Presence of Fragmented QRS may be Associated with Ventricular Arrhythmias in Hemodialysis Patients

Fragmente QRS'nin Varlığı Hemodiyaliz Hastalarında Ventriküler Aritmi ile İlişkili Olabilir

Fatih Kardas[1], Gokay Taylan[2], Caglar Kaya[1], İlhan Kurultak[3]

[1] Edirne State Hospital, Department of Cardiology, Edirne, Turkey

[2] Trakya University Faculty of Medicine, Department of Cardiology, Edirne, Turkey

[3] Trakya University Faculty of Medicine, Department of Nephrology, Edirne, Turkey

ABSTRACT

Introduction: Fragmented QRS (fQRS) is a depolarization defect that can be seen in a 12-derivation electrocardiography (ECG). It has been determined that myocardial fibrotic scar plays a role in the formation of ventricular arrhythmias by causing structural and electrophysiological changes that cause fragmentation and ventricular late potentials in QRS. Arrhythmia risk is increased in hemodialysis (HD) patients. Regular ECG monitoring and the presence of fQRS can help in the early diagnosis of ventricular arrhythmias in HD patients. The aim of this study is to investigate the relationship between the presence of fQRS and ventricular arrhythmia in HD patients.

Methods: In this case-control study, 22 HD patients with fQRS and 72 HD patients without fQRS were compared. The ECG parameters and ECG-holter results of the two groups were compared in terms of the frequency of ventricular arrhythmias by multivariate analysis. A p value <0.05 was considered statistically significant.

Results: The compared to ECG-holter data of the both groups, it was statistically detected that the frequency of ventricular premature contraction (VPC) and the number of cases observed in non-susteined ventricular tachycardia (NSVT) increased in the group with fQRS (+) (p <0.001, p:0.01). In addition, it was observed that corrected QT (QTc), dispersion of QTc (QTcd) and transmural dispersion of repolarization (TDR) were extended from ECG parameters in the fQRS (+) group and were statistically significant (p <0.001, p:0.003, p:0.019).

Conclusion: The frequency of VPC and NSVT in the fQRS group was significantly higher than in the control group. The presence of fQRS may be used to predict ventricular arrhythmias in HD patients.

Key words: Electrocardiography, fragmented QRS, hemodialysis, ventricular arrhythmias.

ÖZET

Giriş: Fragmente QRS (fQRS), 12-derivasyon elektrokardiyografide (EKG) görülebilen bir depolarizasyon kusurudur. Miyokardiyal fibrotik skarın, QRS'de parçalanma ve ventriküler geç potansiyellere neden olarak yapısal ve elektrofizyolojik değişiklik sonucu ventriküler aritmilerin oluşumunda rol oynadığı belirlenmiştir. Hemodiyaliz (HD) hastalarında aritmi riski artmıştır. Düzenli EKG izleme ve fQRS' lerin varlığı HD hastalarında ventriküler aritmilerlerin erken teşhisinde yardımcı olabilir. Bu çalışmanın amacı HD hastalarında fQRS' lerin varlığı ile ventriküler aritmi arasındaki ilişkiyi araştırmaktır.

Yöntemler: Bu vaka-kontrol çalışmasında, fQRS saptanan 22 HD hastası ile fQRS saptanmamış 72 HD hastası karşılaştırıldı. İki grubun EKG parametreleri ve EKG-Holter sonuçları, çok değişkenli analiz yoluyla ventriküler aritmiler sıklığı açısından karşılaştırıldı. P değeri <0,05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Her iki grubun EKG-Holter verileri kıyaslandığında, ventriküler erken vuru (VEV) sıklığının ve süreksiz ventriküler taşikardi (NSVT) gözlenen olguların sayısının fQRS (+) grupta arttığı istatistiksel anlamlı görüldü (p <0,001, p: 0,01). Ek olarak, EKG parametrelerinden düzeltilmiş QT intervali (QTc), QTc dispersionu (QTcd) ve repolarizasyonun transmural dispersiyonu (TDR)' nun fQRS (+) grubunda uzadığı ve istatistiksel olarak anlamlı olduğu saptandı (p <0,001, p: 0,003, p: 0,019).

Sonuç: FQRS grubundaki VEV ve NSVT sıklığı, kontrol grubundan anlamlı olarak yüksekti. FQRS' lerin varlığı hemodiyaliz hastalarında ventriküler aritmileri tahmin etmek için kullanılabilir.

Anahtar Kelimeler: Elektrokardiyografi, fragmente QRS, hemodiyaliz, ventriküler aritmi.

