

Assessment of the relationship between reperfusion success and T-peak to T-end interval in patients with ST elevation myocardial infarction treated with percutaneous coronary intervention

Metin Çağdaş, Süleyman Karakoyun, İbrahim Rencüzoğulları, Yavuz Karabağ, Mahmut Yesin¹, Yalçın Velibey², İnanç Artaç, Doğan İliş, Süleyman Çağan Efe³, Onur Taşar⁴, Halil İbrahim Tanboğa⁵

Department of Cardiology, Faculty of Medicine, Kafkas University; Kars-Turkey

¹Department of Cardiology, Kars Harakani State Hospital; Kars-Turkey

²Department of Cardiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital; İstanbul-Turkey

³Department of Cardiology, Ağrı State Hospital; Ağrı-Turkey

⁴Department of Cardiology, Elazığ Education and Research Hospital; Elazığ-Turkey

⁵Department of Cardiology, Faculty of Medicine, Atatürk University; Erzurum-Turkey

ABSTRACT

Objective: T-peak–T-end (TPE) interval, which represents the dispersion of repolarization, is defined as the interval between the peak and end of the T-wave, and is associated with increased malignant ventricular arrhythmia and sudden cardiac death (SCD) in patients with ST elevation myocardial infarction (STEMI). Although prolonged TPE interval is associated with poor short- and long-term outcomes, even in patients with STEMI treated with successful primary percutaneous coronary intervention (pPCI), clinical, angiographic, and laboratory parameters that affect TPE remain to be elucidated. The aim of our study was to evaluate the potential relationship between prolonged TPE interval and reperfusion success using ST segment resolution (STR) in patients with STEMI undergoing pPCI.

Methods: In the current study, 218 consecutive patients with STEMI who underwent pPCI were enrolled; after exclusion, 164 patients were included in the study population.

Results: Patients were divided into two groups according to the presence of complete (STR%≥70) or incomplete (STR%<70) STR. Preprocedural corrected TPE (cTPE_{PRE}; 116±21 ms vs. 108±21 ms; p=0.027), postprocedural TPE (TPE_{POST}; 107±16 ms vs. 92±21 ms; p<0.001), and postprocedural cTPE (cTPE_{POST}; 119±19 ms vs. 102±17 ms; p<0.001) intervals were significantly longer in patients with incomplete STR than in patients with complete STR, whereas there was no statistically significant difference between the two groups in terms of pre- and postprocedural and corrected QT intervals. cTPE_{PRE} and cTPE_{POST} were found to be independent predictors for incomplete STR.

Conclusion: To our knowledge, this is the first study that evaluated the relationship between TPE interval and no-reflow defined by STR in patients with STEMI who were treated with pPCI. (*Anatol J Cardiol* 2018; 19: 50-7)

Keywords: ST elevation myocardial infarction, reperfusion, no-reflow, T-peak–T-end interval

Introduction

T-peak–T-end (TPE) interval, which is defined as the interval between the peak and end of the T-wave, represents the dispersion of repolarization. Abnormal repolarization and prolonged TPE interval are associated with increased malignant ventricular arrhythmia and sudden cardiac death (SCD) in many acquired and congenital cardiac diseases (1, 2). Recently, the relationship between prolonged TPE interval and worse short- and long-term outcomes in patients with STEMI has been established (3-5). Although prolonged TPE interval has been shown to be associated

with poor short- and long-term outcomes, even in patients with ST elevation myocardial infarction (STEMI) who are treated with successful primary percutaneous coronary intervention (pPCI), clinical, angiographic, and laboratory parameters that affect the TPE interval remain unclear.

Coronary no-reflow (NR) is defined as imperfect myocardial perfusion despite successful restoration of epicardial coronary flow (6), and is associated with larger myocardial infarct size, lower left ventricular ejection fraction, adverse left ventricular remodeling, increased mechanical complications, heart failure, and death (7-9). NR has been reported in up to 60% of patients with STEMI,

Address for correspondence: Dr. Metin Çağdaş, Kafkas Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı Kars-Türkiye
E-mail: metin-cagdas@hotmail.com

Accepted Date: 16.10.2017 **Available Online Date:** 28.12.2017

©Copyright 2018 by Turkish Society of Cardiology - Available online at www.anatoljcardiol.com
DOI:10.14744/AnatolJCardiol.2017.7949



and its incidence varies according to the diagnostic method, such as thrombolysis in myocardial infarction (TIMI) grade, corrected TIMI frame count, myocardial blush grade (MBG), and ST segment resolution (STR) (10-18). Despite prolonged TPE interval and NR being associated with poor prognosis in patients with STEMI, no study has investigated the possible relationship between TPE interval and NR using STR. In the present study, we aimed to investigate the relationship between TPE interval and coronary NR using STR in patients with STEMI treated with pPCI.

Methods

Study population

A total of 218 consecutive patients with STEMI who underwent pPCI between January 2014 and January 2015 were enrolled in this cross-sectional study. STEMI was defined based on the following criteria: ongoing ischemic symptoms (within 12 h); typical rise or fall in cardiac biomarker levels; new ST elevation in ≥ 2 contiguous leads, with leads V1, V2, and V3 measuring at least 0.2 mV or remaining leads measuring at least 0.1 mV; or newly developed left bundle branch block pattern (19). Patients with a previous history of MI and structural heart disease (26 patients), inappropriate electrocardiogram (ECG) due to poor image quality, bundle branch block, second- and third-degree AV block, QRS duration (QRSD) of >120 ms (17 patients), and inconclusive clinical data from hospital files and computer records (11 patients) were excluded from the study. Thus, 164 patients constituted the study population. Using hospital records, the patients' baseline clinical and demographic characteristics and past history, including hypertension (HT), diabetes mellitus (DM), CAD, family history of CAD, dyslipidemia, and smoking status were obtained. The study protocol was reviewed and approved by the local Ethics Committee of our university in accordance with the Declaration of Helsinki.

