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Early QTc Interval Prolongation After Primary Percutaneous Coronary Intervention May Have a Positive Impact

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Abstract

Objectives: Corrected QT (QTc) interval is prolonged in acute myocardial infarction and begins to shorten after successful reperfusion. Data on the early change of QTc after reperfusion and the prognostic significance of this change are limited. We aimed to evaluate the change of QTc interval in the first hour following successful primary percutaneous coronary intervention (pPCI) in ST-elevation myocardial infarction (STEMI) patients and its relationship with reperfusion parameters such as myocardial blush grade (MBG) and ST-segment resolution (STR%).

Materials and Methods: Patients who presented with the first STEMI episode and underwent successful pPCI were included in the study. After pPCI, MBG and STR% were calculated. QTc measurements were made from the electrocardiography (ECG) recorded at admission (Pre-pPCI QTc), 1 hour after pPCI (Post-pPCI QTc), and the 24th hour.

Results: One hundred and five patients who had successful pPCI with adequate ECG data were enrolled in the study. The mean Pre-pPCI QTc was 409±34 ms, and the mean post-pPCI QTc was 427±32 ms. A statistically significant prolongation was observed in the QTc interval after pPCI (QTc-Change) [21 ms (-3, 37 interquartile range (IQR)), p<0.001]. The median STR was 71% (60-83 IQR), and the median MBG was 2 (1-3 IQR). In the multivariable linear regression analysis, a significant relationship was observed between QTc-Change with MBG and STR% [β=9.077, 95% confidence interval (CI): 2.55-15.60, p=0.006 and β=9.315, 95% CI: 2.00-16.62, p=0.013, respectively].

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Conclusion: It was found that the QTc interval continued to prolong somewhat in the early period after successful pPCI in STEMI patients, and this QTc-Change was significantly associated with reperfusion parameters such as MBG and STR%. STR% and MBG were higher in those with higher QTc-Change.

Keywords: ST-segment elevation myocardial infarction, QTc interval, myocardial blush grade, ST-segment resolution

Introduction

The QT interval on the surface electrocardiogram (ECG) represents the time from the onset of ventricular depolarization to the completion of repolarization. Previous studies have shown that prolonged corrected QT (QTc) is associated with high arrhythmic event rates, sudden death, and all-cause mortality in the normal population and patients with acute myocardial infarction (AMI)[1-5].

Acute myocardial ischemia has been shown to increase repolarization heterogeneity and prolong the QT interval[5,6]. Studies have shown that the QTc interval is prolonged in AMI and begins to shorten after successful reperfusion[7-9]. However, data on the change of the QTc interval in the early period after revascularization and the prognostic significance of this change are limited. In a study by Bonnemeier et al.[7], it was found that in patients with AMI, the OTc interval initially became prolonged in the first hour following successful primary percutaneous coronary intervention (pPCI) but it was then followed by OTc interval shortening.

ST-segment resolution (STR%) and myocardial blush grade (MBG) are among the early reperfusion parameters that have shown prognostic significance in ST-elevation myocardial infarction (STEMI) patients[10-13]. Our study aimed to evaluate the change of QTc interval during the following hour after successful pPCI in STEMI patients and its relationship to reperfusion parameters such as MBG and STR%.

Materials and Methods

A total of 150 consecutive patients admitted with STEMI were evaluated. The patients enrolled were initially selected from those with clinical history and symptoms suggestive of the first episode of acute STEMI, who had presented within 12 hours after the onset of symptoms. According to current guidelines, the diagnosis STEMI required: Chest pain lasting >20 min and ST-elevation (STE) of >1 mm in at last two contiguous ECG leads without left ventricular hypertrophy and left bundle branch block[14]. Only patients who underwent successful pPCI with thrombolysis in myocardial infarction (TIMI) flow grade 3 were included. After exclusion criteria were applied, 105 patients were enrolled in the study.

