

Tp-e/QTc ratio, SYNTAX, and GRACE score in patients who underwent coronary angiography owing to acute coronary syndrome

Kadriye Gayretli Yayla^{1, 2} , Çağrı Yayla³ , Mehmet Akif Erdöl³ , Mustafa Karanfil³ ,
Hamza Sunman¹ , Faruk Aydın Yılmaz¹ , Nail Burak Özbeyaz¹ ,
Ayşe Nur Özkaya İbiş¹ , Murat Tulmaç¹ 

¹Department of Cardiology, Health Sciences University, Dışkapı Yıldırım Beyazıt Training and Research Hospital; Ankara-Turkey

²Department of Cardiology, Health Sciences University, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital; Ankara-Turkey

³Department of Cardiology, Health Sciences University, Ankara City Hospital; Ankara-Turkey

ABSTRACT

Objective: Ventricular arrhythmias following acute coronary syndrome (ACS) range from benign to life-threatening fatal arrhythmias. Tpeak-end (Tp-e) interval has been shown to be an important parameter in the assessment of repolarization dispersion. We aimed to evaluate the relationship between SYNTAX and Global Registry of Acute Coronary Events (GRACE) risk score calculated on admission and Tp-e interval and Tp-e/QTc ratio.

Methods: A total of 421 patients were included in the study. The patients were divided into 2 groups as low SYNTAX score (≤ 22) and moderate and high risk SYNTAX score (> 22). According to the GRACE risk score, the patients were divided into 2 groups; high-risk patients ≥ 140 and < 140 low-risk patients.

Results: In the group with SYNTAX score > 22 , the Tp-e interval ($p < 0.001$) and Tp-e/QTc ratio ($p < 0.001$) was found to be significantly higher than in the group with a SYNTAX score ≤ 22 . Tp-e interval ($p < 0.001$) and Tp-e/QTc ratio ($p = 0.002$) was higher in patients with GRACE risk score ≥ 140 compared with patients with a GRACE risk score < 140 . The correlation between Tp-e interval and Tp-e/QTc ratio and SYNTAX score ($r = 0.489$; $p < 0.001$) and GRACE risk score ($r = 0.274$; $p < 0.001$) were found to be significant. A significant and independent correlation was found between the SYNTAX score and Tp-e/QTc ratio ($\beta = 0.385$; $p < 0.001$).

Conclusion: Tp-e interval and Tp-e/QT ratio increased in patients with severe coronary artery disease assessed with SYNTAX score. Tp-e interval and Tp-e/QT ratio increased in patients with a high GRACE risk score.

Keywords: acute coronary syndrome, GRACE risk score, SYNTAX score, Tp-e/QTc

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Introduction

Ventricular arrhythmias that occur after acute coronary syndromes (ACS) range from benign to life-threatening deadly arrhythmias. Although the incidence of arrhythmias in ACS is more in ST-segment elevation myocardial infarction (STEMI) than in non-ST segment elevation myocardial infarction

(NSTEMI), clinicians should be careful about arrhythmias in all the patients with ACS.

Approximately 90% of patients with acute myocardial infarction (AMI) develop various cardiac arrhythmias. Arrhythmias occur in the first 24 hours of the onset of infarction. The risk of life-threatening arrhythmia such as ventricular tachycardia (VT) and ventricular fibrillation (VF) is frequently observed in those

Address for Correspondence: Dr. Çağrı Yayla, Sağlık Bilimleri Üniversitesi,
Ankara Şehir Hastanesi, Kardiyoloji Kliniği, Ankara-Türkiye
E-mail: cagriyayla@gmail.com

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HIGHLIGHTS

- Tp-e interval and Tp-e/QT ratio are easily accessible, inexpensive, and non-invasive methods that can be useful markers for predicting ventricular arrhythmias.
- The SYNTAX scoring system was developed to evaluate the severity of coronary artery disease.
- The Global Registry of Acute Coronary Events (GRACE) risk score has a good discriminative power and provides the most accurate classification of risk, both during admission and out of hospital in patients with acute coronary syndromes.
- Tp-e interval and Tp-e/QT ratio increased in patients with severe coronary artery disease assessed with SYNTAX score.
- In patients with a high SYNTAX score, the GRACE risk score was also high. In addition, Tp-e interval and Tp-e/QT ratio increased in patients with a high GRACE risk score.

with left ventricular ejection fraction (LVEF) <30% and multiple vascular disease (1).