Corresponding author: Gokay Taylan, Trakya University Faculty of Medicine, Department of Cardiology, Edirne, Turkey
E-mail: taylan1091@hotmail.com
Eskisehir Med. J. 2022; 3(2):92-100.
Received date:25.04.2022 Accepted date:27.05.2022
Authors: Fatih Kardas (ORCID: 0000-0001-7370-3960), Gokay Taylan (ORCID: 0000-0002-7015-4537), Caglar Kaya (ORCID: 0000-0002-2968-5352), İlhan Kurultak (ORCID: 0000-0001-5607-1375)

INTRODUCTION

Chronic renal disease (CRD), negatively affecting quality of life, an increase in frequency has been detected in recent years, is the disease which has high morbidity and mortality (1). Hemodialysis (HD) treatment is one of the most frequently applied treatments in people with end-stage CRD (2). HD, CRD patients have to continue throughout their life, is an effective and so costly as well renal replacement therapy. It can also negatively affect the quality of life of patients, it is an interventional treatment where various side effects can develop and sudden death can also be seen. For this reason, the treatment process can be complex and such cases need to be approached multidisciplinary. Cardiology is one of the most important departments that provides support to the nephrology department in a multidisciplinary approach and is involved in monitoring patients cardiovascular risk. Because cardiac arrhythmias, congestive heart failure, cardivascular diseases such as coronary artery disease (CAD) are often observed in HD patients (3). Therefore, the elimination of risk factors for cardiovascular disease in CRD, early diagnosis and treatment can improve life expectancy and quality of life for HD patients. HD patients need cardiological evaluation at regular intervals and various examinations such as electrocardiography (ECG), transthoracic echocardiography (TTE) and ECG holter are used.

One of the important cardiological pathologies that can be observed in HD patients is cardiac arrhythmias. Cardiac arrhythmias can reduce quality of life, trigger various comorbid diseases or even cause death (4). Arrhythmias are a common condition in patients receiving regular HD treatment; atrial arrhythmia is present in 68-88% of patients, ventricular arrhythmia in 59-76% and complex ventricular extrasystole in 14-21% (5). 2/3 of sudden cardiac deaths (SCD) in HD centres have been reported to be due to ventricular tachycardia or fibrillation (6). In consequence of increasing in risk of arrhythmia because of various mechanisms in HD patients; regular ECG monitoring can help early diagnosis and save lives. Additionally, by early and effective treatments, the incidence of ventricular arrhythmias that may occur in HD patients can be reduced.

The presence of fragmented QRS (fQRS) in patients with ischemic-nonischemic cardiomyopathy, in arrhythmogenic right ventricular dysplasia / cardiomyopathy, in amyloidosis, storage diseases and at Brugada syndrome is considered as a predictive parameter for increased morbidity and mortality (7-11). It has been determined that myocardial fibrotic scar took a role in the formation of ventricular arrhythmias by leading structural and electrophysiological changes which cause formation of micro–reentry, change in activation potential, fragmentation in QRS and ventricular late potentials in the fragmented area (12-15).

FQRS is a depolarization defect seen in electrocardiography (ECG) with 12 derivations (16). The presence of fQRS is recognized as a predictive parameter for increased morbidity and mortality in various cardiac or non-cardiac pathologies (7, 11). In our study, the risk of ventricular arrhythmia was evaluated in those who detected fQRS on ECGs' of HD patients. The frequency of fQRS in ECGs' of HD patients and whether there was an increase in the frequency of ventricular arrhythmia in patients with fQRS were evaluated by ECG holter examination. The aim of our study is to investigate the association between the presence of fQRS and ventricular arrhythmias in HD patients.

METHODS

Our investigation was designed as a case-control study. This study was approved by the local ethics committee with approval number TUTF-BAEK 2019/262. The patients with illuminated informed consent from all of

patients who were followed up with the diagnosis of chronic renal failure in nephrology outpatient clinic between 11/11/2019 and 14/05/2020 and received HD were included in the study.

Among these patients, a total of 94 volunteers were included in the study, including 22 patients with fQRS on their ECG and 72 patients without fQRS detected. The inclusion criterias; ≥18 years of age, to fill out the informed consent form at their own request / guardian, to receive routine HD treatment for at least 3 months, to have no contraindications for giving blood to the person were determined. The patients who did not receive HD treatment, ≤18 years of age, pregnancy status, lack of illuminated voluntary consent, acute renal failure, acute metabolic disorders, being admitted to an acute coronary syndrome clinic, active infective disease, acute heart failure and uncontrolled arrhythmia were excluded from the study.

Demographic characteristics of patients and cardiovascular risk factors were questioned. The physical examinations were performed. The patients in this study included individuals who were diagnosed with CRD and who had been entering HD for at least 3 months, providing the glomerular filtration rate (GFR) < 15 ml/min/1.73m2 criterion. The biochemical (creatinine, sodium, potassium etc.) and hemogram (leukocyte, neutrophil etc.) parameters, ECG and TTE were evaluated. After the HD session, the presence of arrhythmia in patients was evaluated by connecting a 24-hour ECG holter.

