Relationship between frontal QRS-T duration and the severity of coronary artery disease in who were non-diabetic and had stable angina pectoris

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Abstract

Objective: There is a known relationship between frontal-QRS-T (F-QRS-T) angle and coronary artery disease (CAD). This study examined the relationship between F-QRS-T angle changes and CAD severity in patients with stable CAD.

Methods: A total of 202 patients were included in the study after the implementation of exclusion criteria among 894 patients, who were admitted to the outpatient clinic with stable angina pectoris between September 2018 and September 2019. The F-QRS-T angle calculated on the 12-lead electrocardiograms (ECGs) of the patients (taken in the outpatient clinic), and the CAD severity calculated using the Gensini score in patients undergoing coronary angiography were compared.

Results: Of the patients included in the study, 38.6% were female and 61.4% were male. The mean age was calculated as 60.16±11.27 years, and 52% of the patients had hypertension. There was no difference between the groups in terms of demographic and clinical values. In a comparison of CAD severity and F-QRS-T angles, the F-QRS-T angle was seen to be statistically significantly higher in the severe CAD group [91°° (102/79)] compared to the group with mild CAD [53°° (64/38)]. In the multivariate logistic regression analysis, there was a significant association between the F-QRS-T angle (odds ratio=1.09, 95% confidence interval=1.06-1.11, p<0.001) and CAD severity.

Conclusion: It seems that CAD severity in patients who were non-diabetic and had stable angina pectoris is associated with the F-QRS-T angle.

Keywords: coronary artery disease, stable angina pectoris, frontal QRS-T angle, Gensini score, non-diabetic

Cite this article as: *Akın H, Bilge Ö. Relationship between frontal QRS-T duration and the severity of coronary artery disease in who were non-diabetic and had stable angina pectoris. Anatol J Cardiol 2021; 25: 572-8.*

Introduction

Coronary artery diseases (CADs) are among the most important causes of morbidity and mortality worldwide. Coronary angiography (CAG) is used for the diagnosis and treatment of coronary atherosclerotic diseases (1). Chest pain is seen as a problem in CAD. In patients with stable chest pain characterized by typical symptoms related to the character, location, and effort, the basis of the diagnosis is the patient's clinical history, and in most of these cases, it allows for a reliable diagnosis of angina (2). Patients with diabetes mellitus with acute myocardial infarction (MI) and coronary revascularization have been shown to have a worse prognosis than that seen in patients without diabetes mellitus (3). Although the clinical results of changing the perception of pain in patients with diabetes and CAD remain uncertain, some studies have reported that it is more common in patients with diabetes and atypical acute MI, but no significant relationship has been determined between those with diabetes and those without (4, 5). Studies on stable CAD have shown that the prevalence of atypical ischemia is more consistent among patients with and without diabetes, but there is not enough information on whether there is such a consistent prevalence among patients with atypical angina (6). The misinterpretation of atypical chest pain may result in negative prognostic results for

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Accepted Date: 16.03.2021 **Available Online Date:** 16.07.2021

DOI:10.5152/AnatolJCardiol.2021.33232

HIGHLIGHTS

- The frontal-QRS-T (F-QRS-T) angle; is the absolute value of the difference between the ventricular depolarization and repolarization.
- F-QRS-T angle can be measured automatically in the electrocardiogram as well as simply manually.
- The F-QRS-T angle width is associated with severe coronary artery disease.

angina or may affect the physician's diagnostic strategy by not showing evidence of the typicality of symptoms in patients Who were non-diabetic and had stable angina pectoris in CAD (7).

F-QRS-T angle is expressed as the absolute value of the difference between ventricular depolarization and repolarization and as a marker of myocardial depolarization and repolarization heterogeneity (8). QRS-T abnormalities reflect the electrical imbalance of the ventricular myocardium and affect negative cardiovascular outcomes and overall mortality rates, especially in patients with CAD (9). As the relationship between the QRS-T angle changes and CAD has not been studied in patients who were non-diabetic and had stable angina pectoris in the literature, this study aimed to investigate whether there is a relationship between CAD severity and F-QRS-T angle in these patient groups.

