### **Original Research Article**

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# QT interval dispersion as a prognostic indicator in patients of acute coronary syndromes

## Saurabh Chittora\*, Nirmal K. Sharma, Devendra Ajmera, Pavankumar Pyarsabadi, Sudeep Javedar, Kapil Jaiswal

Department of Medicine, Government Medical College, Kota, Rajasthan, India

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\*Correspondence: Dr. Saurabh Chittora,

E-mail: saurabh85chittora@gmail.com

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#### **ABSTRACT**

**Background:** QT dispersion is a potential marker of arrhythmic risk, myocardial ischemia and myocardial viability. Measurement of QT interval dispersion has failed to establish its place in routine clinical practice. The study aims at predicting risk of life threatening ventricular arrhythmias in patients of acute coronary syndromes using rate adjusted QT interval dispersion (QTcd) as one of the cheapest modalities of investigation.

**Methods:** Serial measurements (at admission, after 24 hours, 48 hours, and 7<sup>th</sup> day) of rate adjusted QT interval dispersion (QTcd) was done in 107 cases of acute coronary syndromes (ACS) namely ST-segment elevated Myocardial infarction (STEMI), non-ST-segment elevated myocardial infarction (NSTEMI) and unstable angina (UA). Patients who reported within 12 hrs of onset of chest pain and typical ECG changes were thrombolysed using streptokinase (15 lack IU).

**Results:** Mean QTcd following acute coronary syndrome was maximum at admission and then gradually falls till day-7 as the patients clinical condition improves but it remains high in case of development of various complications (viz. hypotension, congestive heart failure (CHF), PSVT, VPC, CHB, ventricular fibrillation and death). Patients with STEMI who were thrombolysed at admission showed significantly lower mean QTcd on day-1, as well as complications and death during in-hospital stay as compared to patients who were not thrombolysed (p <0.001).

**Conclusions:** QTcd interval could be helpful as an earliest in-hospital bedside predictor of life-threatening arrhythmias and death. Timely reperfusion by thrombolysis decreases mean Qtcd and thus reduces post-MI mortality and morbidity.

**Keywords:** Arrhythmias, QT interval dispersion, Thrombolysis

#### INTRODUCTION

The QT interval reflects the duration of depolarization and repolarization of the ventricular myocardium thus reflects changes in local myocardial milieu. QT dispersion is defined by Cowan and colleagues in 1988 as "the differences between the maximum and minimum QT interval measurement on the standard 12 lead ECG". Dispersion of repolarisation is thought to reflect regional heterogeneity of the recovery process within the

myocardium, which is believed to be important in the genesis of ventricular arrhythmias.<sup>2-5</sup> Slowed conduction in the ischemic zone of myocardium, electrolyte disturbance and alterations in the level and kind of autonomic control after acute myocardial infarction are responsible for development of arrhythmias.<sup>6-8</sup> After AMI, the effect of thrombolytic therapy and the patency of infarct related artery, history of re-infarction, the size of the infarction scar and left ventricular ejection fraction are linked to QTd.

Medical science has little to offer, in ascertaining the likely prognosis of patients with acute coronary syndromes in terms of morbidity and mortality, once the acute event has occurred. Relevant past studies have focused on Acute STEMI to study prognosis using QTd (QT dispersion). However, to broaden the scope of our study we included unstable angina, Non STEMI, and STEMI (both thrombolysed and non thrombolysed).

#### **METHODS**

This was a prospective study of patients with a diagnosis of acute coronary syndromes admitted in Medical OPD, Emergency and various wards of M.B.S. Hospital, Kota, Rajasthan, India from January to December 2013 after obtaining an informed consent. 107 cases of acute coronary syndromes (ACS) were studied.

#### Inclusion criteria

- Patients with chest pain and ECG changes that suggest unstable angina by standard criteria.
- Patients who have at least 2 out of 3 following criteria for myocardial infarction, as defined by WHO,
  - a) Typical history of severe chest pain radiating to the neck or arms for duration >30 minutes,
  - b) ECG changes of ST elevation >2mm in two or more chest leads or >1mm in two or more limb leads.
  - Rise in serum cardiac enzymes concentration (Troponin-T) more than twice the upper limit of normal.
- Patients with non-ST elevation myocardial infarction as per standard criteria.

#### Exclusion criteria

- Patients reporting after 48 hours,
- Atrial fibrillation or flutter,
- Previous ECG showing Left or right bundle branch block, Patient on drugs affecting QT interval Eg. quinidine, procainamide, tricyclic and tetracyclic antidepressants,
- Valvular heart disease,
- Hypocalcemia,
- Chronic congestive heart failure.

In all patients with ACS, 12 lead ECG was recorded at speed of 25 mm/sec and at a setting of 1mv=10mm at admission, after 24 hours, 48 hours, and on the 7<sup>th</sup> day of admission. QT interval was measured from onset of the QRS to the end of the T wave.

