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Relationship of Frontal QRS-T Angle with Coronary Flow Grade and Adverse Events Before Percutaneous Coronary Intervention in Patients with Non-ST-Elevation Myocardial Infarction

ST Segment Yükselmesiz Miyokard Enfarktüslü Hastalarda Perkütan Koroner Girişim Öncesi Frontal QRS-T Açısının Koroner Akım Derecesi ve Advers Olaylarla Ilişkisi

ABSTRACT

Objective: Electrocardiography is used in the initial risk assessment of patients with non-ST-elevation myocardial infarction. The frontal QRS-T angle is an electrocardiography parameter that may be affected by the alterations in the coronary blood flow. This study aimed to explore the relationship of the frontal QRS-T angle with coronary flow grade and adverse events in non-ST-elevation myocardial infarction patients.

Methods: A total of 191 non-ST-elevation myocardial infarction patients were divided into 2 groups based on the thrombolysis in myocardial infarction (TIMI) flow level on coronary angiography before revascularization, namely TIMI 0/1 and TIMI 2/3. The frontal QRS-T angle obtained before revascularization was compared between the groups and its relationship with adverse events was examined. In-hospital all-cause mortality, repeat target lesion revascularization, new-onset heart failure, ventricular arrhythmias, and atrial fibrillation were defined as adverse events.

Results: Frontal QRS-T angle was wider in the patients with TIMI 0/1 flow compared to the patients with TIMI 2/3 flow ($P < 0.001$). The frontal QRS-T angle was determined to be a predictor of TIMI flow grade 0/1 before revascularization in patients with non-ST-elevation myocardial infarction (odds ratio: 1.51; 95% CI: 1.30-1.75; $P < 0.001$). The frontal QRS-T angle was a predictor of the adverse events during hospitalization in the patients with non-ST-elevation myocardial infarction (odds ratio: 1.11; 95% CI: 1.04-1.19; $P = 0.002$). The cut-off values of the frontal QRS-T angle for TIMI flow grade and adverse events were determined to be 73.5°, based on receiver operating characteristic curve analysis.

Conclusion: Increased frontal QRS-T angle may be a useful electrocardiography parameter for determining TIMI flow grade and the need for an early invasive strategy in patients with non-ST-elevation myocardial infarction.

Keywords: Electrocardiography, frontal QRS-T angle, STYzME, percutaneous coronary intervention

ÖZET

Giriş: Elektrokardiyografi (EKG), ST segment yükselmesiz miyokard enfarktüslü (STYzME) hastaların ilk risk değerlendirmesinde kullanılmaktadır. Frontal QRS-T [F(QRS-T)] açısı koroner kan akımındaki değişiklikten etkilenebilecek bir EKG belirtecidir. Bu çalışmanın amacı, STYzME hastalarında F(QRS-T) açısının koroner akış derecesi ve kötü klinik sonlanımlarla ilişkisini araştırmaktı.

Yöntemler: Toplam 191 STYzME hastası, revaskülarizasyon öncesi koroner anjiyografide (KAG) Thrombolysis in myocardial infarction (TIMI) akış derecesine göre TIMI 0/1 ve TIMI 2/3 olmak üzere iki gruba ayrıldı. Revaskülarizasyon öncesi elde edilen F(QRS-T) açısı gruplar arasında karşılaştırıldı ve kötü klinik sonlanımlarla ilişkisi incelendi. Hastane içi tüm nedenli mortalite, tekrarlanan hedef lezyon revaskülarizasyonu, yeni başlangıçlı kalp yetmezliği, ventriküler aritmiler ve atriyal fibrilasyon kötü klinik sonlanımlar olarak tanımlandı.

Bulgular: F(QRS-T) açısı TIMI 0/1 akışı olan hastalarda TIMI 2/3 akışı olan hastalara göre daha genişti ($P < 0,001$). F(QRS-T) açısı, STYzME'li hastalarda revaskülarizasyon öncesi TIMI akış derecesi 0/1'in göstergesi olduğu belirlendi (olasılık oranı [OO]: 1,51; %95 güven aralığı [GA]:

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KLİNİK ÇALIŞMA

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1,30–1,75; $P < 0,001$). F(QRS-T) açısı, STYzME'li hastalarda hastanede yatış sırasındaki kötü klinik sonlanımların göstergesiydi (OO: 1,11; %95 GA: 1,04–1,19; $P = 0,002$). ROC analizine göre TIMI akış derecesi ve kötü klinik sonlanımlar için F(QRS-T) açısının kesme seviyeleri 73,5° olarak belirlendi.

Sonuç: STYzME hastalarda artmış F(QRS-T) açısı TIMI akış derecesini ve erken dönem invaziv strateji ihtiyacını belirlemek için yararlı bir EKG parametresi olabilir.

Anahtar Kelimeler: Elektrokardiyografi, frontal QRS-T açısı, STYzME, perkütan koroner girişim

Acute myocardial infarction is still a major cause of mortality and morbidity worldwide despite improvements in medical treatment and extensive use of percutaneous coronary revascularization.[1] More than half of these patients present with non-ST-elevation myocardial infarction (NSTEMI) and they are at risk of adverse cardiac outcomes in the long-term follow-up.[2] In most cases, clinical history, electrocardiography (ECG), and cardiac troponin (cTn) levels are used for the diagnosis of ACS and for its prognostication.[3] Thrombolysis in myocardial infarction (TIMI) flow grade is another important parameter used in the prognostication of ACS.[4] The patency of the infarct-related artery (IRA) and its TIMI flow grade are associated with infarct size and survival in patients undergoing primary percutaneous coronary intervention (PCI).[5,6] The importance of determining the TIMI flow grade before PCI in patients with NSTEMI has not been investigated sufficiently despite the considerable significance of blood flux in the IRA.

