Fragmented QRS is associated with frequency of premature ventricular contractions in patients without overt cardiac disease

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Abstract

Objective: In this study, we aimed to demonstrate whether the presence of fragmented QRS (fQRS) is associated with the frequency of premature ventricular contractions (PVCs).

Methods: We retrospectively analyzed 282 cases by 24-hour Holter monitorings (HMs) between August 2012 and February 2013. Firstly, the patients were divided into 2 groups with respect to presence of fQRS and then divided into 3 groups with respect to frequency of PVCs as Group 1: seldom PVC (<120 PVCs/day), Group 2: moderate-frequency PVC (120-720 PVCs/day), and Group 3: frequent PVC (>720 PVCs/day). We investigated the predictors of frequent PVCs by using multinomial logistic regression analysis.

Results: Ninety-eight patients had fQRS. There was no difference between the 2 groups with respect to body mass index, gender, hypertension, and diabetes mellitus. Patients with fQRS were older (54.9±15.6 vs. 47.0±16.3, p<0.001) and had more family history of coronary artery disease (25% vs. 13%, p=0.012). Patients with fQRS was more likely to be on aspirin therapy (28.6% vs. 10.4%, p<0.001) and have a larger left atrium diameter (33.5±5.7 vs. 30.4±5.8, p=0.001). Presence of fQRS was significantly associated with the frequency of PVCs (for frequent PVC 27.7% vs. 7.6%, p<0.001; for moderate-frequency PVC 18.4% vs. 11.4%, p=0.012); 26.2% of Group 1 (n=202) had fQRS, 46.2% of Group 2 (n=39) had fQRS, and 65.9% of Group 3 (n=41) had fQRS. In the multinomial regression analysis, only age (odds ratio: 4.24, 95% confidence interval 2.08-8.64, p=0.001) and fQRS (odds ratio: 2.11, 95% confidence interval 1.00-4.45, p=0.05) were predictors of frequent PVCs.

Conclusion: This study demonstrated that the presence of fQRS is associated with frequent PVCs in patients without overt structural heart disease. *(Anatol J Cardiol 2015; 15: 456-62)*

Keywords: fragmented QRS, premature ventricular contraction, Holter monitoring

Introduction

Premature ventricular contractions (PVCs) are common in the general population, and most of them are not clinically important in the absence of underlying structural heart disease, but it is well known that PVCs are associated with mortality and morbidity when there is an underlying structural heart disease (1-3). It is shown that frequent PVCs have a good prognosis in the absence of structural heart disease (4). On the contrary, some studies demonstrated an increased risk of sudden cardiac death, myocardial infarction, and all-cause mortality in patients with frequent PVCs but without structural heart disease (5, 6). Some investigators found that frequent PVCs may cause cardiomyopathy by itself and may be responsible for increased cardiac risk (7, 8). Additionally, PVCs without underlying heart disease may be associated with ventricular tachycardia (VT), and elimination of these PVCs with catheter ablation prevents further occurrence of VT (9-11).

Fragmented QRS (fQRS) is a finding on the surface electrocardiogram (ECG), and it is associated with cardiac mortality and morbidity in various cardiac conditions (12, 13). Furthermore, fQRS was found to be associated with ventricular arrhythmias in patients with various cardiac disorders, such as chronic heart failure, hypertrophic cardiomyopathy, Brugada syndrome, and idiopathic ventricular fibrillation (14-17), but the association between fQRS and PVCs is not well studied.

In the present study, we aimed to demonstrate whether the presence of fQRS is associated with frequent PVCs on 24-hour Holter monitorings (HMs) in patients without overt structural heart disease.

