What is the Optimal Evaluation Time of the QT Dispersion After Acute Myocardial Infarction for the Risk Stratification?

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The sequential changes of the corrected QT dispersion (QTcD) were studied in 136 patients 1 day to 30 days after a transmural acute myocardial infarction (AMI) to investigate the optimal measurement time of QT dispersion for risk stratification. The study group included 136 patients (89 men; mean age, 57 ±10 years) with transmural AMI who were treated with thrombolytics (Tr+ group, n=73) or not (Tr- group, n=63) and 65 healthy controls (43 men; mean age, 56 ±7 years). Fourteen patients in whom ventricular tachycardia (VT), ventricular fibrillation (VF), or sudden cardiac death developed during the 30-day period were also evaluated as major cardiac arrhythmia (MCA) group. ECGs were obtained for each patient on days 1, 3, 5, 10, 15, and 30 after AMI. QTc dispersion in patients with AMI (for every period of QTcD after MI) was significantly more prolonged than in normal controls (49.3 ±16.3 ms) ($p<0.001$). QTcD was significantly greater in patients without thrombolytics than in patients with thrombolytics for every period (days 1, 3, 5, 10, 15, and 30) of QTcD after MI ($p<0.001$). The mean of QTcD was significantly greater in patients with MCA than in patients without MCA group for every period (days 1, 3, 5, 10, 15, and 30) of QTcD after MI ($p<0.05$). Maximal QTcD was seen on day 10 ($p<0.05$ 1st vs day 10 for each group) after myocardial infarction, and then reached a plateau for an each group. The ideal time to measure the QTD for risk stratification is at least 10 days after AMI.

Introduction

Patients with coronary artery disease are at increased risk of sudden cardiac death mainly caused by ventricular tachyarrhythmias.[1,2] Recent studies have suggested that interlead QT variability on the surface electrocardiogram, defined as QT dispersion (QTD), may reflect regional variations in ventricular recovery of excitability. Increased dispersion of ventricular repolarization time is believed to provide a substrate that facilitates serious ventricular arrhythmias.[3-5] Subsequently, in several studies, the value of QTD for risk stratification was represented in post-myocardial infarction patients.[6-8] However, there are no clear data about optimal time to measure the

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QTD for non-invasive risk stratification after acute myocardial infarction.

Therefore, in this study, we investigated the changes of corrected QT dispersion (QTcD) in post-myocardial infarction patients to clarify the time of risk stratification.

Methods

Patients

A clinical diagnosis of AMI was established according to the presence of at least two of three classic WHO criteria (ST elevation obligatory). The exclusion criteria were: atrial fibrillation or bundle branch block or preexcitation; patients with previous MI or other organic heart disease; nontransmural MI; patients taking oral medications (except beta-blockers) that might alter QT interval; electrolyte imbalance; and patients who underwent revascularization procedures. The study group (Table I) included 136 patients (89 men, 47 women; mean ± standard deviation [SD] age 57 ±10 years) with transmural AMI and 65 healthy controls (43 men, 22 women; mean ± standard deviation [SD] age 56 ±7 years). Seventy-three of 136 in the study group received thrombolytic therapy. ECG localization of MI indicated anterior in 79 patients and inferior in 57 patients. Four patients (n = 1; thrombolytic positive) died of sudden cardiac death between 24 hours and 30 days. Ventricular tachycardia occurred in eight patients (n = 3; thrombolytic positive); six non-sustained and two sustained. Two patients were resuscitated by ventricular fibrillation. QTcD of these 14 patients (n = 4; thrombolytic positive) was also evaluated as part of the major cardiac arrhythmia (MCA) group.

QT Analysis

Corrected QT dispersion (QTcD) measurements were calculated from a 12-lead resting electrocardiogram (ECG) during sinus rhythm at a paper speed of 25 mm/s with 1 mV amplitude. These ECGs were obtained for each patient on days 1, 3, 5, 10, 15 (if possible), and 30 (if possible) after AMI (between 8 and 10 AM). Electrocardiograms of control subjects were also obtained during morning hours (between 8 and 10 AM). Electrocardiograms were magnified 100% with a photocopier. Two blinded observers measured QT interval from the onset of QRS to end of the T wave, defined as a return to T-P baseline. When U waves were present, the QT was measured to the nadir of the curve between the T and U waves. When the end of the T wave could not be identified, the lead was not included. A minimum of seven leads, at least three of them being precordial, were required for QTcD to be calculated. The QTc was calculated using Bazett's formula.[9] QTcD is defined as the difference between the maximal and the minimal QTc intervals occurring in any of the 12 leads.

Reproducibility

We performed a study on the variability of QTc measurements. Twenty-five ECGs were coded and

Table I. Demographic and clinical characteristics of patients and healthy controls.

Characteristic	Total Patients	Thrombolytic (+)	Thrombolytic (–)	Control
Number	136	**73**	63	65
Age (years)	57 ±10	56 ±10	58 ±9	56 ±7
Male/female	89/47	47/26	42/21	43/22
Beta-blocker (+)/(–)	57/79	31/42	26/37	–
Anterior MI	79	**44**	35	–
Inferior MI	57	**32**	25	–

duplicated and measured blindly by two observers. We found an intraobserver variability of 1% to 3% and interobserver variability of 3% to 4%.

