

## Original Research Article

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# Effects of thrombolytic therapy on QT depression following acute myocardial infarction

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## ABSTRACT

**Background:** Arrhythmias remains the major source of mortality from MI but with continuous ECG monitoring and the rapid availability of defibrillators, few with infarction die from ventricular fibrillation (VF) in hospitals. Perhaps for this reason or because of the lack of success in the prediction of VF, this problem has attracted relatively little recent attention. Objective of this study was to study effects of thrombolytic therapy on QT depression following acute myocardial infarction.

**Methods:** Fifty patients of acute myocardial infarction (AMI) admitted to ICCU of a tertiary care hospital were studied for a period of three years. At the time of admission to ICCU a detailed history was taken in all patients. A general examination was done in all patients and vital signs of pulse, blood pressure, temperature was recorded.

**Results:** VPC was the most common type of arrhythmia observed in the present study in 16% of the cases. Out of the 50 cases studied arrhythmias were found in only 23% of the cases. QTd as well as QTcd was more on admission among those who did not receive thrombolytic therapy. QT depression was significantly less in healthy individuals compared to patients with ventricular arrhythmias. Maximum i.e. four patients died due to ventricular arrhythmias or fibrillation. The mean value on admission was more in patients with ventricular arrhythmia compared to patients without ventricular arrhythmia. The mean value on admission as well as at discharge was more in patients with anterior.

**Conclusions:** Present study to a large extent supports the contemporary hypothesis that higher QTc intervals and dispersions on the first day ECG of the patients with AMI caution us about the impending danger of VA and subsequent mortality.

**Keywords:** Acute myocardial infarction, ECG, QT interval

## INTRODUCTION

Great efforts have been expanded in attempts to predict the fatal ventricular arrhythmias (fibrillation) in patients at the earliest phase of myocardial infarction (MI). These arrhythmias remain the major source of mortality from MI but with continuous ECG monitoring and the rapid availability of defibrillators, few with infarction die from ventricular fibrillation (VF) in hospitals. Perhaps for this

reason or because of the lack of success in the prediction of VF, this problem has attracted relatively little recent attention.<sup>1</sup>

Various features are significantly associated with primary VF, time from onset of symptoms; size of infarction, potassium levels etc, but none has clinically useful positive predictive accuracy. R on T ventricular extra systoles has been investigated as predictor of VF. They

appeared an attractive prospect regarding their part initiating primary VF, but their presence and frequency proved neither specific nor sensitive in predicting this arrhythmia. Signal averaged ECG for calculating the late potentials which indicate the presence of substrate for V-Tach/VF in MI, is the latest sophisticated technique for predicting the vulnerability for VF in MI. Late potentials which are low voltage, high frequency signals in the terminal portion of the QRS complex, indicate myocardial activation and are commonly found in patients subject to V-tach.<sup>2</sup>

Recent clinical studies have indicated that the inter lead variability of the QT interval in the surface ECG (viz. the QT dispersion defined as the difference between the maximal and minimal QT interval duration and corrected to heart rate i.e. QTc dispersion) reflects the regional differences in ventricular recovery time. Experimental data have demonstrated a strong link between the vulnerability of the ventricular myocardium to serious tachy-arrhythmia and increased temporal dispersion of refractoriness. The QT dispersion has been linked to the occurrence of arrhythmias in patients with congenital long QT syndrome or with drug induced pro-arrhythmias like Torsade de pointes tachycardia to sudden death in chronic CCF. There are however, several important unresolved issues regarding the techniques and the diagnostic value of assessment of QT dispersion for the surface ECG. For instance, the range of QT dispersion in persons without heart disease is still ill defined. Furthermore, there is a lack of data concerning the intra and inter observer variability of repeated QT dispersion measurements. Another methodological problem relates to the issue of lead selection i.e. 12 leads vs. pre-cordial leads for determination of QT dispersion in order to obtain maximal determination on ventricular recovery time.<sup>3</sup>