Electrocardiography is a frequently used diagnostic tool in ACS diagnosis and prognostication.[7] However, the ECG may be relatively silent in patients with NSTEMI in the absence of acute coronary occlusion (ACO) causing infarction.[8] A non-trivial number of NSTEMI patients may even have ACO without having striking ECG findings (e.g., ST-segment elevation),[9-11] and these patients have more extensive infarct sizes and high mortality rates due to delayed diagnosis and treatment.[12,13] Therefore, additional clinical assistance is needed for the evaluation of these patients.[14] Several other ECG parameters, including frontal QRS-T [F(QRS-T)] angle, can inform clinicians about active or remote ischemia and electrical instability of the ventricular myocardial tissue.[15,16] Although recent studies have shown a change in F(QRS-T) angle secondary to disturbances in coronary flow and subsequent myocardial damage,[17,18] as far as we know, no studies have explored the relationship of F(QRS-T) angle before PCI and coronary flow grade on angiogram, and adverse events in patients with NSTEMI.

The aim of this study was to investigate the predictive value of the F(QRS-T) angle before PCI for TIMI flow grade on angiogram and adverse events in patients with NSTEMI.

ABBREVIATIONS

ACO	Acute coronary occlusion
cTn	Cardiac troponin
ECG	Electrocardiography
IRA	Infarct-related artery
NSTEMI	Non-ST-elevation myocardial infarction
PCI	Percutaneous coronary intervention
TIMI	Thrombolysis in myocardial infarction

Materials and Methods

Study Population

We retrospectively screened all consecutive patients over the age of 18 with a diagnosis of NSTEMI, who were admitted to our coronary care unit at Çanakkale Onsekiz Mart University Hospital, between January 2015 and August 2021. The study was approved by the Ethics Committee of Clinical Research of Çanakkale Onsekiz Mart University (Approval No: 2011-KAEK-27/2021-2100129433). The Declaration of Helsinki was complied to in all study procedures. As a result of the retrospective study design, written informed consent was not obtained from the participants before the study.

Non-ST-elevation myocardial infarction was diagnosed based on the following criteria[19]:

1. Typical chest pain and angina equivalents (such as dyspnea) that persisted for ≥30 minutes.
2. Typical fast increase and slow decrease in high-sensitivity cardiac troponin (hs-cTn) levels exceeding the 99th percentile values of the cut-off value for the particular hs-cTn assay.
3. The absence of STEMI criteria as defined in the fourth universal definition of MI.[19]

Patients with a history of coronary artery disease (CAD), chronic kidney disease (CKD) (estimated glomerular filtration rate < 30 mL/min/1.73 m^2), stroke, coronary artery bypass grafting (CABG) operation, permanent pacemaker, left ventricular ejection fraction (LVEF) below 40%, and cardiomyopathy; the presence of any bundle branch block or hemiblock (complete or incomplete), pathological Q waves, atrial fibrillation (AF), atrioventricular conduction abnormality, right or left ventricular hypertrophy, ST-segment elevation in aVR suggesting active diffuse subendocardial ischemia; any valvular disease at least in moderate severity, use of antiarrhythmic drugs other than beta-blockers, such as amiodarone, propafenone, sotalol; the presence of any electrolyte abnormality, active infection and/or malignant disease were excluded.

Adverse events were defined as the composite of in-hospital all-cause mortality, the need for repeat target lesion revascularization, new-onset heart failure (HF), ventricular arrhythmias, and new-onset AF. The term in-hospital all-cause mortality refers to both cardiovascular (including cardiac arrest, pulmonary edema, and cardiogenic shock) and non-cardiovascular death. The need for repeat target lesion revascularization was defined as the need for revascularization to restore lumen patency after the loss of lumen in the lesion responsible for the index infarct (re-intervention to address an acute re-occlusion within the previous

stent). New-onset HF with reduced ejection fraction was defined as new-onset HF in patients with no history of HF (LVEF ≤40%). New-onset AF was defined as an irregular rhythm in which no P waves were detected on the ECG in a patient who was in sinus rhythm at the time of the admission. Ventricular arrhythmias (such as ventricular fibrillation and sustained ventricular tachycardia) were defined as abnormal heart rhythms originating from the ventricle.

Electrocardiography Evaluation

Electrocardiography samples were taken within 10 minutes of admission to the emergency department (ED) from patients who presented at the ED with chest pain. All patients underwent ECG (Cardioline, Trento, Italy) (12-lead, 25 mm/s paper speed, and 10 mm/mV calibration) before coronary angiography (CAG). Two independent cardiologists blinded to the patient information evaluated the ECG data. Using the ECG machine's automatic report, the F(QRS-T) angle was obtained from the angles between the QRS axis and the T axis. If the obtained F(QRS-T) angle was greater than 180°, this value was subtracted from 360° to obtain the F(QRS-T) angle.[20] The ECG data used in our other studies were also checked by independent cardiologists. Figure 1A-B shows the F(QRS-T) angle calculation method.