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Methods

Study population

We retrospectively evaluated 412 patients who underwent 24 hour HM due to complaints of palpitation in our hospital between August 2012 and February 2013. To exclude possible coronary artery disease (CAD), we did not evaluate and include the patients with complaints of chest pain and dyspnea. Patients with positive noninvasive stress tests were also not done. Among the evaluated 412 patients, 62 patients with missing ECGs, 26 patients with ischemic cardiomyopathy, 18 patients with bundle branch block, 11 patients with moderate to severe valvular disease, 8 patients with nonischemic cardiomyopathy, 4 patients with pacemaker activity, and 1 patient with hypertrophic cardiomyopathy were excluded from study. Finally, 282 patients were included in the study. Firstly, the patients were divided into 2 groups with respect to the presence of fQRS, and then, patients were divided into 3 groups with respect to frequency of PVCs, with groups 1, 2, and 3 representing seldom PVCs (<120 PVCs/day), moderate-frequency PVCs (120-720 PVCs/day), and frequent PVCs (>720 PVCs/day), respectively (18).

Patients' medical history and baseline characteristics were extracted from the medical recordings. Hypertension (HTN), diabetes mellitus (DM), smoking, and family history of coronary artery disease (CAD) were noted. Body mass index (BMI) was calculated by using the standard formula [weight (kilogram)/ square of height (meter)]. Baseline laboratory findings, including fasting plasma glucose (FPG), creatinine, potassium, hemoglobin (Hgb), leukocytes, thyroid-stimulating hormone (TSH), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), and total cholesterol levels, were noted from the laboratory recordings obtained prior to HM. Glomerular filtration rate (eGFR) was measured using the standard Cockcroft-Gault formula.

Echocardiographic recordings (all of them were done with a Vivid 7, General Electric Vingmed, Horten, Norway) were evaluated, and ejection fraction (EF) (by Simpson method), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), interventricular septum (IVS) thickness in diastole, posterior wall (PW) thickness in diastole, and left atrium (LA) diameter in apical for chamber dimensions were noted. All echocardiographies in our institution were performed according to previous guidelines of the American Society of Echocardiography (19).

Electrocardiography

A 12-lead surface ECG was obtained from all patients before connecting the Holter device to the patient. The 12-lead ECGs (Nihon-KohdenCardiofax ECG1350K, Tokyo, Japan, filter range 0.5 Hz to 150 Hz, AC filter 60 Hz, 25 mm/s, 10 mm/mV) were analyzed by 2 independent cardiologists who were blinded to the Holter data. fQRS was defined as the presence of different RSR' patterns (QRS duration <120 ms), which included an additional R wave (R' prime) or notching of the R wave or S wave, or the presence of more than one R' prime without typical bundle branch block in two contiguous leads corresponding to a major coronary artery territory (12-14). ECGs were evaluated with the naked eye by two cardiologists, who were blinded to the Holter results for the presence of fQRS without using any magnification. The inter-observer concordance rate for determining fQRS was 98.5% between the two readers. In cases of disagreement, the final decision was made mutually.

Holter monitoring and interpretation

Holter devices (Universal resting 12-lead Holter dms 300-4A, mtm multitechmed gmbh, Schwarzwaldstrasse, Germany) were applied to the patient by our clinic's nurse; the patient came back after 24 hours, and the nurse took off the device and uploaded the recordings to the Holter archive. Two independent cardiologists evaluated the recordings for PVCs, and the number of PVCs was recorded.

Statistical analysis

All statistical studies were carried out with the SPSS program (version 15.0, SPSS, Chicago, İllinois, USA). Quantitative variables were expressed as the mean value±SD, and qualitative variables were expressed as percentages (%). All measurements were evaluated with the Kolmogorov-Smirnov test. A comparison between two groups, according to the presence of fQRS, was performed using the student t-test. A comparison between three groups, according to the number of PVCs, was performed using one-way ANOVA and Tukey test for post-hoc analysis. Categorical variables were compared by the likelihood ratio $\chi 2$ test or Fisher's exact test. Multinomial logistic regression analysis, which included variables with $p<0.1$, was performed to identify independent predictors of PVC frequency. Age ≥65, increased left atrium diameter (≥35 mm), increased interventricular septum diameter (≥11 mm), male gender, DM, HT, family history, beta-blocker usage, and presence of fQRS were entered into the model. A p value <0.05 was considered statistically significant.

