Colombia Médica

ORIGINAL ARTICLE

Increased para-aortic adipose tissue on echocardiography may closely be related with fragmented QRS.

El aumento del tejido adiposo paraaórtico en la ecocardiografía puede estar estrechamente relacionado con la fragmentación del QRS.

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Citation: Çakan F, Akinci S, Adar A, Köktürk U, Akbay E, Önalan O. **Increased para-aortic adipose tissue on echocardiography may closely be related with fragmented QRS**. Colomb Méd (Cali),2024; 55(2):e2025986.http://doi.org/10.25100/cm.v55i2.5986

Received: 25 Feb 2024
Revised: 15 Apr 2024
Accepted : 21 Jun 2024
Published: 30 Jun 2024

Keywords:
Fragmented QRS, paraaortic, adipose tissue, echocardiography, perivascular, cardiovascular risk factors.

Palabras clave:
TQRS fragmentado, paraaórtico, tejido adiposo, ecocardiografía, perivascular, factores de riesgo cardiovascular.

Abstract

Background:
The association of fragmented QRS (fQRS) with many cardiac pathologies such as cardiac fibrosis has been described previously. Paraaortic adipose tissue (PAT) is thought to be associated with many cardiac diseases and there is only one publication on its echocardiographic evaluation.

Aims:
To describe the possible relationship between fQRS and PAT.

Methods:
Patients presenting to the cardiology outpatient clinic were evaluated for inclusion in the study. Presence of additional R' wave or notching/splitting of S wave in two contiguous ECG leads was defined as fragmented QRS (fQRS) and patients were divided into two groups according to fQRS status on ECG. The hypoechoic space in front of the ascending aorta was considered as PAT in the parasternal long-axis view. The medical history and routine laboratory parameters of the participants were recorded. Univariate and multivariate binary regression analysis was used to determine the relationship between PAT and fQRS.

Results:
A total of 221 patients were enrolled and divided into two groups according to fQRS status. PAT was significantly higher in the fQRS group: 9.2 mm (7.1/12.3) vs 6.8 mm (1.2/10.9), p=0.001. Univariate analysis showed significant association between fragmented QRS and PAT size (OR 1.122, p= 0.001). Binary regression analysis revealed an independent and strong association between aortic size (OR 1.4, CI95% 1.012-1.938, p=0.042), paraaortic adipose tissue (OR 1.483, CI95% 1.084-2.029, p=0.014) and fragmented QRS.

Conclusions:
The presence of fQRS is associated with PAT, a newly defined parameter in echocardiography.

Conflict of interest:
The authors have no conflict of interest to disclose

Author contributions:
Substantial contributions to the conception or design of the work; Fahri Çakan, Uğur Köktürk. Drafting the work or reviewing it critically for important intellectual content; Fahri ÇAKAN, Adem Adar, Sinan Akıncı. Final approval of the version to be published; Fahri Çakan, Orhan Önalan, Ertan Akbay.

Data Statement:
Raw data for this paper is available offline. It can be available online by publishing in a repository on demand anytime.

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Resumen

Antecedentes:
La asociación del QRS fragmentado (fQRS) con muchas patologías cardiacas como la fibrosis cardiaca se ha descrito previamente. Se cree que el tejido adiposo paraaórtico (PAT) está asociado a muchas enfermedades cardiacas y sólo existe una publicación sobre su evaluación ecocardiográfica.

Objetivo:
Describir la posible relación entre el fQRS y el PAT.

Métodos:
Los pacientes que acudieron a la consulta externa de cardiología fueron evaluados para su inclusión en el estudio. Se definió como QRS fragmentado (fQRS) la presencia de una onda R' adicional o una muesca/división de la onda S en dos derivaciones contiguas del ECG y se dividió a los pacientes en dos grupos según el estado del fQRS en el ECG. El espacio hipoecoico delante de la aorta ascendente se consideró PAT en la proyección paraesternal de eje largo. Se registraron los antecedentes médicos y los parámetros de laboratorio habituales de los participantes. Se utilizó un análisis de regresión binaria univariante y multivariante para determinar la relación entre PAT y fQRS.

Resultados:
Se reclutaron 221 pacientes, que se dividieron en dos grupos según el estado de fQRS. La PAT fue significativamente mayor en el grupo fQRS [9.2 mm (7.1/12.3) frente a 6.8 mm (1.2/10.9), p=0.001]. El análisis univariante mostró una asociación significativa entre el QRS fragmentado y el tamaño del PAT (OR 1.122; p=0.001). El análisis de regresión binaria reveló una asociación fuerte e independiente entre el tamaño aórtico (OR 1.4; IC95% 1.012-1.938; p=0.042), el tejido adiposo paraaórtico (OR 1.483; IC95% 1.084-2.029; p=0.014) y el QRS fragmentado.

Conclusiones:
La presencia de QRSf se asocia a PAT, un parámetro de nueva definición en ecocardiografía.

