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Reduced QT dispersion after early thrombolysis – protection of ventricular electrical stability

I. Lőrincz, C. Kun¹, Z. Karányi, F. Wórum

Temporary QT prolongation during acute myocardial infarction predicts ventricular tachyarrhythmias. New data suggest that in acute myocardial infarction and in the pathogenesis of other ventricular arrhythmias the QT dispersion demonstrates ventricular inhomogeneity and ventricular instability better than QT prolongation. The aim of this study was to assess the effect of intravenous streptokinase on the QT, JT dispersions and their corrected values during therapy of acute myocardial infarction.

Twenty patients, 10 patients with acute myocardial infarction treated with streptokinase (Group A), 10 acute myocardial infarction patients without streptokinase (Group B) and 10 healthy volunteers (Group C) were studied. Simultaneous 12 lead ECGs were recorded at the time of admission to hospital (day 1) in patients with acute myocardial infarction and prior to discharge (day 8 ± 2) in a standard setting. The QT intervals for each lead were measured manually on the enlarged ECGs (by a factor 3) using calipers by the same observer. Each QT interval was corrected for patient's heart rate: $QT_c = QT/\sqrt{RR}$ (msec). There were significantly greater mean QT, QT_c , JT, JTc dispersions in Groups A and B in the early hours of infarction compared to Group C ($p < 0.05$). Patients with anterior myocardial infarction showed significantly greater QT, QT_c and JT, JTc dispersions when compared to inferior myocardial infarction patients ($p < 0.02$). There were significantly greater reductions in QT, QT_c , JT, JTc dispersions at day 8 ± 2 after streptokinase therapy compared to patients who were not treated with streptokinase ($p < 0.05$).

Successful fibrinolytic therapy results in reduction in QT and JT dispersions. This can be taken into consideration in the risk stratification for malignant ventricular tachyarrhythmias and it is another evidence of the benefit of thrombolytic therapy in patients with acute myocardial infarction. *J Clin Basic Cardiol 1999; 2: 85–8.*

Key words: electrocardiography, myocardial infarction, reperfusion, thrombolysis

In patients with acute myocardial infarction (AMI) ventricular tachyarrhythmias can cause serious clinical symptoms and can induce sudden cardiac death. They may result from different myocardial abnormalities or may be a side effect of drug treatment or metabolic abnormalities [1]. Experimental data have demonstrated a strong link between the vulnerability of the ventricular myocardium to serious tachyarrhythmias and increased temporal dispersion of refractoriness [2].

From the beginning of this century the electrocardiogram (ECG) has been used in the diagnosis of different cardiac structural and functional abnormalities, and in the identification and prediction of different serious and potentially fatal brady- and tachyarrhythmias. Experimental and clinical studies have recently indicated that interlead variability of the QT interval in surface 12 lead ECG (ie, the QT dispersion defined as the difference between maximal and minimal QT interval duration) reflects regional differences in ventricular recovery time [3]. This QT dispersion has been linked to the occurrence of arrhythmias in patients with congenital long QT syndromes, postinfarction patients, drug-induced tachycardias and sudden death in patients with chronic congestive heart failure, [4–7]. The homogeneity of recovering time protects against arrhythmias, whereas dispersion of recovering time is arrhythmogenic [2, 8].

Thrombolytic therapy has become the basic treatment of acute myocardial infarction. It is well known that thrombolytic agents improve survival and preserve myocardial function [9]. In cases of successfully reperfused heart, lower incidences of early and late mortalities have been demonstrated as compared with conventionally treated patients [10]. In parallel with the improvement in myocardial mechanical function the electrical stability also developed better [10].

Although QT prolongation could appear in the acute phase of myocardial infarction [1], and it is known that temporary QT prolongation during AMI predicts ventricular tachyarrhythmias. New data suggest that in AMI the QT dispersion demonstrates ventricular instability better than QT prolongation [11, 12].

The purpose of our investigation was to compare QT, JT dispersions in the early hours of AMI in healthy volunteers and to determine QT, JT dispersions in patients with anterior and inferior AMI to assess the effect of intravenous streptokinase on the QT, JT dispersions and to compare them to those of AMI patients without streptokinase treatment on admission and before discharge [13].