Patients excluded from the study were those with non-sinus rhythm, bundle branch block, pacemaker rhythm, prior AMI or coronary bypass grafting, coronary occlusions unsuitable for PCI, TIMI flow grade <3, and challenge to determine the end of T-waves.

Angiographic Examination and Definition

Coronary angiography, pPCI, and periprocedural care conformed to the current guidelines[14]. The culprit lesion was crossed with wire within the first 60 minutes of hospital admission in all the cases. After successful revascularization (TIMI-3 flow), MBG was calculated. TIMI flow grade has been defined as follows: TIMI 0 refers to the absence of any antegrade flow beyond a coronary occlusion; TIMI 1 flow is faint antegrade coronary flow beyond the occlusion, although filling of the distal coronary bed is incomplete; TIMI 2 flow is delayed or sluggish antegrade flow with complete filling of the distal territory; TIMI 3 flow is normal flow, which fills the distal coronary bed completely[15]. MBG is an angiographic measure of myocardial perfusion. MBG has been defined as follows: 0, no myocardial blush (MB) or

contrast density (CD); 1, minimal MB or CD; 2, moderate MB or CD but less than that obtained during angiography of a non-infarct related coronary artery; 3, standard MB or CD, comparable with that obtained during angiography of a non-infarct-related coronary artery[13].

Electrocardiographic Analysis

For each patient, standard 12-lead-ECGs (paper speed of 25 mm/s, standardization of 10 mm/1 mV) were recorded at admission, within the first hour after pPCI, and at the 24 hours after pPCI. All analyses were made by two independent observers using a magnifying glass. ECG was performed with the Nihon Kohden Electrocardiograph (model ECG 2350).

ST-Segment Resolution (STR%): STR was calculated from the ECGs taken at admission and the first hour after pPCI. The sum of STR was measured 20 milliseconds after the end of QRS complex: Leads V1-6 for anterior MI and leads II, III, and aVF for inferior infarction. ST resolution was calculated as a percentage reduction of the absolute STE in the single lead, which is associated with the infarct territory with maximum STE on the baseline ECG[10].

QTc Interval Measurement: QT intervals were measured from the recorded ECGs (baseline, 1st and 24th hours after pPCI). Measurements were made using a manual compass in either lead II for inferior MI and V2 or V5 for anterior MI, with the most prolonged QT interval being used. The maximum measured interval in successive 3-5 beats was taken. When leads II, V2, or V5 were deemed unsuitable, one of the remaining leads associated with infarct territory was chosen. QT intervals were measured from the onset of the QRS complex to the point of return of the T wave to the isoelectric line or the nadir between the T and U waves in cases the U wave was present. QT intervals were corrected for heart rate effects using a modified Bazzet's formula (QTc=QT/(R-R)1/2).

Transthoracic echocardiography was performed 24 hours after admission, and the left ventricular ejection fraction (LVEF %) was measured by the modified Simpson method.

The study approved by the local institutional ethics committee. The study protocol conforms to the Declaration of Helsinki [University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital Ethics Committee (approval date: 28/02/2020 number: 413].

Statistical Analysis

Statistical analysis was performed by using R software version 4.02 (R Project, Austria Vienna). Continuous variables were presented as mean ± standard deviations, or if a non-normal distribution was found, they were given as median, interquartile range: 25-75% (IQR). Categorical variables were expressed as percentages. The histogram and Shapiro-Wilks test were used to verify the normal distribution of data. The paired Student's t-test was used to assess QTc change after pPCI. Correlation between variables was performed using Spearman's rank or Pearson correlation test according to the distribution of data.

Outcome Variable: QTc-Change first hour after pPCI.