Methods

Study population

The study was designed as a retrospective cohort study. A total of 202 patients were included in the study after the implementation of the exclusion criteria among 894 patients who got admitted to the outpatient clinic with stable angina pectoris between September 2018 and September 2019. Patients With diabetes, those with a previous history of CAD, those who underwent a coronary artery bypass operation, those with an ischemic change in their ECGs, those with complete and incomplete right or left bundle branch block or pathological Q, those with a history of cerebral infarction, those with heart failure and arrhythmia (atrial fibrillation or atrioventricular block), those with cardiomyopathies, and those with valvular heart disease were excluded from the study. The patients were given a stress test, and patients with >1 mm ST depression in the lateral leads were considered positive. Effort test was positive in all patients included in the study. The F-QRS-T angle calculated on the 12-lead ECGs of the patients (taken in the outpatient clinic) and the CAD severity calculated using the Gensini score (Fig. 1) in patients undergoing CAG were compared. The Gensini score was used to measure the prevalence of CAD in CAG. According to Gensini scores; patients with Gensini score <25 points were accepted as the mild CAD group, whereas patients with Gensini score ≥25 points were accepted as the severe CAD group (10). The patients were compared in terms of QRS-T angle, and an evaluation was conducted to know whether QRS-T angle indicated the prevalence of CAD. The informed consent of the subjects was obtained, and the study protocol was approved by the Human Research Committee of the Institute. The study protocol conforms to the Declaration of Helsinki (Approval number/date: 578. 25/09/2020).

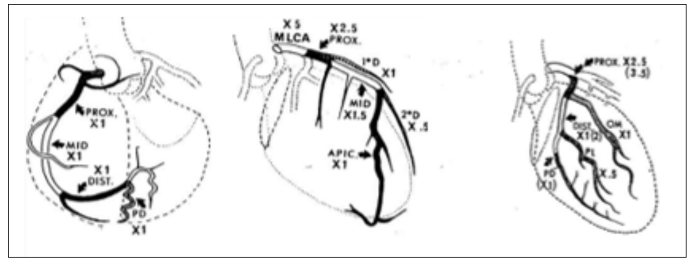

Figure 1. An example demonstrating the measurement of the Gensini score calculation

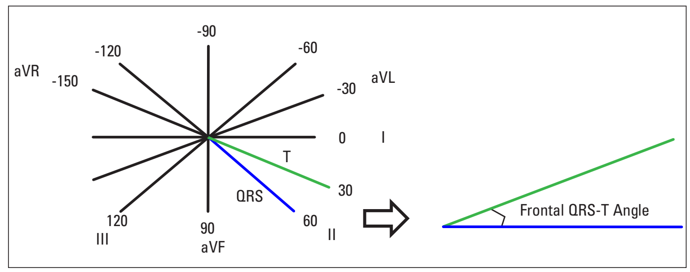

Figure 2. An example demonstrating the measurement of the frontal QRS-T angle

Electrocardiography

A 12-lead ECG was recorded at a paper speed of 25 mm/s and voltage of 10 mm/mV amplitude in the same device (Cardio Soft version 6.0, GE Medical Systems, Milwaukee, USA). The Frontal-QRS and T-wave axes were analyzed automatically (Marquette 12SL software GE Medical Systems, Milwaukee, USA). All ECGs were also checked by a single independent observer. Manual measurement, in short, the QRS deflections, were measured by a ruler in each of the 3 standard leads. The results were then inserted in Einthoven's triangle, and the angle was measured by a protractor. T-waves were measured similarly, and the difference between the QRS- and the T-wave angle was calculated (11). When there was a conflict of >15° between automatic and observer measurements, the observer's measurement applied. The F-QRS-T angle was defined as the absolute value of the difference between the QRS and T-wave axes (Fig. 2 and 3). If the F-QRS-T angle was >180°, the relevant value was determined as follows: 360°- (QRS axis - T axis). According to the 95th percentile values of a population based study, the F-QRS-T angle was classified as abnormal if it was ≥73° for males and ≥67° for females (12). The frontal T-wave axis was considered abnormal when it was >75° or <15° (13).

Coronary angiography

Coronary angiograms were recorded digitally for quantitative analysis (DICOM viewer, MedCom GmbH, Darmstadt, Germany).