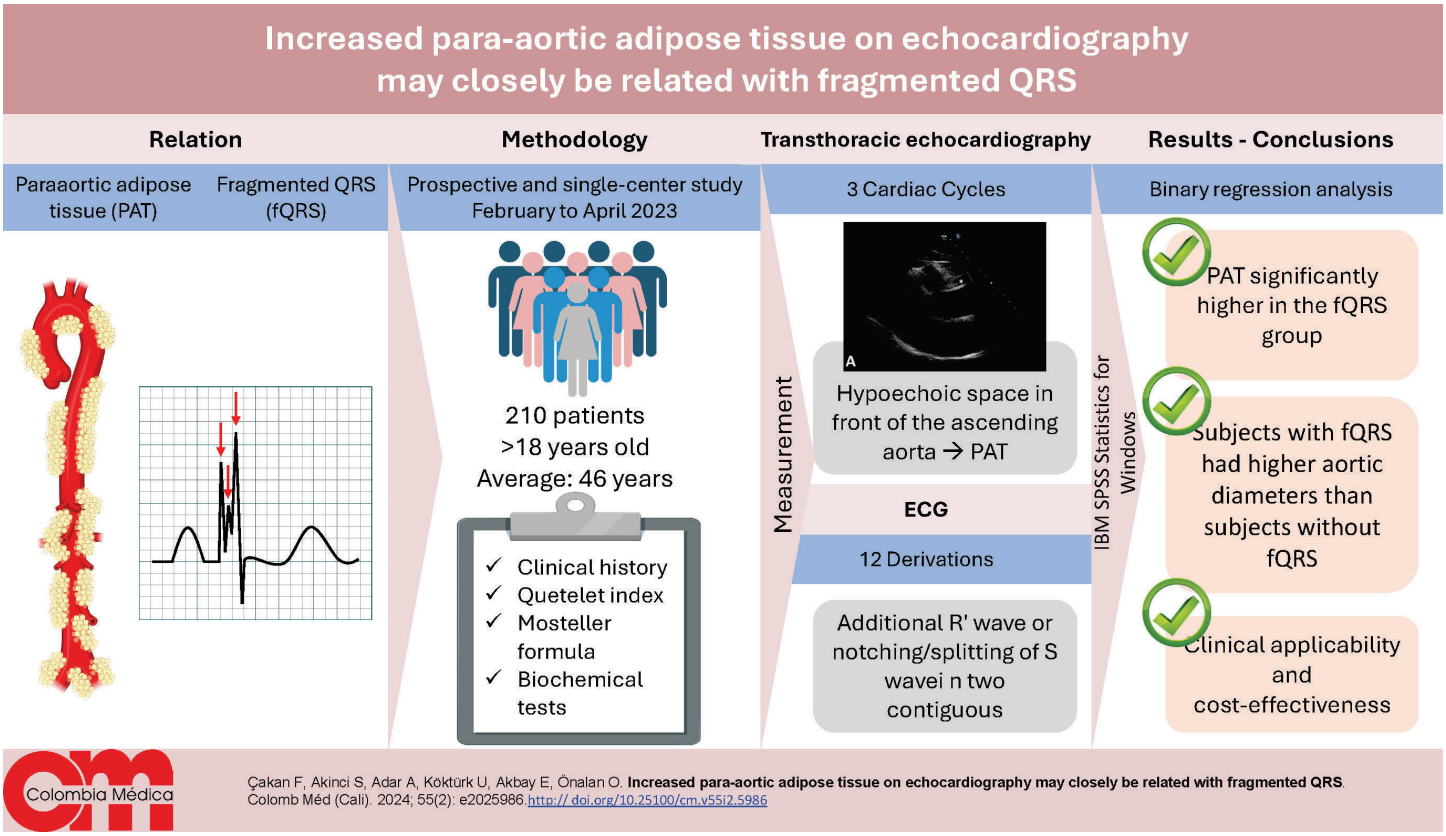
Remark

1) Why was this study conducted?
In this study it was aimed to explore the potential relationship between fragmented QRS (fQRS), a marker linked to cardiac pathologies like fibrosis, and paraaortic adipose tissue (PAT), a factor associated with cardiac diseases, with limited prior echocardiographic research.

2) What were the most relevant results of the study?
Regression analysis showed significant association between fragmented QRS and PAT size and this significance was maintained after eliminating confounding factors.

3) What do these results contribute?
The results from this study supports the idea that PAT being above a certain thickness in echocardiography may be a sign of some cardiac diseases. While fragmented QRS defines this situation electrically, PAT can reveal this situation visually through a fast modality such as echocardiography

Graphical Abstract



Introduction

Fragmented QRS (fQRS) is a reliable and easy-to-use electrocardiographic (ECG) finding in clinical practice. It is defined as notching in R or S waves without typical bundle branch block or additional RSR patterns on the QRS complex. fQRS develops as a result of heterogeneous electrical activation caused by impaired ventricular depolarization [1]. Fibrotic tissue slows electrical conduction and leads to notching of the QRS complexes [2]. It represents myocardial fibrosis or scar tissue and is associated with worse cardiovascular outcomes [3-5]. In addition, fQRS is associated with an increased risk of sudden cardiac death in patients with idiopathic dilated cardiomyopathy and heart failure [2,6,7].

Para-aortic adipose tissue is a localized fat that surrounds the aorta. In addition to protecting the aorta from trauma, paraaortic adipose tissue has been suggested to contribute significantly to aortic atherosclerosis and dilation by secreting bioactive molecules such as adiponectin and growth factors [8]. It has been suggested that epicardial adipose tissue (EAT), as measured by echocardiography, is associated with cardiac fibrosis [5]. In addition, periaortic adipose tissue has been shown to be associated with current metabolic status [9]. Most previous studies have described and investigated paraaortic adipose tissue using computed tomography. Adar et al. [10], were the first to describe paraaortic adipose tissue by echocardiography and to demonstrate its association with ascending aortic dilatation. Demonstration of this tissue by echocardiography is faster, cheaper and safer in terms of radiation compared to other modalities (especially tomography).