Statistical Modeling: Multiple linear regression analysis was used to assess the relationship of QTc-Change with the STR% and MBG after adjusting common clinical predictors (age, gender, diabetes mellitus, hypertension, peak troponin, infarct location, symptom to door time, potassium, Glycoprotein IIb/IIIa inhibitor use). Continuous variables were included in the model by restricted cubic spline transformation (3 knot) to attain the nonlinearity of data. Continuous variables were presented in regression analysis as their interquartile range (25-75 IQR). In all the statistical analyses, a p-value of <0.05 was considered statistically significant. The correction for p-value was performed where needed.

Results

One hundred and five patients who had successful pPCI with adequate ECG data were enrolled in the study. The mean age was 55±10 years in the study population. Nineteen (18%) patients were female, and 44 (42%) patients had anterior STEMI. Baseline characteristics,

clinical, laboratory, and electrocardiographic findings of patients were given in Table 1.

The mean Pre-pPCI QTc was 409±34 ms, the mean post-pPCI QTc was 427±32 ms, and the mean 24th hour QTc was 424±34 ms (Figure 1). After pPCI, the median 21 ms (-3, 37 IQR) prolongation was observed in the QTc interval and this prolongation (QTc-Change) was statistically significant (p<0.001). The median STR was 71% (60-83 IQR), the median MBG was 2 (1-3 IQR), the median symptom to door time was 3 (1.75-4 IQR) hours. The median LVEF measured at 24 hours was 55% (47-57 IQR). In-hospital mortality occurred in one patient who presented with anterior STEMI, and non-sustained ventricular tachycardia was observed within the first 24 hours after revascularization in another patient.

A weak negative correlation was observed between admission Pre-pPCI QTc and STR (%) (r=-0.237), LVEF (%) (r=-0.383) and MBG (r=-0.355). A weak positive correlation was observed between symptom to door time and pre-pPCI QTc (r=0.382). A moderate negative correlation was observed between QTc-Change and Pre-pPCI QTc (r=-0.422). A moderate positive correlation was observed between QTc change and STR% (r=0.402), MBG (r=407), and LVEF% (r=0.437). A weak negative correlation was observed between QTc-Change and symptom to door time (r=-333). In the multivariable linear regression analysis, a significant relationship was

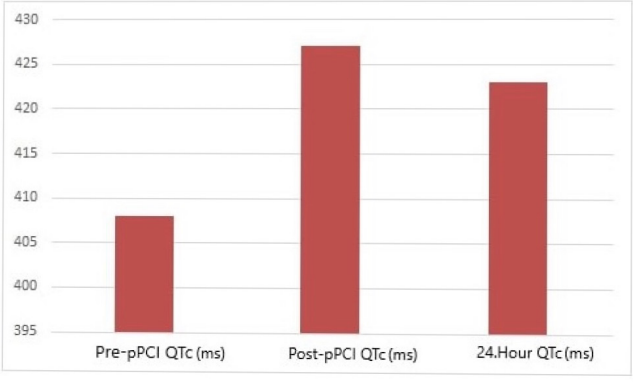

Figure 1. Temporal change of QTc interval: Pre-pPCI QTc, Post-pPCI QTc, and 24th-hour QTc
pPCI: Primary percutaneous coronary intervention, QTc: Corrected QT

Table 1. Baseline characteristics, and clinical, laboratory, and electrocardiographic findings of patients