The SYNTAX scoring system was developed to evaluate the severity of coronary artery disease (CAD). This scoring system is a guide in terms of deciding treatment in patients who are candidates for percutaneous coronary intervention (PCI) or coronary artery bypass surgery (2). The Global Registry of Acute Coronary Events (GRACE) is a scoring system that is used for risk classification in patients with a risk of ACS and is calculated by clinical parameters such as age, heart rate, systolic blood pressure, creatinine value, arrest history at admission, Killip classification, and abnormal cardiac enzyme value. The GRACE risk score, which is based on direct comparisons, has a good discriminative power and provides the most accurate classification of risk both in admission and out of hospital.

The Tpeak-end (Tp-e) interval, which is one of the ventricular repolarization parameters used in recent years as a predictor of arrhythmic events, has been shown to be an important parameter in evaluating the transmural and global dispersion of repolarization and can be used to evaluate arrhythmic risk (3).

In this study, we aimed to evaluate the relationship between Tp-e interval and Tp-e/QTc ratio and the SYNTAX score and GRACE risk score in patients who underwent coronary angiography for ACS.

Methods

Our study was performed retrospectively and cross sectionally in patients diagnosed with ACS who presented to our hospital between July 2018 and May 2019 in the cardiology clinic.

Patients who underwent coronary angiography for the diagnosis of ACS were included. Patients with serious valve disease, severe chronic kidney disease, serious lung disease, chronic systemic inflammatory disease, history of malignancy, complete and/or incomplete branch block, atrial fibrillation, antiarrhythmic drug use, and pace rhythm were excluded from the study. Of the 502 patients with ACS who were screened retrospectively, 81 were excluded because they did not meet the inclusion criteria or had exclusion criteria. Our study was conducted in accordance with the guidelines proposed in the Helsinki Declaration and approved by Local Ethics Committee (Decision date-no: 28/06/2019-66/16).

Demographic characteristics of the patients, height, weight, troponin, glucose, creatinine, sodium, potassium, calcium, magnesium, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride, hemoglobin, and platelets, and electrocardiography, echocardiography, and coronary angiography images were examined from archives of patient files.

Hypertension was defined as documentation of systolic blood pressure of 140 mm Hg and/or diastolic blood pressure \geq 90 mm Hg in at least 2 measurements or as active use of any antihypertensive agent.

Diabetes mellitus was defined as fasting plasma glucose level >126 mg/dL or glucose level >200 mg/dL in any measurement or actively using an antidiabetic agent.

The patients were divided into 2 groups on the basis of SYNTAX score as low (\leq 22) and moderate and high risk (>22). Images of the angiogram were evaluated by 2 experienced interventional cardiologists. The SYNTAX score was calculated using the site "<http://www.syntaxscore.com>." Interobserver and intraobserver coefficients of variation were 2.0% and 2.3% respectively.

The GRACE risk score was calculated using the site, "<https://www.mdcalc.com/grace-acs-risk-mortality-calculator>." Parameters on admission such as age, heart rate, systolic blood pressure, creatinine value, history of arrest during on admission, Killip classification, and abnormal cardiac enzyme were calculated. The patients were divided into 2 groups according to the GRACE risk score of \geq 140 with high risk and GRACE risk score of <140 as low risk.

Echocardiography

Echocardiographic assessment was performed using a VIVID 7 Dimension Cardiovascular Ultrasound System (Vingmed-General Electric, Horten, Norway) with a 3.5 MHz transducer. Echocardiographic examination was performed in the left lateral decubitus position. Parasternal long- and short-axis views and apical views were used as standard imaging windows. Ejection fraction was calculated using the modified Simpson method. Septal and posterior wall thickness and end-systolic and end-diastolic dimensions were measured from parasternal long-axis view. All the echocardiographic examinations were performed by an experienced cardiologist.

Electrocardiography

The 12-lead ECG was recorded at a paper speed of 50 mm/s (Hewlett Packard, Page-writer, USA) in the supine position. To decrease the error in measurements, all the ECGs were scanned and transferred to a personal computer and then used at 400x% magnification by Adobe Photoshop software. ECG measurements of QT and Tp-e intervals were performed by 2 cardiologists who were blinded to the patient data. Patients with U waves on their ECGs were excluded from the study. The QT interval was measured from the beginning of the QRS complex to the end of the T wave and corrected for heart rate using the Bazett formula: $cQT = QT\sqrt{(R-R \text{ interval})}$. Measurements of the Tp-e interval were performed from V4-V6 precordial leads, and an average value of at least 3 readings was calculated for each lead and measurement. The measurement of each parameter was obtained by averaging 3 consecutive beats. Because of the dispersion of Tp-e interval between infarction-related and non-infarction related leads, the maximum of Tp-e in all measured leads was in the infarction-related lead and entered into the analysis. The Tp-e interval was obtained from the peak of the T-wave to the end of T-wave in ST-segment elevated leads. In the case of negative or biphasic T-waves, QTpeak was measured to the nadir of the T-wave. Twenty-one patients whose elevated ST-segment and T-waves on ECG fused into a monophasic curve were excluded from the study. The Tp-e/QT ratio was calculated from these measurements (Fig. 1) (4, 5). Interobserver and intraobserver coefficients of variation were 2.9% and 2.1% respectively.

