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Fragmented QRS in the relatives of patients with coronary artery disease

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Abstract

Background: Coronary artery disease (CAD) is one of the important causes of mortality. It has been emphasized that the risk of CAD may be increased in the relatives of CAD patients. Fragmented QRS (fQRS) is an electrocardiography (ECG) marker showing myocardial damage.

Methods: A study group of 62 symptomatic individuals (31 males, mean age 38.5 ± 7.12 years) with first-degree relatives with coronary artery disease and 64 healthy volunteers (24 males, mean age 37.9 ± 11.6 years) were included in this study. The study did not include those with known cardiac disease, metabolic disease, or drug use that may cause a change in ECG parameters.

Results: There was no significant difference between the groups regarding gender, heart rate, QRS complex, QTc, frontal QRS-T angle, and left ventricle ejection fraction. Compared to the control group, the QT interval and fQRS count were significantly higher in the study group ($p < .05$ for both). Low-density lipoprotein cholesterol (LDL-C), hemoglobin, and neutrophil counts were significantly higher in the study group compared to the control group ($p < .05$ for all).

Conclusions: Our study showed that fQRS was increased in individuals with symptomatic first-degree relatives with coronary artery disease compared to healthy volunteers.

KEYWORDS
coronary artery disease, fragmented QRS, myocardial scar

1 | INTRODUCTION

Cardiovascular diseases are one of the leading causes of mortality and morbidity worldwide. Classical risk factors determined due to epidemiological studies are insufficient to explain the prevalence of coronary artery disease in the population. Early diagnosis of patients with symptoms such as palpitations, chest pain, and high blood pressure makes positive contributions to preventing morbidity and mortality (Brown et al., 2021). Individuals with a familial history of coronary artery disease can be detected in normal controls, even with mild symptoms. For this reason, cardiac parameters and electrocardiograms should be followed up at certain intervals in their routine follow-up if the first-degree relatives of coronary artery patients have complaints such as palpitations, fainting, high blood pressure, and chest pain (Shea et al., 1984).

Fragmented QRS (fQRS) and frontal QRS-T angle are non-invasive and specific ECG parameters that can be easily measured from surface electrocardiogram (ECG) without any computer program. fQRS

is defined as the RSR pattern and/or the presence of notching in the R and S waves in at least two consecutive leads on the ECG, while the frontal QRS-T angle is defined as the absolute angle difference between the mean QRS and T-wave axes. These ECG parameters are relatively new and provide essential information about the depolarization and repolarization of the myocardium (Dilaveris et al., 2001). Studies have shown that fragment fQRS and frontal QRS-T angle can predict future heart disease in different patient populations, and it has been reported that these parameters are associated with the risk of arrhythmia and sudden death (Take & Morita, 2012; Tekin et al., 2022).

This study compares fQRS complexes and frontal QRS-T angles on ECG examinations in first-degree relatives of patients diagnosed with coronary artery disease with healthy controls.

2 | METHODS

2.1 | Study design

This study is a cross-sectional and descriptive study. Within the scope of the study, symptomatic first-degree relatives of patients with coronary artery disease followed in the cardiology outpatient clinic were examined. The permission of the local ethics committee was obtained for the study (dated 18/01/2022, decision number 2022/1–24). The study group consisted of 62 individuals over 18 who had first-degree coronary artery disease but did not have any known cardiac disease.

The control group was recruited from healthy individuals who did not have any other disease and applied to the cardiology outpatient clinic to obtain a sound report for employment examination, military service examination, and medical report for driver's license. The control group consisted of 64 people over the age of 18. Patients with rheumatic heart disease, systemic autoimmune disease, heart valve disease, thyroid dysfunction, liver disease, pulmonary disease, acute or chronic infection, electrolyte disorder, anemia, kidney disease, diabetes mellitus, and stable or acute coronary artery disease were excluded from the study. In addition, those with sinus arrhythmia, atrioventricular conduction defect, and right and/or left bundle branch block were excluded from the study. Those using drugs such as antidepressants, antipsychotics, antiarrhythmics, and antihistamines that affect the QRS complex and T wave in the ECG were also excluded from the study.