	Total (n=105)
Age (year)	55±10
Gender (female)	19 (18%)
Diabetes mellitus	14 (13%)
Hypertension	35 (33%)
Smoking	34 (32%)
Hyperlipidemia	36 (34%)
Symptom to door time (h)	3 (1.75-4)
Troponin (ng/mL)	3.8 (0.34-21)
Peak troponin (ng/mL)	34 (13-50)
Killip class >1	21 (20%)
Infarct location (anterior)	44 (42%)
Infarct vessel	
Left anterior descending	44 (42%)
Left circumflex	23 (22%)
Right	38 (36%)
Left ventricular ejection fraction (%)	55% (47-57)
ST-segment resolution (%)	71 (60-83)
Myocardial blush grade	
0	6 (6%)
1	20 (19%)
2	44 (42%)
3	35 (33%)
Glycoprotein IIb/IIIa inhibitor use	40 (38%)
Hemoglobin (g/dL)	13.7±1.7
Creatinine (mg/dL)	0.80±0.18
Potassium (mmol/L)	4.03±0.35
Heart rate pre-pPCI (beat/min)	75±17
Heart rate post-pPCI (beat/min)	76±14
Heart rate 24th hour (beat/min)	71±11
Pre-pPCI QT interval (ms)	371±39
Post-pPCI QT interval (ms)	381±36
24th hour QT interval (ms)	392±37
Pre-pPCI QTc interval (ms)	409±34
Post-pPCI QTc interval (ms)	427±32
24th-hour QTc interval (ms)	424±34
QTc-Change (ms)	21 (-3, 37)

Values are expressed as number of patients (%), mean ± SD, or median (25th-75th percentile).
pPCI: Primary percutaneous coronary intervention, SD: Standard deviation

observed between QTc-Change with MBG and STR% (β-coefficient=9.077, 95% CI: 2.55-15.60, p=0.006 and β coefficient=9.315, 95% CI: 2.00-16.62, p=0.013, respectively). Multivariable linear regression analysis between the QTc-Change and clinical variable was given in Table 2. Partial effect plots of MBG and STR% with QTc-Change were given in Figure 2a and 2b. It is seen that as STR% and MBG increase, QTc-Change increases. In Figure 3, we summarized the relative importance of each predictor in the model. MBG was ranked as the most contributing predictor for QTc-Change, and followed by STR%.

Discussion

There are insufficient data regarding the prognostic significance of the change in the QTc interval after revascularization in STEMI patients, and our study is important in terms of showing the relationship between this QTc-change and prognostic parameters. This study showed that the QTc interval was significantly prolonged

Table 2. Multivariable Linear Regression analysis of QTc-Change with clinical variables

	β-coefficient	95% CI	p-value
Age (year) (from 48 to 61)	3.42	-4.62, 8.98	0.775
Sex (male/female)	5.18	-8.79, 19.06	0.460
Hypertension (from 0 to 1)	2.84	-9.12, 14.81	0.637
Diabetes mellitus (from 0 to 1)	-5.20	-20.98, 10.56	0.513
Troponin (ng/mL) (from 0.34 to 18.9)	-7.18	-11.33, 17.12	0.703
Symptom to door time (hour) (from 2 to 4)	-8.79	-8.79, 6.37	0.07
Infarct type (anterior/nonanterior)	1.59	-9.29, 12.48	0.772
STR% (from 60 to 83)	9.31	2.00, 16.62	0.013
MBG (from 1 to 3)	9.07	2.55, 15.60	0.006
Glycoprotein IIb/IIIa inhibitor	4.81	-4.86, 14.48	0.320
Potassium (3.8 to 4.2) (mmol/L)	-4.56	-11.21, 2.09	0.039

Regression coefficients were given according to the IQR 25-75% (interquartile-range) changes of the continuous variables. Because of nonlinearity of some data (we used restrictive cubic splines 3 knot) such-as Potassium, corresponding CI includes zero; however, p-value is significant.
STR: ST-segment resolution, MBG: Myocardial blush grade, CI: Confidence interval.

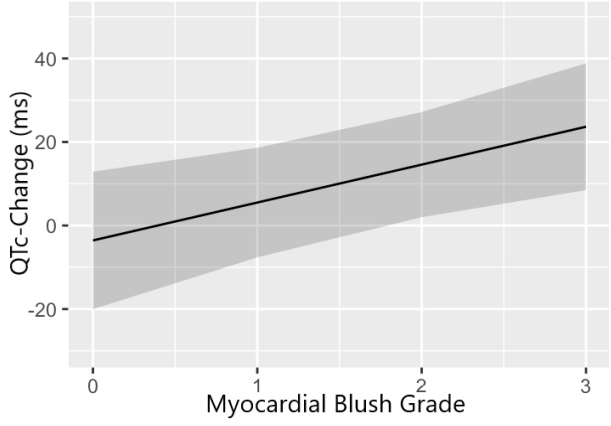

Figure 2a. Partial effect plot in the model for QTc-change and myocardial blush grade
QTc: Corrected QT