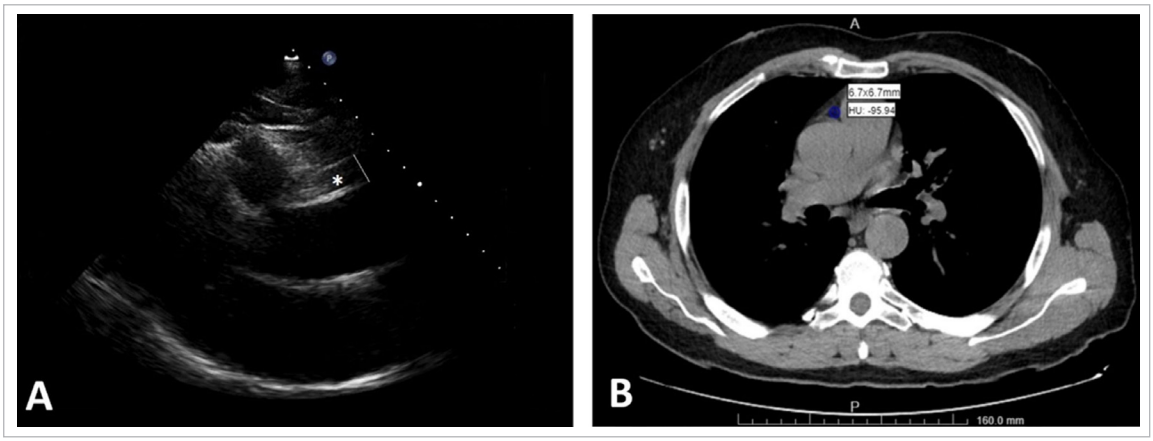


Figure 1. A. Measuring the para-aortic adipose tissue with transthoracic echocardiography on parasternal long axis view. B. Determination of adipose tissue characteristics of para-aortic tissue via computed tomography

Paraaortic adipose tissue, a metabolically active tissue, may also be an indicator of cardiac fibrosis and may be associated with fQRS, another indicator of cardiac fibrosis. This tissue, which can be easily measured by echocardiography in appropriate acoustic windows, may aid in the identification and assessment of cardiac fibrosis. The aim of this study is to describe the relationship between echocardiographic paraaortic adipose tissue thickness and the presence of fQRS.

Materials and Methods

General Information

This is a prospective and single-center study designed to evaluate the association between the presence of fQRS on 12-lead ECG and paraaortic adipose tissue. In the calculation of the estimated sample size, paraaortic tissue measurement was taken as the primary variable. When the sample size was calculated using Student's t paired test with 95% power, $\alpha = 0.05$ probability of error and Cohen's effect size 'medium', it was found appropriate to complete the study with at least 210 patients. All patients aged 18 years or older who presented to our outpatient clinic for any reason between february 2023 and april 2023 and were followed up on an outpatient basis were evaluated for inclusion. Patients with active infection, active malignancy, bundle branch block, history of coronary artery bypass graft or valve replacement, congenital heart disease and pregnancy were excluded from the study. All patients who agreed to participate were included in the study.

A detailed medical history was obtained from all enrolled participants, and information on hypertension, diabetes mellitus, coronary artery disease, chronic renal insufficiency, alcohol and tobacco use, and medication use was recorded.

Body mass index (BMI) was calculated as body weight (kg) divided by height squared (meters) (Quetelet index), and body surface area (BSA) was calculated as the square root of height (cm) multiplied by weight (kg) divided by 3,600 (Mosteller formula). Routine biochemical tests, lipid profiles, thyroid function tests, and complete blood counts were recorded for all participants. Glomerular filtration rate (eGFR) was calculated according to the CKD-EPI equations [11].

12-lead resting ECG was taken in all patients (Welch Allyn, Mortara ELI150c, NY, USA). The presence of fQRS was defined as the presence of notching in R or S waves in at least two consecutive leads, in the absence of typical bundle branch block, with a normal QRS duration, consistent with a coronary artery supply area. In addition, heart rate, PR interval, QRS duration, QTc interval, P-axis, QRS axis, and T-axis values automatically calculated by the ECG device were recorded.

Echocardiographic measurements

Transthoracic echocardiography was performed in all patients with a 2.5-3.25 MHz transducer (Philips Affiniti 50 S4-2 probe system, Andover, USA) according to the recommendations of the American Society of Echocardiography [12-14].

Left ventricular ejection fraction was calculated by the modified Simpson method [15]. Left ventricular mass (g) was calculated according to the Devereux formula [16]. Left ventricular mass index was calculated by dividing left ventricular mass by body surface area. Relative wall thickness was calculated as twice posterior wall thickness divided by left ventricular diastolic diameter [17].

Periaortic adipose tissue, as defined by Adar et al. [10], was identified as a hypoechoic space anterior to the ascending aorta located 2 cm above the sinotubular junction at end-systole (Figure 1A, Video 1). Measurements were obtained over three cardiac cycles, and the average of these measurements was used. The interobserver consistency of paraaortic adipose tissue measurements was calculated to be almost perfect (κ= 0.803, p= 0.001). By using computed tomography imaging, tissue analysis was performed in order to determine adipose characteristics of hypodense space. The mean attenuation (Hounsfield Units, HU) interval for adipose tissue was defined as -190 to -30 HU [18]. The mean Hounsfield Units (HU) of paraaortic adipose tissue was found to be -95.94 HU (Figure 1B).

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (Armonk, NY). For absence or handling of missing data, the respective participant was excluded from the analysis. Categorical variables were expressed as numbers and percentages. Normality of continuous variables was assessed using the Kolmogorov-Smirnow test, skewness, and kurtosis. Normally distributed continuous variables were expressed as mean and standard deviation, while non-normally distributed variables were expressed as median and 25/75 quartiles. Categorical variables were compared between groups using the chi-squared test. Normally distributed continuous variables were compared using the independent samples t-test, whereas non-normally distributed variables were compared using the Mann-Whitney U test. To determine the parameters to be included in the multivariate regression analysis, preliminary univariate regression analyses were initially conducted. Binary logistic regression analysis was performed for parameters whose significance was less than 0.1 in the univariate analysis. Non-normally distributed variables were normalized by Box-Cox transformation before regression analysis. The backward conditional method was used to determine independent variables associated with fragmented QRS in binary logistic regression analysis. All analyses were two-tailed, and $p < 0.05$ was considered statistically significant.