Patients who were diagnosed with hypertension (HT) in the anamnesis of the patients who used antihypertensive drugs or had systolic/diastolic blood pressure ≥140/90 mmHg were considered HT. (17). Diabetes mellitus (DM) diagnosed and antidiabetic drug and/or insulin treatment or fasting blood glucose (FBG) ≥126mg/dL was considered DM (18). Patients with triglyceride (TG) levels above 150 mg/dl and low density lipoprotein (LDL) levels above 130 mg/dl were considered hypertriglyceridemia and hyperlipidemia (17). Drugs used by patients; antiaggregation and anticoagulation therapy, beta blockers (BB), calcium channel blockers (CCB), angiotensin converting enzyme inhibitors (ACEI), loop diuretic (Furosemide), statins and nephrological drugs were grouped.

Defining Fragmented QRS

12 Lead ECGs from all patients for the study were taken with Schiller AT-102 plus brand device. In these records, the filter was 100 Hz, the alternative current filter 60 Hz, the paper speed 25 mm/s and the amplitude 10 mm/mV. The presence of fQRS in these traces was evaluated by a cardiologist.

FQRS was defined as the presence of at least one of the following in two consecutive derivations corresponding to the areas feed by major coronary arteries (16).

In patients with narrow QRS complexes; a) an additional R wave (R'), b) notching at the bottom of the S wave, c) notching of the R wave, d) detecting the presence of more than one R'. In patients with large QRS complexes (QRS duration> 120 ms); a) various patterns of RsR with 2 R, b) 2 notches in the R wave, c) 2 notches in the up or down direction of the S wave.

Echocardiographic analysis

TTE; HD patients was monitored by using Vivid 7 Pro, General Electric Medical System, Milwaukee, Winconsin echocardiography device to obtain 2.5-3.5 MHz transducer made parasternal long and short axis, apical four and two chamber images.

The images were evaluated by an experienced cardiologist. In this evaluation; left ventricular ejection fraction (EF), left ventricular end-diastolic diameter (LVEDD), left ventricular endsystole diameter (LVESD), valve abnormalities, left ventricular wall thickness, aortic calcification, pulmonary arterial pressure,

tricuspid annular plan systolic difference were used. Left ventricular EF was measured by Simpson method.

ECG - Holter analysis

24-hour Holter monitoring of all patients with a 3-channel ECG recorder (DMS Holter Recorder, DM Systems (Beijing) Co., Ltd. (China) was done. Mean heart rate and R-R variability were obtained from 24-hour records. Heart rate variability parameters and arrhythmias analysis (Cardioscan version 11.5, DM Software Inc, USA software) were processed in computer. Holter records and analyses were evaluated both automatically and manually by cardiologist.

According to the 2017 American Heart Association guidelines for management of patients with ventricular arrhythmia and prevention of sudden cardiac death; ventricular premature contraction (VPC) >30 per hour or >720 beats per day were considered pathological (19). In our study, VPC >720 beats monitored in ECG-Holter for 24 hours; arrhythmia load patients were evaluated as a high group and it was accepted as a VPC positive group. In the second group, VPC ≤720 beats monitored in ECG-Holter for 24 hours; arrhythmia load patients were evaluated as a low group and it was accepted as a VPC negative group.

Statistical analysis

Normal distribution was controlled by Shapiro-Wilk test. In comparison of the two groups, Student t test was used for variables that match the normal distribution, and MannWhitney U test was used for variables that do not match the normal distribution. When investigating the associations between quantitative variables, Pearson correlation coefficient for variables that match the normal distribution and Spearman correlation coefficient for variables that do not match the normal distribution were calculated. Associations between qualitative variables were investigated by Pearson chi-square test. Risk factors affecting arrhythmia were determined using logistic regression analysis (stepwise binary). For quantitative variables, mean and standard deviation were used in variables that match the normal distribution, and median and quarters were used in variables that do not match the normal distribution. For qualitative variables, frequency and percentage were given.

Regression analysis was planned and modelling was designed in terms of evaluating factors affecting arrhythmia load in patients. In the first modelling, the factors affecting the number of VPC >720beats group that we group as high arrhythmia load were investigated. In the second modelling, the factors affecting non-susteined ventricular tachycardia (NSVT) were investigated by grouping by the number of NSVT. All modelling was evaluated by stepwise binary logistic regression analysis. Significance level was determined as 0.05 in all statistical analyses. All statistical analyses were processed by using TURCOSA (Turcosa Analytics Ltd. Co., Turkey, www.turcosa.com.tr) statistical software.