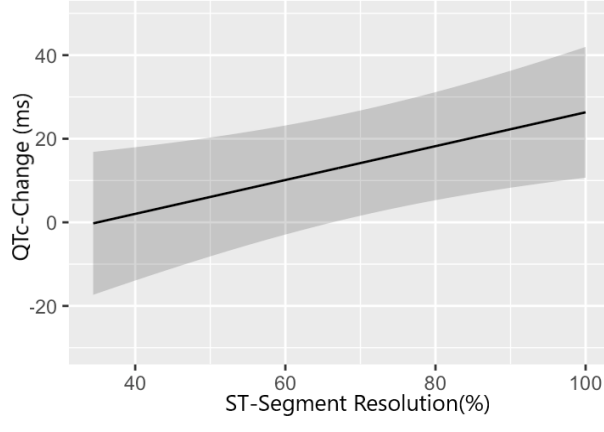

Figure 2b. Partial effect plot in the model for QTc-Change and ST-Segment resolution (%)
QTc: Corrected QT

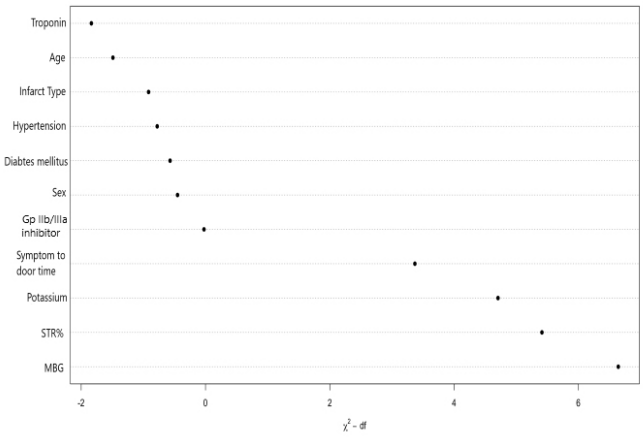

Figure 3. Relative importance of each variable in the model for QTc-change; STR%: ST-segment resolution (%), MBG: Myocardial blush grade

in the early period after successful reperfusion in STEMI patients. QTc-Change was significantly associated with STR% and MBG by multivariable linear regression analysis, and STR% and MBG were higher in patients with prolonged QTc interval. Moreover, the QTc change demonstrated a moderately negative correlation with both LVEF% and Pre-pPCI QTc.

Acute myocardial ischemia has been shown to modify the QT interval duration, increase repolarization heterogeneity, and prolong the maximum electrocardiographic QT interval[6]. Numerous mechanisms have been proposed for ischemia to prolong the QTc duration. Increased sympathetic activity, together with structural myocardial damage, electrolyte imbalance, and dysfunction of the ion channels in the acute phase of ischemia, may cause QT prolongation[9]. Many studies have shown that a long admission QTc interval is associated with a poor prognosis in AMI. In one study, a QTc interval >445 ms on admission to the emergency department was an independent predictor for all-cause mortality and heart failure in STEMI patients[16]. In our study, the Pre-pPCI QTc interval, measured on admission to the emergency department, showed a negative correlation with STR%, MBG, and LVEF%, respectively. Again, the Pre-pPCI QTc interval was prolonged in patients with increased symptom to door time in our study.