Statistical analysis

The data analysis was performed using the Statistical Package for Social Sciences Program for Windows version 21.0 (SPSS Inc., Chicago, IL, USA). To test normality of distribution, the Kolmogorov-Smirnov test was used. Quantitative variables with a

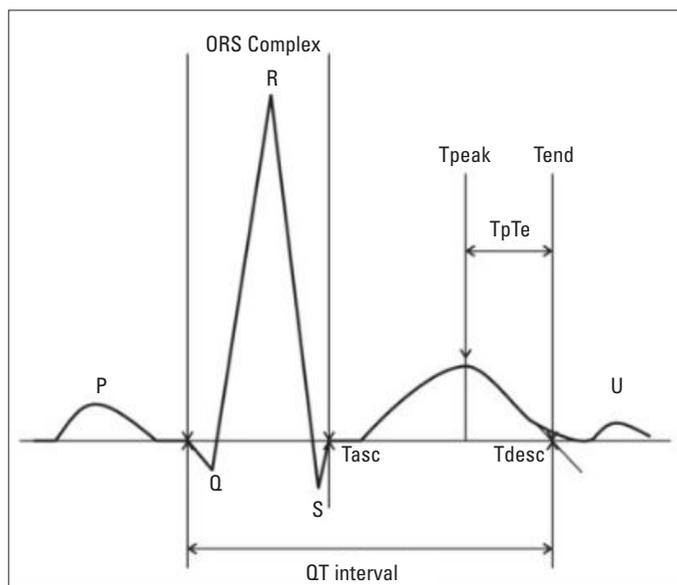


Figure 1. Measurement of Tp-e interval

Table 1. Clinical characteristics and laboratory findings of the study population

Parameters	n=421
Age, years	59.6±12.4
Sex, male, n (%)	302 (71.7)
Hypertension, n (%)	226 (53.6)
Diabetes mellitus, n (%)	289 (68.6)
Smoking, n (%)	228 (54.1)
Type of ACS, n (%)	
USAP	39 (9.2)
NSTEMI	140 (33.2)
STEMI	242 (57.4)
LVEF, %	50 (38.5–60)
Systolic blood pressure, mm Hg	132 (120–151.5)
Diastolic blood pressure, mm Hg	80 (70–90)
Height, cm	169 (162–175)
Weight, kg	78 (70–85)
Troponin on admission, pg/mL	140 (18–1815)
Peak troponin, pg/mL	5443 (597–22100)
CK, U/l	134 (83–301)
CKMB, U/l	21 (15–36)
Glucose, mg/dL	132 (107–180)
Creatinine, mg/dL	0.99 (0.88–1.13)
Sodium, mEq/L	137 (135–138)
Potassium, mmol/L	4.1±0.4
Calcium, mg/dL	9.4±0.5
Magnesium, mg/dL	1.9±0.1
ALT, IU/l	21 (15–33)
TSH, µIU/mL	1.17 (0.68–2.02)
Total cholesterol, mg/dL	178 (147–205)
LDL cholesterol, mg/dL	126.7±37.8
HDL cholesterol, mg/dL	37 (32–43)
Triglyceride, mg/dL	134 (97–197)
Hemoglobin, g/dL	14.1±1.8
Platelet count, 10 ³ /mm ³	250 (210–301.5)
SYNTAX score	12.5±8.7
GRACE score	105.0±28.3
Heart rate, beat/min	79.3±17.5
Tp-e interval, ms	78.9±11.7
QT interval, ms	374.1±42.2
QTc interval, ms	405.4±31.8
Tp-e/QT ratio	0.21±0.04
Tp-e/QTc ratio	0.19±0.03
Drugs, n (%)	
Antiplatelets	331 (78.6)
ACEi/ARBs	296 (70.3)
Statins	175 (41.5)
β-blockers	246 (58.4)
Calcium channel blocker	107 (25.4)