Coronary Angiography and Thrombolysis in Myocardial Infarction and Flow Grade

Coronary angiography (GE Healthcare Innova 2100, New Jersey, USA) was performed by a sophisticated cardiologist using the standard Judkins technique and iobitridol (Xenetix-350, Guerbet BP, Roissy, CdG Cedex, France). Angiographic images were evaluated by 2 experienced cardiologists who were blinded to patient details. All patients were treated in accordance with the current guidelines of the European Society of Cardiology.[3,21] The patients were administered clopidogrel (600 mg) or ticagrelor (180 mg) in addition to 300 mg aspirin for pre-procedural antiplatelet therapy. Various image planes were considered while identifying the lesions responsible for infarction. The IRA was identified based on CAG imaging (coronary arteries with occlusive defects such as thrombus, ulcerated plaque, lumen dissection, or flaps) in combination with ECG and TTE results. After the intravenous administration of heparin (70 U/kg bolus) into the IRA, coronary revascularizations were performed with coronary bare metal stents or drug-eluting stents (DES) (the selection of DES was at the discretion of

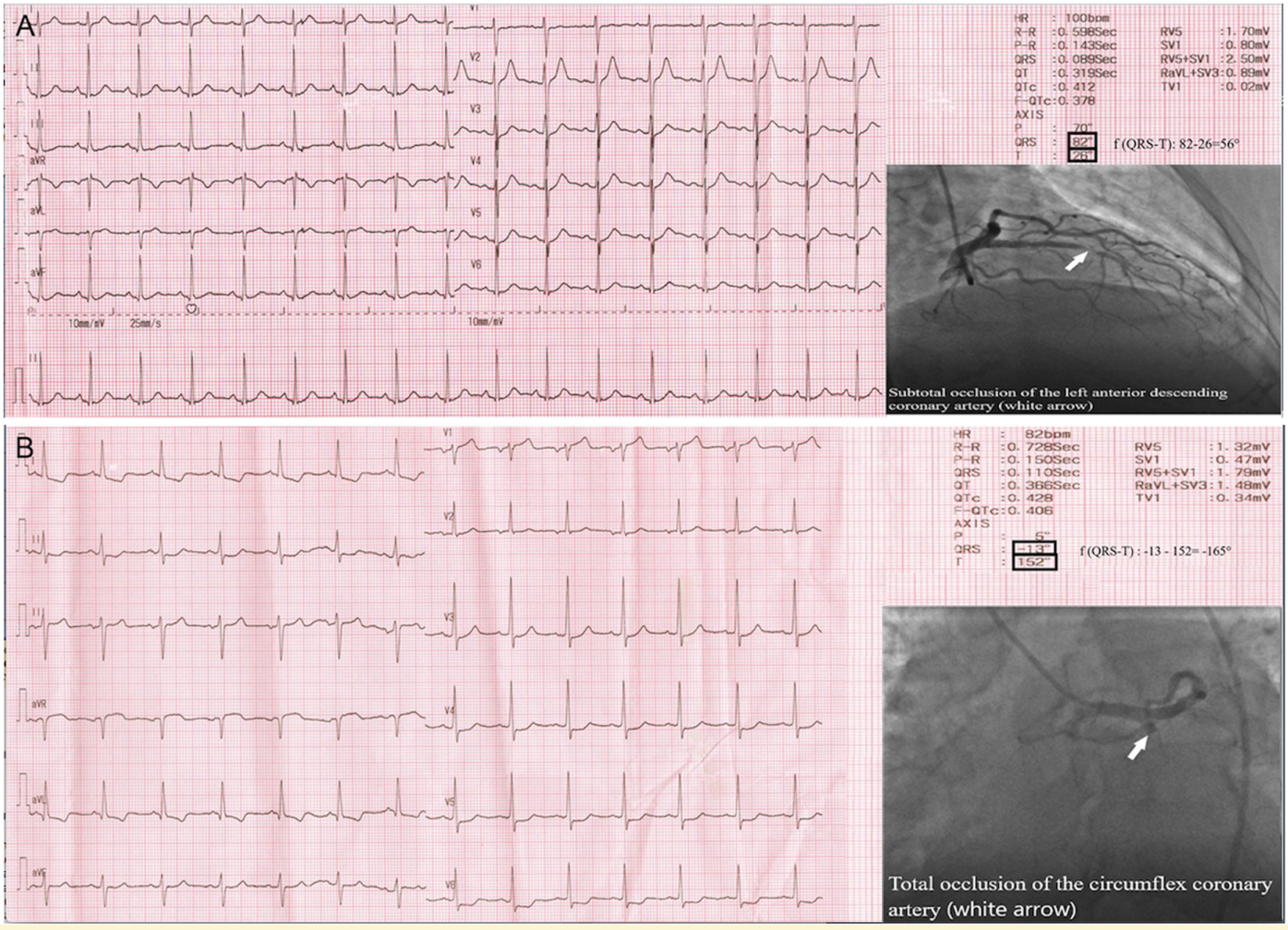


Figure 1. A, B. Calculation of anterior QRS-T angle on electrocardiogram and visualization of the responsible lesion causing this coronary angiographic. The QRS axis and T axis were calculated automatically. Frontal QRS-T angle was calculated as the absolute value of the difference between the frontal plane QRS and T axes (frontal QRS-T angle = QRS axis − T axis).