Patients and controls

The data of three groups were analysed: Two groups of ten patients each with AMI in the Coronary Care Unit of the 1st Department of Medicine, University Medical School of Debrecen, and ten normal healthy volunteers were studied. Ten patients with AMI presented with ST-segment elevation associated with typical ischaemic symptoms and received streptokinase therapy within 4 hours of symptom onset (Group A). Standard exclusion criteria included >4 hours duration of chest pain, hypotension, or uncorrected hypertension, history of bleeding diathesis, recent surgery or trauma, any previous cerebrovascular accident or prior coronary bypass surgery. Ten patients were not treated with streptokinase (Group B). Both groups were on standard cardiac care including serial ECGs, serial creatinine phosphokinase measurements and use of intravenous nitroglycerine, heparin, lidocaine, beta-blockers and inotropic support where appropriate. The con-

control group comprised 10 healthy volunteers (Group C). (Table 1). The exclusion criteria for our study were (1) unmeasurable T waves, (2) atrial fibrillation, (3) bundle branch block, (4) antiarrhythmic drugs which affect the QT interval, (5) serum potassium level below 3.9 mmol/l or above 5.0 mmol/l.

Methods

In patients with AMI (Groups A and B) simultaneous 12 lead ECGs were recorded for assessment of QT and JT dispersion by means of a 12 channel ECG recorder (Hewlett Packard) at a paper speed of 25 mm/s, within 24 hours of hospital admission and before discharge. All ECGs were examined by one observer who was unaware of the patients' drug and coronary status. In the healthy control group (Group C) ECG was obtained after a 5-minute resting period, with the patients lying comfortably in the supine position. For analysis of the QT and JT intervals, the 12 lead ECGs were enlarged on the same photostat by a factor of three. The RR, QT and JT intervals for each lead were measured by one observer manually with calipers. The QT interval was measured from the first deflection of the QRS complex to the point of the T wave offset, defined by the return of the terminal T wave to the isoelectric TP baseline. In the presence of U wave interrupting T wave, the terminal portion of the visible T wave was extrapolated to the TP baseline in order to define the point of T wave offset. If the end of the T wave could not be reliably determined, the lead was not included in the analysis. JT in-

Table 1. Clinical data of different subjects

	Group A	Group B	Group C
Number of subjects	10	10	10
Average age (years)	61±12	63±11	61±14
Range (years)	39-73	44-79	42-74
Male/Female	6/4	5/5	4/6
Heart rate	90±17	79±14	77±13
Measurable leads	6-12	6-12	7-12

tervals were measured from J point to the end of the T wave (Figure 1 and Figure 2). Each QT and JT interval was corrected for patient's heart rate using Bazett's formula: $QTc = QT/\sqrt{RR}$ (msec), where QTc is the corrected QT interval. QT, QTc and JT, JTc dispersions were defined as the differences between the minimal and maximal QT or QTc, and JT and JTc values in each of the 12 leads studied [1, 3, 6].

Statistical analysis

Data were expressed as mean ± SD. Differences in group means were analysed using the 2-tailed unpaired T-test or χ -square test. A p-value < 0.05 was considered significant.

Results

The QT and QTc maximal interval, the QT and QTc dispersion (mean values and their standard deviations), the JT and

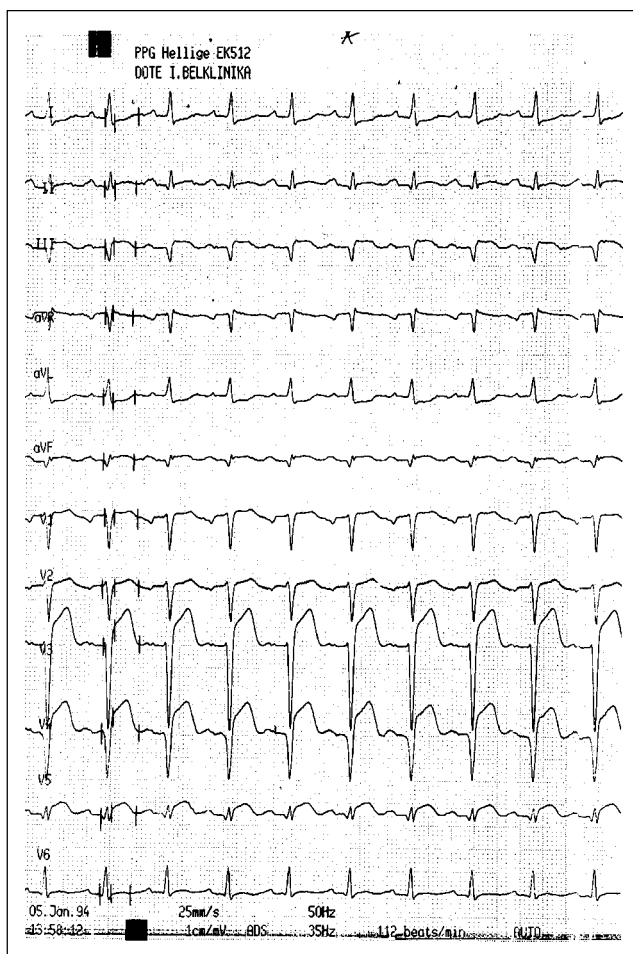


Figure 1. The illustrative example of the typical measurement of JT and QT intervals I, II, III, aVR, aVL, aVF and V1-5 ECG leads