RESULTS

The demographic characteristics of patients are shown in Table 1. Only atrial fibrillation (AF) was statistically different among groups (p:0.004).

Compared to laboratory values, lymphocyte values in the control group were lower than in the fQRS group, and statistically significant was found (p:0.027). Although potassium levels in both groups were within normal limits, the FQRS group was statistically significantly low (p:0.016) (Table 2).

Among the drugs that patients taken, there was no statistical significance other than usage of warfarin (p:0.004) (Table 3). No significant differences were detected between the groups in terms of parameters compared to TTE data of both groups (Table 4).

It was detected that when ECG data were evaluated, QT dispersion (QTd), dispersion of corrected QT

Table 1. Baseline demographic parameters of the study population

	Control Group n: 72	fQRS Group n: 22	p
Gender			
-Male	50 (%69.45)	14 (%63,63)	-
Age	59.83	59.72	0.979
Height (cm)	165.25 (±8.83)	166.45 ±9.97	0.588
Weight (kg)	69.86±15.17	66.63±12.72	0.368
Body mass index	25.54±5.32	23.93±4.22	0.197
Blood pressure (systole)	132.50±17.78	130.00±17.99	0.566
Blood pressure (diastole)	76.53±9.77	73.63±9.02	0.220
Renal Transplant	4(%5.5)	0	0.259
Hypertension	60%83.33)	20(%90.90)	0.382
Diabetes Mellitus	22(%30.5)	10(%4545)	0.197
MI	12(%16.66)	2(%9.09)	0.382
Coronary Stent	10(%13.88)	0	0.064
CABG-O	4(%5.55)	4(%18.18)	0.063
Heart Failure	2(%2.77)	2(9.09)	0.199
Atrial Fibrillation	4(%5.55)	6(%27.27)	0.004
Peripheral Artery Disease	6(%8.3)	0	0.162
Stroke	2(%2.77)	2(%9.09)	0.199
Malignancy	8(%11.11)	2(%9.09)	0.788

Abb. MI: Myocardial Infarctus, CABG-O: Coronary Artery Bypass Graft-Operation, n: Number of patients.

Table 2. Laboratory parameters of the cases in the study

	Control Group	fQRS Group	p
Wbc ($10^{\wedge 3}$/µL)	7.53±3.15	8.02±2.44	0.507
Hb (g/dl)	11.23±1.49	11.42±2.00	0.621
Htc (%)	34.02±4.51	32.39±9.51	0.264
Rdw-cv	15.69±1.75	15.54±1.76	0.728
Plt ($10^{\wedge 3}$/µL)	212.75±69.55	211±82.99	0.922
Neutrophile	4.99±2.08	5.63±2.48	0.227
Lymphocyte	1.55±1.17	3.8±8.30	0.027
Urea (mg/dl)	75.22±31.92	69.54±33.32	0.472
Creatinine (mg/dl)	4.99±2.19	4.08±2.04	0.086
Na (mmol/L)	139.41±5.04	138.36±1.91	0.342
K (mmol/L)	4.54±0.70	4.14±0.50	0.016
Cl (mmol/L)	100.33±2.95	101.54±2.55	0.086
Ca (mg/dl)	9.41±0.90	9.51±0.81	0.651
Mg (mg/dl)	2.23±0.26	2.18±0.21	0.3636
Total Protein	7.15±0.81	6.92±0.74	0.237
Albumin (g/dl)	4.89±6.01	3.72±0.48	0.367
Alt (U/L)	11.27±6.33	8.63±4.62	0.073
Ast (U/L)	15.05±7.71	13.72±4.94	0.449
Triglycerides (mg/dl)	226.22±290.70	157.36±65.51	0.275
Total Cholesterol (mg/dl)	196.86±55.25	181.91±64.53	0.289
Ldl (md/dl)	124.72±41.32	124.45±49.27	0.980
Hdl (mg/dl)	43.00±13.91	38.27±14.07	0.167
Crp (mg/dl)	1.83±2.76	2.39±2.72	0.409
Troponin-I (pg/ml)	14.5 (6.9-29.5)	13.7(9.4-54.4)	0.211

Abb. Wbc: White blood cell count, Plt: Thrombocytes count, Hb: Hemoglobin, Htc: Hematocrit , Rdw-cv: Red Cell Distribution Width- coefficient of variation, Na: Sodium, K: Potassium, Cl: Chlorine, Ca: Calcium, Mg: Magnesium, Alt: Alanine aminotransferase, Ast: Aspartate aminotransferase, Ldl: Low density lipoprotein, Hdl: High density lipoprotein, Crp: C reactive protein, n: Number of patients.