The QT interval therefore is one of the most controversial and least understood features of the surface ECG. What is clearly understood is that the homogeneity of recovery time protects against arrhythmias whereas dispersion of recovery time is arrhythmogenic. A single derived value of surface ECG embodies the concept of a global value for cardiac repolarisation time. But QT interval varies for lead to lead off the surface ECG. If such a variation is merely a technical artefact caused for example, by differences in unipolar vs. bipolar leads, by differential time attenuation or by cancellation of vectors, then a desired average QT value from surface ECG is scientifically valid. Thus, QT dispersion corrector to heart rate (Q-Tcd) or a standard ECG has been shown to reflect the regional variation in ventricular repolarisation and is significantly greater in patients with than in those without arrhythmic events. One study which looked critically in the comparative values of QT dispersion in normal healthy subjects, patients with uncomplicated MI and patients with complicated MI (VF), concluded that QT dispersion is increased after MI and the levels are still higher in those MI complicated with VF. They observed

that changes in QT dispersion are dynamic and may reflect the changing pattern of underlying ventricular recovery of ventricular excitability which is profoundly disturbed at the earliest phase of acute infarction.<sup>1</sup>

Another study of a large number of acute MI patients showed that the thrombolytic therapy which has become now the corner stone of treatment of acute MI and which indisputably improves the survival and preserves the myocardial function reduces the ventricular excitability and therefore the QT dispersion especially those with very successful reperfusion.<sup>4</sup>

Keeping all these observations in mind, we planned the present study with the objective to study the QT dispersion status in patients with acute MI in ICCU.

## METHODS

Fifty patients of acute myocardial infarction (AMI) admitted to ICCU of a tertiary care hospital were studied for a period of three years. Criteria for the diagnosis of AMI was chest pain classical for MI of more than 20 minutes duration not responding to sublingual nitrates, ECG changes of MI. ST segment elevation equal to or more than 1mV in two or more continuous leads and CPKMB more than 40 units per liter. Patients having at least two of the above mentioned three were included in the present study. Informed consent was taken for all included patients.

At the time of admission to ICCU a detailed history was taken in all patients. A general examination was done in all patients and vital signs of pulse, blood pressure, temperature was recorded.

A meticulous physical examination was done and recorded in the proforma. Routine investigations including HB, CBC, ESR, urine was done. Blood sugar levels were estimated. Renal functions of blood urea and serum creatinine was also estimated. Cardiac enzymes of CPKMB were estimated in all patients immediately after admission.

A 12 lead ECG was taken at admission. ECG was also taken before discharge of the patient. For recording a three channel ECG machine was used and the recordings were made 25 mm/sec and 1 mV for 10 mm setting. The same ECG machine was used throughout the study. The points on the chest used for recording the ECG was marked with the surface marking pencil, so that the same points were used in the follow up ECG. All the patients were classified as per Killip's classification. Class I were those with no signs of pulmonary venous congestion. Class II was those with moderate heart failure as evidenced by rales at lung bases, S2 gallop tachypnoea, and signs of right sided heart failure. Class III was those with severe heart failure and pulmonary edema. Class IV was those with cardiogenic shock.

All the patients were managed in the ICCU as per the standard protocol. Thrombolytic therapy (TLT) was given in 24 out of 50 patients who were eligible for such therapy. Thrombolysis was done with streptokinase 1.5 million units given as per the recommended regimen. Other treatment included heparin, aspirin, beta blockers, vasodilators, dopamine, dobutamine, NTG drips, ACE inhibitors were also used in appropriate cases.

QT interval and QTc interval measurements were carried out as per the standard guidelines.

The data was analysed using proportions, mean values, and other statistical tests as and when required.

## RESULTS

**Table 1: Distribution of various types of arrhythmias noted in the present study.**

Type of arrhythmia	Number	Percentage
VPC	8	16
Ventricular bigeminy	2	4
Ventricular trigeminy	2	4
Ventricular tachycardia	1	2
Total	13	23

VPC was the most common type of arrhythmia observed in the present study in 16% of the cases. Out of the 50 cases studied arrhythmias were found in only 23% of the cases. Ventricular bigeminy and trigeminy was found in two cases each.

