Transient QT Interval Prolongation With Inverted T Waves Indicates Myocardial Salvage on Dual Radionuclide Single-Photon Emission Computed Tomography in Acute Anterior Myocardial Infarction

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In patients with acute myocardial infarction (AMI), transient QT interval prolongation with a prominent negative T wave is frequently observed in cases of early spontaneous reperfusion and often indicates a good prognosis. Additionally, in nuclear cardiac imaging, technetium-99m/thallium-201 overlap on dual single-photon emission computed tomography (dual SPECT) in AMI patients indicates the presence of viable myocardium and early recanalization. To elucidate the clinical significance of this transient QT interval prolongation, 34 patients (64±8 years) admitted within 24 h of the onset of anterior AMI were enrolled and classified into 2 groups according to the presence (group A, n=24) or absence (group B, n=10) of scintigraphic overlap on simultaneous dual SPECT imaging. The maximal QTc interval was 0.59±0.06 s in group A and 0.52±0.06 s in group B (p<0.01). The peak creatine kinase was lower in group A (2650±2160 IU/L) than in group B (3490±2060 IU/L). The left ventricular ejection fraction (LVEF) at discharge was 62±11% in group A and 49±14% in group B (p<0.01). The scintigraphic overlap group had a smaller infarct and better LVEF, which suggests that the QT interval prolongation that appears transiently in the acute phase of AMI indicates scintigraphically the presence of salvaged myocardium. (*Jpn Circ J* 2001; 65: 7–10)

Key Words: Acute myocardial infarction; Dual SPECT (dual single-photon emission computed tomography); Scintigraphic overlap; Transient QT interval prolongation

In patients with acute myocardial infarction (AMI), QT interval prolongation is commonly seen when standard 12-lead ECG are serially recorded^{1–3} and is characteristically transient (36–48 h after the onset of AMI) and associated with a prominent negative T wave.⁴ QT prolongation has been considered a poor prognostic sign leading to ventricular tachycardia or sudden cardiac death,^{5,6} but it is frequently observed in cases of early spontaneous reperfusion and often indicates a good prognosis.⁴ Nuclear imaging in the early post-infarction period is useful in estimating the extent of myocardial salvage,^{7,9,14} but there are few previous reports on the relation between this transient ECG change and the scintigraphy findings during the acute phase of AMI.⁸ The present study aimed to elucidate the clinical significance of transient QT interval prolongation with a prominent negative T wave, using scintigraphic technetium-99m (^{99m}Tc) pyrophosphate/thallium-201 (²⁰¹Tl) chloride dual single-photon emission computed tomography (dual SPECT).⁹

Methods

Patient Selection

Of 154 consecutive survivors of AMI evaluated during a

30-month period, 34 patients who had been admitted within 24 h of onset of first anterior AMI, had maintained sinus rhythm without bundle branch block and who had undergone dual SPECT, were enrolled in this study. The diagnosis of AMI was based on typical chest pain lasting more than 30 min with ST-segment elevation of >0.2 mV in at least 2 continuous precordial leads on ECG and an increase in serum creatine kinase to at least twice the upper level of normal. Patients with severe congestive heart failure and those who had been given catecholamines were excluded. There were 25 men and 9 women, with a mean age of 64±8 years (range, 49–81). Of these 34 patients, 30 underwent coronary angiography: 21 had single-vessel coronary artery disease (CAD), 3 had double-vessel CAD and 6 had triple-vessel CAD. The patients were classified into 2 groups according to the presence (group A, n=24) or absence (group B, n=10) of scintigraphic overlap on simultaneous dual SPECT imaging, on the basis that previous reports have suggested that the overlap phenomenon indicates the presence of viable myocardium.^{4,14,15}

ECG Recording

Standard 12-lead ECGs were serially recorded every 6 h after admission for 2 days, every 12 h for the next 2 days, every 24 h for the following 3 days, 2 weeks later and just before discharge. The QT and RR interval were measured in 3 consecutive beats; the QTc was obtained from the Bazett's formula: $QTc = QT / \sqrt{RR}$.^{10,11} The QT interval was measured in each lead from the onset of QRS to the end of the T wave on the isoelectric baseline. The end of the T wave was defined as return to the isoelectric baseline. When the U

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Table 1 Patient Characteristics

Overlap	Group A (+) (n=24)	Group B (-) (n=10)	p value
Age (years)	65.3±8.3	59.2±6.6	<0.05
(age >70 years)	7	0	
M/F	17/7	8/2	NS
pCK (IU)	2,650±2,160	3,490±2,060	NS
pCKt (h)	13.1±4.9	15.8±6.9	NS
No. of diseased vessels	1.4±0.7	1.9±0.9	NS
Patency of culprit lesion (%)	80.0 (16/20)	66.7 (6/9)	NS

pCK, value of peak CK; pCKt, time to peak CK.