(QTcd), transmural dispersion of repolarization (TDR) were statistically significant. (p:<0.001, p:0.003, p:0.019). No significant differences were found between the groups in terms of other ECG parameters (Table 5).

The number of VPC did not match the normal distribution, and the median and quarters were used. It was statistically significant that the number of VPC was measured as 130 (71,5-299.75) in the control group, and 830 (160.75-1027.75) in the fQRS group was monitored (p:<0.001). No patient's ECG-Holter data was followed by ventricular tachycardia longer than 30 seconds.

It was seen that while the number of patients who was detected NSVT was 2 (2.77%) people in the control group, it was 4 (18.18%) people in the fQRS group and it was statistically significant (p:0.010). No significant differences were found between the groups in terms of other ECG-holter data (Table 6).

As a result of the regression analysis, fQRS presence (p<0.001 and p:0.047) were statistically significant in terms of ventricular arrhythmias (Table 7A and 7B).

Table 3. Drug usage of patients in the study

	Control Group	fQRS Group	p
Acetyl salicylic aside	34(%47.22)	10(%45.45)	0.884
Clopidogrel	10(%13.88)	2(%9.09)	0.555
Warfarin	4(%5.55)	6(%27.57)	0.004
Beta-Blocker	38(%52.77)	14(%63.63)	0.370
Calcium Channel Blocker	22(%30.55)	10(%45.45)	0.197
ACEI	4(%5.55)	2(%9.09)	0.553
ARB	6(%8.33)	0	0.162
Furosemide	26(%36.11)	4(%18.18)	0.114
Statin	16(%22.22)	2(%9.09)	0.171
Nephrological Drugs	68(%94.44)	20(%90.90)	0.553

Abb. **ACEI:** Angiotensin converting enzyme inhibitor, **ARB:** Angiotensin receptor blocker, **n:** Number of patients.

DISCUSSION

Cardiovascular diseases is the most common cause of death in HD patients (20). Cardiac arrhythmias, one of the cardiovascular diseases, adversely affect the quality of life in HD patients and increase the risk of sudden cardiac death (21). Ventricular arrhythmias, in particular, have increased in frequency in HD patients

and can trigger sudden cardiac death. In this study, a significant relationship was found between the presence of fQRS in HD patients and the frequency of ventricular arrhythmia in the ECG-Holter follow-up. This result is the first study in the literature in which the presence of fQRS, which may be used to predict ventricular arrhythmias as well as the frequency of VPC in HD patients, was determined as an independent predictor.

Table 4. Echocardiographic characteristics of groups

	Control Group	fQRS Group	p
Ejection fraction (%)	54.77±6.58	53.27±9.33	0.730
End-diastole diameter (mm)	45.13±3.62	46.54±4.74	0.143
End-systole diameter (mm)	30.25±4.12	31.18±5.78	0.404
Septum thickness (mm)	12.22±2.32	11.91±2.56	0.591
Posterior wall thickness (mm)	11.58±1.76	11.45±2.02	0.773
Aortic velocity	1.52±0.61	1.65±0.82	0.424
Mitral annular calcification	16(%22.22)	2(%9.09)	0.171
Aortic annular calcification	24(%33.33)	4(%18.18)	0.174
Right ventricular diameter (mm)	34.58±3.96	35.54±4.37	0.334
Pulmonary artery pressure (mmHg)	24.19±10.07	28.91±13.84	0.082
Valve Disease	4(%5.55)	4(%18.18)	0.063

Abb. n: Number of patients, p: Significance value.

In a study in which Das et al. investigated the specificity and sensitivity of fQRS in the detection of myocardial perfusion abnormalities, it was found that sensitivity and negative predictivity were higher for fQRS than the Q wave (16). But in another study, it was found that the sensitivity of the fQRS was less compared to the Q wave, and its specificity was quite high (12).

Table 5. Electrocardiographic characteristics of groups

	Control Group	fQRS Group	p
QRS (ms)	90.89±12.04	93.82±18.51	0.641
QT (ms)	374.22±39.46	391.00±38.44	0.081
QTc	432.65±27.74	441.18±17.76	0.093
QTd	40.00±16.78	57.27±17.79	<0.001
QTcd	46.29±17.45	58.50±11.85	0.003
MQTc	430.77±27.57	440.36±18.46	0.129
TDR	34.44±16.18	40.00±8.73	0.019
RBBB	2(%2.77)	0	0.429
LBBB	2(%2.77)	0	0.429

Abb. QTc: Corrected QT interval, QTd: QT dispersion, QTcd: Corrected QT dispersion, MQTc: Median corrected QT interval, TDR: Transmural repolarization dispersion, RBBB: Right bundle branch block, LBBB: Left bundle branch block , n: Number of patients.