**Table 2: Comparison of QT depression in patients of MI who received and who did not receive thrombolytic therapy.**

Received thrombolytic therapy	On admission (mean values)		On discharge (mean values)	
	QTd m-sec	QTcd m-sec	QTd m-sec	QTcd m-sec
Yes (N = 24)	62.5	73.75	64.16	71.66
No (N = 26)	75	101	69	86

Table 2 shows comparison of QT depression in patients of MI who received and who did not receive thrombolytic therapy. The QTd as well as QTcd was more on admission among those who did not receive thrombolytic therapy. On discharge also, it was more among this group compared to the other group.

Table 3 shows comparison of QT depression in various groups. The QT depression was significantly less in healthy individuals compared to patients with ventricular arrhythmias.

The QT depression was also significantly lesser in patients with ventricular arrhythmias compared to patients who died during the hospital stay.

**Table 3: Comparison of QT depression in various groups.**

Groups	QTd m-sec (mean values)	QTcd m-sec (mean values)
Healthy (N = 10)	32	44
Patients with ventricular arrhythmias (N = 13)	92	71
Patients who died during hospital stay (N = 6)	123	87

**Table 4: Causes of death among patients who died during hospital stay.**

Cause of death	Number
Congestive cardiac failure	1
Cardiogenic shock	1
Ventricular arrhythmias/fibrillation	4

Table 4 shows causes of death among patients who died during hospital stay. Maximum i.e. four patients died due to ventricular arrhythmias or fibrillation. One patient died due to congestive cardiac failure and one patient died due to cardiogenic shock.

**Table 5: Mean QTcd values in cases of AMI with and without ventricular arrhythmias (VA).**

Group	Mean QTcd value on admission (m-sec)	Mean QTcd value on discharge (m-sec)
AMI without VA (N = 37)	92	89
AMI with VA (N = 13)	103	80

Table 5 shows mean QTcd values in cases of AMI with and without ventricular arrhythmias (VA). The mean value on admission was more in patients with ventricular arrhythmia compared to patients without ventricular arrhythmia. But on discharge the mean value was more among patients without ventricular arrhythmia compared to patients with ventricular arrhythmia.

**Table 6: Mean QTcd values on admission and at discharge according to site of infarction.**

Site of infarction	Mean QTcd value on admission (m-sec)	Mean QTcd value on discharge (m-sec)
Anterior wall (N = 29)	94	82
Inferior wall (N = 23)	70	60

Table 6 shows mean QTcd values on admission and at discharge according to site of infarction. The mean value on admission as well as at discharge was more in patients with anterior wall infarction compared to patients with inferior wall infarction.

**Table 7: Mean QTcd values among expired and survived patients.**

Outcome	Mean QTcd value on admission (m-sec)	Mean QTcd value on discharge (m-sec)
Expired (N = 6)	123	87
Alive (N = 44)	77	76

Table 7 shows mean QTcd values among expired and survived patients. The mean value on admission as well as at discharge was more in patients who died compared to patients who survived.

## DISCUSSION

In the present study, among the 10 normal subjects there was a wide inter individual variation of QT intervals and the QTc dispersions. QTc dispersion varied from 10-80 msec (mean = 44msec). In the series of 50 normal subjects Van de Loo et al found that mean QTc dispersion was  $34 \pm 11$  msec and a wide inter-individual variation in QT interval and dispersions was evident there also.<sup>3</sup>