Table 2 QT Interval and LV Function

Overlap	Group A (+) (n=24)	Group B (-) (n=10)	p value
mQTc (s)	0.59±0.06	0.52±0.06	<0.01
LVEF (%)	62.1±10.5	49.3±13.5	<0.01
pCK <3,000 IU (%)	73.9 (17/23)	30.0 (3/10)	<0.02

mQTc, maximal QTc; LVEF, left ventricular ejection fraction; pCK, value of peak CK.

wave followed the T wave immediately, QT interval was measured to the nadir of the curve between the T and U waves. Biphasic T waves were measured to the time of final return to baseline. The measurement was made in the lead with the longest QTc interval (usually V₃, V₄).¹² The maximal QTc (mQTc) and the time to maximal QTc (mQTt) were decided from these serial QTc measurements.

Biochemical Analysis

Blood samples were obtained every 4 h from admission until serum creatine kinase (CK) activity returned to normal levels. The value of peak CK (pCK) and the time to peak CK (pCKt) were determined on the basis of analysis of the serial changes in serum CK activity.¹³

Cardiac Catheterization

Four weeks after the onset, left ventriculography was performed in the 30-degree right anterior oblique projection at 25 frames/s after injecting 25 ml of non-ionic contrast medium at a rate of 6 ml/s. The left ventricular ejection fraction (LVEF) was calculated by the area-length method. Coronary angiograms were obtained on admission and/or at discharge using the Judkins technique or the trans-brachial/radial approach.

Scintigraphic Evaluation

Simultaneous dual SPECT imaging was performed 3–5 days after the onset of AMI using the method of Hashimoto et al;¹⁴ 25% and 40% background subtractions were used for ²⁰¹Tl chloride and ^{99m}Tc pyrophosphate cardiac images, respectively. Color tomograms were described in identical slices and regions on the green image for ²⁰¹Tl chloride, indicating viable myocardium, and on the red image for ^{99m}Tc pyrophosphate, indicating necrotic tissue. The overlap, reflecting the presence of salvaged myocardium, was defined as more than one-quarter of the cardiac silhouette in at least 2 contiguous slices. Scintigraphic overlap was judged from identical slices of SPECT by visual inspection. The presence or absence of the scintigraphic overlap was determined by 2 independent investigators and resolved by consensus. There was neither subtle analysis nor inter- or intraobserver variability in the judgement of overlap.

Statistics

Data are presented as mean values ± SD. For statistical analysis, unpaired Student's t-test was used for comparison of continuous variables between group A and B, and repeated measures analysis of variance (ANOVA) was used for comparison of serial changes of QTc intervals. Multiple comparison within QTc intervals was tested with Bonferroni correction. Differences between categorical variables were examined by chi-squared test. Differences were considered statistically significant at the p<0.05 level.

Results

Patient Characteristics (Table 1)

There were no significant differences between the 2 groups in gender, number of diseased vessels or the patency of culprit lesions.

Biochemical Analysis (Table 1)

The pCK was lower in group A (2,650±2,160 IU/L) than in group B (3,490±2,060 IU/L), but the difference between the 2 groups was not statistically significant.

However, there were 17/23 (74%) patients with small-sized infarcts whose pCK levels were less than 3,000 IU in group A and 3/10 (30%) in group B (p<0.02) (Table 2). The pCKt was shorter in group A (13±5 h) than in group B (16±7 h), although no differences were observed between the groups.

Standard 12-Lead ECG

A typical ECG with a prolonged QT interval and a prominent negative T wave is shown in Fig 1, and the serial changes in the QTc intervals are shown in Fig 2. In all the patients, T wave inversion was associated with QT interval prolongation. Prolongation of the QTc interval peaked 36 h after the onset of AMI (0.54±0.07) and returned to a normal value 4 weeks later (0.46±0.04). This QTc interval prolongation appeared transiently (p<0.01 by repeated measures ANOVA with Bonferroni correction). The mQTc intervals were longer in patients with scintigraphic overlap (Fig 3).

Fig 1. Typical ECG with a prolonged QT interval and a prominent negative T wave in V4 lead. The peak QTc interval is 0.61 s at 36h after the onset of acute myocardial infarction (AMI).

Fig2. Serial changes in the QTc intervals. Prolongation of the QTc interval peaked 36h after the onset of acute myocardial infarction (AMI) and returned to a normal value 4 weeks later ($p<0.01$ by repeated measures ANOVA with Bonferroni correction). Data are presented as mean $\pm$ SD.

QT Intervals and Left Ventricular (LV) Function (Table 2)

The mQTc interval was 0.59 ± 0.06 s in group A and 0.52 ± 0.06 s in group B. The patients in group A showed significantly prolonged mQTc intervals compared with those in group B ($p<0.01$). Differences in the QTc intervals between the 2 groups disappeared 4 weeks after the onset of AMI. The LVEF was $62\pm11\%$ in group A and $49\pm14\%$ in group B, significantly better in the former ($p<0.01$).