Ethical Statement

The study was approved by Tekirdağ City Hospital Non-Interventional Clinical Research Ethics Committee on January 31, 2023 (approval number: 20). Written informed consent was obtained from all participants in accordance with the ethical principles for research involving human subjects as stated in the Second Declaration of Helsinki.

Results

In study were evaluated 312 patients for enrollment. Of these, 38 patients were excluded to insufficient paraaortic adipose tissue visualization window and 7 patients refused to participate in the study. An additional 46 patients who met one or more of the exclusion criteria were excluded from the study (Figure 2). The study included a total of 221 participants, 152 in the fQRS group and 69 in the non-fQRS group. The median age of the participants was 46 years (range: 38.5-53), and 76 (34.4%) were female. Baseline characteristics, biochemical parameters, echocardiographic measurements, and ECG parameters are summarized in Table 1. Compared to the control group, patients with fQRS were older [median age: 47 years (range: 41-54) vs. 43 years (range: 32-49.5), p = 0.003], and the gender distribution was similar between the groups. BMI was significantly higher in patients with fQRS (30.1 vs. 29.4, p= 0.034).

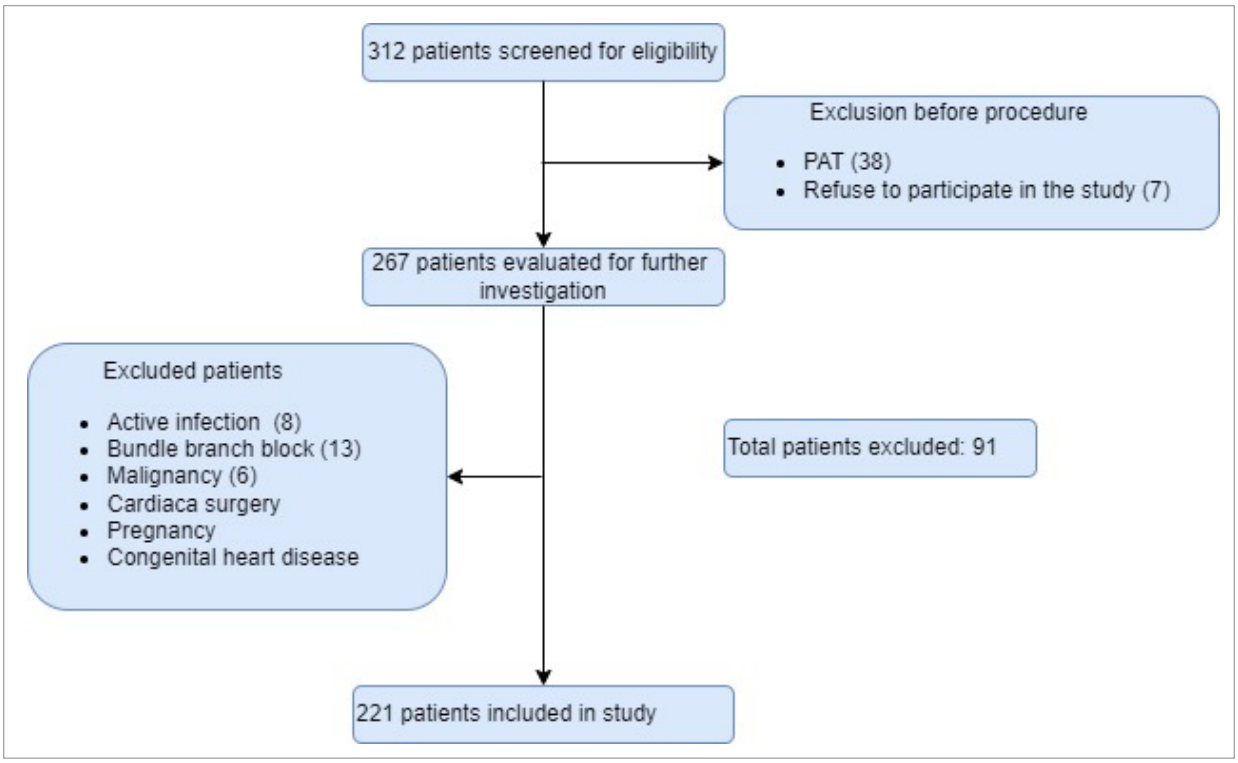


Figure 2. Flow chart for patient selection

Significant differences were observed in the prevalence of hypertension (p= 0.003) and diabetes (p= 0.008) between the groups, while the groups were similar in terms of hyperlipidemia, smoking, and coronary artery disease.

Laboratory parameters showed no significant differences between groups except for GFR. GFR values were significantly lower in the fQRS group (105.8 ±8.3 vs 109.5 ±9.4, p= 0.004).

Regarding echocardiographic measurements, there was no statistically significant difference in left ventricular end-diastolic diameter, interventricular septal thickness, relative wall thickness, left ventricular mass index, and ejection fraction between the fQRS group and the control group. However, left ventricular mass (188.6 g (164.5/217.2) vs 178.2 g (142.5/200.1), p= 0.046) and aortic size (32 mm (30/35) vs 30 mm (28/34), p= 0.001) were significantly higher in the fQRS group. Paraaortic adipose tissue thickness was also significantly higher in subjects with fQRS (9.2 mm (7.1/12.3) vs 6.8 mm (1.2/10.9), p= 0.001) (Table 1).

Regarding electrocardiographic parameters, there was no statistically significant difference in heart rate, PR interval, P-axis and T-axis between the fQRS group and the control group. However, QRS duration (94 msec (66/102) vs. 90 msec (86/94), p= 0.002) and corrected QT interval (403 msec (392/419) vs. 395 msec (387/410), p= 0.002) were significantly higher, while QRS axis (32° (8/53) vs. 47° (30/67), p <0.001) was significantly lower in the fQRS group.

