Relationship Between Epicardial Adipose Tissue Thickness and Fragmented QRS

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ABSTRACT

Introduction: Fragmented QRS (fQRS) on a 12-lead electrocardiogram (ECG) has been demonstrated as a marker of myocardial fibrosis. The main purpose of present study was to investigate the association between epicardial adipose tissue (EAT) and fragmented QRS.

Materials and Method: Study population consisted of 151 patients had fQRS detected on a routine 12-lead ECG and 114 controls without fQRS. Epicardial adipose tissue was assessed by measuring epicardial fat thickness with echocardiography. Fragmented QRS was defined by the presence of various RSR' patterns included an additional R wave (R), notching of the R wave, notching of the downstroke or upstroke of the S wave, or the presence of >1 R′ in 2 contiguous leads corresponding to a major coronary artery territory.

Results: Patients with fQRS had higher EAT values compared with those without fQRS (5.9 ± 2.7, 3.8 ± 2.3, p<0.001). Univariate analyse demonstrated significant association between fQRS and EAT (P< 0.001), hypertension (p: 0.015). Binary logistic regression analysis revealed EAT (95% confidence interval [CI] 1.053 – 1.938, p: 0.022) and total cholesterol (95% CI: 1.001 – 1.030, P: 0.037) as an independent determinant of fQRS.

Conclusion: In present study, we found higher amounts of epicardial adipose tissue in subjects with fQRS. In addition, presence of fQRS was found to be independently associated with EAT.

Keywords: Fragmented QRS, epicardial adipose tissue, myocardial fibrosis

Epikardiyal Yağ Dokusu Kalınlığı ve Parçalı QRS Arasındaki İlişki

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ÖZET

Giriş: On iki kanallı elektrokardiyografide (EKG) tespit edilen parçalı QRS'in (pQRS) miyokart fibrozunun bir belirteci olduğu gösterilmiştir. Bu çalışmanın amacı epikardiyal yağ dokusu kalınlığı (EYK) ile parçalı QRS (pQRS) arasındaki ilişkiyi incelemektir.

Hastalar ve Metod: Çalışmaya kardiyoloji polikliniğimize müracaat edip rutin eloktrokardiyografik incelemede pQRS i olan 151 hasta ve kontrol grubu olarak pQRS i olmayan 114 hasta alındı. Epikardiyal yağ dokusu kalınlığı ekokardiyografide hesaplandı. Parçalanmış QRS birbirini takip eden iki EKG derivasyonunda ilave R dalgası (R') veya R veya S dalgasında çentiklenme veya bölünme varlığı olarak alındı.

Bulgular: pQRS olan hastalarda EYK değerleri daha yüksekti (5.9 ± 2.7, 3.8 ± 2.3, p <0.001). Tek değişkenli analiz EYK ile pQRS(P <0.001) ve hipertansiyon (p: 0.015) arasında anlamlı bir ilişki olduğunu göstermiştir. Binary lojistik regresyon analizi, EYK (% 95 güven aralığı [CI] 1.053 - 1.938, p: 0.022) ve total kolesterolü (% 95 GA: 1.001 - 1.030, P: 0.037) pQRS 'in bağımsız bir belirleyicisi olarak ortaya koydu.

Sonuç: Bu çalışmada, pQRS li hastalarda Epikardiyal yağ dokusu kalınlığını artmış olarak tespit ettik. Buna ek olarak, epikardiyal yağ dokusu kalınlığı pQRS in güçlü ve bağımsız bir belirteci olarak bulunmuştur.

Anahtar Kelimeler: Parçalı QRS, epikardiyal yağ dokusu, miyokardiyal fibrozis

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Introduction

Fragmented QRS (fQRS) was defined by the presence of various RSR' patterns with or without a Q wave and included an additional R wave (R), notching of the R wave, notching of the downstroke or upstroke of the S wave, or the presence of >1 R′ without a typical bundle branch block in 2 contiguous leads, corresponding to a major coronary artery territory (1). Several studies have demonstrated that fQRS on a routine 12-lead ECG signifies a myocardial scar in different clinical situations. Also, fQRS represents conduction delay from inhomogeneous activation of the ventricles due to myocardial scar (2,3,4).