ALT - alanine aminotransferase; ACEi - angiotensin-converting-enzyme inhibitors; ARB - angiotensin II receptor blockers; ACS - acute coronary syndrome; CK - creatine kinase; CKMB - creatine kinase myocardial band; HDL - high-density lipoproteins; LDL - low-density lipoproteins; LVEF - left ventricular ejection fraction; NSTEMI - non-ST segment elevation myocardial infarction; STEMI - ST segment elevation myocardial infarction; TSH - thyroid-stimulating hormone; USAP - unstable angina pectoris

normal distribution were specified as the mean \pm standard deviation, and variables with non-normal distribution were presented as median (interquartile range). Categorical variables were shown as number and percentage values. Categorical variables were compared with the chi-squared test. Differences between the groups were evaluated using Student's t-test. Mann-Whitney U test was used to compare the parameters with non-normal distribution. Pearson correlation analysis was performed to examine the relationship between Tp-e interval, Tp-e/QTc ratio, and SYNTAX and GRACE scores. A p value of <0.05 was accepted as statistically significant. Multiple linear regression analysis was performed to determine the independent predictors of the Tp-e/QTc ratio. Possible confounding factors were tested in univariate regression model and confounders with a p value of <0.1 were tested in multivariate linear regression analysis. A p value of <0.05 was accepted as statistically significant.

Results

Clinical and demographical characteristics of study groups are shown in Table 1. The mean age of the participants was 59.6 ± 12.4 years and 71.7% of patients were men. The patients were divided into 2 groups according to the SYNTAX scores; low (≤ 22) and moderate–high group (>22). Among baseline characteristics, the type of ACS ($p=0.002$), EF ($p<0.001$), peak troponin level ($p<0.001$), and the GRACE risk score ($p=0.008$) were significantly higher in the moderate–high SYNTAX group. In addition, Tp-e interval, QTc interval, Tp-e/QT ratio, and Tp-e/QTc ratio were significantly higher in the group with a moderate–high SYNTAX score (Table 2).

Patients with a high GRACE risk score (≥ 140) were older ($p<0.001$), and the rate of hypertension was lower than patients

with low–moderate GRACE risk score (<140) ($p<0.001$). In addition, systolic and diastolic blood pressures were lower ($p<0.001$), the patients were shorter and weaker ($p<0.001$), peak troponin levels were higher ($p=0.011$), and creatinine values were increased in patients with a high GRACE risk score ($p<0.001$). In addition, heart rate, Tp-e interval, QTc interval, Tp-e/QT ratio, and Tp-e/QTc ratio were significantly higher in the group with a high GRACE risk score (Table 3).

The correlation between Tp-e interval and SYNTAX score ($r=0.489$; $p<0.001$) and GRACE risk score ($r=0.274$; $p<0.001$) was statistically significant. The Tp-e/QTc ratio and SYNTAX score ($r=0.364$; $p<0.001$) and GRACE risk score ($r=0.134$; $p=0.006$) was statistically significant (Fig. 2 and 3). Multivariate linear regression analysis showed a significant and independent correlation between SYNTAX score and Tp-e/QTc ratio ($\beta=0.385$; $p<0.001$) (Table 4).

Discussion

This is the first study comparing noninvasive ECG parameters such as Tp-e interval and Tp-e/QTc ratio with the severity of coronary artery disease and mortality risk at admission in patients who underwent coronary angiography for ACS. Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios were also increased in patients with a high SYNTAX score and high GRACE risk score in patients underwent coronary angiography owing to ACS. We also found a significant and independent correlation between SYNTAX score and Tp-e/QTc ratio.

Since 2009, several studies have tested the accuracy of SYNTAX score as a risk algorithm for predicting negative results. There is an increased risk of many negative outcome events, including ventricular arrhythmia in patients with a high SYNTAX