In the univariate regression analysis, parameters with a significance level of p <0.1 were selected for inclusion in the multivariate regression model (Table 2). According to the results of this analysis, age, hypertension, diabetes mellitus, body mass index, glomerular filtration rate, ejection fraction, left ventricular mass, aortic diameter, and periaortic fat thickness were included in the regression analysis model In binary regression analysis, an independent and strong association was found between aortic size (OR: 1.4, CI 95%: 1.012-1.938, p= 0.042), paraaortic adipose tissue (OR: 1.483, CI 95%: 1.084-2.029, p= 0.014) and fQRS (Table 3).

Table 1. Comparison of characteristics of the study population according to the presence of fragmented QRS.

Variables	Total (n = 221)	fQRS (+) (n= 152)	fQRS (-) (n= 69)
Age, years	46(38.5/53)	47(41/54)	43(32/49.5) **
Sex (Male/female), n (%)	145(65.6)/76(34.4)	102(67.1)/50(32.9)	43(62.3)/26(37.7)
BMI, kg/m^2	29.9(26.7/32.8)	30.1(27.2/33.5)	29.4(25.5/32.1) *
HT, n (%)	144(66.1)	108(72.5)	36(52.2) **
DM, n (%)	23(10.5)	21(13.9)	2(2.9) **
Hyperlipidemia, n (%)	23(10.4)	16(10.5)	7(10.1)
Smoking, n (%)	47(21.3)	33(21.7)	14(20.3)
CAD, n (%)	8(3.6)	6(3.9)	2(2.9)
Glucose, mg/dL	103(94/109.5)	103.5(94/109)	102(94/110.5)
Creatinine, mg/dL	0.9(0.76/1)	0.9(0.78/1)	0.9(0.72/0.99)
GFR, ml/min	106.9±8.8	105.8±8.3	109.5±9.4**
Total Cholesterol, mg/dL	199(170/238)	200(169/240)	193(168/228)
HDL-C, mg/dL	45(38/53)	45(37/53)	46(39.5/53.5)
LDL-C, mg/dL	118(97/147)	124.5(97/148)	116(96/142)
Triglyceride	150(92/230)	157(105/250)	133(81/209)
Hemoglobin, g/dL	14.6(13.2/15.8)	14.6(13.2/15.9)	14.5(13.3/15.6)
WBC, x10^3/µL	7.8(6.4/9.2)	7.8(6.6/9.2)	7.8(6.2/9.25)
LVEDD, mm	44(42/47)	45(42/47)	44(42/46)
IVS, mm	12(10/13)	12(11/13)	12(10/12)
EF, %	62.9(59.9/65.8)	62.4(59.6/65.8)	64(61.8/66.7)
RWT	0.51±0.08	0.51±0.07	0.5±0.08
LVM, g	184.7(157.1/212)	188.6(164.5/217.2)	178.2(142.5/200.1)*
LVMI, g/m^2	89.9(77.6/104)	90(79.4/106.4)	89.9(76.2/102.1)
Aorta, mm	32(30/35)	32(30/35)	30(28/34)**
PAT, mm	8.9(5.95/11.7)	9.2(7.1/12.3)	6.8(1.2/10.9)**
Heart rate, bpm	75(68/85)	75(68/85)	76(67/84)
PR, msec	150(138/162)	150(140/162)	150(136/162)
QRS, msec	92(86/100)	94(66/102)	90(86/94)**
QTc, msec	401(390/415)	403(392/419)	395(387/410)**
P axis, degree	50(33.7/60)	48(34/60)	52(33/61)
QRS axis, degree	37(12/56)	32(8/53)	47(30/67)**
T axis, degree	41(25/55)	39(22/54)	45(32/59)

BMI, body mass index; CAD, coronary artery disease; DM, diabetes mellitus; EF, ejection fraction; GFR, glomerular filtration rate; HDL-C, high density lipoprotein cholesterol; HT, hypertension; IVS, interventricular septum; LDL-C, low density lipoprotein cholesterol; LVEDD, left ventricular end diastolic diameter; LVM, left ventricular mass; LVMI, left ventricular mass index; PAT, paraaortic adipose tissue; RWT, relative wall thickness; WBC, white blood cell.

* <0.05; ** <0.001

Discussion

The present study showed that paraaortic adipose tissue thickness was significantly increased in the group with fQRS on admission ECG compared with the control group. To our knowledge, this is the first report of this association. In the literature, the measurement of paraaortic adipose tissue is usually performed by more sophisticated and expensive modalities such as computed tomography. However, this study was performed using echocardiography, which allows for rapid assessment in individuals with appropriate acoustic windows. We believe that this approach may be valuable in terms of clinical applicability and cost-effectiveness.

The fQRS is a simple yet highly effective parameter that is readily available to clinicians. It has been shown to be associated with myocardial fibrosis and scar tissue in coronary artery disease and heart failure [6]. While it is observed in approximately 7.2% of healthy individuals, it is found in approximately one in five patients with ST-elevation myocardial infarction, one in four patients with metabolic syndrome, and three in four patients with cardiac sarcoidosis [19-21]. In particular, these data suggest that the frequency of fQRS is higher in the presence of myocardial damage. It has also been explained that people with a fragmented QRS complex in the absence of obvious heart disease do not have an increased risk of death [22].