2.2 | Laboratory evaluation

Venous blood samples were examined at hospital admission. Low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels were analyzed using the Architect c8000 Chemistry System (Abbott Diagnostics, USA) commercial kits. Complete white blood (WBC) counts, including neutrophil and lymphocyte counts, were measured using an automated hematology analyzer CELL-DYN Ruby (Abbott Diagnostics) and expressed as $\times 1000\,\text{cells/mm}^3$. Hemoglobin, hematocrit, platelet count, mean platelet volume (MCV), and red blood cell distribution width (RDW) were also calculated. Neutrophil to lymphocyte ratio (NLR) was calculated by dividing the neutrophil count by the lymphocyte count, and platelet to lymphocyte ratio (PLR) was calculated as the number of platelets divided by the lymphocyte count. C-reactive protein (CRP) levels were analyzed using biochemistry kits (Abbott Diagnostics) and an Architect c8000 Chemistry System (Abbott Diagnostics) device.

2.3 | Electrocardiographic and echocardiographic evaluation

The 12-lead ECG of each patient was analyzed blindly by two independent cardiologists. The 12 lead ECG recordings (50 mm/s, 10 mm/mV) were obtained in the supine position using a CardioFax S device (Nihon Kohden). Resting heart rate was measured using the ECG data, and calipers and magnifying glasses were used to reduce measurement errors. The QRS duration was defined as the

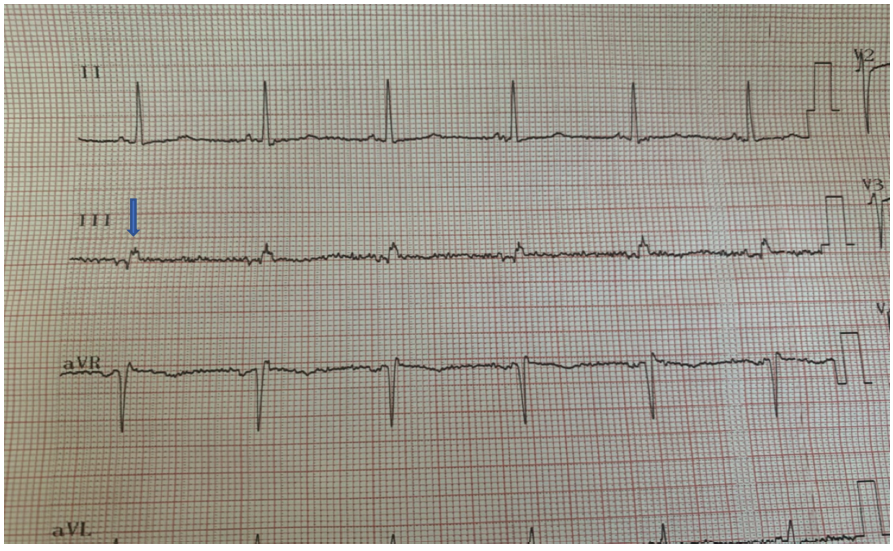

FIGURE 1 fQRS was seen as RSR′ patterns (QRS duration <120 ms) in Lead DIII

time interval onset to the end of the QRS complex. The QT interval was calculated as the time from the start of the QRS complex to the end of the T wave. QT interval was corrected for heart rate by using Bazett's formula (Bazett, 1920).

Frontal QRS and T-wave axes were available in the automatic reports of the ECG machine. The f(QRS-T) angle was calculated from these axes as the absolute difference between the frontal plane QRS axis and frontal plane T axis. If the angle exceeds 180°, it was calculated by subtracting from 360°. fQRS was said to be present when different QRS morphologies with varying RSR' patterns (QRS duration <120 ms) were detected, such as the presence of an additional R wave (R′), notching of the nadir of the R or S wave, or the presence of more than one R′ (fragmentation) in two contiguous leads (Figure 1).

Transthoracic echocardiographic evaluations of all patients included in the study were performed using the Vivid 5 Pro (General Electric) brand ECO device. Parasternal long-axis and short-axis images were obtained in the lateral decubitus position, and four-chamber and two-chamber views were obtained from the apical window. Left ventricular ejection fraction (LVEF) was assessed using Simpson's method (Lang et al., 2015).

2.4 | Statistical analysis

Statistical Package for the Social Sciences version 26.0 (SPSS Inc.) was used for statistical analysis. Numerical variables were posted as mean ± standard deviation values, whereas qualitative variables were given numbers and percentages. The Kolmogorov–Smirnov test evaluated data distribution. Independent sample *t*-tests were used to compare numerical variables, whereas Mann–Whitney *U* tests were used for discontinuous parametric variables. Qualitative variables were compared by using chi-square tests within the study group. For correlation analysis, the Pearson correlation test was used. It was considered statistically significant if the *p* values were less than .05.