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DOI:10.5152/AnatolJCardiol.2021.33232

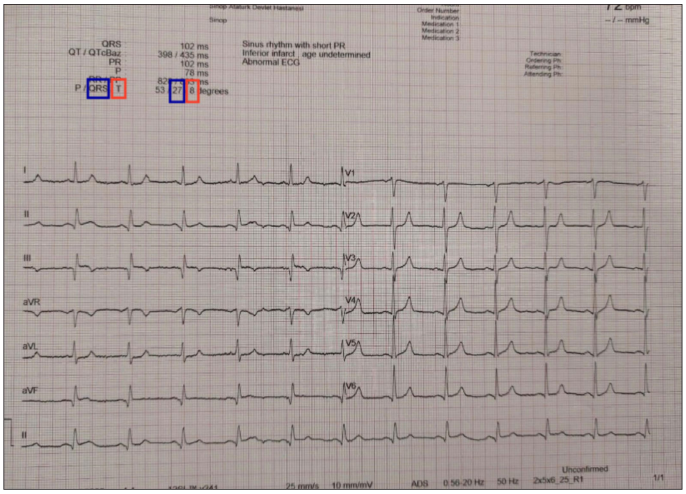

Figure 3. An electrocardiogram example demonstrating the measurement of the frontal QRS-T angle. The QRS axis and T axis were calculated automatically (arrowheads). Then, the frontal QRS-T angle was calculated as the absolute value of the difference between the frontal plane QRS and T axes (frontal QRS-T angle=QRS axis - T axis). For the ECG of the patient demonstrating aforementioned measurement, frontal QRS-T angle=21° (QRS axis=27°, T axis=8°)

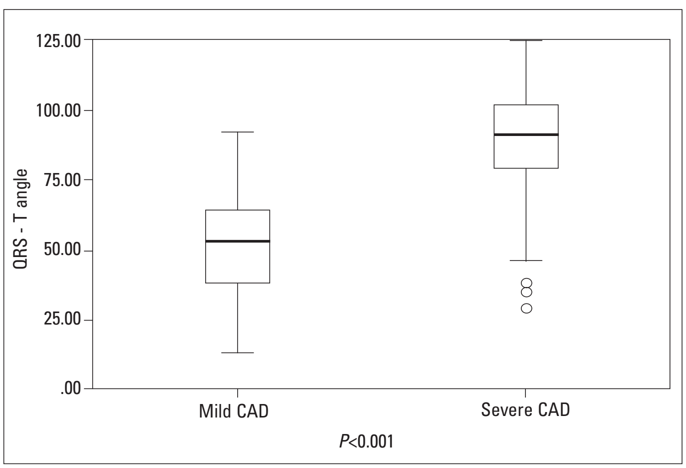

Figure 4. Operating characteristics showing the distinctive utility of frontal QRS-T angles

These digital angiograms were evaluated by 2 experienced cardiologists blinded to other patient information. In case of any contradiction regarding the evaluations, a consensus was reached by discussing the issue. Gensini scores were obtained by multiplying the myocardial area fed by the vascular area with 1, 2, 4, 8, 16, and 32 stenoses, respectively, by the coefficient determined according to functional importance. Accordingly, The left main coronary artery was multiplied by 5, the proximal left descending artery by 2.5, the proximal circumflex artery by 2.5, the left anterior descending artery middle segment by 1.5, the right coronary artery, the distal left anterior descending artery, and the posterolateral artery and obtuse marginal artery by 1, and others by 0.5 (Fig. 1) (14). Patients with CAD were divided into the following 2 groups: those below the cut-off value and those above the cut-off value. The first group was composed of those with mild atherosclerosis [Gensini score <25 points (mild CAD group)], whereas the second group was composed of those with severe atherosclerosis [Gensini score ≥25 points (severe CAD group)], with this classification compatible with the literature (10).

Statistical methods

The SPSS 25.0 (IBM Corporation, Armonk, New York, United States) program was used in the analysis of the variables. The conformity of the data to normal distribution was evaluated by the Shapiro-Wilk Francia test. The independent samples *t*-test was used with the Bootstrap results to compare 2 independent groups according to the quantitative data, whereas the Mann-Whitney U test was used with the Monte Carlo results. The Pearson chi-square test was used with the Exact results to compare categorical variables with each other. The logistic regression test was used with the Enter method to determine the cause-effect relationship between the 2 category response variables and explanatory variables. The quantitative variables were shown as mean (standard deviation) and median [quartile (Q)1 / Q3], while the categorical variables were shown as n (%) in the tables. The variables were examined at a 95% confidence interval (CI), and the p-value was considered significant when it was less than 0.05.