In our study, the frequency of fQRS was found to be significantly higher in individuals with hypertension and diabetes. The effects of hypertension on myocardial remodeling and fibrosis are evident. Worsening of left ventricular geometry and left ventricular hypertrophy have been

Table 2. Univariate regression analysis of variables with fragmented QRS

Variable	Exp(B)	95% Confidence Intervals
Age	1.041	1.014-1.069 ***
Sex (Male/female)	1.233	0.682-2.232
Body Mass Index	1.064	0.999-1.134 *
HT	0.414	0.229-0.750 ***
DM	0.185	0.042-0.812 **
Hyperlipidemia	0.96	0.376-2.451
Smoking	0.918	0.455-1.852
CAD	0.726	0.143-3.693
Glucose	1.012	0.998-1.028
Creatinine	2.207	0.364-13.364
GFR	0.953	0.921-0.985 ***
Total Cholesterol	1.003	0.997-1.009
HDL-C	0.991	0.969-1.014
LDL-C	1.005	0.997-1.012
Triglyceride	1.002	0.999-1.005
Hemoglobin	0.92	0.836-1.154
WBC	1.036	0.9-1.193
LVEDD	1.063	0.968-1.168
IVS	1.099	0.928-1.302
EF	0.939	0.888-0.992 **
RWT	10.03	0.221-454.5
LVM	1.006	0.999-1.012 **
LVMI	1.005	0.99-1.02
Aorta	1.139	1.047-1.24 ***
PAT	1.122	1.051-1.197 ***

CAD, coronary artery disease; DM, diabetes mellitus; EF, ejection fraction; GFR, glomerular filtration rate; HDL-C, high density lipoprotein cholesterol; HT, hypertension; IVS, interventricular septum; LDL-C, low density lipoprotein cholesterol; LVEDD, left ventricular end diastolic diameter; LVM, left ventricular mass; LVMI, left ventricular mass index; PAT, paraaortic adipose tissue; RWT, relative wall thickness; WBC, white blood cell.
* p <0.05; ** p <0.01; ***p <0.001

demonstrated in hypertensive subjects with fQRS [23]. Hypertension was approximately 40% more common in the group with fQRS (72.5% vs. 52.2%) in the present study. Although this is the case, the over-observation of fQRS frequency in our study of hypertensive individuals is compatible with previous studies. Although left ventricular mass was higher in individuals with fQRS, no significant difference was found in left ventricular mass index in this study. We believe that this finding is mainly due to the young patient population. Considering that the hypertensive state takes years for ventricular remodeling, our results are in line with current evidence [24].

fQRS is common in the presence of diabetes. The frequency of fQRS has been previously reported to be in the range of 28-60% in individuals with diabetes mellitus [25,26]. Vascular damage, which is the underlying cause, ultimately affects myocardial cells. In this study, the rate of diabetes in individuals with fQRS was 13.9%. According to previous studies, the difference is mainly due to the content and group characteristics of the population.

fQRS status has also been studied in renal failure. One study reported that the frequency of fQRS was 30% in a cohort of 310 patients with chronic kidney failure [27]. In our study, the GFR values are statistically lower in the group with fQRS. However, we believe that these low values are not clinically meaningful. This finding may be due to the older age of the population with fQRS. There was no significant difference in creatinine levels between the two groups. However, these data are thought-provoking for further studies. Indeed, renal dysfunction stimulates cardiac remodeling via uncontrolled hypertension and hemodynamic effects in the following periods, and cardiac fibrosis is ultimately inevitable. Based on these data, it can be assumed that this effect may start earlier.

Another finding for this study, subjects with fQRS had significantly higher measured aortic diameters than subjects without fQRS. This has not been previously reported in the literature.

Table 3. Multivariate binary regression analysis for covariates of fragmented QRS

	B	Standard error	Wald	Sig.	Exp(B)	95% Confidence Intervals for Exp(B)
DM	-1.451	0.764	3.614	0.057	0.234	0.052-1.046
Aorta	0.337	0.166	4.131	0.042*	1.400	1.012-1.938
PAT	0.394	0.160	6.068	0.014*	1.483	1.084-2.029
Constant	2.172	0.745	8.506	0.004	8.780	

Variables included in model: Age*, hypertension, diabetes mellitus, body mass index*, glomerular filtration rate, ejection fraction*, left ventricular mass*, aortic diameter*, periaortic fat thickness*
*Non-normally distributed variables are normalized using Box-Cox transformation before regression analysis

Kim et al. compared the effect of hypertension on aortic dimensions and reported that aortic dimensions are statistically higher in individuals with hypertension, especially at the tubular level [28]. In terms of causality, the more frequent observation of hypertension in individuals with fQRS and the shear stress imposed on the aorta by the hypertensive state may have caused this.

Some vascular-related adipose tissue distributions in the body differ from white adipose tissue. One example is epicardial adipose tissue (EAT). Increased EAT volume creates a prothrombotic and proinflammatory state and is considered a possible risk factor in the pathogenesis of cardiovascular disease [29]. It is also known that activin-A secreted by this tissue is an effective paracrine substance on myocardial fibrosis [30]. Based on this, a study conducted in a healthy population found that EAT thickness was higher in individuals with fQRS than in non-fQRS [29]. Perivascular adipose tissue is also known to behave like an organ with local paracrine effects rather than energy storage. It has been suggested that the cardiovascular effects may be higher due to the anatomical proximity of this adipose tissue [31]. They have negative effects on vascular and cardiac structures in their neighborhood through paracrine effects of secreted inflammatory substances [32,33]. Paraaortic adipose tissue is a regional tissue surrounding the aorta in the class of perivascular fat. It has been suggested that adiponectin and growth factors play a role in the atherosclerosis and dilatation of the aorta through the mechanisms and pathways mentioned above [8]. The same study suggested that periaortic adipose tissue is associated with coronary calcification and systemic inflammation, independent of the amount of body fat [8]. However, this adipose tissue is known to be similar to brown adipose tissue and has thermoregulatory effects with beneficial effects. The clinical utility of fQRS may be greater than thought. The relationship between paraortic adipose tissue and fQRS may be dichotomous. Increased adipose tissue can be considered a combination of poorly managed risk factors. Poorly managed cardiovascular risk factors ultimately lead to cardiac fibrosis and remodeling with mediators secreted by this and similar tissues and contribute to the formation of fQRS. In addition, this adipose tissue is a tissue with different functions and different adipose characteristics compared to other adipose tissues. It is stated that it plays a role in the distribution of thermoregulatory and systemic energetics, having a character similar to brown adipose tissue [34]. One study found that this tissue is associated with systemic inflammation regardless of body fat content [8]. In light of these data, this tissue may also be one that increases in size to slow, stop, or prevent cardiac fibrosis from any cause. To be clear, the primary reason for increasing this tissue may be to prevent cardiac remodeling and fibrosis. fQRS is reflected in the ECG paper as a cumulative result of this. Therefore, studies requiring histopathological and chemical examination are needed.