3 | RESULTS

A study group of 62 symptomatic individuals (31 males, mean age 38.5 ± 7.12 years) with first-degree relatives with coronary artery disease and 64 healthy volunteers (24 males, mean age 37.9 ± 11.6 years) were included in this study. Demographic, electrocardiographic, and echocardiographic characteristics of the study groups are given in Table 1. There was no significant difference between the groups regarding gender, heart rate, QRS complex, QTc, frontal QRS-T angle, and LVEF. Compared to the control group, the QT interval and fQRS count were significantly higher in the study group ($p < .05$ for both).

Comparative laboratory findings of the two groups are given in Table 2. LDL-C, hemoglobin, and neutrophil counts were significantly higher in the study group compared to the control group ($p < .05$ for all). The PLR value was higher in the control group, and there was no statistical difference between the groups regarding other laboratory parameters.

TABLE 1 Comparison of sociodemographic features and electrocardiographic parameters of CAD relatives and healthy volunteers

	CAD relatives ($n = 62$)	Healthy ($n = 64$)	*p*
Age	38.5 ± 7.12	37.98 ± 11.6	.764[a]
Gender			
Female	31 (50)	40 (66)	.157[b]
Male	31 (50)	24 (34)	
Smoking	21 (35)	19 (30)	.358[b]
BMI, kg/m^2	27.5 ± 4.6	26.8 ± 4.8	.214[a]
Systolic blood pressure mmHg	120.3 ± 12.3	114.5 ± 15.4	.562[a]
Diastolic blood pressure mmHg	74.3 ± 6.9	72.8 ± 8.9	.456[a]
LVEF, %	60.2 ± 5.2	57.3 ± 4.7	.213[a]
Heart rate, bpm	83.84 ± 14.91	81.91 ± 15.19	.502[a]
QRS, ms	89 ± 8.92	89.78 ± 8.01	.448[a]
QT, ms	362.74 ± 29.91	350.05 ± 28.58	**.016**[a]
QTc, ms	405 [430–393]	402 [423–387]	.266[c]
Frontal QRS-T angle	32 [48–20]	24 [40–12]	.074[c]
Having fQRS	48 (77)	7 (11)	**<.001**[b]
fQRS count	1.00 [2.25–1.00]	0.00 [1.00–0.00]	**<.001**[c]

Abbreviations: BMI, body mass index; CAD, coronary artery disease; fQRS, fragmented QRS; LVEF, left ventricular ejection fraction; QTc, corrected QT interval.

Bold indicates statistically significant value ($p < .05$).

[a]Independent *t* test was used.

[b]Chi-square test was used.

[c]Mann–Whitney *U* test was used.

TABLE 2 Comparison of laboratory parameters of CAD relatives and healthy volunteers

	CAD relatives ($n = 62$)	Healthy ($n = 64$)	p
Hemoglobin, mg/dl	14.2 ± 1.56	13.61 ± 1.65	**.041**[a]
Hematocrit, %	43.72 ± 4.87	42.67 ± 4.81	.226[a]
MCV, fL	85.01 ± 4.28	84.23 ± 7.05	.751[a]
RDW, %	11.88 ± 1.33	12.39 ± 1.79	.072[a]
WBC, 10^3/μl	8.2 ± 1.7	7.8 ± 2.0	.336[a]
Platelet, 10^3/μl	214 [294–173]	275 [342–247]	**<.001**[b]
Neutrophil, 10^6/μl	5.0 ± 1.4	4.6 ± 1.8	**.046**[a]
Lymphocyte, 10^3/μl	2.3 ± 0.8	2.3 ± 0.7	.924[a]
LDL-C, mg/dl	109.3 ± 23.3	100.1 ± 26.7	**.042**[a]
HDL-C, mg/dl	45.5 ± 12.3	46.2 ± 13.1	.782[a]
CRP, mg/dl	0.2 [0.2–0.2]	0.3 [0.6–0.1]	.527[b]
NLR	2.47 ± 1.13	2.21 ± 1.18	.093[a]
PLR	116 [166–70]	125 [173–100]	**.043**[b]

Abbreviations: CAD, coronary artery disease; CRP, c-reactive protein; HDL-C, high-density cholesterol; LDL-C, low-density cholesterol; MCV, mean corpuscular volüme; NLR; neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; RDW, red cell distribution width; WBC, white blood cell.

Bold indicates statistically significant value ($p < .05$).

[a]Independent *t* test was used.

[b]Mann–Whitney *U* test was used.