Results

Of the 894 patients who applied to the outpatient clinic with stable angina pectoris between September 2018 and September 2019, a total of 202 patients were included in the study after the implementation of the exclusion criteria. The QRS-T angle recorded by the 12-lead ECGs of the patients were compared with their CAD severities. The demographic and clinical variables of the patients included in the study are shown in Table 1. Of all the patients, 38.6% were female and, 61.4% were male, and their mean age was calculated as 60.16±11.27, 52% of the patients had hypertension (HT). According to the CAG results, 48% of the patients had mild CAD (Gensini score <25) and 52% had severe CAD (Gensini score ≥25). The mean QRS duration of all patients included in the study were measured as 79.12±3.90 seconds the mean QRS-T angle as 71.18±26.39°°, and the mean QTc as 429.52±16.65. No significant relationship could be determined between the patients' ages, patients, gender, presence of HT in the patients, patients lipid profiles, patients whole blood parameters, patients kidney function tests, patients pulse, patients QRS durations, and patients QTc data (p>0.05) (Tables 1 and 2).

While comparing the CAG data and the F-QRS-T angles of the patient groups, the F-QRS-T angle was found to be average 91°° (between 79 and 102) in the severe CAD group, 53°° (between 38 and 64) for the mild CAD group; there was a significant relationship between the 2 groups (p<0.001) (Fig. 4). In the multivariate logistic regression analysis to determine the association of the F-QRS-T angle with CAD severity in patients with stable angina pectoris, a significant association was found between the F-QRS-T angle [odds ratio (OR)=1.09, 95% CI=1.06-1.11, p<0.001] and CAD severity (Table 3). In addition, the total cholesterol level

Table 1. An evaluation of coronary angiography according to age, gender, HT, and laboratory parameters				
	Total (n=202)	**Mild CAD (n=97)**	**Severe CAD (n=105)**	
Variables	**Median (Q1/Q3)**	**Median (Q1/Q3)**	**Median (Q1/Q3)**	***P*-value**
Age (years)	58 (51/69)	58 (69/51)	59 (71/52)	0.345[u]
Gender, n (%)				
Female	78 (38.6)	41 (42.3)	37 (35.2)	0.315[p]
Male	124 (61.4)	56 (57.7)	68 (64.8)	
HT, n (%)				
Absent	97 (48.0)	46 (47.4)	51 (48.6)	0.889[p]
Present	105 (52.0)	51 (52.6)	54 (51.4)	
LDL cholesterol (mg/dL)	132.57 (37.67)	132.28 (34.41)	132.85 (40.62)	0.912[t]
HDL cholesterol (mg/dL)	46.56 (38/65.4)	49 (41.64/65.8)	45.2 (37.37/65.3)	0.317[u]
Triglyceride (mg/dL)	162.65 (130.7/208.92)	159 (126/208.92)	163 (135/208.92)	0.554[u]
Total cholesterol (mg/dL)	189.6 (172.82/220)	195 (178.9/230)	186 (169/207.9)	0.068[u]
Hemoglobin (g/dL)	13 (12/14.5)	13.3 (12/14.7)	13 (11.8/14.4)	0.157[u]
Hematocrit %	41 (38.4/44.2)	41.2 (38.7/44.3)	40.33 (37.2/44)	0.164[u]
Red blood cell (M/uL), mean (SD)	5.06 (0.78)	5.17 (0.73)	4.96 (0.82)	0.046[t]
White blood cell count (10^3/mL)	8.45 (6.8/9.75)	7.99 (6.8/9.76)	8.47 (6.8/9.74)	0.872[u]
Red cell distribution width (%)	14 (13.2/14.7)	14 (13/14.6)	13.9 (13.3/14.7)	0.343[u]
Mean platelet volume (fL)	11.2 (10.3/11.65)	11 (10/11.6)	11.3 (10.5/11.65)	0.158[u]
Uric acid (mmol/L)	6 (5/7)	6 (5/6)	6 (5/7)	0.057[u]
e-GFR (mL/min)	55 (46/60)	55 (48/60)	55 (46/60)	0.366[u]
Urea (mg/dL)	33.46 (27.65/41.1)	33.46 (27.45/40.75)	33.46 (28.13/41.7)	0.459[u]
Creatinine (mmol/L)	0.905 (0.69/1.2)	0.95 (0.71/1.19)	0.9 (0.69/1.2)	0.929[u]
Ejection fraction (%)	47 (42/55)	49 (44/55)	45 (42/55)	0.373[u]
Heard rate (beat/min)	78.82 (4.93)	78.99 (4.68)	78.66 (5.17)	0.609[t]
QRS-T angle	73 (50/92)	53 (38/64)	91 (79/102)	<0.001[u]
QRS duration (ms)	79 (76/82)	79 (76/81)	79 (76/82)	0.617[u]
QTc (ms)	427 (420/438)	428 (419/438)	427 (421/437)	0.928[u]