This study has several limitations. First, it was a single-center study and has a relatively small sample size in terms of providing high-quality evidence. In addition, histopathologic and magnetic resonance evidence of myocardial fibrosis was not provided. Patients with bundle branch block were excluded from the study. In addition, paraaortic adipose tissue was measured only by echocardiography. Another point is that the ECGs were also evaluated only once. In some studies, it has been reported that only prolonged duration of fQRS gains prognostic importance [35]. This is both a limitation and an indication of the strength of the paraaortic adipose tissue that the data is still significant despite this situation. It has been reported that standard ECG devices can filter high frequency fQRs [36]. In this context,

device-assisted filtering systems were not used and only the presence of fragmented QRS was evaluated on the doctor's interpretation. Despite all these and other variables, only paraaortic adipose tissue continued to be associated with fQRS more than all other variables without losing its statistical significance.

Conclusions

The presence of fQRS on ECG is associated with increased paraaortic adipose tissue thickness in this ambulatory population. This study can be considered as pioneering. fQRS has been associated with cardiac fibrosis and in this study, we shed light on the potential association of para-aortic adipose tissue with various clinical characteristics. Further investigation of the results of this study in other studies will provide an opportunity to better understand the significance of paraaortic adipose tissue over time. Further studies with larger patient groups are needed to clarify the exact pathophysiological mechanisms underlying these findings.

References

1. Pietrasik G, Zareba W. QRS fragmentation: diagnostic and prognostic significance. Cardiol J. 2012; 19(2): 114-21. doi: 10.5603/cj.2012.0022.

2. Das MK, Zipes DP. Fragmented QRS: a predictor of mortality and sudden cardiac death. Heart Rhythm. 2009; 6(3 Suppl): S8-14. doi: 10.1016/j.hrthm.2008.10.019.

3. Akgul O, Uyarel H, Pusuroglu H, Surgit O, Turen S, Erturk M, et al. Predictive value of a fragmented QRS complex in patients undergoing primary angioplasty for ST elevation myocardial infarction. Ann Noninvasive Electrocardiol. 2015; 20(3):263-72. doi: 10.1111/anec.12179.

4. Das MK, Michael MA, Suradi H, Peng J, Sinha A, Shen C, et al. Usefulness of fragmented QRS on a 12-lead electrocardiogram in acute coronary syndrome for predicting mortality. Am J Cardiol. 2009; 104(12): 1631-7. doi: 10.1016/j.amjcard.2009.07.046.

5. Bekar L, Katar M, Yetim M, Çelik O, Kilci H, Önalan O. Fragmented QRS complexes are a marker of myocardial fibrosis in hypertensive heart disease. Turk Kardiyol Dern Ars. 2016; 44(7):554-60. doi: 10.5543/tkda.2016.55256.

6. Sha J, Zhang S, Tang M, Chen K, Zhao X, Wang F. Fragmented QRS is associated with all-cause mortality and ventricular arrhythmias in patient with idiopathic dilated cardiomyopathy. Ann Noninvasive Electrocardiol. 2011; 16(3): 270-5. doi: 10.1111/j.1542-474X.2011.00442.x.

7. Pei J, Li N, Gao Y, Wang Z, Li X, Zhang Y, et al. The J wave and fragmented QRS complexes in inferior leads associated with sudden cardiac death in patients with chronic heart failure. Europace. 2012;14(8):1180-7. doi: 10.1093/europace/eur437.

8. Yun CH, Lin TY, Wu YJ, Liu CC, Kuo JY, Yeh HI, et al. Pericardial and thoracic peri-aortic adipose tissues contribute to systemic inflammation and calcified coronary atherosclerosis independent of body fat composition, anthropometric measures and traditional cardiovascular risks. Eur J Radiol. 2012;81(4):749-56. 10.1016/j.ejrad.2011.01.035.

9. Lehman SJ, Massaro JM, Schlett CL, O´Donnell CJ, Hoffmann U, Fox CS. Peri-aortic fat, cardiovascular disease risk factors, and aortic calcification: the Framingham Heart Study. Atherosclerosis. 2010;210(2):656-61. doi: 10.1016/j.atherosclerosis.2010.01.007.

10. Adar A, Onalan O, Cakan F, Keles H, Akbay E, Akinci S, et al. Evaluation of the relationship between para-aortic adipose tissue and ascending aortic diameter using a new method. Acta Cardiol. 2022;77(10):943-949. doi: 10.1080/00015385.2022.2121537.

11. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. New England Journal of Medicine. 2021;385(19):1737-49. doi: 10.1056/NEJMoa2102953.

12. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1): 1-39.e14. doi: 10.1016/j.echo.2014.10.003.

13. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: A report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr. 2010;23(7):685-713; doi: 10.1016/j.echo.2010.05.010.

14. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2016;29(4):277-314. doi: 10.1016/j.echo.2016.01.011.

15. Starling MR, Walsh RA. Accuracy of biplane axial oblique and oblique cineangiographic left ventricular cast volume determinations using a modification of Simpson's rule algorithm. Am Heart J. 1985;110(6):1219-25. doi: 10.1016/0002-8703(85)90016-x.

16. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, et al. Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. Am J Cardiol. 1986;57(6):450-8. doi: 10.1016/0002-9149(86)90771-x.