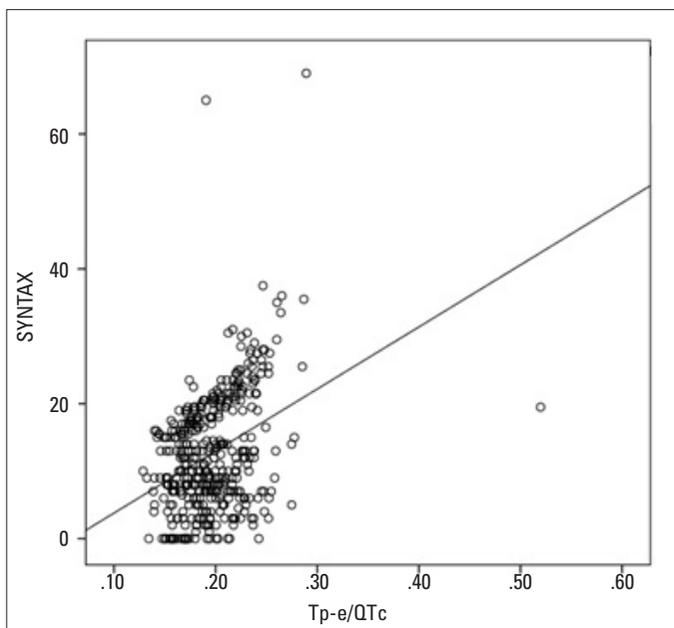


Figure 2. The correlation between Tp-e/QTc ratio and SYNTAX score

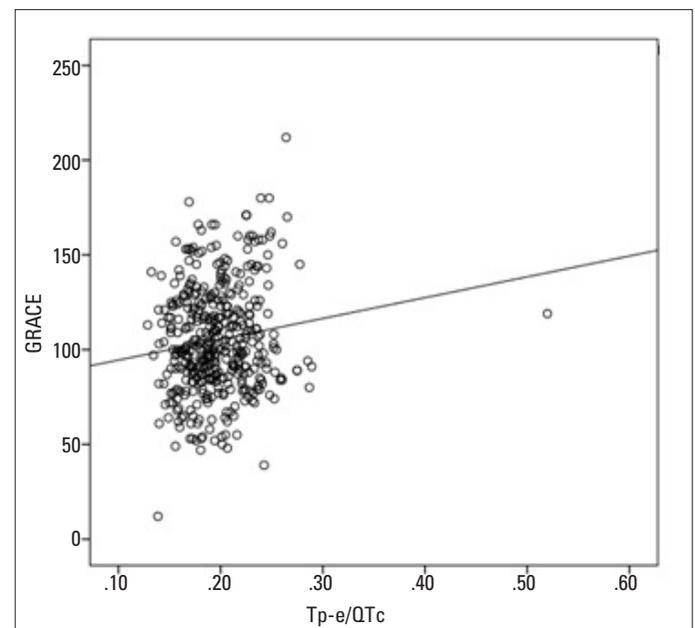


Figure 3. The correlation between Tp-e/QTc ratio and GRACE score

Table 2. Basal characteristics of patients according to SYNTAX score severity

Parameters	SYNTAX ≤22 (n=369)	SYNTAX >22 (n=52)	P-value
Age, years	59.3±12.2	61.8±13.7	0.173
Sex, male, n (%)	263 (71.2)	39 (75.0)	0.576
Hypertension, n (%)	198 (53.6)	28 (53.8)	0.995
Diabetes mellitus, n (%)	254 (68.8)	35 (48.0)	0.781
Smoking, n (%)	197 (53.3)	31 (59.6)	0.410
Type of ACS, n (%)			
USAP	39 (10.5)	0 (0)	0.002
NSTEMI	129 (34.9)	11 (21.1)	
STEMI	201 (54.4)	41 (78.8)	
LVEF, %	50 (40–60)	35 (32–45)	<0.001
Systolic blood pressure, mm Hg	134 (120–152)	130 (107–149)	0.089
Diastolic blood pressure, mm Hg	80 (70–90)	80 (61–90)	0.314
Height, cm	168 (162–175)	170 (165–174)	0.645
Weight, kg	78 (70–85)	77 (70–84)	0.934
Troponin on admission, pg/mL	137 (15–1764)	325 (62–3403)	0.096
Peak troponin, pg/mL	4189 (539–18750)	23631 (13544–119440)	<0.001
CK, U/l	129 (80–271)	168 (101–626)	0.082
CKMB, U/l	21 (15–35)	23 (17–44)	0.104
Glucose, mg/dL	132 (106–173)	145 (113–222)	0.048
Creatinine, mg/dL	0.98 (0.88–1.12)	1.04 (0.89–1.25)	0.157
Sodium, mEq/L	137 (135–138)	136 (134–138)	0.342
Potassium, mmol/L	4.0±0.4	4.1±0.4	0.840
Calcium, mg/dL	9.4±0.6	9.3±0.5	0.117
Magnesium, mg/dL	1.9±0.2	1.8±0.1	0.152
ALT, IU/L	21 (15–32)	24 (16–42)	0.083
TSH, µIU/mL	1.16 (0.68–2.00)	1.22 (0.66–2.18)	0.848
Total cholesterol, mg/dL	177 (146–204)	184 (149–207)	0.685
LDL cholesterol, mg/dL	126.6±38.3	127.7±35.2	0.857
HDL cholesterol, mg/dL	37 (32–42)	38 (32–44)	0.740
Triglyceride, mg/dL	134 (97–198)	138 (96–193)	0.786
Hemoglobin, g/dL	14.1±1.8	13.9±2.0	0.393
Platelet count, 10 ³ /mm ³	249 (213–298)	256 (212–335)	0.391
SYNTAX score	10.3±6.1	28.0±8.7	<0.001
GRACE score	103.7±27.6	114.8±31.9	0.008
Heart rate, bpm	79.0±17.1	81.8±20.1	0.280
Tp-e interval, ms	76.5±10.1	96.2±6.5	<0.001
QT interval, ms	373.1±40.6	381.1±52.5	0.210
QTc interval, ms	404.0±30.5	415.1±38.7	0.019
Tp-e/QT ratio	0.21±0.04	0.25±0.03	<0.001
Tp-e/QTc ratio	0.19±0.03	0.23±0.02	<0.001