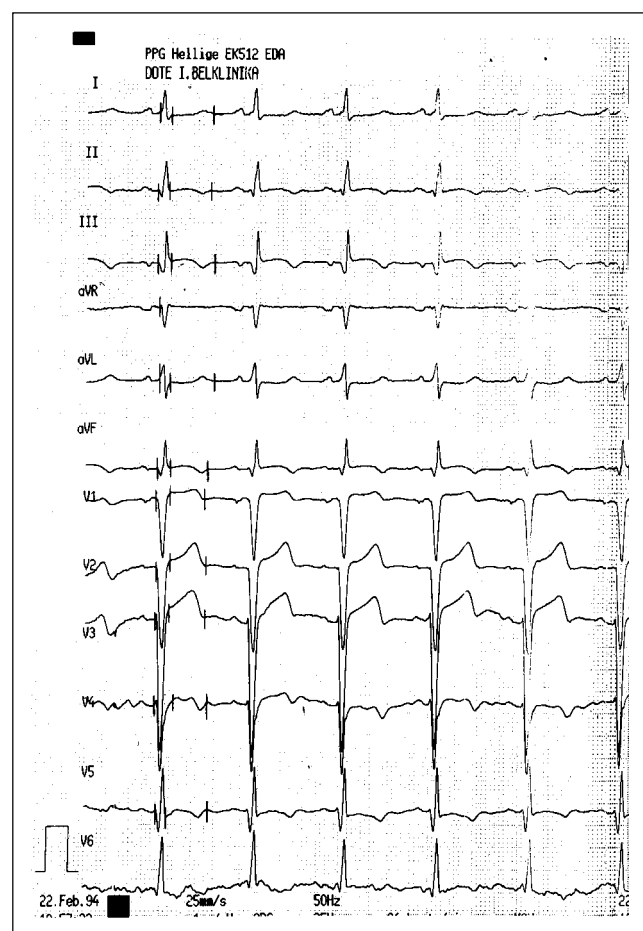


Figure 2. The illustrative example of the typical measurement of JT and QT intervals. It shows the inability to measure the end of T wave in leads aVR and V6. I, II, III, aVR, aVL, aVF and V1-5 ECG leads

Table 2. Findings of measured QT, JT dispersions in AMI patients with and without SK treatment

	Group A admission mean \pm SD	Group A after SK 8 \pm 2 days mean \pm SD	Group B admission mean \pm SD	Group B after 8 \pm 2 days mean \pm SD	Group C mean \pm SD
QT dispersion (ms)	88 \pm 11	59 \pm 9	85 \pm 11	80 \pm 11	39 \pm 7
QTc dispersion (ms)	99 \pm 14	68 \pm 9	96 \pm 16*	88 \pm 14*	42 \pm 8
JT dispersion (ms)	71 \pm 9	49 \pm 8	67 \pm 13	63 \pm 12	42 \pm 5
JTc dispersion (ms)	86 \pm 10	56 \pm 12	76 \pm 13	69 \pm 13	46 \pm 5

p < 0.01, except p < 0.05*

JTc maximal interval, and the JT and JTc dispersions of the three groups are shown in Table 2. There were significantly greater mean QT, QTc, JT, JTc dispersions in both Groups A and B in the early hours of infarction compared to Group C (p < 0.03).

Patients with anterior AMI showed significantly greater QT, QTc (88 \pm 9, 105 \pm 11 versus 73 \pm 6, 83 \pm 8) and JT, JTc (73 \pm 9, 86 \pm 9 versus 62 \pm 10, 70 \pm 9) dispersions compared to postero-inferior AMI patients (p < 0.02) as shown in Table 3.

There were significantly greater reductions in QT, QTc, JT, JTc dispersions at day 8 (SD \pm 2) after SK therapy compared to patients who were not treated with SK (p < 0.05). Successful SK therapy resulted in reduction of QT and JT dispersions (Table 2).

Discussion

QT and QTc dispersion reduction during treatment of the acute phase of myocardial infarction showed the effectiveness of thrombolytic therapy, which was determined before the discharge from hospital after 8 \pm 2 days from onset of AMI signs. This kind of decrease in QT dispersion and improvement of cardiac repolarization homogeneity could not be demonstrated by Glancy and coworkers [14]. In the acute phase of myocardial infarction the degree of QT and QTc dispersion depends on the localization of myocardial damage. In patients with anterior AMI larger QT and QTc dispersions than in patients with inferior AMI could be verified. These results were found by other authors, too [10, 15]. The effect of thrombolysis on QT/QTc and JT/JTc dispersion was not evaluated in subgroups of anterior and inferior AMI because of the limited number of patients.