Discussion

Several studies support that the scintigraphic overlap phenomenon in AMI patients indicates the presence of viable myocardium.^{4,14,15} $^{99m}\text{Tc}/^{201}\text{Tl}$ overlap on dual SPECT can be used as an index for documenting early recanalization and may reflect the presence of salvaged myocardium adjacent to necrotic tissue. Hashimoto et al reported that the patients with scintigraphic overlap have a shorter interval between onset of AMI and reflow, compared with the patients without overlap (2.5 ± 0.8 vs 4.8 ± 1.3 h, $p<0.001$).¹⁴ Our data showed that the pCKt was shorter in group A than in group B, although no significant differences were observed between the groups (13 ± 5 vs 16 ± 7 h, $p=0.216$). Areas with overlapping of dual SPECT may contain jeopardized myocardium.¹⁵ $^{99m}\text{Tc}/^{201}\text{Tl}$ overlap in the delayed image early after AMI can be used as an index for predicting

Fig3. A maximal QTc (mQTc) scattergram is shown. The mQTc interval was 0.59 ± 0.06 s in group A (scintigraphic overlap(+) group) and 0.52 ± 0.06 s in group B (overlap(-) group). The patients in group A had significantly prolonged mQTc intervals compared with those in group B ($p<0.01$). Data are presented as mean $\pm$ SD.

successful early recanalization and probably viable myocardium.⁹ On ECG, T wave inversion in the left precordial leads and prominent negative T wave with QT prolongation in V3 or V4 reaching their peak values within 1–5 days after successful reperfusion in patients with acute coronary syndrome, may indicate reperfusion injury and the presence of myocardial stunning in the anterior wall of the left ventricle. Hirota et al reported that serial echocardiograms showed normalization of wall motion within 4 to 28 days after the onset of acute coronary syndrome.⁴ The present study demonstrated that the transient QT interval prolongation and the scintigraphic overlap on the dual SPECT imaging were closely related in patients experiencing their first anterior AMI, and also showed that the scintigraphic overlap group had a smaller infarct and better LVEF. These findings suggest that QT interval prolongation, appearing transiently in the acute phase of AMI, is associated with myocardial salvage, which is also observed on scintigraphy.

On the other hand, a consistently prolonged QT interval may indicate an increase in arrhythmias and lowering of the ventricular fibrillation threshold. Among patients with previous myocardial infarction a prolonged QTc interval indicates a 2-fold greater risk of sudden cardiac death.⁵ Multivariate analysis of risk factors reveals that the QTc interval at discharge is of significant independent value for predicting major cardiac events after discharge from the

hospital⁶ In general, delayed ventricular repolarization produces QT prolongation and may increase the vulnerable period. Such responses enhance susceptibility to ventricular arrhythmias.¹⁶ However, a transient QT prolongation with prominent negative T waves is clinically different from the consistent QT prolongation observed with arrhythmogenic substrate, because this arrhythmogenic QT prolongation is consistent, not transient.

There are numerous reported causes and mechanisms for QTc lengthening: congenital, neurogenic, hypothermia, hypocalcemia, myocardial ischemia, antiarrhythmic drugs, anaphylactic reactions, post-resuscitation, catecholamines, severe bradycardia, atrioventricular block, and unknown causes.^{8,17–22} An ECG pattern closely resembling the QTc prolongation in AMI occurs in patients with intracranial hemorrhage⁸ and in patients with pheochromocytoma. The QTc prolongation in these patients is characterized by its acquired QTc interval lengthening, transient appearance and association with prominent T waves inversion.²³ Several studies have shown that QT prolongation with deeply inverted T waves can be produced by various manipulations of autonomic innervation to the heart in animal models.^{20,21,24} However, the exact mechanism of this peculiar ECG change in AMI patients is still uncertain.

Lead selection for the measurement of the QT interval is important. Measurements of the QT interval in precordial unipolar leads are more precise than in bipolar limb leads, because more subtle and much smaller changes of the QT interval and T wave inversion are canceled and masked in bipolar leads.¹² For these reasons, patients with inferior AMI were excluded from this study.

Patency of the culprit coronary lesion did not relate to scintigraphic overlap in this study. Of the 29 patients undergoing emergency coronary angiography, recanalization of the culprit lesion failed in 7 and 5 of these had rich collaterals. In total, 27/29 (93.1%) of patients undergoing emergency coronary angiography reestablished coronary flow to the jeopardized myocardium; therefore, coronary patency of the lesions did not affect statistically the presence of scintigraphic overlap.

Study Limitations

The study subjects were consecutively entered into the study, but because of the importance of lead selection for QT interval measurement and the acute phase scintigraphic study only 22% (34/154) were enrolled. Thus the subgroup subjected to the various analyses became very small. As the judgement of scintigraphic overlap was not quantitative, the presence of the overlap as assessed on the identical slices in the dual SPECT was obvious and did not require a more detailed analysis.

Although there was a significant difference in age between the groups, it was accidental that all the 7 patients older than 70 years old belonged to group A, and that this group of patients were older than the patients in group B. There was no evidence that age was an independent factor for scintigraphic overlap.

Conclusions

The present study demonstrated that transient QT interval prolongation and scintigraphic overlap on the dual (^{99m}Tc pyrophosphate/²⁰¹Tl chloride) SPECT imaging are closely related in patients experiencing their first anterior AMI, and

also showed that the scintigraphic overlap group had a smaller infarct and better LVEF. These findings suggest that QT interval prolongation, which appears transiently on ECG in the acute phase of AMI, indicates the presence of salvaged myocardium observable on scintigraphy.

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