17. Krumholz HM, Larson M, Levy D. Prognosis of left ventricular geometric patterns in the Framingham Heart Study. J Am Coll Cardiol. 1995;25(4):879-84. doi: 10.1016/0735-1097(94)00473-4.

18. Sjöström L. A computer-tomography based multicompartment body composition technique and anthropometric predictions of lean body mass, total and subcutaneous adipose tissue. Int J Obes. 1991; 15(Suppl 2):19-30.

19. Adar A, Kiris A, Ulusoy S, Ozkan G, Bektas H, Okutucu S, et al. Fragmented QRS is associated with subclinical left ventricular dysfunction in patients with chronic kidney disease. Acta Cardiol. 2014;69(4):385-90. doi: 10.1080/ac.69.4.3036654.

20. Oner E, Erturk M, Birant A, Kalkan AK, Uzun F, Avci Y, et al. Fragmented QRS complexes are associated with left ventricular systolic and diastolic dysfunctions in patients with metabolic syndrome. Cardiol J. 2015;22(6):691-8. doi: 10.5603/CJ.a2015.0045.

21. Schuller JL, Olson MD, Zipse MM, Schneider PM, Aleong RG, Wienberger HD, et al. Electrocardiographic characteristics in patients with pulmonary sarcoidosis indicating cardiac involvement. J Cardiovasc Electrophysiol. 2011;22(11):1243-8. doi: 10.1111/j.1540-8167.2011.02099.x.

22. Terho HK, Tikkanen JT, Junttila JM, Anttonen O, Kentta TV, Aro AL, et al. Prevalence and prognostic significance of fragmented QRS complex in middle-aged subjects with and without clinical or electrocardiographic evidence of cardiac disease. Am J Cardiol. 2014; 114(1):141-7. doi: 10.1016/j.amjcard.2014.03.066.

23. Kadi H, Kevser A, Ozturk A, Koc F, Ceyhan K. Fragmented QRS complexes are associated with increased left ventricular mass in patients with essential hypertension. Ann Noninvasive Electrocardiol. 2013;18(6):547-54. doi: 10.1111/anec.12070.

24. Yun M, Li S, Yan Y, Sun D, Guo Y, Fernandez C, et al. Blood pressure and left ventricular geometric changes: a directionality analysis. Hypertension. 2021;78(5):1259-66. doi: 10.1161/HYPERTENSIONAHA.121.18035

25. Bayramoglu A, Tasolar H, Kaya Y, Bektas O, Kaya A, Yaman M, et al. Fragmented QRS complexes are associated with left ventricular dysfunction in patients with type-2 diabetes mellitus: a two-dimensional speckle tracking echocardiography study. Acta Cardiol. 2018; 73(5):449-56. doi: 10.1080/00015385.2017.1410350.

26. Eren H, Kaya Ü, Öcal L, Öcal AG, Genç Ö, Genç S, et al. Presence of fragmented QRS may be associated with complex ventricular arrhythmias in patients with type-2 diabetes mellitus. Acta Cardiol. 2021;76(1):67-75. doi: 10.1080/00015385.2019.1693117.

27. Liu P, Wu J, Wang L, Han D, Sun C, Sun J. The prevalence of fragmented QRS and its relationship with left ventricular systolic function in chronic kidney disease. J Int Med Res. 2020;48(4):300060519890792. doi: 10.1177/0300060519890792.

28. Kim M, Roman MJ, Cavallini MC, Schwartz JE, Pickering TG, Devereux RB. Effect of hypertension on aortic root size and prevalence of aortic regurgitation. Hypertension. 1996;28(1):47-52. doi: 10.1161/01.hyp.28.1.47.

29. Yaman M, Arslan U, Bayramoglu A, Bektas O, Gunaydin ZY, Kaya A. The presence of fragmented QRS is associated with increased epicardial adipose tissue and subclinical myocardial dysfunction in healthy individuals. Rev Port Cardiol (Engl Ed). 2018;37(6):469-75. doi: 10.1016/j.repc.2017.09.022.

30. Venteclef N, Guglielmi V, Balse E, Gaborit B, Cotillard A, Atassi F, et al. Human epicardial adipose tissue induces fibrosis of the atrial myocardium through the secretion of adipo-fibrokines. Eur Heart J. 2015;36(13):795-805a. doi: 10.1093/eurheartj/eht099.

31. Lehman SJ, Massaro JM, Schlett CL, O'Donnell CJ, Hoffmann U, Fox CS. Peri-aortic fat, cardiovascular disease risk factors, and aortic calcification: the Framingham Heart Study. Atherosclerosis. 2010;210(2):656-61. doi: 10.1016/j.atherosclerosis.2010.01.007.

32. Thalmann S, Meier CA. Local adipose tissue depots as cardiovascular risk factors. Cardiovasc Res. 2007;75(4):690-701. doi: 10.1016/j.cardiores.2007.03.008.

33. Iacobellis G, Corradi D, Sharma AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. Nat Clin Pract Cardiovasc Med. 2005; 2(10): 536-43. doi: 10.1038/ncpcardio0319.

34. Singh R, Barrios A, Dirakvand G, Pervin S. Human Brown Adipose Tissue and Metabolic Health: Potential for Therapeutic Avenues. Cells. 2021;10(11): 3030. doi: 10.3390/cells10113030.

35. Allescher J, Sinnecker D, von Goeldel B, Barthel P, Muller A, Hapfelmeier A, et al. QRS fragmentation does not predict mortality in survivors of acute myocardial infarction. Clin Cardiol. 2024;47(1):e24218. doi: 10.1002/clc.24218.

36. Malik M. Electrocardiographic smoke signals of fragmented QRS complex. J Cardiovasc Electrophysiol. 2013;24(11):1267-70. doi: 10.1111/jce.12226.