Statistical Analysis

Categorical variables were compared by chi-square analysis. Continuous variables are presented as mean value ± standard deviation and compared by a two-tailed Student's t test, either paired or unpaired as appropriate. Comparison of QTcD between days 15, 30 and 1, 3, 5, 10 of infarction are applied the same number of patients when we used the paired Student's t test. A value of $p < 0.05$ was considered statistically significant. SPSS release 6.0 for MS Windows was used for statistical analysis.

Results

There were no significant differences among the three groups (Tr+, Tr–, and control) with regard to age and sex ($p > 0.05$). We also found no significant differences between the Tr+ and the Tr– groups when ECG MI localization and beta-blocker usage were compared ($p > 0.05$).

Measures of QTcD on days 1, 3, 5, 10, 15, and 30 of infarction are shown in Table II and Figure 1 for all patients and according to whether thrombolytic therapy was given (Tr+ group) or not (Tr– group). QTc dispersion in patients with AMI (for every period of QTcD after MI) was significantly more prolonged in patients than in normal controls (49.3 ±16.3 ms) ($p < 0.001$). QTcD was significantly greater in patients without thrombolytics (Tr–) than in patients with thrombolytics (Tr+) for every period (days 1, 3, 5, 10, 15, and 30) of QTcD after MI ($p < 0.001$). Maximal QTcD was seen on day 10 of myocardial infarction, and then reached a plateau for each group. Although in Tr– group, QTcD showed an increase continuously after the first day MI, we found no significant difference until the 10th day (Table III). However, in Tr+ group, QTcD showed a rapid increase and reached a statistical difference ($p = 0.048$) on the 3rd day (see Table III). QTcD of the MCA group also followed the same course (see Tables II, III, and Figure 1). The mean of QTcD was significantly greater in patients with MCA than in patients without MCA (Tr+ or –group) for every period (days 1, 3, 5, 10, 15, and 30) of QTcD after MI ($p < 0.05$).

Discussion

Risk stratification for arrhythmogenic events and sudden death in patients with coronary heart disease and a history of MI continues to be a major challenge for clinical cardiologists, although advanced management strategies including thrombolysis[10] and revascularization procedures[11] dramatically reduced the percentage of sudden deaths following AMI. Recent studies proposed that QTD may represent heterogeneity of ventricular repolarization, and therefore be a potential measure of substrates for re-entrant ventricular tachyarrhythmias.[3-5] Subsequently, the potential value of QTD for risk stratification was examined post-myocardial infarction.

In some studies, QTD was found to be useful in the identification of subjects developing major cardiac arrhythmias.[6-8] Our data were in accordance with these studies that reported an increased QTD in patients in whom MCA develops

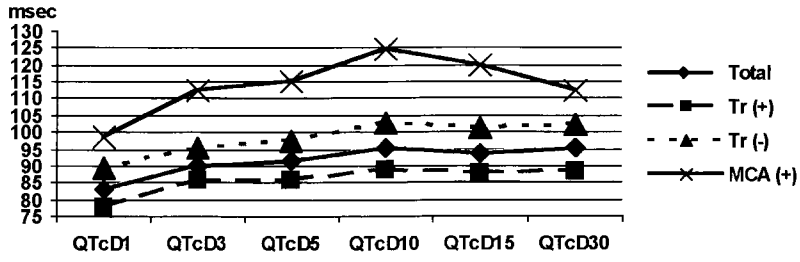

Figure 1. The sequential changes of the corrected QT dispersion (QTcD) 1 day to 30 days after a transmural acute myocardial infarction (AMI) for all patients, according to whether thrombolytic therapy was given (Tr+ group) or not (Tr– group), including the MCA group.

Table II. Measures of QTcD on days 1, 3, 5, 10, 15, and 30 of infarction for all MI patients according to whether thrombolytic therapy was given (Tr+ group) or not (Tr– group), and major arrhythmia group.

QTcD (day)	Total	Thrombolytic (+)	Thrombolytic (–)	Major arrhythmia
QTcD1	83.1 ±21.9 (n=136)	77.6 ±20.2* (n=73)	89.5 ±22.1 (n=63)	98.3 ±24.7† (n=14)
QTcD3	90.1 ±30.8 (n=136)	85.6 ±31.2* (n=73)	95.2 ±29.8 (n=63)	112.4 ±31.0† (n=14)
QTcD5	91.4 ±31.2 (n=136)	85.9 ±30.4* (n=73)	97.6 ±31.2 (n=63)	115.0 ±25.2† (n=14)
QTcD10	95.2 ±29.3 (n=136)	88.8 ±29.3* (n=73)	102.7 ±27.7 (n=62)	124.7 ±30.8† (n=13)
QTcD15	93.9 ±26.5 (n=77)	88.0 ±26.7* (n=42)	100.9 ±24.6 (n=35)	120.1 ±25.8† (n=12)
QTcD30	95.2 ±29.7 (n=61)	88.4 ±29.2* (n=33)	102.1 ±28.8 (n=27)	112.4 ±28.7† (n=10)