the operator), while balloon predilatation was performed before coronary stenting for some lesions. In all patients without contraindications, isosorbide dinitrate was administered by an interventional cardiologist before the first angiographic images to exclude the coronary slow flow phenomenon. The intervention was terminated after obtaining images following the administration of isosorbide dinitrate in all patients without contraindications. The classification of the coronary lesions was based on the recommendations found in the relevant literature.[22] The SYNTAX (synergy between percutaneous coronary intervention with taxus and cardiac surgery) score, GRACE (global registry of acute coronary events) score, and TIMI flow grade were calculated with reference to the respective websites (http://www.syntaxscore.com, http://www.outcomesumassmed.org/grace, and http://www.timi.org). The TIMI flow grade was defined as in the literature (No flow or perfusion at the obstructed distal is defined as TIMI 0, penetration without perfusion as TIMI 1, partial perfusion as TIMI 2, and complete perfusion as TIMI 3).[23] Two groups were created of TIMI flow degree 0/1 and 2/3. All patients received guideline-recommended long-term drug therapy, including statins, beta-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers, as necessary.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences version 19.0 software (SPSS Inc., Chicago, Ill, USA). The conformity of continuous variables to normal distribution was analyzed using the Kolmogorov–Smirnov test. Data were expressed as mean ± SD, or median (interquartile range) values. Categorical variables were expressed as number (n) and percentage (%). Parameters showing normal distribution were compared using the student's *t*-test, while those not showing normal distribution were compared with the Mann–Whitney *U* test or the Kruskal–Wallis test. The chi-square test or Fisher's exact test was used to compare the probability ratios of categorical variables. Pearson and Spearman's tests were used for correlation analysis. The F(QRS-T) angle with this cut-off value was used to group patients and predict TIMI flow grade and adverse events. Receiver operating characteristic (ROC) analysis was performed to determine the optimal cut-off value of the F(QRS-T) angle for the prediction of TIMI 0/1 flow and adverse events, with mark sensitivity and specificity determined according to the Youden J index. To estimate TIMI flow grade and adverse events, possible confounding independent variables (e.g., age, sex, systolic blood pressure, hs-cTn level, diabetes, hypertension, GRACE score, SYNTAX score, time from chest pain to PCI, IRA, LVEF, and F(QRS-T) angle) were included in the univariate analysis. Variables with a non-adjusted *P*-value less than 0.1 in the univariate analysis were determined as potential risk factors and were then included in the multivariate analysis. Multivariate analysis was performed to determine the independent predictors of TIMI flow grade and adverse events in NSTEMI patients. The Hosmer–Lemeshow test was used to evaluate the suitability of the model. Statistical significance was defined as a value of $P < 0.05$.

Results

We screened 456 patients within the study period. In total, 265 patients were excluded because of the presence of one or more of the exclusion criteria. Patients with CAD (n=58), CKD (n=8), stroke (n=5), CABG (n=35), permanent pacemaker (n=5), any cardiomyopathy (n=4), any bundle branch block or hemiblock (complete or incomplete) (n=17), pathological Q waves (n=4), AF (n=22), atrioventricular conduction abnormality (n=21), right or left ventricular hypertrophy (n=28), ST-segment elevation in aVR suggesting active diffuse subendocardial ischemia (n=3); any valve disease of at least moderate severity (n=14), use of antiarrhythmic drugs other than beta-blockers such as amiodarone, propafenone, sotalol (n=16); any electrolyte abnormality (n=14), and active infection and/or malignant disease (n=11) were excluded from the study. The final study population was comprised of 191 patients. TIMI flow grade 0/1 was seen in 62 patients (40 males; 22 females) whereas TIMI flow grade 2/3 was seen in 129 patients (72 males; 57 females). No variation was noted between the 2 groups in terms of demographic data, such as the presence of hypertension, diabetes, and the medical treatment before PCI (Table 1).

A review of the angiographic data indicated that the left anterior descending artery (LAD) represented the most frequently noted IRA. Both groups had mostly non-proximal LAD lesions. SYNTAX and GRACE scores were significantly higher in TIMI flow grade 0/1 patients ($P=0.013$ and $P=0.027$, respectively). In the intergroup comparison of the lesion types, type B lesions were determined to be the most common lesions in both groups. Drug-eluting stents were extensively used during PCI (Table 2). There was a statistically significant decrease in post-procedural compared to the pre-procedural F(QRS-T) angle in the TIMI 0-1 group (95.89 ± 25.31 and 67.22 ± 10.86, respectively, $P < 0.001$). There was a statistically significant decrease in the postoperative compared to the pre-procedural F(QRS-T) angle in the TIMI 2-3 group (42.10 ± 14.38 and 34.01 ± 11.88, respectively, $P < 0.001$).

In patients with TIMI flow grade 0/1, F(QRS-T) angle was significantly wider than in patients with TIMI flow grade 2/3 (95.89 ± 25.31 vs. 42.10 ± 14.38; $P < 0.001$) (Figure 2). In patients with TIMI flow grade 0/1, post-PCI F(QRS-T) angle was also significantly wider compared to patients with TIMI flow grade 2/3 (67.22 ± 10.86 vs. 34.01 ± 11.88; $P < 0.001$). The number of leads with ST-segment depression (2.41 ± 1.13 vs. 1.54 ± 1.36; $P < 0.001$) and maximal ST depression (mV) (0.25 ± 0.07 vs. 0.21 ± 0.06; $P=0.001$) were significantly higher in patients with TIMI flow grade 0/1 compared to patients with TIMI flow grade 2/3. T-wave inversion (TWI) limb and precordial leads were seen at a similar frequency in both groups (Table 2).

The predictive value of the F(QRS-T) angle for the TIMI 0/1 degree of flow and adverse events was confirmed using a ROC curve analysis. The cut-off value of the F(QRS-T) angle was 73.50 (area under the curve [AUC]: 0.85; 95% CI: 0.78-0.91; $P < 0.001$; sensitivity, 69.3%, specificity, 91.4%; positive predictive value, 79.63%; and negative predictive value, 88.29%) (Figure 3).

A significant correlation was observed between the F(QRS-T) angle and GRACE score ($r=0.52$; $P < 0.001$), pain to PCI time ($r=0.16$; $P=0.020$), and hs-cTn ($r=0.45$; $P=0.010$). A negative correlation was observed between LVEF and the F(QRS-T) angle ($r=-0.37$, $P=0.030$). Patients with TIMI flow grade 0/1 were seen to have a longer hospitalization than those with TIMI

Table 1. Comparison of Baseline Clinical and Demographic Characteristics of Groups