ECG analysis

A digital 12-lead ECG recorded at a speed of 25 mm/s and voltage of 10 mm/mV was obtained for all patients at admission (preprocedural ECG) and 60 min after pPCI (postprocedural ECG). All ECGs were scanned, loaded on a computer, sufficiently magnified, and analyzed with a digital image processing software (imagej.nih.gov/ij/). All measurements were evaluated by two independent cardiologists who were blinded to other patients' clinical information. STR $\geq 70\%$ was defined as successful reperfusion. The TPE interval was measured from the lead that had the longest TPE interval to no ST-T wave change by the tail method (22). Heart rate and QRS and QT intervals were also measured. Because the QT and TPE intervals vary with heart rate, Bazett's formula (corrected index interval=index interval/ $\sqrt{R-R}$) was applied to the QT and TPE intervals to determine corrected values of QT (cQT) and TPE (cTPE) intervals, respectively (23). The durations in milliseconds (ms) were obtained from pre- and postprocedural ECGs. The sum of the pre- and postprocedural

ST segment elevation ($\sum \text{STE}_{\text{PRE}} - \sum \text{STE}_{\text{POST}}$) was measured 20 ms after the end of QRS complex of the infarct-related artery (IRA) leads. The percentage of STR was calculated according to the following formula: $100 * (\sum \text{STE}_{\text{PRE}} - \sum \text{STE}_{\text{POST}}) / \sum \text{STE}_{\text{POST}}$

Coronary angiography

Coronary angiography and PCI were performed according to standard practice. All patients received anticoagulation therapy with unfractionated heparin [70–100 units/kg (maximum dose, 10,000 U)] and dual antiplatelet therapy with aspirin (300 mg) and clopidogrel (600 mg) before the procedure. Coronary blood flow patterns before and after primary PCI were thoroughly evaluated using TIMI flow grades (0–3) (10). MBG was assessed according to the technique defined by van't Hof et al. (20). Thrombus burden was assessed according to TIMI thrombus grading scale, ranging from grade 0 (no thrombus) to 5 (very large thrombus causing vessel occlusion). Patients with grade 5 thrombus were reclassified into grades 0–4 after recanalization with guidewire or small balloon (21).

Statistical analysis

Data were analyzed using the SPSS 17.0 version (SPSS Inc., Chicago, Illinois, USA). Intra- and interobserver variabilities in TPE measurements were estimated by calculating the Lin's concordance correlation coefficient. Concordance correlation coefficients were 0.991 [95% confidence interval (CI), 0.988–0.994] for the preprocedural TPE interval and 0.992 (95% CI, 0.989–0.994) for the postprocedural TPE interval, evaluated by the same observer. Concordance correlation coefficients were 0.990 (95% CI, 0.986–0.992) for the preprocedural TPE interval and 0.988 (95% CI, 0.984–0.991) for the postprocedural TPE interval between the two observers. Normality of the data distribution was analyzed using the Kolmogorov-Smirnov test. The numerical variables with a normal distribution were presented as the mean \pm standard deviation, whereas those without a normal distribution were presented as the median (interquartile range). Categorical variables were presented as number and percentage (%). Continuous variables between the two independent groups were compared using the Student's t-test or Mann-Whitney U test. Continuous variables with normal distribution between the two dependent groups were compared using the paired t-test. Categorical data were compared using the chi-square or Fisher's exact test. Statistical significance was defined as a p value of <0.05 . Multiple variable logistic regression analysis was performed to identify the independent predictors for incomplete STR (STR $<70\%$) using variables that showed marginal association with STR ($p < 0.05$) on univariate testing. Receiver operating characteristic (ROC) curve analyses were performed to determine the best cut-off value of pre- (cTPE_{PRE}) and postprocedural cTPE (cTPE_{POST}) intervals for predicting incomplete STR. The effect size (Cohen's d) and power value ($1 - \beta$) for cTPE_{PRE} and cTPE_{POST} intervals, compared between patients with complete and incomplete STR, were calculated using the G*Power software

Table 1. Demographic, clinical, laboratory and coronary angiographic characteristics of all patients, patients with incomplete STR and complete STR with P value