Epicardial adipose tissue (EAT) is true visceral fat deposit that presents on the surface of the heart between the visceral pericardium and myocardium and covers more than three quarters of the surface of the heart (5). Due to its paracrine and endocrine activity, secreting pro-inflammatory and anti-inflammatory chemokines and cytokines, including interleukin-6, interleukin-1β, tumor necrosis factor-α, and monocyte chemoattractant protein-1, it has been supposed to influence both structural and ultrastructural change in myocardium such as increased LV mass, development of coronary atherosclerosis, atrial enlargement and diastolic dysfunction (5,6,7,8) that may lead to the development of fQRS. However, the relationship between EFT and fQRS has not been investigated. Thus, the purpose of present study was to investigate this association in patients without known structural heart disease.

Material and Methods

Patients

Study population consisted of 151 patients had fQRS detected on a routine 12-lead ECG and 114 controls without fQRS. Exclusion criteria were the presence of structural heart disease including known coronary artery disease (previous myocardial infarction, percutaneous coronary intervention coronary by-pass and angina pectoris), heart failure (ejection fraction<50%), dilated or hypertrophic cardiomyopathy, moderate and severe valvular disease, valve replacement and poor echocardiographic imaging. The presence of blood pressure >140/90 mmHg or the use of antihypertensive medication were defined as hypertension. Demographic data, biochemical blood tests and ECG were obtained from the entire study population. Informed consent was obtained from

all participants and the study protocol was approved by the Ethics Committee of the Trabzon Kanuni Training and Research Hospital.

Electrocardiography

All standard 12‑lead ECGs were obtained simultaneously using a recorder set at a 25 mm/s paper speed and a voltage calibration of 1 mV/cm (Nihon Kohden-cardiofax S ECG-1250 K, filter range 0.5 Hz to 150 Hz, alternating current filter 60 Hz). All examinations were carried out in a quiet room during spontaneous breathing, following 10 min of rest in the supine position. The ECGs were each numbered and presented to the analyzing investigators who were blind both to patient name and group information. ECG assesments were maden by two medically qualified observers blind to the name and group of patients. Presence of fQRS was determined with consensus. fQRS comprises various morphologies of QRS wave with or without a Q wave. fQRS was diagnosed with the presence of an additional R wave (R') or notching in the nadir of the R wave or the S wave, or the presence of more than one R' (fragmentation) in two consecutive leads, corresponding to a certain myocardial territory.

Measurement of Epicardial Adipose Tissue

EAT thickness was evaluated by transthoracic echocardiography. Two-dimensional transthoracic echocardiography in the left lateral decubitus position was performed by a Vivid S5 cardiovascular ultrasound system (GE Healtcare, Wauwatosa, WI, USA). Measurements were performed by a an experienced physician who was unaware of the subjects' clinical and demographic data. Epicardial fat was defined as an echo- free space in front of the right ventricle free wall between the outer wall of the myocardium and the pericardial layer. Epicardial fat thickness was measured perpendicularly on the free wall of the right ventricle at end diastole. Aortic annulus was used as anatomical reference to standardize the measurement point. All measurements were performed for three consecutive cardiac cycles and an average value was obtained. For the parasternal short-axis view, epicardial adipose tissue thickness was measured on the right ventricular free wall along the midline of the ultrasound beam, 2 cm from the ventricular septum (fig. 1).

Statistical Analyse

Continuous variables were expressed as mean+standard deviation, and categorical variables were expressed as percentage. An analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. A comparison of the categorical variables between the groups was performed using a chi-square test. Continuous variables were compared using independet t test and Mann-Whitney U test. Binary logistic regression analysis was performed to find the independent determinant of fQRS. A P < .05 (2-tailed) was considered significant. Statistical analysis was carried out using SPSS 17.0 statistical software. (SPSS Inc., Chicago,Illinois, USA).