	TIMI 0-1 (n=62)	TIMI 2-3 (n=129)	*P*	F(QRS-T) angle ≥ 73.5 (n=54)	F(QRS-T) angle < 73.5 (n=137)	*P*
Age (years)	65.34 ± 9.97	64.01 ± 10.85	0.416	62.88 ± 10.38	65.45 ± 10.60	0.103
Gender (M/F)	40/22	72/57	0.253	35/19	77/60	0.329
BMI (kg/m^2)	25.40 ± 1.74	26.0 ± 2.71	0.117	25.56 ± 2.16	25.97 ± 2.62	0.257
Smoking, n (%)	17 (27.4)	29 (22.5)	0.455	17 (31.5)	29 (21.2)	0.189
Hypertension, n (%)	38 (61.3)	79 (61.2)	0.995	36 (66.7)	81 (59.1)	0.424
Diabetes mellitus, n (%)	26 (41.9)	52 (40.3)	0.831	26 (48.1)	52 (38)	0.260
Family history of CAD, n (%)	13 (21)	24 (18.6)	0.699	11 (20.4)	26 (19)	0.826
SBP (mmHg)	126.02 ± 13.04	129.44 ± 19.04	0.148	125.70 ± 15.01	129.36 ± 18.15	0.156
DBP (mmHg)	72.45 ± 10.64	74.26 ± 10.30	0.268	73.89 ± 8.56	73.59 ± 11.09	0.843
Laboratory data						
Glucose (mg/dL)	135 (100-160)	123 (104-165)	0.354	135 (103-162)	123 (100-165)	0.219
Creatinine (mg/dL)	0.95 ± 0.33	1.02 ± 0.52	0.203	0.97 ± 0.30	1.01 ± 0.52	0.567
Hemoglobin (g/dL)	12.80 ± 1.01	12.56 ± 1.99	0.381	12.89 ± 1.31	12.54 ± 1.87	0.210
WBC count (10^9/L)	8.15 ± 2.32	8.75 ± 2.86	0.150	8.76 ± 3.15	8.48 ± 2.52	0.529
Platelet count (10^9/L)	228.90 ± 34.90	227.25 ± 47.45	0.807	224.0 ± 43.26	229.28 ± 3.15	0.454
LDL cholesterol	123.17 ± 28.06	127.86 ± 53.58	0.519	127.87 ± 32.68	125.73 ± 51.42	0.734
HDL cholesterol	44.13 ± 14.96	43.08 ± 8.89	0.545	43.34 ± 13.92	43.46 ± 9.98	0.112
Cardiac Tn (ng/L)	209 (98.72-879.50)	195 (34.14-400)	0.001	209 (98.72-480.75)	195 (35.28-400)	0.091
Peak hs-cTn (ng/L)*	461 (343-1794)	446 (44.3-709)	<0.001	446 (311.83-1345)	346 (47.2-817.70)	0.026
Echocardiographic data						
LVEF (%)	50.65 ± 5.65	50.16 ± 5.96	0.584	51.20 ± 5.98	49.96 ± 5.80	0.196
LA (mm)	30.62 ± 3.82	31.58 ± 4.65	0.136	31.40 ± 4.64	31.21 ± 4.33	0.798
RA (mm)	23.61 ± 3.68	24.56 ± 4.25	0.132	23.88 ± 4.20	24.40 ± 4.05	0.445
IVS (mm)	10.56 ± 1.56	10.84 ± 1.57	0.249	10.75 ± 1.63	10.75 ± 1.55	0.977
PW (mm)	8.75 ± 1.27	9.02 ± 1.44	0.200	8.70 ± 1.34	9.02 ± 1.40	0.140
Medical therapy before admission, n (%)						
Aspirin, n (%)	13 (21)	37 (28.7)	0.256	9 (16.7)	41 (29.9)	0.090
Clopidogrel, n (%)	9 (14.5)	31 (24)	0.130	7 (13)	33 (24.1)	0.133
Beta-bloker, n (%)	7 (11.3)	17 (13.2)	0.712	5 (9.3)	19 (13.9)	0.534
Statin, n (%)	3 (4.8)	15 (11.6)	0.133	2 (3.7)	16 (11.7)	0.105
ACEI/ARB, n (%)	21 (33.9)	43 (33.3)	0.941	24 (44.4)	40 (29.2)	0.061
MRA, n (%)	3 (4.8)	12 (9.3)	0.264	3 (5.6)	12 (8.8)	0.563

*Peak hs-cTn levels are 48 hours after successful reperfusion.

ACEI, angiotensinogen converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; IVS, interventricular septum; LA, left atrium, RA, right atrium; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; PW, posterior wall; SBP, systolic blood pressure; TIMI, thrombolysis in myocardial infarction; Tn, troponin; WBC, white blood cell.

flow grade 2/3 (5.06 ± 1.14 vs. 4.22 ± 0.98, $P < 0.001$). Clinical outcomes, in-hospital mortality, newly-diagnosed AF and HF, ventricular arrhythmias, and the need for repeat target vessel revascularization were more prevalent in patients with TIMI flow grade 0/1 than in those with TIMI flow grade 2/3 ($P=0.002$) (Table 3). Total adverse events were more common in the group with F(QRS-T) angle ≥73.5 than in the group with F(QRS-T) angle <73.5 ($P=0.015$) (Table 3).