	All patients (n=164)	STR %<70 (n=102)	STR %≥70 (n=62)	P
Age, years	62±12	65±11	57±11	<0.001
Female sex, n (%)	42 (25.6)	28 (27.5)	14 (22.6)	0.308
Hypertension, n (%)	71 (43.3)	56 (54.9)	15 (24.2)	<0.001
Diabetes mellitus, n (%)	58 (35.4%)	46 (45.1)	12 (19.%)	0.001
Dyslipidemia, n (%)	50 (30.5%)	35 (34.3)	15 (24.2)	0.172
Smoking, n (%)	93 (56.7%)	64 (62.7)	29 (46.8)	0.045
Family history, n (%)	48 (29.3%)	28 (27.5)	20 (32.3)	0.512
Systolic blood pressure, mm Hg	134±21	136±18	131±24	0.193
FGL, mg/dL	107 (95-127)	117 (98-132)	97 (88-112)	<0.001
Creatinine, mg/dL	0.90±0.18	0.88±0.18	0.94±0.18	0.05
Hemoglobin, g/dL	14.9±1.7	14.7±1.8	15.2±1.4	0.071
White blood cell, 10 ³ /μL	11.4±3.2	11.7±2.9	11.1±3.5	0.22
Platelet, 10 ³ /mm ³	195 (171-243)	198 (176-256)	195 (171-234)	0.067
Total cholesterol, mg/dL	169 (159-192)	171 (151-194)	167 (159-189)	0.454
CRP, mg/dL	0.59 (0.17-1.45)	0.83 (0.47-1.48)	0.15 (0.08-0.88)	<0.001
Peak CK-MB, mg/dL	199 (115-311)	252 (160-332)	127 (63-195)	<0.001
Symptom to balloon time, hours	2.7±0.9	3.1±0.8	2.1±0.8	<0.001
IRA of LAD n (%)	63 (38.4)	43 (42.2)	20 (32.3)	0.206
Proximal lesion, n (%)	80 (48.8)	48 (47.1)	32 (51.6)	0.572
Preprocedural TIMI 0, n (%)	103 (62.8)	75 (73.5)	28 (45.2)	<0.001
Thrombus grade ≥2, n (%)	92 (56.1)	72 (70.6)	20 (32.3)	<0.001
Postprocedural IRA TFC	15 (11-21)	19 (14-30)	13 (10-14)	<0.001
Angiographic No-reflow n (%)	81 (49.4)	70 (68.6)	11 (17.7)	<0.001
Stent length, mm	23 (23-28)	28 (23-33)	23 (18-23)	<0.001
3 vessel disease, n (%)	18(11)	15 (14.7)	3 (4.8)	0.05
LVEF %	47 (40-52)	45 (35-52)	48 (46-52)	0.013

CK-MB-creatinine kinase-myocardial band, CRP-C-reactive protein, FGL-fasting glucose level, IRA - infarct related artery, LAD-left anterior descending, LVEF-left ventricular ejection fraction, STR-ST segment resulation, TFC-TIMI frame count, TIMI-trombolysis in myocardial infarction

Continuous variables with normal distribution presented as mean±standard deviation were compared using Student t test. Continuous variables without normal distribution presented as median and interquartile range were compared using Mann-Whitney U test. Categorical variables presented as number and percentiles were compared using chi-square test

(version 3.1.9.2). The alpha level used for this analysis was <0.05. The effect size and power value were 0.94 and 0.99 for cTPE_{POST} and 0.38 and 0.76 for cTPE_{PRE}.

Results

The study population consisted of 164 patients with STEMI (mean age, 62±12 years; females, 25.6%) who underwent pPCI. Patients were divided into two groups: with STR% <70 (n=102) and STR% ≥70 (n=62). Patients with STR% <70 had older age, higher incidence of HT, DM, current smoking, fasting blood glucose, C-reactive protein (CRP) levels, and peak CK-MB levels compared with those with STR% ≥70. Increased symptom to balloon time, longer lesion length, preprocedural TIMI grade 0,

TIMI thrombus grade ≥2, and angiographic NR were seen more frequently in patients with STR% <70. The baseline characteristics, and clinical, angiographic, and laboratory findings of all study patients are summarized in Table 1.

The patients with STR% <70 had higher Q wave on admission ECG and longer cTPE_{PRE} (116±21 vs. 108±21; p=0.027), TPE-_{POST} (107±16 vs. 92±21; p<0.001), and cTPE_{POST} (119±19 vs. 102±17; p<0.001) than those with STR% ≥70 (Table 2, Fig. 1a-1b). There was no statistically significant difference between pre- and postprocedural QT, cQT, TPE, and cTPE intervals in patients with STR <70, but there was a statistically significant decrease in TPE and cTPE intervals after pPCI in patients with STR% ≥70 (Table 3). cTPE_{PRE}, TPE_{POST}, and cTPE_{POST} were correlated with STR%, peak CK-MB levels, and postprocedural IRA TFC, with statisti-