If in an ECG, U waves were present, the QT interval was measured to the nadir of the curve between the T and U waves. If the end of the T wave could not be identified, that lead was not included. A minimum of eight leads had been measured to calculate QT dispersion. Heart rate was measured from average of 3 RR intervals. Each QT

interval was corrected for the patient's heart rate using BAZETT's formula,

 $QTcd = QT interval/\sqrt{RR}$  (sec)

(Where QTc is the corrected QT interval).

Various parameters to judge the short-term prognosis of patients admitted with diagnosis of acute coronary syndrome were as follows:

- Hypotension (a systolic BP ≤ 90 mmHg or diastolic BP < 60 mmHg).</li>
- Life threatening arrhythmias (diagnosed by standard criteria) - paroxysmal supraventricular tachycardia (PSVT), ventricular premature contractions (VPC), complete heart block (CHB) and ventricular fibrillation.
- Congestive heart failure (killip class II and III)
- Death/asystole.

Patients who presented with STEMI within 12 hours period were thrombolysed with streptokinase 15 lack Units over 30mins after ruling out any contraindication.

All values of QTcd has been represented as mean  $\pm$  standard deviation, comparison of mean levels between 2 groups was done by Z-test for large samples (>50 samples in each group) and student's 't' test for small samples (<50 samples in a group) a value of p <0.05 was considered as the minimum level of statistical significance.

#### **RESULTS**

Out of 107 patients under study, 76 (71%) were males and 31 (29%) were females. The mean age of males was 57±13 years and that of females was 54±12 years. 13.08 % patients were less than 40 years of age. Maximum no. of patients i.e. 27.1% belong to age group 51-60 years. As shown in Table 1 there had been 33 patients with diagnosis of unstable angina (30.8%), 48 patients of STEMI (44.9%) and 26 patients with NSTEMI (24.3%). Mean QTcd on day-0 in patients with UA, STEMI and NSTEMI was 122.970±14.836 msec, 158.440±14.895 msec and 153.870±17.995 msec respectively. This is significantly higher (p <0.0001) than mean QTcd on day-0 in patients with NSTEMI and STEMI is significantly higher (p<0.0001) than in patients with UA.

This suggests that STEMI and NSTEMI cause greater rise of QTcd as compared to UA. The most common complication among different patients of ACS was Congestive heart failure (26), then hypotension (7), followed by ventricular arrhythmias and deaths (5 each); figure 1. The least common observed complication was complete heart block (3).

Table 2 shows that the mean QTcd on day-0 in controls is  $65.891 \pm 16.571$  msec and in cases with no complication was  $138.241 \pm 16.882$  msec. There was statistically significant difference (p<0.0001). However in patients with various complications following acute coronary syndromes the mean QTcd on day-0 (172.862±15.156 msec), day-1 (148.178±19.601 msec), day-2 (123.097±17.141 msec) and day-7 (100.075±15.407 msec) which was significantly higher as compared to patients without any complication on all 4 days. Table 3 shows that mean QTcd on day-0, day-1 and day-2 in patients who died was (180.895±10.467, 160.542±5.708

and 122.395±3.221 msec respectively), which is higher than mean QTcd on similar days among survivors. P value for day-0, day-1 and day-2 is highly significant. To study the effect of thrombolysis (with streptokinase) on QTcd in patients with acute STEMI presenting within 12 hrs of onset of chest pain. Mean QTcd on day 0, day-1, day-2 and day-7 was calculated. Table 4: Figure 2 shows that 15 out of 48 patients with STEMI that underwent thrombolysis with STK showed statistically significant reduction in QTcd on day 1 (p<0.0001) and till day 7 (p<0.05). No death was observed among the group who were thrombolysed.

Table 1: Comparison of mean QTCD on day-0, day-1, day-2 and day-7 in various types of acute coronary syndromes.

Type of ACS		No. of	Mean QTcd (msec)			
Type of ACS		patients	Day-0	Day-1	Day-2	Day-7
Controls		50	65.130±17.046	-	-	-
ACS	Unstable Angina	33	122.970±14.836 (p<0.0001)*	102.355±17.165	89.474±18.320	76.094±16.184
	STEMI	48	158.440±14.895 (p<0.0001)**	132.045±17.189	109.816±13.548	89.652±10.609
	NSTEMI	26	153.870±17.995 (p<0.0001) **	131.020±15.409	108.719±13.813	87.907±15.215

<sup>\*</sup>p value for significance of difference between unstable angina and controls; \*\*p value for significance of difference between Unstable angina and STEMI/NSTEMI.

Table 2: Comparison of mean QTcd on day-0, day-1, day-2 and day-7 in cases with no complication and cases with complications.

Patient group		No. of	Mean QTcd (msec)				
		patients	Day-0	Day-1	Day-2	Day-7	
Controls		50	65.130±17.046	-	-	-	
ACS	With no. complications	55	138.241±16.882 (p<0.0001)*	115.027±15.234	97.831±13.824	81.377±12.793	
	With various complications	52	172.862±15.156 (p<0.0001)*	148.178±19.601	123.097±17.141	100.075±15.407	

<sup>\*</sup>p-value signifies correlation between controls and different ACS with/without complications.

Table 3: Comparison of mean QTcd on day-0, day-1, day-2 and day-7 in patient who died during hospital stay, with patients who survived.