Table 6. ECG-Holter characteristics of groups

	Control Group	fQRS Group	p
Recording Time (hours)	22.08±2.47	21.27±2.09	0.167
Median Heart Rate (beats/minute)	78.88±12.96	79.72±19.52	0.816
Minimum Heart Rate (beats/minute)	58.19±10.98	62.55±14.91	0.140
Maximum Heart Rate (beats/minute)	114.88±20.08	114.09±22.72	0.874
Ventricular Extra Sistole	130.5 (71.5-299.75)	830 (160.75-1027.75)	<0.001
Susteined Ventricular Tachycardia	0	0	-
NSVT	2 (%2.77)	4 (%18.18)	0.010
Atrial Fibrillation	6 (%8.03)	4 (%18.18)	0.190
Supraventricular Tachycardia	0	0	-
Atrial Extra Sistole	778.22±2078.85	1575.55±2471.33	0.136
Pause (longer than 3 seconds)	0	0	-

Abb. **NSVT**: Non-sustained Ventricular Tachycardia, **n:** Number of patients.

In two different studies conducted by Homsi et al., using the gadolinium magnetic resonance imaging (MRI) method, it was reported that the sensitivity of fQRS was high in predicting myocardial scar areas associated with CAD and not CAD. (22). Again, in a study conducted by Park et al. with gadolinium MRI in patients with Tetralogy of opere fallot, it was reported that there was a association between fQRS and scar tissue (23). In addition, many studies have shown association between scar tissue and myocardial perfusion disorder and fQRS (12, 24, 25). In our study, a significant association was determined between fQRS and ventricular arrhythmia (VPC frequency and NSVT) in HD patients. It has been thought that this association is due to increased cardiac scar formation and CAD frequency in HD patients.

In the study of demographic data, the absence of significant differences other than AF, which has been shown to increase in frequency in HD patients in many studies, increases the proportional distribution of groups and their statistical significance. A study by Winkelmayer et al. on the increased prevalence of AF in HD patients reported an increased risk of AF development in HD patients (26). As a result of our study, we found that the frequency of AF increases in HD patients with fQRS (p:0.004). We believe that the increase in AF frequency is due to increased atrial remodelling and scar development in HD patients.

Table 7A. First modelling in which factors affecting VPC frequency

VPC+	O.R.	%95 GA	p
fQRS	18.304	4.51-74.15	<0.001
QTc	1.037	1.009-1.065	0.008
QTd	1.037	0.991-1.072	0.135
QT	-	-	-
QTcd	-	-	-
MQTc	-	-	-
QRS	-	-	-

Abb. VPC: Ventricular prematüre contraction, fQRS: Fragmente QRS, QTc: Corrected QT interval, QTd: QT dispersion, QTcd: Corrected QT dispersion, MQTc: Median corrected QT interval, Stepwise binary logistic regression.

Table 7B. Second modelling in which ECG parameters acting on patients with NSVT

NSVT	O.R.	%95 GA	p
fQRS	10.01	1.031-97.207	0.047
QTc	0.938	0.865-1.017	0.120
MQTc	1.151	1.037-1.277	0.008
Qt	-	-	-
QTcd	-	-	-
QRS	-	-	-

Abb. NSVT: Non-sustained Ventricular Tachycardia, fQRS: Fragmente QRS, QTc: Corrected QT interval, MQTc: Average corrected QT interval, QTcd: Corrected QT dispersion, Stepwise binary logistic regression.

In the evaluation of biochemical parameters between groups, there were no statistical differences other than lymphocyte count and chlorine levels, and again, there was no statistical significance other than warfarin in the evaluation of the drugs used. This study shows that our groups are homogeneous and balanced. We thought that high detection of lymphocyte count in the fQRS group may be due to cellular immunity response associated with increased scar formation. It has been thought that the difference in warfarin use was statistically significant due to increased AF frequency in HD patients and fQRS patients.

No statistically significant findings were found between the groups in the TTE examination of the patients. These groups show that they are balanced, and that they do not have structural heart disease that will affect them in terms of ventricular arrhythmias.

We found that QTd, QTcd and TDR were statistically significantly longer in the fQRS (+) group when ECG parameters were evaluated in the FQRS (+) and fQRS (-) groups. It has been thought that fragmentation is the base factor in the elongation of these values. Increased QTd and QTcd are reported to be predictors of ventricular arrhythmias in the study of QT dispersion as a predictor of arrhythmic events in patients with Ankylosing Spondylitis, conducted by Yildirim et al (27). In this study conducted by Yildirim et al, it was found that the frequency of VPC was associated with increased QTd (p: <0.01) and QTcd (p: <0.01) (27). In a study conducted by Castro et al. investigating risk factors for ventricular arrhythmias in patients with Brugada syndrome, it was found that TDR is a good predictor of arrhythmogenic risk (28).