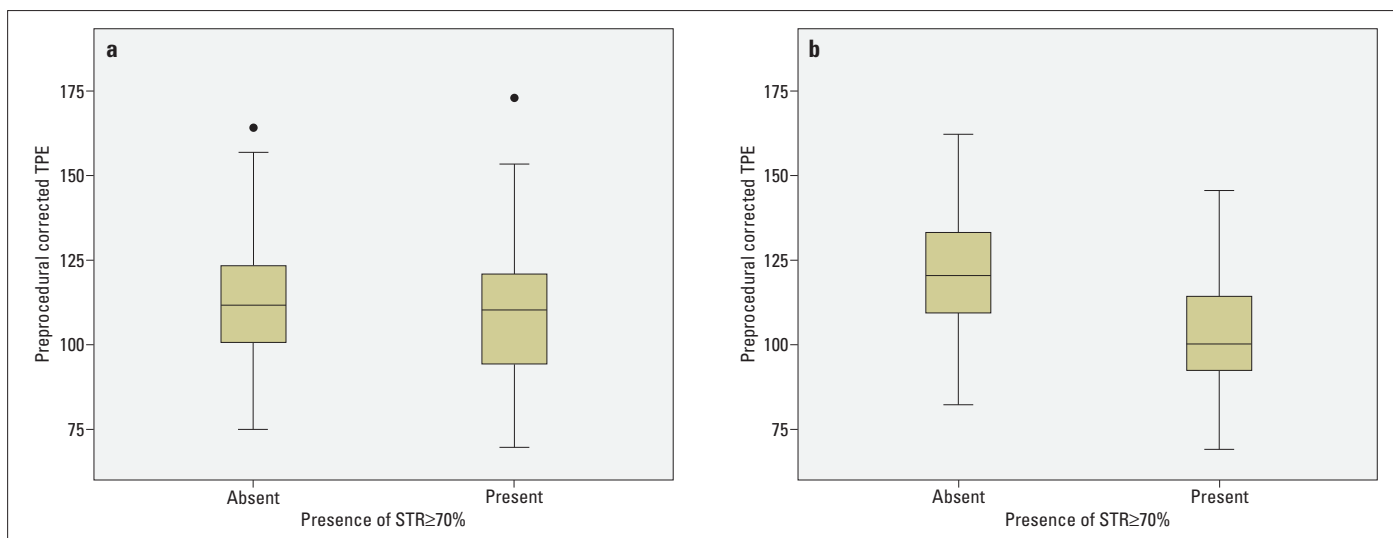


Figure 1. Box plot showing the comparison of $cTPE_{PRE}$ (A) and $cTPE_{POST}$ (B) intervals in patients with complete and incomplete STR

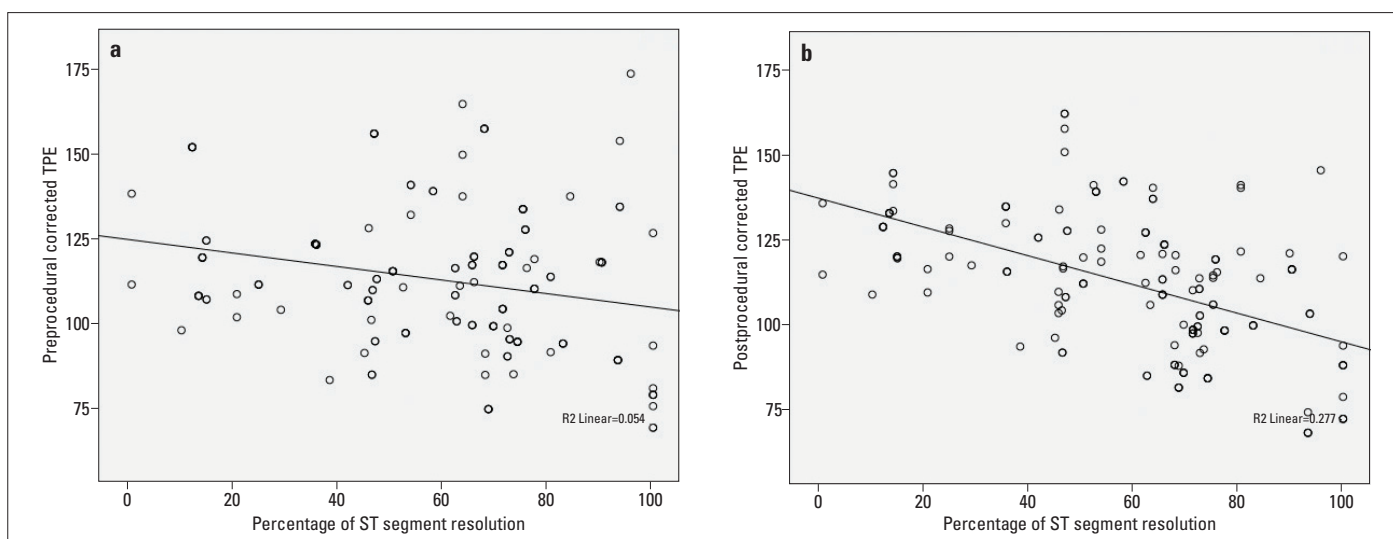


Figure 2. Scatter plot of correlation between STR% and $cTPE_{PRE}$ (a) and $cTPE_{POST}$ (b) intervals

cally significant correlations between the parameters (Table 4, Fig. 2a-2b).

Multiple variable logistic regression analysis was used for determining the independent predictors for $STR\% < 70$. Univariate analysis showed that age, HT, DM, smoking, fasting glucose level, CRP level, peak CK-MB level, symptom to balloon time, preprocedural TIMI grade 0, thrombus grade ≥ 2 , angiographic NR, stent length, left ventricular ejection fraction, Q wave on admission, $cTPE_{PRE}$, TPE_{POST} and $cTPE_{POST}$ were significantly associated with $STR\% < 70$. However, in multiple variable analysis, age, symptom to balloon time, angiographic NR, $cTPE_{PRE}$ and $cTPE_{POST}$ were found to be independent predictors for $STR\% < 70$ (Table 5). The cut-off values of $cTPE_{PRE}$ and $cTPE_{POST}$ intervals for predicting $STR\% < 70$ were 96 with a sensitivity of 87.3% and specificity of 40.3% (AUC, 0.592; $p=0.048$) and 103 with a sensitivity of 81.4% and specificity of 62.9% (AUC, 0.756; $p<0.001$), respectively (Fig. 3).