Results

Clinical and laboratory characteristics between subjects with and without fragmented QRS was demonstrated in table 1. Patients with fQRS had higher EAT values compared with those without fQRS (5.9 ± 2.7, 3.8 ± 2.3, p<0.001). (fig2). Also, in univariate analyse there was significant association between fQRS and EAT (P< 0.001), hypertension (p: 0.015). Binary logistic regression analysis revealed EAT (95% confidence interval [CI] 1.053 – 1.938, p: 0.022) and total cholesterol (95% CI: 1.001 – 1.030, P: 0.037) as an independent determinant of fQRS (table 2).

Discussion

In the present study, we found increased epicardial fat thickness in subjects with fQRS as compared to controls. It was also shown that EAT was independently associated with presence of fQRS.

Fragmented QRS on ECG has been regarded as a marker of myocardial fibrosis or scarring in different diseases and independent predictor of cardiac events in patients with coronary artery disease (9,10,11) Several studies have showed that the region of a myocardial fibrosis is associated with inhomogeneous activation of the left ventricle, leading to terminal conduction delay or fragmentation of QRS (12,13). Another study demonstrated that the fQRS complex on ECG is a highly sensitive and specific marker of myocardial scarring as detected by regional perfusion abnormalities on a nuclear stress test (1). Also, fQRS on a standard 12-lead ECG can be used in the detection of myocardial scar with higher sensitivity and negative predictive value than Q wave. Furthermore, simultaneous occurrence of fQRS and Q wave on 12-lead ECG improves the predictive value in predicting the presence of myocardial scar (14).

EAT is visceral fat which has a close interaction with the myocardium and coronary arteries. EAT also plays an important role in the inflammatory process in the cardiovascular system via its endocrine and paracrine activity (6, 15). Several studies showed that EAT is associated with a variety of disorders such as atherosclerosis, xanthelasma palpebrarum, hypertension, arterial stiffness, enlarged atrial and ventricular dimensions, ventricular premature beats, atrial fibrillation and increased LV mass (16,17,18,19,20).

Some potential mechanisms can be proposed to explain relationship between EAT and fQRS. EAT cause both structural and ultrastructural changes in myocardium that might be considered as a possible mechanism. Iacobellis et al showed that EAT is associated with structural and ultrastructural myocardial changes, including myocardial fibrosis. (20,21). EAT also releases pro-inflammatory cytokines, including TNF-α, IL1-β and IL-6, it has been supposed to influence both structural and ultrastructural change in myocardium including myocardial fibrosis (5, 6, 20). Myocardial remodeling and fibrosis may produce some changes in action potential characteristics and predispose the fQRS on the surface ECG.

Limitations of the study

Firstly, our study population had a relatively small number patients. Secondly, no evaluation of magnetic resonance imaging or computed tomography was performed to assess EFT. Thirdly, detailed echocardiographycal assessment, diastolic parameters were not obtained all patients that are known to be related to myocardial fibrosis, such as mass, wall thickness and hypertrophy but earliest studies showed this association(20,21). Finally, our study is a case-control study, which has some limitations concerning matching methodology.

Conclusions

In the present study, we found higher amounts of epicardial adipose tissue in subjects with fQRS. In addition, EAT was found to be independently associated with presence of fQRS. EAT thickness may be a new mechanism to explain fQRS pathogenesis. Further studies are required to explain the patophysiological mechanism in fQRS and EAT.