In a study in which Bekar et al. investigated the association of fQRS with ventricular arrhythmias in hypertensive patients, the number of VPC and NSVT in ECG-Holter in the fQRS (+) group was significantly increased (29). In addition, a significant association was found in the rate of paroxysmal AF (PAF) in this study conducted by Bekar et al. In our study, we also found an association between fQRS and ventricular arrhythmias. It was observed that the number of VPC (p<0.001) and the number of patients with NSVT (p:0.01) were significant in the group with fQRS (+). But in our study, no significant association was found in the number of PAF patients in the fQRS(+) group.

In a study in which Sheldon et al. investigated the association of VPC and NSVT with SCD, it was reported that increased VPC frequency was associated with mortality (30). In our study, we found that the frequency of VPC and the frequency of NSVT increased in the fQRS group. There is literature information that shows that the frequency of VPC of 30 beats / hour can be a predictive finding in terms of VT and mortality development (19). In our study, we therefore determined the number of VPC >720 beats/24 hours as a criterion and found that the frequency of fQRS increased in the VPC (+) group in statistical comparison of groups and that there was an

independent risk factor in multiple regression analysis. In addition, we found that the frequency of fQRS increased in the NSVT (+) group and that there was an independent risk factor in multiple regression analysis.

As a result of our study, fQRS may be used as a predictor for ventricular arrhythmias with ECG-holter in HD patients. In this way, during the treatment process of HD patients, it may regulate antiarrhythmic medical treatment, catheter ablation may be performed or implantable cardiac defibrillator (ICD) implantation may be applied. As a result, our study may be used to reduce cardiovascular symptoms and cardiac mortality in HD patients. In particular, patients with fQRS present and increased VPC load should be closely followed for cardiac events.

The limitations of our study; low number of patients, it may not reflect the general community because it is done in the university hospital, single-centered and the ECG-Holter period is limited to 24 hours. In addition, electrophysiological studies have not been carried out in the evaluation of ventricular arrhythmias.

The presence of fQRS in the early prediction of ventricular arrhythmias in HD patients should be investigated in multicenter and randomized controlled trials.

CONCLUSION

We found that the frequency of NSVT and VPC increased in HD patients with fQRS, regardless of structural heart disease, biochemical results, or medications used. FQRS may be an independent predictor of ventricular arrhythmias in HD patients.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: None.

Ethics approval: The study protocol conforms to the ethical guidelines of the1964 *Declaration of Helsinki* and its later amendments. This study was approved by the Trakya University ethics committee with approval number TUTF-BAEK 2019/262.

REFERENCES

1. Hesketh CC, Knoll GA, Molnar AO, Tsampalieros A, & Zimmerman DL. Vitamin D and kidney transplant outcomes: a protocol for a systematic review and meta-analysis. Systematic reviews, 2014;3(1):1-5.

2. Veitenhansl M, Stegner K, Hierl FX., et al. 40th EASD Annual Meeting of the European Association for the Study of Diabetes. Diabetologia, 2004;47:1-464.

3. Cheung AK, Sarnak MJ, Yan G, et al. Cardiac diseases in maintenance hemodialysis patients: results of the HEMO Study. Kidney international, 2004;65(6):2380-89.

4. Turakhia MP, Blankestijn PJ, Carrero JJ, et al. Chronic kidney disease and arrhythmias: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference. European heart journal, 2018;39(24):2314-25.

5. Akpolat T, Utaş C. Renal transplantasyon ve hasta seçimi. Hemodiyaliz hekimi el kitabı, 2011.

6. Becker L, Eisenberg M, Fahrenbruch C, Cobb L. Cardiac arrest in medical and dental practices: implications for automated external defibrillators. Archives of internal medicine, 2001;161(12):1509-12.

7. Pietrasik G, Goldenberg I, Zdzienicka J, et al. Prognostic significance of fragmented QRS complex for predicting the risk of recurrent cardiac events in patients with Q-wave myocardial infarction. The American journal of cardiology, 2007;100(4):583-86.

8. Morita H, Kusano KF, Miura D, et al. Fragmented QRS as a marker of conduction abnormality and a predictor of prognosis of Brugada syndrome. Circulation, 2008;118(17):1697.

9. Wang DD, Buerkel DM, Corbett JR, & Gurm HS. Fragmented QRS complex has poor sensitivity in detecting myocardial scar. Annals of Noninvasive Electrocardiology, 2010;15(4):308-14.