ALT - alanine aminotransferase; ACEi - angiotensin-converting-enzyme inhibitors; ARB - angiotensin II receptor blockers; ACS - acute coronary syndrome; CK - creatine kinase; CKMB - creatine kinase myocardial band; HDL - high-density lipoproteins; LDL - low-density lipoproteins; LVEF - left ventricular ejection fraction; NSTEMI - non-ST segment elevation myocardial infarction; STEMI - ST segment elevation myocardial infarction; TSH - thyroid-stimulating hormone; USAP - unstable angina pectoris

Table 3. Basal characteristics of patients according to GRACE score severity

Parameters	GRACE <140 (n=367)	GRACE ≥140 (n=54)	P-value
Age, years	56.9±10.5	78.2±8.4	<0.001
Sex, male n (%)	277 (75.4)	25 (46.2)	<0.001
Hypertension, n (%)	211 (57.4)	15 (27.7)	<0.001
Diabetes mellitus, n (%)	253 (68.9)	36 (66.6)	0.860
Smoking, n (%)	182 (49.5)	46 (85.1)	<0.001
Type of ACS, n (%)			
USAP	38 (10.3)	1 (1.8)	0.098
NSTEMI	123 (33.5)	17 (31.4)	
STEMI	206 (56.1)	36 (66.6)	
LVEF, %	50 (40–60)	35 (45–55)	0.108
Systolic blood pressure, mm Hg	136 (120–155)	123 (109–140)	<0.001
Diastolic blood pressure, mm Hg	80 (70–92)	70 (60–80)	<0.001
Height, cm	170 (164–175)	165 (160–170)	<0.001
Weight, kg	79 (70–85)	70 (65–80)	<0.001
Troponin on admission, pg/mL	133 (16–1752)	244 (34–2820)	0.300
Peak troponin, pg/mL	4449 (549–20783)	17122 (3452–57265)	0.011
CK, U/l	140 (87–302)	101 (66–254)	0.038
CKMB, U/l	21 (15–35)	21 (16–53)	0.450
Glucose, mg/dL	132 (107–175)	147 (107–223)	0.184
Creatinine, mg/dL	0.97 (0.86–1.09)	1.24 (1.05–1.59)	<0.001
Sodium, mEq/L	137 (135–138)	137 (135–138)	0.524
Potassium, mmol/L	4.1±0.4	4.1±0.5	0.208
Calcium, mg/dL	9.4±0.5	9.2±0.6	0.003
Magnesium, mg/dL	1.9±0.1	1.9±0.2	0.720
ALT, IU/L	23 (16–33)	15 (11–25)	<0.001
TSH, µIU/mL	1.21 (0.70–2.03)	1.03 (0.63–1.87)	0.280
Total cholesterol, mg/dL	179 (148–205)	177 (135–194)	0.438
LDL cholesterol, mg/dL	127.2±32.5	123.3±40.2	0.525
HDL cholesterol, mg/dL	37 (32–42)	37 (32–44)	0.868
Triglyceride, mg/dL	138 (100–200)	107 (82–183)	0.017
Hemoglobin, g/dL	14.3±1.8	12.8±1.6	<0.001
Platelet count, 10 ³ /mm ³	255 (213–302)	231 (206–290)	0.040
SYNTAX score	12.2±8.6	14.8±9.0	0.036
GRACE score	97.6±21.7	155.4±13.2	<0.001
Heart rate, bpm	78.4±16.7	85.8±21.3	0.004
Tp-e interval, ms	77.8±11.3	86.7±11.5	<0.001
QT interval, ms	374.0±41.3	374.7±48.3	0.916
QTc interval, ms	403.9±30.8	415.3±36.7	0.015
Tp-e/QT ratio	0.21±0.04	0.23±0.04	<0.001
Tp-e/QTc ratio	0.19±0.03	0.21±0.03	0.002