Discussion

Our study demonstrated that prolonged $cTPE_{PRE}$ and $cTPE_{POST}$ intervals were significantly associated with reperfusion success and independent predictors for imperfect STR.

In clinical practice, there are several methods to define reperfusion success in the setting of STEMI, including TIMI grade, corrected TIMI frame count, MBG, and STR (10-18). ST segment changes reflect myocardial rather than epicardial flow and thus yield prognostic information beyond that provided by coronary angiogram alone. Numerous studies have shown that $STR\% \geq 70$ (complete resolution) was significantly associated with lower infarct size and subsequent morbidity and mortality (14-18). In our study, incomplete STR ($< 70\%$) was seen in 62.2% ($n=102$) of patients. Consistent with the results of previous studies, we found that older age, history of DM, smoking, large infarct size (higher

Table 2. Electrocardiographic characteristics of all patients, patients with incomplete STR and complete STR with P value

	All patients (n=164)	STR %<70 (n=102)	STR %≥70 (n=62)	P
Preprocedural HR; /min	72±14	73±13	69±15	0.151
Postprocedural HR; /min	72±13	73±12	70±14	0.172
Q wave on admission; n (%)	60 (36.6)	53 (52)	7 (11.3)	<0.001
ΣSTE _{PRE}	8 (6-13)	8 (6-12)	8 (4-20)	0.495
ΣSTE _{POST}	3 (2-5)	4 (2-8)	2 (1-3)	<0.001
STR %	66 (47-75)	48 (36-64)	78 (73-93)	<0.001
QT _{PRE}	392±26	391±27	393±23	0.699
cQT _{PRE}	426±40	429±42	420±36	0.155
QT _{POST}	392±20	393±22	390±17	0.332
cQT _{POST}	432±31	434±32	428±29	0.168
TPE _{PRE}	103±17	105±16	101±19	0.146
cTPE _{PRE}	113±21	116±21	108±21	0.027
TPE _{POST}	102±17	107±16	92±14	<0.001
cTPE _{POST}	112±20	119±19	102±17	<0.001

ΣSTE_{PRE}-preprocedural sum of ST segment elevation, ΣSTE_{POST}-postprocedural sum of ST segment elevation, cQT_{POST}-postprocedural corrected QT interval, cQT_{PRE}-preprocedural corrected QT interval, cTPE_{POST}-postprocedural corrected TPE interval, cTPE_{PRE}-preprocedural corrected TPE interval, HR-heart rate, QT_{POST}-postprocedural QT interval, QT_{PRE}-preprocedural QT interval, STR-ST segment resolution, TPE_{POST}-postprocedural TPE interval, TPE_{PRE}-preprocedural TPE interval

Continuous variables with normal distribution presented as mean±standard deviation were compared using Student t test. Continuous variables without normal distribution presented as median and interquartile range were compared using Mann-Whitney U test. Categorical variables presented as number and percentiles were compared using chi-square test

symptom to balloon time, presence of Q wave on admission ECG, peak CK-MB level, decreased LVEF), more frequent preprocedural TIMI grade 0, high thrombus burden, and angiographic NR were associated with incomplete STR (7-13). In addition, we found that history of HT was more prevalent in patients with NR despite lack of evidence regarding the relationship between NR and HT. This

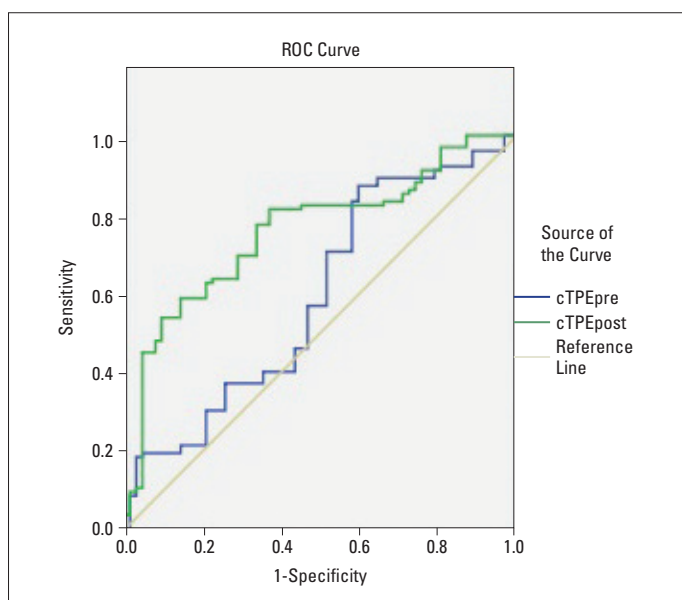


Figure 3. ROC graphs to detect the best cut-off value of cTPE_{PRE} and cTPE_{POST} intervals in the prediction of incomplete STR. ROC, receiver operating characteristic; cTPE_{PRE}, preprocedural corrected TPE interval; cTPE_{POST}, postprocedural corrected TPE interval

contradictory result could be explained by the relationship between HT, endothelial dysfunction (24), slow coronary flow (25), and increased atherosclerotic burden (26) in stable CAD.