10. Das MK, Maskoun W, Shen C, et al. Fragmented QRS on twelve-lead electrocardiogram predicts arrhythmic events in patients with ischemic and nonischemic cardiomyopathy. Heart rhythm, 2010;71:74-80.

11. Peters S, Trümmel M, Koehler B. QRS fragmentation in standard ECG as a diagnostic marker of arrhythmogenic right ventricular dysplasia–cardiomyopathy. Heart Rhythm, 2008;5(10):1417-21.

12. Das MK, Suradi H, Maskoun W, et al. Fragmented wide QRS on a 12-lead ECG: a sign of myocardial scar and poor prognosis. Circulation: Arrhythmia and Electrophysiology, 2008;1(4):258-68.

13. Sha J, Zhang S, Tang M, et al. Fragmented QRS is associated with all-cause mortality and ventricular arrhythmias in patient with idiopathic dilated cardiomyopathy. Annals of Noninvasive Electrocardiology, 2011;16(3):270-75.

14. Carey MG, Luisi Jr AJ, Baldwa S, et al. The Selvester QRS Score is more accurate than Q waves and fragmented QRS complexes using the Mason-Likar configuration in estimating infarct volume in patients with ischemic cardiomyopathy. Journal of electrocardiology, 2010;43(4):318-25.

15. Abdelrahman TM. QRS Fragmentation as a Prognostic Test in Acute Coronary Syndrome. World Journal of Cardiovascular Surgery, 2013;3(2):42-51.

16. Das MK, Khan B, Jacob S, et al. Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. Circulation, 2006;113(21):2495-2501.

17. Visseren FL, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). European heart journal, 2021;42(34), 3227-3337.

18. American Diabetes Association. Glycemic targets: standards of medical care in diabetes-2021. Diabetes Care, 2021;44(1):73-84.

19. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology, 2018;72(14):91-220.

20. Qureshi AR, Alvestrand A, Divino-Filho JC, et al. Inflammation, malnutrition, and cardiac disease as predictors of mortality in hemodialysis patients. Journal of the American Society of Nephrology, 2002;13(1):28-36.

21. Genovesi S, Pogliani D, Faini A, et al. Prevalence of atrial fibrillation and associated factors in a population of long-term hemodialysis patients. American journal of kidney diseases, 2005;46(5):897-902.

22. Homsi M, Alsayed L, Safadi A, et al. Fragmented QRS complexes on a 12-lead ECG as a marker of non-coronary artery disease related myocardial disease by gadolinium delayed enhancement cardiac magnetic resonance imaging. Journal of Cardiovascular Magnetic Resonance, 2009;11(1):1-316.

23. Park SJ, On YK, Kim JS, et al. Relation of fragmented QRS complex to right ventricular fibrosis detected by late gadolinium enhancement cardiac magnetic resonance in adults with repaired tetralogy of fallot. The American journal of cardiology, 2012;109(1):110-15.

24. Basaran Y, Tigen K, Karaahmet T, et al. Fragmented QRS complexes are associated with cardiac fibrosis and significant intraventricular systolic dyssynchrony in nonischemic dilated cardiomyopathy patients with a narrow QRS interval. Echocardiography, 2011;28(1):62-68.

25. Damar Hİ. Kardiyak sendrom x hastalarında fragmente qrs sıklığı, Tıpta uzmanlık tezi, Tokat , Gaziosmanpaşa Üniversitesi Tıp Fakültesi, 2014;26-27.

26. Winkelmayer WC, Patrick AR, Liu J, Brookhart MA, Setoguchi S. The increasing prevalence of atrial fibrillation among hemodialysis patients. Journal of the American Society of Nephrology, 2011;22(2):349-57.

27. Yildirir A, Aksoyek S, Calguneri M, et al. QT dispersion as a predictor of arrhythmic events in patients with ankylosing spondylitis. Rheumatology, 2000;39(8):875-79.

28. Castro Hevia J, Antzelevitch C, Tornés Bárzaga F, et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. Journal of the American College of Cardiology, 2006;47(9):1828-34.

29. Bekar L, Kalçık M, Kilci H, et al. Presence of fragmented QRS may be associated with complex ventricular arrhythmias in patients with essential hypertension. Journal of electrocardiology, 2019;55:20-25.

30. Sheldon SH, Gard JJ, Asirvatham SJ. Premature ventricular contractions and non-sustained ventricular tachycardia: association with sudden cardiac death, risk stratification, and management strategies. Indian pacing and electrophysiology journal, 2010;10(8):357.

Cite as: Kardas F, Taylan G, Kaya C, Kurultak I. Presence of fragmented QRS may be associated with ventricular arrhythmias in hemodialysis patients. Eskisehir Med J. 2022;3(2):92-100.