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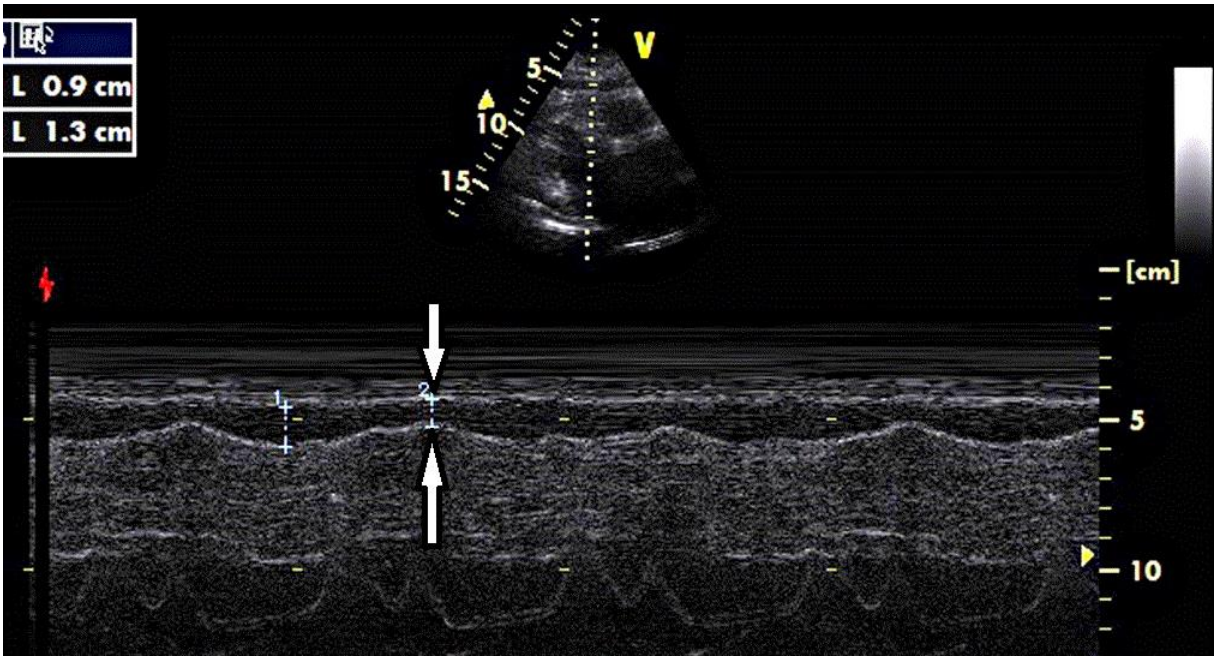