In cases of acute MI who had received TLT (N = 24), QT intervals and QT dispersion have been analysed and compared to those cases who did not have the benefit for TLT (N = 26). It was obvious that the QTc dispersion values were higher in those who did not have TLT than in those who had TLT. Among those who received TLT the QTcd values of the first day i.e. before TLT came down marginally to a mean of 71.66 msec after TLT thereby indicating the reduced excitability of the myocardial hence vulnerability for ventricular arrhythmias. But this was not statistically significant. A study by Moreno et al looked into similar parameters in a large number of post myocardial infarction patients (N = 244) and has shown the appropriate and successful thrombolysis is associated with reduction in QTcd values, a measure of dispersion of ventricular repolarisation.<sup>4</sup> This study assessed the success of the thrombolysis by coronary angiography and knowing the flow status. Higher grades of flow were associated with far lower QTcd values compared to lower grades of flow. Thus, establishing the patency, TLT may reduce the degree to which an abnormal electrophysiological milieu develops after AMI. This study also demonstrated that QT or QTc dispersion is greater with LAD coronary artery occlusion and with anterior wall site of infarction. Our study is limited by the lack of angiographic data and therefore to say which patient had a successful revascularization by TLT among our patients is difficult. However, in our patients with anterior wall

MI QTcd values were much higher compared to those who had inferior wall MI both on admission and discharge day supporting the observation given by Monero et al.<sup>4</sup>

Author also looked into QT intervals and dispersion in the subsets of the patients of AMI who experienced VA and compared to others without VA. This again emphasizes the earlier observations that QTcd values are higher in the sub group of AMI patients with VA compared to AMI with no VA. This may be a significant factor although mean QTcd values in the patient with VA on admission came down significantly on the discharge or death day, the group as a whole had higher QTcd value than in the AMI cases with no VA.

From our study it was obvious that QT intervals and QT dispersions corrected to the heart rate are significantly increased in patients with acute MI as a whole compared to the normal healthy subjects. Secondly, higher QTc and QTcd values found on first day AMI came down marginally after TLT when appropriately and selectively given compared to those who did not receive TLT. Thirdly that case of AMI who had ventricular arrhythmia had higher values of QTc and QTcd compared to those who did not have VA.

Analysis of the expired patients in this cohort showed that the QTcd values were far higher in than those of survived patients. An earlier study of sudden death and its relation to prolongation of QT interval after AMI showed that QT prolongation though seen in some patients after AMI, reduced LVEF and frequent ventricular arrhythmias are the most important factors for predicting sudden death in the patient population. They however did not look for QT dispersions, the significant of which was not known at that time.<sup>5</sup>

Priori et al has shown that QT dispersion was a predictor of sudden death in the idiopathic long QT syndrome and can be used as a marker of therapeutic efficacy of drugs used in this condition.<sup>6</sup> A much earlier study by Taylor et al showed that prolonged QT interval in the acute phase of MI patients was a predictor of V-Tach, VF and sudden death.<sup>7</sup> They did not however look into the QT dispersions.

There are some studies recently published which have shown that QT dispersion on the admission ECG was not clear-cut predictor of higher mortality. For instance, Glancy et al observed that the initial QT dispersions although higher did not differ much between the patients who died and the survivors.<sup>8</sup> However, the QTc dispersion values seem at least four weeks after the infarct were associated with the subsequent mortality but cautioned that this finding must be confirmed on a prospective trial basis.

In another study by Leitchh J et al has shown 24 patients of acute MI who developed VF within 12 hours of

admission, authors analyzed QTc interval and dispersions measured on the presenting ECG and concluded that their values failed to predict early VF after MI compared to 24 control patients who did not develop VF.<sup>9</sup>

Other studies including by Xiang H et al, Yunus et al, and Hohnloser SH et al has conclusively shown that higher QTc intervals and QTc dispersions with AMI represent the significant marker of in-homogeneous repolarisation prone to VF and that this may allow early identification of high risk patients soon after hospital admission.<sup>10-12</sup>

The above studies represent the varied and often conflicting opinions regarding the values of QT intervals and dispersions in patients presenting with AMI.

## CONCLUSION

The present study to a large extent supports the contemporary hypothesis that higher QTc intervals and dispersions on the first day ECG of the patients with AMI caution us about the impending danger of VA and subsequent mortality. The TLT is beneficial in reducing the QTc intervals and dispersions and subsequent possible survival benefit to such patients.

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