[u]Mann-Whitney U test , [t]Independent Samples t-test , [p]Pearson chi-square test
CAD - coronary artery disease; HDL - high-density lipoprotein; HT - hypertension; LDL - low-density lipoprotein; GFR - glomerular filtration rate; Q - quartile

Table 2. Electrocardiographic parameters of groups created by coronary angiography classification		
	QRS-T angle	
(n=202)	**Median (Q1/Q3)**	***P*-value**
Gender		
Female	68 (54/93)	0.816
Male	76 (49.5/92)	
Hypertension		
Absent	73 (49/92)	0.665
Present	73 (52/91)	

Mann-Whitney U test (Monte Carlo): Q1: Percentile 25, Q3: Percentile 75
Q - quartile

was found to be significantly higher in the severe CAD group (OR=1.01, 95% CI=1.00-1.02, p=0.031).

Discussion

To the best of our knowledge, this study is the first study in the literature to investigate F-QRS-T angle and the severity of CAD in patients who were non-diabetic and had SAP. In the study, a significant relationship was found between the F-QRS-T angle and the intensity of CAD severity. Of the patient population included in the study, 38.6% were female and, 61.4% were male, and their mean age was calculated as 60.16±11.27; 52% of the patients had HT. In addition, no significant correlation was found between the study groups in terms of the demographic characteristics and biochemical parameters of the patients included in the study.

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DOI:10.5152/AnatolJCardiol.2021.33232

Table 3. OR, *P* values, and 95% CI of independent predictors of severity of CAD according to multiple logistic regression analysis

					95% CI for OR	
Reference group: Severe CAD	**B**	**SE**	***P*-value**	**OR**	**Lower bound**	**Upper bound**
Age	0.018	0.019	0.360	1.018	0.980	1.057
Gender	0.037	0.445	0.402	0.688	0.288	1.647
HT	0.369	0.454	0.417	1.446	0.593	3.524
LDL cholesterol	0.004	0.006	0.519	1.004	0.992	1.016
Triglyceride	0.002	0.002	0.481	1.002	0.997	1.006
Total cholesterol (↑)	0.013	0.006	0.031	1.013	1.001	1.025
Red blood cell, M/uL	–0.246	0.272	0.365	0.782	0.458	1.333
QRS-T angle (↑)	0.087	0.011	<0.001	1.091	1.067	1.115
Constant	–5.810	1.672	0.001			

Dependent variables: CAD, predicted mild CAD (sensitivity) = 84.5, predicted severe CAD (sensitivity) = 83.8, PPV=84.2, NPV=84.8, predicted total (accuracy rate) = 86.1, *P* model <0.001, bold values: *P*<0.005.
Multiple logistic regression (Method = Enter)
B - regression coefficients; CAD - coronary artery disease; CI - confidence interval; LDL - low-density lipoprotein; NPV - negative predictive value; OR - odds ratio; PPV- positive predictive value; SE - standard error

CAD is a leading cause of morbidity and mortality in patients with diabetes. Diabetes is known to be associated with the development of CAD, and the prognosis of the disease worsens owing to diabetes (15). According to the information obtained in a study conducted with multivariate-adjusted risk models, it is noted that the spatial QRS-T angle is a significant and strong predictor of CAD in females compared with in males, with a hazard ratio of 2.14 (11).

In this study, the comparison of the F-QRS-T angle and the CAG data of patients with stable angina pectoris was conducted. According to the literature, as CAD is common in patients with diabetes, this study compared CAG data and F-QRS-T angle of patients who were non-diabetic and stable angina pectoris. It was seen that there was almost no previous study on this subject, and it was thought that this gap in the literature could be addressed by this study.

