	0.048*
Absent	6 (37.5%)	5 (13.5%)	

**p*-value significant (< 0.05)

Table-2: QTc interval and severity of arrhythmias in patients with chronic heart failure (n=42).

QTc interval	Severity of ventricular arrhythmias			<i>p</i> value
	Mild	Moderate	Severe	
Normal (n=10)	4 (40%)	4 (40%)	2 (20%)	0.032*
Prolonged (n=32)	4 (12%)	7 (22%)	21 (66%)	

**p*-value significant (< 0.05)

intervals of 16 patients (30.2%) were within normal range. The results were statistically significant as *p*-value calculated was < 0.05. Karaye and Sani studied 113 patients with heart failure for the analysis of QTc interval¹⁹. They reported prolonged QTc interval to be present in 71.4% of their patients. The results were almost similar to present study as 69.8% of our patients also had prolonged QTc interval. Vrtovec et al, analyzed QTc interval in 241 patients with heart failure²⁰. They reported that 51% of their patients had prolonged QTc interval whereas the remaining 49% had the normal interval. Vrtovec et al, recorded 12 lead ECG and calculated QTc manually with the help of calipers and by using Bazett formula. In this study we determined QTc with the help of computer software. This might be the reason for difference in the results of the two studies.

Prolongation of QTc interval increases the incidence of life threatening ventricular

arrhythmias such as polymorphic ventricular tachycardia^{8,21}. We compared QTc interval of heart failure patients with a reference value of 450 milliseconds which is the internationally accepted upper limit of normal QTc interval. The results showed that QTc interval value of our study population was significantly higher than the test value. Vrtovec et al, studied the effect of prolonged QTc interval on mortality in 241 patients with heart failure²⁰. They found that prolonged QTc interval was a strong and independent predictor of sudden death in heart failure patients. Straus et al, carried out a population based cohort study to determine the effects of prolonged QTc interval on sudden cardiac death¹⁰. The study comprised of 7983 subjects and the average follow up period was 6.7 years. They also used the cutoff point of 450 ms for normal QTc interval. They concluded that prolonged QTc interval was associated with a threefold increase in sudden cardiac death. Bruyne et al., studied 5241 patients for association of QTc with mortality and reported the same results²². The results of present study combined with those of Vrtovec et al, Straus et al, and Bruyne et al, suggest that heart failure patients with prolonged QTc interval are at risk of sudden cardiac death and need to be isolated for further evaluation.

We also studied the association of prolonged QTc interval with ventricular arrhythmias. Results revealed 86.4% patients with prolonged QTc and 62.5% patients with normal QTc interval had ventricular arrhythmias. Tedesco et al, studied sudden cardiac death in patients with chronic heart failure²³. Results of their study showed that approximately 50% of deaths in patients with chronic heart failure were due to severe ventricular arrhythmias. In our study, 66% of heart failure patients were also found to have severe arrhythmias. These results are comparable to those of Bounhoure et al, and Chakko et al, who reported incidence of sudden death in heart failure patients due to ventricular arrhythmias as 60% and 50% respectively^{24,25}.

In this study, we analysed the severity of ventricular arrhythmia with reference to QTc interval. Twenty one patients (66%) with prolonged QTc interval had severe ventricular arrhythmias. Aggarwal et al, carried out a study for QTc analysis and fatal outcomes in patients with heart failure²⁶. They found 22% patients with prolonged QTc interval had higher mortality. We could not follow up our patients to determine mortality, however by combining prolonged QTc interval with severity of arrhythmias, an indirect inference can be made about the future outcomes. A high percentage of our study population had prolonged QTc interval along with severe ventricular arrhythmias predicting higher rate of future mortality. Out of 53, 86.4% of chronic heart failure patients had ventricular arrhythmias along with QTc interval prolongation and 66% of these patients had severe ventricular arrhythmias. These findings are consistent with other studies which have revealed that percentage of patients with chronic heart failure terminating into sudden cardiac death ranges from 40 to 60%^{23,27}. Apart from electrophysiological changes in failing heart, multiple other factors such as degree of ventricular dysfunction and etiology could be responsible for genesis of severe ventricular arrhythmias in heart failure. However, prolongation of QTc interval is one of the important factors responsible for arrhythmia leading to sudden cardiac death in heart failure.

CONCLUSION

The QT analysis in our study revealed that the prolongation of QTc interval is associated with increased frequency and severity of ventricular arrhythmias in chronic heart failure. This indicates that prolonged QTc is a significant predictor of potentially lethal ventricular arrhythmias leading to sudden cardiac death in patients with heart failure.

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