Although many studies in patients with AMI report shortening of the QTc interval after successful reperfusion, studies on the QTc interval change during the following hour after reperfusion are limited. Reperfusion may affect the QTc interval, either directly by influencing the electrophysiological milieu or indirectly by interfering with cardiac autonomic nervous control[17]. In a study by Bonnemeier et al.[7], it was found that the QTc interval continued to lengthen in the first hour after reperfusion in AMI patients who underwent pPCI and then began to shorten following hours. In our study, a significant prolongation was observed in the QTc interval (QTc-Change) at the 1st hour after successful pPCI [21 ms (-3, 37 IQR) p-value <0.001], and although a decrease was observed in the QTC interval measured at the 24th hour, it was still found to be higher than the baseline. MBG is an angiographic measure of myocardial perfusion and a strong predictor of mortality in patients with TIMI-3 flow after pPCI[12]. Furthermore, STR% is an electrocardiographic indicator of myocardial perfusion and has a strong relationship with mortality and reinfarction[10]. Even if TIMI-3 flow is provided in the infarct-related vessel, there may be a problem in myocardial perfusion at the microvascular level. Therefore, patients with low STR% and MBG are associated with heart failure and poor outcomes[10-12]. In the study of Poli et al.[13], patients with both MBG 2/3 and STR >50% immediately after pPCI showed a significant 7-day and 6-month functional recovery on echocardiography. In our study, a significant relationship was observed between QTc-Change with STR% and MBG in regression analysis. STR%, MBG, and LVEF were higher in patients with prolongation of QTc interval after pPCI. QTc-Change was lower in patients with increased symptom to door time.

In one study evaluating patients who underwent elective PCI, it was observed that QTc was prolonged in 100% of patients during balloon inflation and began to decrease immediately after deflation, and QTc prolongation

could be the earliest sign of transmural ischemia[18]. In a study of AMI patients comparing successful with unsuccessful reperfusion, it was found that the QTc interval peaked towards the 12th hour in the revascularization group and started to shorten afterward, and it was observed that it continued to increase without peaking in the patient group without reperfusion. LVEF% was better in the patient groups with transient prolongation[19]. In our study, LVEF% measured at the 24th hour was higher in patients with a prolonged QTc interval after reperfusion. Considering that cellular mechanisms are disrupted for a longer period in myocardial infarction than in elective balloon angioplasty (just as echocardiographic stunning does not improve immediately after reperfusion), the QT interval may continue to prolong for a while until the electrophysiological factors that cause QT prolongation recover and then begin to shorten. Reflecting on the relationship of QTc-Change with prognostic parameters such as STR, MBG, LVEF%, and symptom to door time, the moderate prolongation in the early period in the QTc interval may be an indicator of viable myocardial tissue, just like in myocardial stunning. The reversible impairment of ventricular repolarization after reperfusion for patients without adverse event may be interpreted as "electrical stunning" of the ventricular myocardium[7].

The moderate prolongation of the QTc interval in the early hours after pPCI may be prognostically valuable due to its association with better myocardial perfusion and better left ventricular function in some patient groups.

Study Limitations

An important limitation of this study was the small cohort of patients. Another limitation of the study was that the QTc interval change was not monitored after the first hour. Perhaps, examining the relationship of QT prolongation with parameters such as the infarct area may be valuable in terms of showing the presence of living tissue.

Conclusion

It was found that the QTc interval continued to prolong somewhat in the early period after successful pPCI in STEMI patients, and this QTc-Change was significantly associated with reperfusion parameters such as MBG and STR%. STR% and MBG were higher in those with higher QTc-Change.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital Ethics Committee (approval date: 28/02/2020, number: 413).

Informed Consent: Informed consent form was obtained.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Ç., Concept: M.Ç., T.A., Ç.G., Design: M.Ç., Ö.B., F.I., A.K., Data Collection or Processing: M.Ç., Ö.B., F.I., T.G., Analysis or Interpretation: A.K., T.A., Ç.G., Literature Search: E.E., Ö.B., Writing: M.Ç., E.E., C.K., N.Ö.

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