4 | DISCUSSION

In this study, the frequency of fQRS and LDL-C values was higher in individuals with first-degree relatives with coronary artery disease. There was no difference between the groups in terms of frontal QRS-T.

Cardiovascular diseases are the single most significant cause of mortality and morbidity for men and women. In the study of Onat et al. in Turkey, coronary artery disease ranked first among all causes of death with a 43% share (Onat et al., 2001). Family history is a non-modifiable risk factor for coronary artery disease.

fQRS, an arrhythmia marker, shows myocardial damage and fibrosis (Das et al., 2007). In coronary artery disease and non-ischemic cardiomyopathies, fibrosis and scarring can disrupt myocardial electrical current and cause malignant ventricular arrhythmias. It has also been stated that fQRS can predict sudden cardiac death. Late gadolinium enhancement cardiac magnetic resonance imaging showed that myocardial fibrosis was associated with fQRS on ECG (Basaran et al., 2011). In a study conducted with myocardial single-photon emission tomography, fQRS was found to show better myocardial perfusion and functional abnormalities when compared with the Q wave on the ECG (Das et al., 2008). The authors reported that the sensitivity of fQRS in detecting myocardial scar was 85%, and its negative predictive value was 93%. Furthermore, the presence of fQRS in the precordial leads (V1-5) indicates myocardial scarring in the left anterior descending territory; the presence of fQRS in the lateral leads (I, aVL, and V6) indicates myocardial scarring in the lateral myocardial segment; It has been reported that the presence of fQRS in the lower extremity leads (II, III, and aVF) predicts myocardial scarring in the lower myocardial segment or the right coronary artery region (Tanriverdi et al., 2015).

Eyuboglu et al. (Eyüboğlu & Akdeniz, 2018) reported that the presence of fQRS in the ECG is an essential indicator of the extent of coronary artery disease determined by the Gensini score and the total atherosclerotic burden in patients with stable coronary artery disease. The presence of fQRS in the ECG is associated with poor prognosis in patients with coronary artery disease (Das et al., 2008). It has been observed that fQRS is an independent predictor of mortality in patients with acute coronary syndrome (Das et al., 2009). It has been reported that the presence of fQRS is associated with collaterals in patients with chronic total occlusion who have not had acute myocardial infarction before (Kadı et al., 2011). It has been observed that the incidence of fQRS is high in patients with ischemic cardiomyopathy and non-ischemic cardiomyopathy with low EF and is associated with adverse cardiac events (Sha et al., 2011; Tigen et al., 2009). There was no difference in LVEF between the two groups in our study. The fQRS was significantly higher in the study group, which may indicate the presence of coronary artery disease in these individuals.

There are many markers of myocardial repolarization in the literature. One of the newest markers, the QRS-T angle in the frontal plane, was defined as the angle between the mean QRS (ventricular depolarization) and T-wave (ventricular repolarization) axes. QRS-T angle measurement with a spatial method requires special computer programs. However, the frontal QRS-T angle can be easily detected from the surface ECG (subtracting the QRS axis from the T axis). In addition, most ECG devices have a QRS axis and T axis in the automatic report section. It has been suggested that mortality increases threefold in patients with an increased frontal QRS-T angle compared to those with a normal frontal QRS-T angle in patients with cardiovascular disease (Rautaharju et al., 2006). In a study involving 202 patients with stable angina pectoris, a statistically significant correlation was found between the severity of coronary artery disease and the frontal QRS-T angle. There was no difference between the groups in terms of frontal QRS-T angle in our study.

5 | CONCLUSION

Our study showed that fQRS was increased in individuals with symptomatic first-degree relatives with coronary artery disease compared to healthy volunteers.

5.1 | Limitation

The study's main limitations are: First, the study was a single-center and cross-sectional study with a small number of patients. Second, the association of fQRS with coronary artery disease in symptomatic patients was not demonstrated by coronary angiography or myocardial perfusion scintigraphy.

AUTHORS' CONTRIBUTIONS

S Abuş carried out conception and design of the research and acquisition of data. S Abuş and A Afşin contributed to analysis and interpretation of the data, writing of the manuscript and critical revision of the manuscript for intellectual content. All authors read and approved the final draft.

CONFLICT OF INTEREST

There is no conflict of interest declared by the authors.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

No funding was received for this study. The Ethical Committee of the Faculty of Medicine approved the study (Decision Date:18/01/2022, Meeting Number:1, Decision Number:2022/1–24).

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