Acute MI involves electrochemical and metabolic alterations of cardiac muscles, which in turn affect electrochemical gradient, tissue oxygen level, ion channel conditions, and pH. These changes have a complex effect on the duration of action potentials in the ischemic zone and ischemic border zone; thus, TPE and QT intervals display modestly compatible changes (1-5, 27, 28). We hypothesized that the severity of these changes is related with reperfusion success, and that prolongation of QT and TPE intervals could be predictors for imperfect myocardial flow despite successful restoration of the epicardial flow. It is known that myocardial ischemia prolongs QT interval while reperfusion shortens it (29, 30); however, there was no statistically significant relationship between QT interval and reperfusion features in our study. We observed that TPE and cTPE intervals reduced after pPCI in patients with complete STR; no statistically significant change was observed in patients with incomplete STR despite numerical increase. In addition, patients with incomplete STR had significantly longer cTPE_{PRE}, TPE_{POST}, and cTPE_{POST} intervals than those with complete STR; cTPE_{PRE} and cTPE_{POST} intervals were independent predictors for incomplete STR. Similar to our results, Eslami et al. (5) and Duyuler et al. (31) found that reperfusion success was more closely related with shortened TPE interval than with QT interval. However, there were some differences between the results of our and previous studies. We assessed reperfusion success according to STR,

Table 3. Pre-postprocedural change of QT, cQT, TPE and cTPE in patients with incomplete STR and complete STR with P value

	STR %<70 (n=102)			STR %≥70 (n=62)		
	Before pPCI	After pPCI	P	Before pPCI	After pPCI	P
QT	391±27	393±22	0.344	393±23	390±17	0.106
cQT	429±42	434±32	0.182	420±36	428±29	0.063
TPE	105±16	107±16	0.088	101±19	92±14	<0.001
cTPE	116±21	119±19	0.089	108±21	102±17	0.001

cQT-corrected QT interval, cTPE-corrected T peak-T end interval, QT-QT interval, TPE-T peak-T end interval
Units msec (millisecond) Paired t-test was used for comparisons

Table 4. Correlation between cTPE_{PRE}, TPE_{POST}, cTPE_{POST} and STR%, peak CK-MB level, postprocedural IRA TFC, LVEF

		STR %	CK-MB	Postprocedural IRA TFC	LVEF
cTPE _{PRE}	Correlation Coefficient	-0.233	0.156	0.347	-0.121
	Sig. (2-tailed)	0.003	0.046	<0.001	0.123
TPE _{POST}	Correlation Coefficient	-0.555	0.458	0.393	-0.313
	Sig. (2-tailed)	<0.001	<0.001	<0.001	<0.001
cTPE _{POST}	Correlation Coefficient	-0.538	0.430	0.397	-0.340
	Sig. (2-tailed)	<0.001	<0.001	<0.001	<0.001

CK-MB-creatin kinase-myocardial band, cTPE_{POST}-postprocedural corrected TPE interval, cTPE_{PRE}-preprocedural corrected TPE interval, IRA-infarct related artery, LVEF-left ventricular ejection fraction, STR-ST segment resolution, TFC-TIMI frame count, TPE_{POST}-postprocedural TPE interval
Spearman's test was used for correlation analysis

Table 5. Independent predictors of incomplete STR with univariate and multivariate P value, OR with 95% CI

	Univariate P value, OR, 95% CI				Multivariate P value, OR, 95% CI			
	P	OR	Lower	Upper	P	OR	Lower	Upper
Age, years	<0.001	1.072	1.038	1.108	.001	1.078	1.013	1.148
Symptom to balloon time, hours	<0.001	4.437	2.663	7.393	.002	2.874	1.455	5.676
Angiographic no-reflow n (%)	<0.001	4.525	2.546	8.042	.001	5.411	2.065	14.181
cTPE _{PRE} ms	0.027	1.018	1.002	1.034	.019	1.015	1.001	1.029
cTPE _{POST} ms	<0.001	1.054	1.032	1.076	.009	1.043	1.011	1.073

cTPE_{POST}-postprocedural corrected TPE interval, cTPE_{PRE}-preprocedural corrected TPE interval, STR-ST segment resolution
Multiple variable logistic regression analysis with backward elimination was performed

which was claimed to better reflect reperfusion at cellular level, but not according to angiographic indices. Also, we observed that prolonged cTPE_{PRE} interval was an independent predictor for imperfect reperfusion, which was not found in previous studies (5, 31). Shortening of the TPE interval, without shortening of the QT interval, in patients with complete STR can be explained by the fact that these parameters, which have similar clinical applications, represent electrophysiologically different properties in healthy and ischemic myocardia. The duration of the action potential represented by the QT interval on surface ECG is prolonged due to myocardial ischemia/infarction. Moreover, this prolongation could last for hours and days due to the presence of nonischemic causes, such as autonomic alterations, even when tissue perfusion is successfully restored. Interventricular,

intraventricular, and transmural heterogeneity in the repolarization duration of myocytes is represented by TPE on surface ECG. During myocardial infarction/ischemia, the heterogeneity in ventricular repolarization becomes more prominent because of increased differences in repolarization duration between normal, ischemic, and ischemic border zones, thus prolonging the TPE interval. Furthermore, the prolongation of TPE interval is more closely related with ischemia-induced metabolic alteration (intra-extracellular electrolyte concentration, electrochemical gradient, and pH), which rapidly improves with the restoration of the blood supply (28).