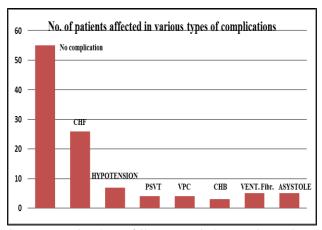
	No. of patients	Day-0	Day-1	Day-2	Day-7
Survivors	102	145.189±21.367	121.649±20.701	103.003±17.950	85.093±15.107
Death	5	180.895±10.467 p<0.001*	160.542±5.708 p<0.0001*	122.395±3.221 p<0.05*	-

<sup>\*</sup>p-value signifies correlation Qtcd (msec) in survivors and patients who died.

Table 4: Progression of QTcd in patients with STEMI.

STEMI patients	Mean QTcd (msec)					
	Day 0	Day 1	Day 2	Day 7		
Not thrombolysed $(n = 33)$	158.347±16.129	134.725±16.091	114.473±12.722	94.467±8.475		
Thrombolysed (n = 15)	158.628±12.281	126.329±18.603	100.504±10.111	80.544±7.866		
Thrombolysed $(n = 15)$	p<0.94*	p<0.0001*	p<0.0006*	p<0.0121*		

<sup>\*</sup>p-value signifies correlation between STEMI patients who were thrombolysed and not thrombolysed on corresponding days after admission.



CHF- congestive heart failure; HYPO hypotension; PSVT-paroximal supraventricular tachycardia; VPC- ventricular premature beats; CHB- complete heart block; VF- ventricular fibrillation.

Figure 1. Graphical representation of various types of complications and the affected no. of patients following ACS as whole.

Figure shows number of patients among all cases (ACS) affected with different types of complications during inhospital stay.

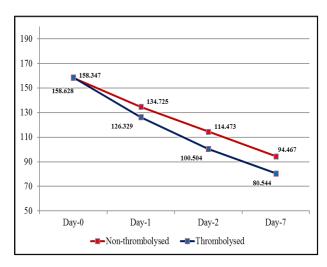


Figure 2: Cumulative frequency curve to compare progressive fall in mean QTcd following thrombolysis on day 0, day 1, day 2 and day 7 as compared to non thrombolysed STEMI patients.

Figure 3 shows comparision of patients of STEMI who underwent thrombolysis with those who were not thrombolysed. Mean QTcd on day-0 in both groups were nearly same however on day-1 after thrombolysis there is significant fall in mean QTcd (p <0.0001), this difference is also seen in mean QTcd on day-7, where p value is p<0.05.

#### **DISCUSSION**

Amongst the acute complications of Acute myocardial infarction, ventricular arrhythmias are very important yet

preventable cause of death.<sup>9</sup> Identification of patients at high risk of life-threatening ventricular tachyarrhythmias represents one of the most challenging issues in patient care, especially after acute myocardial infarction (AMI). The clinical significance of QT interval prolongation has been the subject of much debate, with the evidence till date favoring an association between a prolonged QT interval or an increased QTd, and an increased risk of sudden death due to arrhythmia.<sup>10</sup>

Out of 107 patients of acute coronary Syndromes 71 % patients were male (n=76) and 29% patients were female (n=31). Wahab A et al (11), reported similar results with 86 (69.4%) male and 38 (31.6%) female. Maximum no. of patients i.e. 27.1% belong to age group 51-60 years, this was similar to study by Wahab A et al, who noted maximum cases in 5th decade accounting 30% of all cases.11 Mean QTcd on day-0 in cases (ACS) is 146.858±22.282 msec which is higher than in previous studies.11-13 Also mean QTcd on day-0 in controls (65.891±16.571 milliseconds) was in the same range established in the studies of Sylven et al (54±27 milliseconds), Mirvis (59±12.9 milliseconds) and Cowan et al (48±18 milliseconds). 14,15 The difference in QTcd between Cases and controls is highly significant (p < 0.001).

Mean QTcd in patients with STEMI and NSTEMI on all days of observation was higher than the controls, similar results were observed by Wahab et al, Higham et al (NSTEMI,55 patients), Piventi S et al.<sup>11,16,17</sup> This suggests that STEMI and NSTEMI cause greater rise of QTcd as compared to unstable angina. It is one of a significant finding in our study.

In our study we found that mean QTcd following Acute coronary syndrome is maximum at admission and then gradually falls till day-7 as the patients clinical condition improves but it remains high in case of development of various complications (viz. hypotension, congestive heart failure (CHF), PSVT, VPC, CHB, Ventricular fibrillation and death). These results were consistent with previous studies. 11,13,18 In patients with acute STEMI the fall in QTcd is more in patients who received thrombolytic therapy as compared to those who did not received thrombolytic therapy. These results are similar to studies by Wahab et al, Kabakci G et al and Parale GP et al. 11,19,20

Hence, mean QTcd is a strong and independent risk factor in predicting the morbidity in patients of various acute coronary syndromes during hospital stay independent of established classical risk factors and is also a univariate predictor of short term mortality including sudden cardiac death.

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