Univariate analysis identified the F(QRS-T) angle, GRACE score, and hs-cTn level as significant predictors of TIMI flow grade 0/1. In the multivariate analysis, hs-cTn level and F(QRS-T) angle were determined to be significant predictors. The model had a good fit as evidenced by the result of the Hosmer–Lemeshow test (χ^2, 6.35; $P=0.440$). Univariate analysis revealed that the F(QRS-T) angle and GRACE score were significant predictors of clinical outcomes, and multivariate analysis identified the F(QRS-T) angle

Table 2. Comparison of Angiographic Characteristics and Electrocardiographic Parameters of Study Groups

Angiographic Data	TIMI 0-1 (n=62)	TIMI 2-3 (n=129)	*P*	F(QRS-T) angle ≥ 73.5 (n=54)	F(QRS-T) angle < 73.5 (n=137)	*P*
Pain to PCI time (hours)	9.17 ± 4.74	9.94 ± 4.81	0.299	5.5 ± 2.5	5.0 ± 2.5	0.229
Admission to PCI time (hours)	4.90 ± 2.58	5.54 ± 2.35	0.09	4.45 ± 2.6	3.96 ± 2.5	0.246
SYNTAX score	16.50 ± 5.82	14.12 ± 6.79	0.013	16.04 ± 6.04	14.44 ± 6.67	0.121
GRACE score	141.70 ± 14.97	136.48 ± 15.39	0.027	146.94 ± 12.78	134.72 ± 15.02	<0.001
TIMI risk score	3.43 ± 1.01	3.35 ± 1.08	0.624	3.40 ± 1.05	3.37 ± 1.06	0.837
Initial TIMI flow, n (%)			<0.001			<0.001
TIMI 0-1	62 (100)	-		43 (79.6)	19 (13.9)	
TIMI 2	-	70 (54.3)		5 (9.3)	65 (47.4)	
TIMI 3	-	59 (45.7)		6 (11.1)	53 (38.7)	
Vessel disease, n (%)						
Single vessel	49 (79)	105 (81.4)	0.699	42 (77.8)	112 (81.8)	0.673
Two vessels	11 (17.7)	21 (16.3)	0.800	12 (22.2)	20 (14.6)	0.291
Three or more vessels	2 (3.2)	3 (2.3)	0.666	0 (0)	5 (3.6)	0.328
IRA, n (%)						
LAD, n (%)	35 (56.5)	72 (55.8)	0.934	41 (75.9)	66 (48.2)	0.001
LAD lesion			0.973			0.674
Proximal	2 (5.7)	4 (32.7)		3 (7.3)	3 (4.5)	
Non-proximal	33 (94.3)	68 (67.3)		38 (92.7)	63 (95.5)	
LCX, n (%)	8 (12.9)	14 (10.9)	0.178	1 (1.9)	16 (11.7)	0.062
RCA, n (%)	19 (30.6)	43 (33.3)	0.710	12 (22.2)	50 (26.2)	0.084
ACA/AHA lesion type						
Type A, n (%)	16 (25.8)	27 (20.9)	0.450	14 (25.9)	29 (21.2)	0.605
Type B, n (%)	31 (50)	82 (63.6)	0.074	25 (46.3)	88 (64.2)	0.023
Type C, n (%)	15 (24.2)	20 (15.5)	0.146	15 (27.8)	20 (14.6)	0.040
Stents used						
Bare metal stent	8 (12.9)	9 (7)	0.186	6 (11.1)	11 (8)	0.501
Drug-eluting stent	54 (87.1)	120 (93.0)	0.178	48 (88.9)	126 (92)	0.574
Stent diameter (mm)	3.02 ± 0.41	2.92 ± 0.36	0.127	3.06 ± 0.43	2.91 ± 0.34	0.032
Stent length (mm)	27.33 ± 5.26	25.96 ± 6.52	0.123	26 ± 4.5	26.57 ± 6.71	0.561
Number of stents	1.56 ± 0.59	1.61 ± 0.65	0.613	1.55 ± 0.60	1.61 ± 0.64	0.573
Electrocardiographic data						
Heart rate (beats/min)	70.39 ± 12.65	73.05 ± 17.18	0.278	72.37 ± 13.37	72.12 ± 16.72	0.921
PR interval (ms)	135.58 ± 9.46	133.81 ± 8.92	0.221	138.12 ± 9.51	132.91 ± 8.54	0.001
Number of leads with ST	2.41 ± 1.13	1.54 ± 1.36	<0.001	2.24 ± 1.42	1.67 ± 1.31	0.013
depression	0.25 ± 0.07	0.21 ± 0.06	0.001	0.24 ± 0.07	0.22 ± 0.06	0.146
Maximal ST depression (mV)						
Corrected QT interval (ms)	450.24 ± 38.03	445.45 ± 35.05	0.405	448.96 ± 37.44	446.23 ± 35.55	0.647
TWI in any lead, n (%)	9 (14.5)	11 (8.5)	0.206	11 (20.4)	9 (6.6)	0.011
TWI in limb leads, n (%)	3 (4.8)	5 (3.9)	0.756	4 (7.4)	4 (2.9)	0.225
TWI in precordial leads, n (%)	5 (8.1)	4 (3.1)	0.130	5 (9.3)	4 (2.9)	0.121
Frontal QRS-T angle (°)	95.89 ± 25.31	42.10 ± 14.38	<0.001			
Post-PCI frontal QRS-T angle (°)	67.22 ± 10.86	34.01 ± 11.88	<0.001			

ACC/AHA, American College of Cardiology/American Heart Association; GRACE, global registry of acute coronary events; IRA, infarct-related artery; LAD, left anterior descending artery; LCx, left circumflex artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery; TIMI, thrombolysis in myocardial infarction; TWI, T-wave inversion.