*Thrombolytic (+) vs thrombolytic (–): $p < 0.001$. †Major arrhythmia vs Thrombolytic (+), thrombolytic (–), and total: $p < 0.001$.

after MI ($p < 0.05$). On the other hand, the time of measurement of QTD is not clear for risk evaluation after AMI. To our knowledge, there is only one study that investigates this subject: Glancy and associates[12] investigated the time course of QT interval changes during days 1, 2, 3, and 6 after MI. They found QTcD on day 1 of AMI as 107 ±44.8 ms, and 141.8 ±44 ms, 162.3 ±63.8 ms, 117.4 ±67.4 ms on days 2, 3, and 6 of MI, respectively. These results are consistent with our observations in general. However, there are conflicting data: Glancy and co-workers suggested that at hospital discharge, QTcD had returned to beginning levels. Their study group consists of only 20 patients, and have no data after day 6 of MI. The day 6 value might be the result of the small number in the patient group. In the MCA group in our study, which contains a relatively small number of patients, we observed an evident QTD decrease when some patients were removed (because of death) from the data. In contrast to this report, our series involved a relatively large number of patients and compared the data according to whether they received thrombolytics or not.

Several investigators assessed the time course of QT interval after MI,[13,14] indicating the dynamic ventricular recovery changes after myocardial infarction.[14] Mechanisms of these effects are not clear. It has been shown that in animal experiments, action potential durations shorten promptly after coronary ligation. However, after 1 day, action potential durations and refractory period measurements are abnormally prolonged.[15,16] Such prolongation has been reported in human myocardium excised at the time of transplantation.[17] In a new report, Schneider and his co-workers[18] observed that QTD after myocardial infarction is determined by the extent of scarred tissue. It has been known that the majority of myocardial scar tissue formation occurs during first 2 weeks after MI.[19] Heterogeneity of electrophysiological changes associated with the dynamic events of ischemic and subsequent healing, with intermingling of fibrous and viable tissue, has been suggested as an explanation for the increase of QTD during 10 days after MI.

Thrombolytic therapy could play a role in the restoration of the electrophysiological stability of myocardial cells supplying reperfusion.[20,21] The group of patients receiving thrombolysis (Tr+) showed lesser QTD than patients not given thrombolytics (Tr–) ($p < 0.05$). Studies have indicated that successfully reperfused patients demonstrated a lower incidence of early and late mortality compared with conventionally treated patients.[10] Our data have demonstrated that QTcD shows a tendency to increase during the first 10 days after AMI. This increasing pattern shows early prominence ($p < 0.05$) in patients in the Tr+ group as compared to Tr– group after MI. In-hospital and long-term benefits of thrombolysis are closely re-

Table III. Comparison of QTcD on days 1, 3, 5, 10, 15, and 30 of infarction according to whether thrombolytic therapy was given (Tr+ group) or not (Tr– group), and major cardiac arrhythmia (MCA) group.

QTcD (day)	Total	Thrombolytic (+)	Thrombolytic (–)	MCA Group
QTcD1 vs QTcD3	0.018	0.048	NS	0.02
QTcD1 vs QTcD5	0.006	0.038	NS	0.011
QTcD1 vs QTcD10	<0.001	0.002	<0.001	0.014
QTcD1 vs QTcD15	<0.001	0.002	0.001	0.011
QTcD1 vs QTcD30	<0.001	0.013	0.001	NS
QTcD3 vs QTcD5	NS	NS	NS	NS
QTcD3 vs QTcD10	NS	NS	0.04	NS
QTcD3 vs QTcD15	NS	NS	NS	0.04
QTcD3 vs QTcD30	NS	NS	NS	NS
QTcD5 vs QTcD10	NS	NS	NS	NS
QTcD5 vs QTcD15	NS	NS	NS	NS
QTcD5 vs QTcD30	NS	NS	NS	NS
QTcD10 vs QTcD15	NS	NS	NS	NS
QTcD10 vs QTcD30	NS	NS	NS	NS
QTcD15 vs QTcD30	NS	NS	NS	NS

lated to early reestablishment and maintenance of coronary blood flow.[22] In the first few days, coronary blood flow has dramatically decreased after thrombolysis because of rethrombotic process at the occlusion area.[23,24] Probably, subsequent new ischemic tissue may augment the repolarization heterogeneity. Rapid increases in QTD of Tr+ group patients might be explained by this event. The time course of changes of QTD in our patients with MCA also resembled that of other groups.

The time of QT interval and QTD measurements are another important point of this subject. QT interval and QTD may show circadian variations also in day-time period.[25,26]

Conclusion

Further confirmation of our finding that the QTD increases in the first days after MI in larger numbers of patients may have important clinical implications. First, this study seems to demonstrate changes in QT dispersion in the first month after a AMI; maximal QTcD was seen on day 10 of myocardial infarction, and then reached a plateau for each group after AMI. Therefore QTD measurement must be done 10 days after AMI for risk stratification. Second, comparison of studies of QTD after MI must take into consideration the time of the ECGs recorded.

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