QRS-T angle is defined as the angle between the depolarization and repolarization electrical directions and as a new marker of myocardial depolarization and repolarization heterogeneity (12). Studies have shown that the QRS-T angle is both more robust and reproducible and less sensitive to noise and definition problems when compared with other conventional electrocardiographic myocardial repolarization parameters (16). The QRS-T angle is determined by the 3 dimensional spatial QRS-T angle method and the frontal QRS-T angle calculation method using a projection on the frontal plane in the standard 12-lead ECG (8). As most ECG devices automatically report the QRS and T-axes, the F-QRS-T angle can be easily calculated from the surface ECG by subtracting the QRS-axis from the T-axis (17). F-QRS-T angle abnormalities reflect electrical instability and the heterogeneity of myocardial repolarization. The F-QRS-T angle is effective in detecting repolarization abnormalities before significant ECG changes occur (18). Normally, the result of balanced regulation of electrical activity and recovery; and the ventricular depolarization and repolarization axis are in the same direction, and it results in a sharp QRS axis change (19). Chronically, ischemic myocardium causes delayed conduction in the local Purkinje fibers and partial depolarization and repolarization of the ventricle (20). It results in slow activation of the myocardium. This slow activation is one of the most important reasons for the instability of depolarization and repolarization homogeneity (21). In conclusion, damaged or inhomogeneous areas of the myocardium owing to ischemia results in abnormal ventricular repolarization, and a widening F-QRS-T angle appears. In a study, it was reported that the F-QRS-T angle was an appropriate clinical substitute for the spatial QRS-T angle in risk estimation. With a correction for demographic and clinical features, the F-QRS-T angle wideness was a strong predictor of total mortality with a >50% increased risk and was a strong predictor of incident CAD with a 74% increased risk (11). On the basis of the CAG results of all patients included in this study, a medical treatment was decided for 31.2%, coronary slow flow for 16.8%, percutaneous coronary intervention for 37.1%, and coronary bypass for 14.9% of the patients. When CAD severity was calculated with the Gensini score, mild and severe CAD were detected in 48% and 53% of patients, respectively. The mean QRS duration of all patients included in the study was measured as 79.12±3.90 seconds, the QRS-T angle as 71.18±26.39°°, and the QTc as 429.52±16.65. Considering the study groups created, no significant relationship could be found between the groups according to the pulse, QRS durations, and QTc data of all patients.

In some studies, the relationship between F-QRS-T angle and the severity of CAD was investigated, and it was found that the prevalence of CAD with 2 or 3 vascular occlusions was significantly higher in patients with a planar QRS-T angle >90° Than in patients with a planar QRS-T angle ≤90° (22). In a study conducted on patients with 3 vascular occlusions, a statistically significant difference was found between the number of patients with a F-QRS-T angle ≥95.6° and the number of patients with a F-QRS-T ≤95.6°. They thought that the possible cause of this may be related to an increase in the F-QRS-T angle of the lesion accompanying CAD not associated with infarction and found that patients with a F-QRS-T angle ≥95.6° more frequently had proximal vascular disease (23). In a recent study, damaged or inhomogeneous areas of ischemia-induced myocardium resulted in abnormal ventricular repolarization and revealed a widening QRS-T angle. In the same study, it was shown that hemodynamically significant occlusion in the epicardial coronary artery resulted in a wider QRS-T angle associated with ischemia and a significant narrowing in the QRS-T angle after revascularization (24). In another study, it was found that QRS and T-axes changes were associated with transient ischemic attacks in patients with coronary artery occlusion (25). They also revealed that the association of a wide QRS-T angle with a 6-year mortality risk in patients with ischemic chest pain was 1.5 times greater (26). In this study, however, when the severe CAD group [average 91°° (between 79 and 102)] and the mild CAD group [average 53°° (between 38 and 64)] were compared, it was seen that there was a statistically significant relationship between the F-QRS-T angles. These findings suggest that the F-QRS-T angle may be a useful parameter in demonstrating CAD severity in patients with stable angina pectoris.

Study limitations

The small sample size of the study was the main limitation. In addition, in some studies, it was demonstrated that spatial QRS-T angle can be more superior to the frontal planar QRS-T angle for cardiac risk protection. The lack of data reated to the spatial QRS-T angle values is the other limitation.

Conclusion

In the light of these data, it was seen that there was a significant relationship between the changes in F-QRS-T angles and CAD in patients who were non-diabetic and had angina, and if the F-QRS-T angle is greater than 91°, severe CAD should be considered. Besides, before performing an invasive procedure, the method employed in measuring F-QRS-T angles, one of the repolarization markers for detecting CAD severity, was considered to be of broad utility for these patient groups.

Acknowledgements: We would like to thanks Ass. Prof. Bernas Altıntaş for his support for the statistics of our study.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Author contributions: Concept – H.A.; Design – H.A., Ö.B.; Supervision – H.A., Ö.B.; Fundings – None; Materials – H.A., Ö.B.; Data collection &/or processing – H.A., Ö.B.; Analysis &/or interpretation – H.A., Ö.B.; Literature search – H.A., Ö.B.; Writing – H.A.; Critical review – H.A., Ö.B.

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