Fig. 1. Measurement of epicardial fat by echocardiography

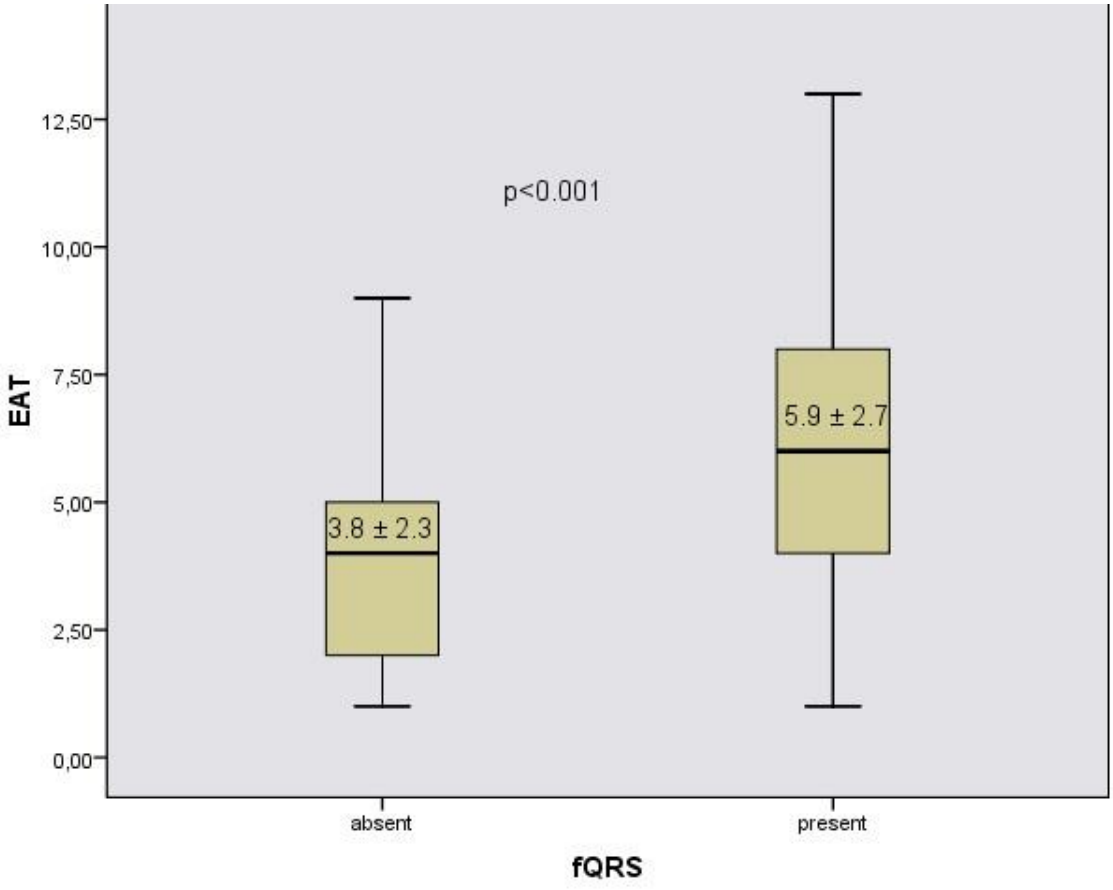

Fig. 2. Epicardial adipose tissue thickness in subjects with and without fQRS

Table 1. Comparison of clinical and laboratory characteristics between subjects with and without fragmented QRS

	fQRS absent (n=114)	fQRS present (n=151)	*p*
Age, years	53± 15	56 ± 13	0.027
Sex, F/M	59/55	82/69	0.68
BMI (kg/m²)	28.4 ± 5.1	29.1 ± 5	0.27
Diabetes mellitus, n(%)	7 (6)	18 (12)	0.11
Hypertension, n(%)	47 (41)	85 (56)	0.015
Dyslipidemia, n(%)	23(20)	56(37)	0.003
Current smokers, n(%)	13(11)	18 (12)	0.89
Cardiovascular medications			
ACE inhibitors or ARB, n(%)	18(16)	49(32)	0.002
Calcium channel blockers, n(%)	8(7)	14(9)	0.51
β-Blockers, n(%)	11(9)	14(9)	0.91
Cholesterol-lowering drugs, n(%)	8(7)	14(9)	0.51
Oral antidiabetic drugs n(%)	6(5)	18(12)	0.06
Biochemical parameters			
Glucose (mg/dl)	94 ± 15	105 ± 46	0.048
Total cholesterol (mg/dl)	197 ± 48	212 ± 47	0.026
HDL-c (mg/dl)	49 ± 12	48 ± 12	0.64
LDL-c (mg/dl)	127 ± 37	130 ± 36	0.49
Triglyceride (mg/dl)	144 ±77	168 ±104	0.05
Serum creatinine (mg/dl)	0.75 ± 0.16	0.76 ± 0.21	0.84
Epicardial fat (mm)	3.8 ± 2.3	5.9 ± 2.7	<0.001

Data are expressed as no. (%) or mean ± standard deviation. ACE, Angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMI, body-mass index; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol

Table 2. Binary logistic regression analysis showing independent factors associated with Fragmented QRS EAT, Epicardial adipose tissue; LDL-c, low-density lipoprotein cholesterol

Variables	%95 CI	P
Age	0.984 – 1.032	0.517
Hypertension	0.575 – 2.09	0.78
Diabet	0.578 – 5.804	0.304
EAT	1.053 – 1.938	0.022
Total cholesterol	1.001 – 1.030	0.037
Triglyceride	0.996–1.004	0.928
LDL-c	0.968-1.000	0.053