ALT - alanine aminotransferase; ACEi - angiotensin-converting-enzyme inhibitors; ARB - angiotensin II receptor blockers; ACS - acute coronary syndrome; CK - creatine kinase; CKMB - creatine kinase myocardial band; HDL - high-density lipoproteins; LDL - low-density lipoproteins; LVEF - left ventricular ejection fraction; NSTEMI - non-ST segment elevation myocardial infarction; STEMI - ST segment elevation myocardial infarction; TSH - thyroid-stimulating hormone; USAP - unstable angina pectoris

Table 4. Multiple linear regression analysis for the prediction of Tp-e/QT ratio

Variables	Univariate		Multivariate	
	β	P-value	β	P-value
LVEF	-0.114	0.030	0.026	0.981
Age	0.048	0.333	-	-
Peak troponin	0.121	0.044	0.037	0.540
SYNTAX score	0.364	<0.001	0.385	<0.001
GRACE score	0.134	0.006	0.063	0.303

LVEF - left ventricular ejection fraction

score. In a recent study, the severity of CAD was investigated in patients with cardiac arrest after non-hospital refractory VF, and a high prevalence of CAD, acute thrombotic lesions, and chronic total obstruction was found in the patient group with arrest caused by refractory VF/VT (6).

Arrhythmic events are higher in patients with increased coronary artery stenosis and severity. Enhanced dispersion of repolarization as a major factor in the development of serious and fatal arrhythmias, especially in the presence of myocardial ischemia. Myocardial ischemia in patients with extensive and severe CAD is a process affecting larger areas of the ventricular myocardium. Therefore, the severity of localized ischemia will have a dominant effect on ventricular repolarization parameters. Di Marco et al. (7) showed that in ischemic patients implanted with an ICD for primary prevention, a chronic total occlusion, one of the most important parameters in increasing the SYNTAX score, associated with a previous infarction in its territory, is an independent predictor of VA, especially of fast VT/VF. Kul et al. (8) found that VT/VF was significantly higher in patients with a high SYNTAX score (>21.75) than in the lower group in 646 patients with STEMI undergoing primary PCI. Stierle et al. (9) found that increased dispersion of ventricular repolarization parameter as measured QT dispersion associated with the extent of myocardial ischemia in patients with multivessel CAD. Yilmaz et al. (10) showed the rest QT dispersion is increased and related to the extent and severity of coronary atherosclerosis as measured with gensini score in patients with stable CAD. Helmy et al. (11) observed a significant positive correlation between corrected QT dispersion and severity of coronary artery disease as assessed by SYNTAX score. Recently, Kahraman et al. (12) found a strong and positive correlation between CAD severity as measured by SYNTAX score and prolonged Tp-e interval and increased Tp-e/QT and Tp-e/QTc ratios.

The GRACE risk score estimates the risk of in-hospital death and death within 6 months after discharge. There are several studies demonstrating that the risk of ventricular arrhythmia also increases in patients with high GRACE risk score. Zorzi et al. (13) prospectively examined 1,325 consecutive patients who were admitted with NSTEMI. The primary endpoint of the study was spontaneous (unrelated to coronary interventions) of in-

hospital, life-threatening ventricular arrhythmias, including continuous VT and VF. The secondary endpoint was in-hospital death for all reasons. They showed that GRACE risk score >140 and LVEF <35% were found to be independent predictors of life-threatening ventricular arrhythmias in hospital. Masuda et al. (14) researched 4,283 consecutive hospitalized patients within 12 hours from the onset of STEMI and undergoing PCI. Subgroup analysis showed that VT/VF in the acute phase was associated with a 5-year mortality increase after discharge in patients with a GRACE risk score \geq 115.