Prolonged TPE_{POST} interval in patients with incomplete STR is an expected finding; however, it was surprising that cTPE_{PRE} interval was also longer in these patients. This unusual finding can

be explained in several ways: First, the infarct size of patients with NR in our study was larger than those without NR before pPCI, because they had a delayed symptom to balloon time and more frequent presence of Q waves on admission ECG. Large infarct size causes imperfect tissue perfusion due to tissue edema, endothelial dysfunction, and ischemia-reperfusion injury (9). Second, patients with NR had more frequent risk factors for NR development, including older age, history of HT, DM, and smoking in the present study. These factors may have contributed to the expansion of the infarct size and thus the prolongation of the TPE interval before the procedure. Finally, the association of prolonged TPE interval with HT and DM could not only be explained by these being risk factors for NR but also by the results of recent studies which demonstrated that HT and DM could cause prolongation of TPE interval in patients without acute medical illness (32, 33). The presence of more frequent history of DM and HT in patients with NR may have contributed to the prolongation of cTPEPRE interval in these patients.

Study limitations

The present study had a cross-sectional design; hence, it does not provide prognostic data. Reperfusion success was evaluated by visual assessment of coronary angiogram and STR; a more specific and sensitive method, such as coronary flow reserve, contrast ECG, or cardiac magnetic resonance, was not used. Although the ECGs were scanned, loaded on a computer, sufficiently magnified, and analyzed using a digital image processing software for precise measurement, standard calibration of ECG recordings (speed, 25 mm/s, voltage calibration, 10 mm/mV) may have caused errors during TPE and QT interval measurement.

Conclusions

The present study demonstrated that prolonged TPE interval is associated with reperfusion features in patients with STEMI, and that TPE could be used as a marker for reperfusion success. These results may provide valuable information about the factors that play a role in TPE prolongation which leads to poor prognosis in patients with STEMI. It also should be noted that the presence of more frequent history of DM and HT in patients with incomplete STR may contribute to the presence of prolonged cTPE_{PRE} interval in these patients.

Acknowledgment: The authors would like to thank www.meta-stata.com for their contributions in statistical analysis and trial design.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – M.Ç., Y.V., İ.R.; Design – M.Ç., S.K.; Supervision – S.K., H.İ.T.; Data collection &/or processing – D.İ.,

İ.R., İ.A., Y.K., M.Y.; Analysis &/or interpretation – Y.K., H.İ.T., O.T.; Literature search – İ.R., Y.V., S.Ç.E.; Writing – M.Ç., Y.V., H.İ.T.; Critical review – S.K., H.İ.T.

References

1. Tse G, Yan BP. Traditional and novel electrocardiographic conduction and repolarization markers of sudden cardiac death. *Europace* 2017; 19: 712-21.
2. Tse G, Gong M, Wong WT, Georgopoulos S, Letsas KP, Vassiliou VS, et al. The Tpeak - Tend interval as an electrocardiographic risk marker of arrhythmic and mortality outcomes: A systematic review and meta-analysis. *Heart Rhythm* 2017; 14: 1131-7.
3. Zhao X, Xie Z, Chu Y, Yang L, Xu W, Yang X, et al. Association between Tp-e/QT ratio and prognosis in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. *Clin Cardiol* 2012; 35: 559-64.
4. Tatlısu MA, Özcan KS, Güngör B, Ekmekçi A, Çekirdekçi EI, Aruğarslan E, et al. Can the T-peak to T-end interval be a predictor of mortality in patients with ST-elevation myocardial infarction?. *Coron Artery Dis* 2014; 25: 399-404.
5. Eslami V, Safi M, Taherkhani M, Adibi A, Movahed MR. Evaluation of QT, QT dispersion, and T-wave peak to end time changes after primary percutaneous coronary intervention in patients presenting with acute ST-elevation myocardial infarction. *J Invasive Cardiol* 2013; 25: 232-4.
6. Morishima I, Sone T, Mokuno S, Taga S, Shimauchi A, Oki Y, et al. Clinical significance of no-reflow phenomenon observed on angiography after successful treatment of acute myocardial infarction with percutaneous transluminal coronary angioplasty. *Am Heart J* 1995; 130: 239-43.
7. Wu KC, Zerhouni EA, Judd RM, Lugo-Olivieri CH, Barouch LA, Schulman SP, et al. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. *Circulation* 1998; 97: 765-72.
8. Ndrepepa G, Tiroch K, Keta D, Fusaro M, Seyfarth M, Pache J, et al. Predictive factors and impact of no reflow after primary percutaneous coronary intervention in patients with acute myocardial infarction. *Circ Cardiovasc Interv* 2010; 3: 27-33.
9. Bouleti C, Mewton N, Germain S. The no-reflow phenomenon: State of the art. *Arch Cardiovasc Dis* 2015; 108: 661-74.
10. Gibson CM, Cannon CP, Murphy SA, Marble SJ, Barron HV, Braunwald E; TIMI Study Group. Relationship of TIMI myocardial perfusion grades, flow grades, frame count and percutaneous coronary intervention to long-term outcomes after thrombolytic administration in acute myocardial infarction. *Circulation* 2002; 105: 1909-13.
11. Hoffmann P, Haager P, Lepper W, Franke A, Hanrath P. Relation of coronary flow pattern to myocardial blush grade in patients with first acute myocardial infarction. *Heart* 2003; 89: 1147-51.
12. Henriques JP, Zijlstra F, van't Hof AW, de Boer MJ, Dambrink JH, Gosselink M, et al. Angiographic assessment of reperfusion in acute myocardial infarction by myocardial blush grade. *Circulation* 2003; 107: 2115-9.
13. Niccoli G, Burzotta F, Galiuto L, Crea F. Myocardial no-reflow in humans. *J Am Coll Cardiol* 2009; 54: 281-92.
14. Schröder R. Prognostic impact of early ST-segment resolution in acute ST-elevation myocardial infarction. *Circulation* 2004; 110: e506-10.