Exact spatial dispersion of ventricular myocardium recovery can be determined by invasive methods such as measurement of monophasic action potentials of the left and right ventricle, and it can also be measured by noninvasive methods such as surface mapping. Both methods are time consuming and require special technical devices, which limit their use in everyday clinical practice. The QT interval as recorded on the cheap, simple surface ECG represents the sum of unconcealed potential differences during ventricular depolarization and repolarization. Previous clinical studies of QT dispersions have shown to be increased in patients after acute myocardial infarction and showed differences between anterior and posterior localization of infarction [6, 10–12, 16].

The cellular basis of QT dispersion is still not fully established, but QT variations in surface electrocardiography in humans have been correlated with epicardial monophasic action potential durations [17]. In acute ischaemia and infarction, multiple ionic and metabolic changes result in marked electrophysiological inhomogeneity at the cellular level, in which post-repolarization refractoriness and cellular uncoupling are involved in conduction disturbances [18]. Twenty-

Table 3. Findings of measured QT, JT dispersions in anterior and postero-inferior AMI

	anterior mean \pm SD n = 12	postero-inferior mean \pm SD n = 8	p-value
QT dispersion (ms)	88 \pm 09	73 \pm 06	0.001
QTc dispersion (ms)	105 \pm 11	83 \pm 08	0.001
JT dispersion (ms)	73 \pm 09	62 \pm 10	0.020
JTc dispersion (ms)	86 \pm 09	70 \pm 09	0.001

four to 72 hours after coronary occlusion, action potential abnormalities, and abnormal impulse generation in surviving cell layers in the border zone of the infarct and in the infarcted area itself contribute mainly to arrhythmias. In healed infarcted myocardium, changes in intercellular impulse propagation as well as non-uniform anisotropic cardiac tissue play a major role in the maintenance of arrhythmias. A major factor leading to the genesis of ventricular arrhythmias during ischaemia is the non-uniformity of the electrical refractory period, which allows excitation to become fragmental during the initiating beat. Ischaemia alters refractoriness through its effects on resting potential and action potential duration. These effects are non-uniform during regional ischaemia because of local variations in blood flow and diffusion of substrate and metabolites across the ischaemic boundary. The instability of the repolarization process may manifest itself as variability in duration and/or depolarizations that interrupt action potential repolarization, and early afterdepolarizations that can initiate triggered arrhythmias including torsade de pointes ventricular tachycardia. An important additional mechanism for creating dispersion of the refractory period is alteration of the action potential duration from beat to beat. Electrical alternans lead to ischaemia-induced ventricular arrhythmias. Alteration in action potential duration is associated with spatial and temporal non-uniformities of the intracellular Ca transient. Abnormalities in the regulation of cytosolic Ca by the ischaemic myocardium may be a principal cause of the dispersion of refractoriness that leads to ventricular fibrillation in acute ischaemia. The ischaemic damage may cause local extracellular hypocalcaemia, resulting in QT interval prolongation [19]. In experimental models of ischaemic damage followed by reperfusion, damaged myocardial cells take up large amounts of calcium, which results in subsequent local extracellular hypocalcaemia [20].

Ventricular arrhythmias are frequently seen in patients with ventricular dysfunction, such as volume or pressure overload, or dyssynergistic ventricular contraction and relaxation. One mechanism suggested to cause arrhythmias under these conditions is mechano-electrical feedback, also known as contraction-excitation feedback. In patients with acute myocardial ischaemia and/or infarction mechanical stretch may cause shortening of the action potential duration and may decrease

in diastolic membrane potential. In some studies, stretch was also shown to cause afterdepolarizations, which in turn were associated with arrhythmias [21, 22].

Autonomic neural mechanisms play a significant role in the regulation of ventricular repolarization and this process may itself increase or decrease dispersion of refractoriness. Heterogeneity of sympathetic innervation is well described in cardiomyopathy patients and has been correlated with the heterogeneity of recovery of excitability [17]. Imbalances in the sympathetic innervation of the heart in acute myocardial infarction or increased tissue sensitivity to catecholamines can result in lower thresholds for ventricular fibrillation [23, 24].

Conclusions of present investigation

- 1) There were significantly greater mean QT, QTc, JT, JTc dispersions in the early hours of AMI.
- 2) Patients with anterior AMI showed significantly greater QT, QTc, JT, JTc dispersions compared to those with inferior localization of AMI.
- 3) There were significantly greater reductions in QT, QTc, JT, JTc dispersions after treatment with SK than without it.
- 4) QT and JT dispersions are greatest in the early hours of AMI and fall with time and successful thrombolysis.
- 5) These results can be taken into consideration in the risk stratification for malignant ventricular tachyarrhythmias and they are another evidence for the benefit of thrombolytic therapy in patients with acute myocardial infarction.

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