Ventricular repolarization markers have been used for risk classification in various clinical settings, including the corrected QT (QTc) interval (15) and QT dispersion (16). Increasing ventricular repolarization dispersion is associated with malign arrhythmias and has prognostic importance in terms of mortality and sudden cardiac death (17). QT dispersion was clarified as a sign of increased dispersion of repolarization but finally lost its importance as a defective concept (18, 19). Nowadays, the Tp-e interval and Tp-e/QT ratio have been evaluated as actual markers of increased dispersion of ventricular repolarization (20-22). Prolongation of Tp-e interval was related with increased mortality in Brugada syndrome, long QT syndrome, and in patients with acute STEMI (20). Nevertheless, Tp-e interval is affected by alterations in body weight and heart rate (23). In recent studies, the Tp-e/QT ratio was proposed to be a more accurate measure of the dispersion of ventricular repolarization than QT dispersion, QTc dispersion, and Tp-e intervals and to be independent of variations in the heart rate (21, 23).

Tp-e interval >0.1 second and Tp-e/QT ratio >0.3 predicted VF with 100% sensitivity in a prospective case-control study with 50 patients with STEMI. Both Tp-e interval and Tp-e/QT ratios were found to be predictors of malignant ventricular arrhythmias in the acute phase of STEMI (24). Erikssen et al. (25) found that Tp-e interval was a particularly strong determinant of fatal cardiac arrhythmia in patients with STEMI and NSTEMI. In a cross-sectional study, prolonged Tp-e interval observed before and after the procedure was a predictor of incomplete ST segment resolution and incomplete reperfusion in patients who underwent primary PCI after myocardial infarction (4). Çoner et al. (26) found that Tp-e interval was a predictor for reperfusion success in patients with STEMI treated with fibrinolytic agents.

Patients after MI have a lifetime risk of ventricular arrhythmia and sudden cardiac death, 4 times higher than the general population (27). Arrhythmias may be caused not only by the death of cardiomyocytes and fibrotic scar replacement, but also by the exposure of dramatic electrophysiological reconstruction, altered action potential, and conductive properties near the infarct (border region) (28).

Atherosclerosis is a chronic inflammatory disease and the leading cause of myocardial infarction. In atherosclerotic mice models, there is a 14-fold increase in circulating monocytes than in healthy mice (29); this results in an increased inflammatory response after myocardial infarction characterized by

increased uptake of inflammatory cells in the infarction, increased protease activity in the myocardium, and increased serum cytokines (30). Increased proinflammatory status has important functional consequences. For example, increased circulating monocyte levels following MI are associated with decreased functional recovery and adverse left ventricular remodeling (31). High serum cytokines are also associated with accelerating the progression to heart failure (32). Increased inflammation and the effects of inflammatory cytokines and proteases, such as interleukin-1 and matrix metalloproteinase-7 may affect susceptibility to electrophysiological remodeling and arrhythmia (33).

Factors such as the complex structure of coronary artery lesions, location of severe lesions and presence of calcification, location and frequency of bifurcation lesions, presence of chronic total occlusion increase the risk of ventricular arrhythmia (34). Therefore, as expected, the Tp-e interval and Tp-e/QT ratio increased in the patient group with severe coronary artery disease. In addition, in patients with a high GRACE risk score, the Tp-e interval and Tp-e/QT ratio increased more than in patients with a lower GRACE risk score. According to the results of our study, in patients with increased Tp-e and Tp-e/QT ratio and with high risk classification at the time of hospital admission, close follow-up and early administration of anti-arrhythmia approaches in the early period can reduce the risk of mortality and morbidity owing to ventricular arrhythmia.

Study limitations

There are some limitations of this study. First, our study had a relatively small sample size. Second, the study was a single-center study. The relationship between ventricular arrhythmias and Tp-e interval and Tp-e/QT ratio was not assessed in patients. Therefore, long-term follow-up and large-scale prospective studies are needed to investigate the predictive value of the Tp-e interval and Tp-e/QT ratio in patients with high risk scores.

Conclusion

In our study, the Tp-e interval and Tp-e/QT ratio, indicators of ventricular repolarization dispersion, increased in patients with severe coronary artery disease. GRACE risk score was also higher in the group with a high SYNTAX score. However, the Tp-e interval and Tp-e/QT ratio also increased in patients with a high GRACE risk score. To the best of our knowledge, our study is the first to evaluate the Tp-e interval and Tp-e/QT ratio together with the SYNTAX and GRACE risk scores in patients with ACS. Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios are simple, easily accessible, inexpensive, and non-invasive methods that could be a useful index of ventricular repolarization and may also predict ventricular arrhythmias, a major problem in patients with high risk scores and severe CAD.

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