15. Sorajja P, Gersh BJ, Costantini C, McLaughlin MG, Zimetbaum P, Cox DA, et al. Combined prognostic utility of ST-segment recovery and myocardial blush after primary percutaneous coronary intervention in acute myocardial infarction. *Eur Heart J* 2005; 26: 667-74.
16. Giugliano RP, Sabatine MS, Gibson CM, Roe MT, Harrington RA, Murphy SA, et al. Combined assessment of thrombolysis in myocardial infarction flow grade, myocardial perfusion grade and ST-segment resolution to evaluate epicardial and myocardial reperfusion. *Am J Cardiol* 2004; 93: 1362-7.
17. Buller CE, Fu Y, Mahaffey KW, Todaro TG, Adams P, Westerhout CM, et al. ST-segment recovery and outcome after primary percutaneous coronary intervention for ST-elevation myocardial infarction: insights from the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial. *Circulation* 2008; 118: 1335-46.
18. van't Hof AW, Liem A, de Boer MJ, Zijlstra F. Clinical value of 12-lead electrocardiogram after successful reperfusion therapy for acute myocardial infarction. Zwolle Myocardial Infarction Study Group. *Lancet* 1997; 350: 615-9.
19. Steg PG, James SK, Atar D, Badano LP, Blömmstrom-Lundqvist C, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012; 33: 2569-619.
20. van't Hof AW, Liem A, Suryapranata H, Hoorntje JC, de Boer MJ, Zijlstra F. Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction: myocardial blush grade. Zwolle Myocardial Infarction Study Group. *Circulation* 1998; 97: 2302-6.
21. Gibson CM, de Lemos JA, Murphy SA, Marble SJ, McCabe CH, Cannon CP, et al. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction – a TIMI 14 substudy. *Circulation* 2001; 103: 2550-4.
22. Salles GF, Cardoso CRL, Leocardio SM, Muxfeldt ES. Recent ventricular repolarization markers in resistant hypertension: are they different from the traditional QT interval? *Am J Hypertens* 2008; 21: 47-53.
23. Erikssen G, Liestøl K, Gullestad L, Haugaa KH, Bendz B, Amlie JP. The terminal part of the QT interval (T peak to T end): a predictor of mortality after acute myocardial infarction. *Ann Noninvasive Electrocardiol* 2012; 17: 85-94.
24. Higashi Y, Nakagawa K, Kimura M, Noma K, Hara K, Sasaki S, et al. Circadian variation of blood pressure and endothelial function in patients with essential hypertension: a comparison of dippers and non-dippers. *J Am Coll Cardiol* 2002; 40: 2039-43.
25. Evola S, Cuttitta F, Evola G, Macaione F, Piraino D, Meschisi MC, et al. Early detection of coronary artery flow and myocardial perfusion impairment in hypertensive patients evidenced by Myocardial Blush Grade (MBG) and Thrombolysis in Myocardial Infarction (TIMI) Frame Count (TFC). *Intern Med* 2012; 51: 1653-60.
26. Jankowski P, Kawecka-Jaszcz K, Czarnecka D. Ascending aortic blood pressure waveform is related to coronary atherosclerosis in hypertensive as well as in normotensive subjects. *Blood Press* 2007; 16: 246-53.
27. Shenthathar J, Deora S, Rai M, Nanjappa Manjunath C. Prolonged Tpeak-end and Tpeak-end/QT ratio as predictors of malignant ventricular arrhythmias in the acute phase of ST-segment elevation myocardial infarction: a prospective case-control study. *Heart Rhythm* 2015; 12: 484-9.
28. Michael G, Xiao L, Qi XY, Dobrev D, Nattel S. Remodelling of cardiac repolarization: How homeostatic responses can lead to arrhythmogenesis. *Cardiovasc Res* 2009; 81: 91-9.
29. Endoh Y, Kasanuki H, Ohnishi S, Shibata N, Hosoda S. Influence of early coronary reperfusion on QT interval dispersion after acute myocardial infarction. *Pacing Clin Electrophysiol* 1997; 20: 1646-53.
30. Nikiforos S, Hatzisavvas J, Pavlides G, Voudris V, Vassilikos VP, Manginas A, et al. QT-interval dispersion in acute myocardial infarction is only shortened by thrombolysis in myocardial infarction grade 2/3 reperfusion. *Clin Cardiol* 2003; 26: 291-5.
31. Duyuler PT, Duyuler S, Demir M. Impact of myocardial blush grade on Tpe interval and Tpe/QT ratio after successful primary percutaneous coronary intervention in patients with ST elevation myocardial infarction. *Eur Rev Med Pharmacol Sci* 2017; 21: 143-9.
32. Demir M, Uyan U. Evaluation of Tp-e interval and Tp-e/QT ratio in patients with non-dipper hypertension. *Clin Exp Hypertens* 2014; 36: 285-8.
33. Tokatlı A, Kılıçaslan F, Alış M, Yiğiner O, Uzun M. Prolonged Tp-e Interval, Tp-e/QT Ratio and Tp-e/QTc Ratio in Patients with Type 2 Diabetes Mellitus. *Endocrinol Metab (Seoul)* 2016; 31: 105-12.