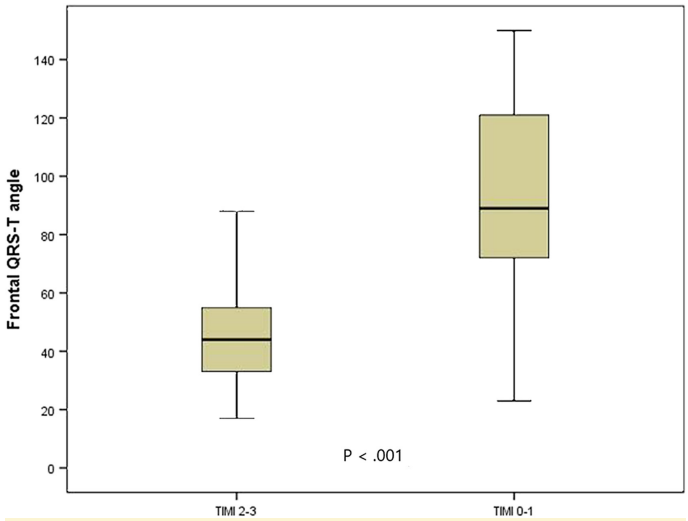
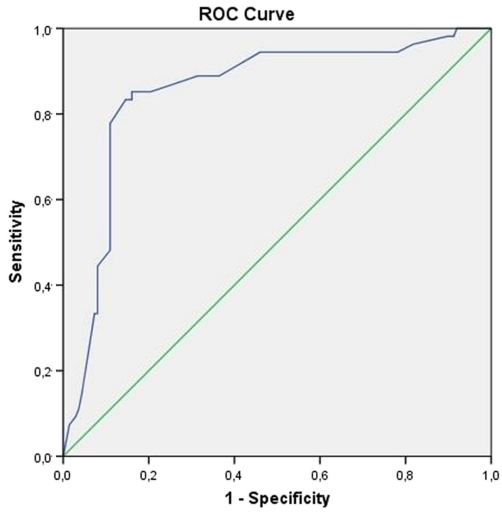


Figure 2. Comparison of frontal QRS-T angle for TIMI 2-3 and TIMI 0-1 groups. TIMI, Thrombolysis in Myocardial Infarction.



	AUC	95% CI	P value	Cut-off value	Sensitivity	Specificity
F(QRS-T) angle	0.851	0.78-0.91	< .001	73.5	69.3	91.4

Figure 3. ROC analyses for frontal QRS-T angle to predict TIMI flow grade and adverse events in NSTEMI. AUC, area under curve; CI, confidence interval; NSTEMI, non-ST-elevation myocardial infarction; ROC, receiver operator characteristic; TIMI, Thrombolysis in Myocardial Infarction.

as a significant predictor. The study model exhibited a good fit in Hosmer–Lemeshow test (χ^2, 3.89; $P=0.860$) (Table 4).

Discussion

The important findings of the present study regarding the relationship between the F(QRS-T) angle and the TIMI flow grade and adverse events in patients with NSTEMI were as follows: (1) prior to PCI, patients with TIMI flow grade 0/1 had wider F(QRS-T) angles compared to those with TIMI flow grade 2/3, (2) a higher proportion of patients with TIMI flow grade 0/1 had adverse events during hospitalization than patients with TIMI flow grade 2/3, (3) F(QRS-T) angle and hs-cTn level were predictors of pre-PCI TIMI 0/1 in patients with NSTEMI, and (4) F(QRS-T) angle was the predictor of adverse events in NSTEMI patients after PCI.

Patients with NSTEMI account for an important majority of patients diagnosed with ACS.[24] Patients with NSTEMI are generally older than those with STEMI, and patients with NSTEMI who undergo PCI are likely to exhibit an increased rate of adverse events during follow-up as comorbid conditions are more prevalent in elderly patients than in younger patients.[25] The diagnosis of NSTEMI is more complex than that of STEMI. STEMI can be more easily diagnosed than NSTEMI based on an interpretation of the ECG. Moreover, it is difficult to predict the lesion responsible for ischemia in patients with NSTEMI or to exclude the presence of a total or subtotal occlusion in the coronary vessel before CAG.[26] Despite the fact that ECG results are instrumental in the diagnosis of patients with STEMI, they may not be so striking in

Table 3. Comparison of Adverse Events

Clinical Outcomes	TIMI 0-1 (n=62)	TIMI 2-3 (n=129)	*P*	F(QRS-T) angle ≥73.5 (n=54)	F(QRS-T) angle <73.5 (n=137)	*P*
Length of stays (days)	5.06 ± 1.14	4.22 ± 0.98	<0.001	4.70 ± 1.23	4.36 ± 0.9	0.032
Total adverse events	8 (12.9)	2 (1.6)	0.002	8 (10.7)	2 (1.7)	0.015
In-hospital all-cause mortality	3	1		4	0	
Atrial fibrillation	2	0		1	1	
Heart failure	1	0		1	0	
Ventricular arrhythmias	1	1		1	1	
Target lesion revascularization	1	0		1	0	
Adverse events and culprit vessel						
LAD	5	2		6	1	
LCx	2	0		1	1	
RCA	1	0		1	0	

F(QRS-T) angle, frontal QRS-T angle; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

Table 4. Univariate and Multivariate Analysis for Prediction of TIMI Flow Grade and Adverse Events

	TIMI Flow Grade Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Age	1.01 (0.98-1.04)	0.414	1.51 (1.30-1.75)	<0.001
Sex, male	1.43 (0.77-2.69)	0.254		
Systolic blood pressure	0.98 (0.97-1.00)	0.203		
DM	1.09 (0.53-223)	0.801		
HT	0.95 (0.46-1.97)	0.905		
Time from chest pain to PCI	0.96 (0.90-1.03)	0.296		
IRA	0.96 (0.68-1.34)	0.815		
LVEF	0.58 (0.96-1.069)	0.588		
Frontal QRS-T angle (°)	1.45 (1.28-1.65)	<0.001		
GRACE score	1.02 (1.00-1.04)	0.022	1.02 (0.91-1.14)	0.686
Cardiac Tn	1.01 (0.98-1.09)	0.040	1.07 (1.00-1.137)	0.024
Adverse Events				
	Univariate Analysis		**Multivariate Analysis**	
	OR (95% CI)	***P***	**OR (95% CI)**	***P***
Age	0.98 (0.92-1.04)	0.559	1.11 (1.04-1.19)	0.002
Sex, male	0.69 (0.19-2.47)	0.578		
Systolic blood pressure	1.02 (0.98-1.05)	0.220		
DM	0.74 (0.17-3.18)	0.694		
HT	1.73 (0.37-8.14)	0.482		
Time from chest pain to PCI	0.99 (0.97-1.01)	0.631		
IRA	0.68 (0.31-1.51)	0.353		
LVEF	1.03 (0.92-1.16)	0.516		
Frontal QRS-T angle (°)	1.02 (1.00-1.04)	0.009		
GRACE score	1.04 (1.00-1.09)	0.043	1.06 (0.97-1.17)	0.179
Cardiac Tn	0.99 (0.99-1.00)	0.515		

GRACE, global registry of acute coronary events; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery; TIMI, thrombolysis in myocardial infarction; Tn, troponin.

patients with NSTEMI. For example, although the maximal ST depression differs between the TIMI 0-1 and TIMI 2-3 groups, when we examine the groups in which the F(QRS-T) angle of the maximal ST depression is greater or less than 73.5, it is concluded that there is no difference between the groups. Similarly, the presence of TWI in the limb or precordial leads does not provide us with sufficient information about coronary vessel occlusion in patients with NSTEMI.

Early revascularization in patients with high-risk NSTEMI has been reported to be associated with better clinical and angiographic outcomes than delayed revascularization.[27,28] Furthermore, a widespread infarction area has been identified in patients with NSTEMI with completely occluded vessels, with patients determined with high mortality incidence during long-term follow-up.[29] In recent studies, optimal revascularization time has been the focus of attention in patients with NSTEMI in order to reduce adverse events such as recurrent ischemia, death, and length of stay in hospital.[30,31] Although in-hospital mortality is higher in patients with STEMI than in those with NSTEMI, the mortality rates are equalized during the 6-month follow-up, and the rate has been reported to be twice as high in patients with NSTEMI.[32]

An increased F(QRS-T) angle may be a worthwhile variable in prediction of long-term risk.[33] The absence or reduction of blood flow in the coronary arteries and myocardial ischemia resulting from lack of perfusion due to increased resistance in myocardial capillaries are associated with an increased F(QRS-T) angle.[32] In line with the outcomes of this study, the F(QRS-T) angle before the procedure has been demonstrated to be affected by the TIMI flow grade. Therefore, it was hypothesized that the F(QRS-T) angle may be related to the coronary flow degree, and it was seen that the decrease in the F(QRS-T) angle, especially after revascularization, is a momentous supporter of this. The cardiac electrical and metabolic systems may be affected at the cellular level due to the decreased blood flow and subsequent intercellular depolarization and repolarization changes, which may be one of the most important mechanisms underlying the condition. In normal subjects, a narrow F(QRS-T) angle is hoped because the depolarization and repolarization axis tend to be in a similar direction in healthy myocardial cells.[35] There is a significant relationship between F(QRS-T) angle and mortality in STEMI patients.[36] In addition, the F(QRS-T) angle measured after revascularization in STEMI patients has been shown to predict in-hospital mortality in this patient group.[37] On the other hand, there is limited information about the relationship of the F(QRS-T) angle

with the coronary flow degree and adverse events in patients with NSTEMI in the literature.

In the current study, the group with more frequent adverse events had a wider F(QRS-T) angle after the procedure, and the frequency of type C lesions was found to be higher in patients with a wide F(QRS-T) angle. Similarly, cTn is a significant indicator of cardiac injury and is associated with cardiovascular adverse outcomes.[38] As seen in our study, a strong correlation was observed between F(QRS-T) angle and cardiac troponins. In addition, a negative correlation was found between the F(QRS-T) angle and LVEF in this study. In light of these findings, the results of this study suggest that a cascade of events such as decreased TIMI flow grade, and increased microvascular ischemia may be important mechanisms responsible for the increase in the F(QRS-T) angle and adverse events in NSTEMI patients.

Our study has several limitations. Among these are single-center design, relatively limited, and highly selected study cohorts. The patients with a previous history of CAD and coronary artery bypass were not included in this study on the grounds that vessels with chronic occlusion might have led to misinterpretation of the study results, and therefore, the relationship of the F(QRS-T) angle with the degree of coronary flow and adverse events before PCI could not be investigated in those patients. Previous ECGs of the patients before the coronary event were not available, and so there was no information about the change between the F(QRS-T) angle at the time of the coronary event and the F(QRS-T) angle when the patient was healthy. Finally, the relationship between the F(QRS-T) angle and adverse events of patients with NSTEMI was not investigated in the long term as the present study did not include a follow-up. F(QRS-T) angle was strongly correlated with the GRACE score suggesting that further studies are warranted to investigate whether it is independently associated with long-term adverse events.

In conclusion, the F(QRS-T) angle measured before PCI in patients with NSTEMI appears to be an independent indicator of decreased coronary flow rate and adverse events. Therefore, the F(QRS-T) angle may help screen patients with NSTEMI for early PCI and identify the patients who will experience adverse events during hospitalization.

Ethics Committee Approval: Ethical committee approval was received from Ethics Committee of Clinical Research of Çanakkale Onsekiz Mart University (Approval No: 2011-KAEK-27/2021-2100129433).

Informed Consent: As a result of the retrospective study design, written informed consent was not obtained from the participants before the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – U.K., K.A., U.Ö., B.A.; Design – U.K., K.A., U.Ö., B.A.; Supervision – U.K., K.A., U.Ö., B.A.; Materials – U.K., K.A., U.Ö., B.A.; Data Collection and/or Processing – U.K., K.A., U.Ö., B.A.; Analysis and/or Interpretation – U.K., K.A., U.Ö., B.A.; Literature Review – U.K., K.A., U.Ö., B.A.; Writing – U.K., K.A., U.Ö., B.A.; Critical Review – U.K., K.A., U.Ö., B.A.;

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