Results

In total, the study included 282 patients. Fragmented QRS was present in 98 (34.7%) of them. The baseline characteristics of the patients are shown in Table 1. There were no differences between the 2 groups (defined according to the presence of fQRS) with respect to gender, HTN, DM, BMI, and smoking status. Patients with fQRS were older (54.9±15.6 vs. 47.0±16.3, $p<0.001$) and more likely to be on aspirin therapy for primary prevention (28.6% vs. 10.4%, $p<0.001$) and β-blocker therapy (29.6% vs. 15.8%, $p=0.007$). The baseline laboratory findings, except TSH and FPG, were not different between the 2 groups. Patients with fQRS had higher TSH levels (2.3±1.6 vs. 1.82±1.3, $p=0.016$) and higher FPG levels (111.2±44.4 vs. 99.7±24.9, $p=0.006$) than patients without fQRS. Patients with fQRS had a larger left atrium (33.5±5.7 vs. 30.4±5.8, $p=0.001$) and thicker IVS (10.2±1.8 vs. 9.5±2.3, $p=0.042$) than patients without fQRS. Frequency of PVCs was significantly higher in patients with fQRS (27.6% vs.

Table 1. Baseline characteristics of study patients according to the presence of fragmented QRS

Age, years	fQRS- (n=184) 47.0±16.3	fQRS+ (n=98) 54.9±15.6	*P* <0.001
Gender, female n (%)	114 (62)	50 (49)	0.053
BMI, kg/m^2	27.1±6.1	27.6±5.0	0.491
Hypertension, n (%)	53(28.8)	38 (39.2)	0.077
Diabetes mellitus, n (%)	11.4 (21)	19.8 (19)	0.057
Family CAD history, n (%)	24 (13)	24 (25)	0.012*
Smoking, n (%)	47 (25.5)	22 (22.7)	0.596
Ejection fraction, %	63.3±4.1	61.6±6.4	0.086
LVEDD, mm	42.7±4.7	44.1±4.7	0.067
LVESD, mm	28.0±5.0	28.6±4.1	0.495
LAD, mm	30.4±5.8	33.5±5.7	0.001*
IVSD, mm	9.5±2.3	10.2±1.8	0.042
LVPWD, mm	9.7±1.8	10.2±2.4	0.131
FPG, mg/dL	99.7±24.9	111.2±44.4	0.006*
Hemoglobin, g/dL	12.8±1.6	13.0±1.4	0.518
Leukocyte, ×10^3 /mL	7.4±2.0	7.6±2.4	0.693
Creatinine, mg/dL	0.78±0.27	0.79±0.30	0.719
Potassium, mg/dL	5.0±1.4	4.4±0.4	0.360
eGFR	99.8±28.0	96.7±27.2	0.478
Total cholesterol, mg/dL	200±37	227±93	0.048*
LDL-C, mg/dL	127±36	128±31	0.789
HDL-C, mg/dL	51±12	52±12	0.748
Triglyceride, mg/dL	112±50	131±70	0.078
TSH, UI/mL	1.82±1.3	2.3±1.6	0.016
ASA, n (%)	19 (10.4)	28 (28.6)	<0.001*
β blocker, n (%)	29 (15.8)	29 (29.6)	0.007*
ACEi, n (%)	15 (8.7)	13 (13.3)	0.235
ND-CCB, n (%)	15 (8.7)	15 (15.3)	0.068
Moderate PVCs, n (%)	21 (11.4)	18 (18.4)	0.012†
Frequent PVCs, n (%)	14 (7.6)	27 (27.7)	<0.001†

*significant differences
†significantly different than fewer PVCs.
ASA - asetil salicylic acite; BMI - body mass index; CAD - coronary artery disease; eGFR - estimated glomerular filtration rate; FPG - fasting plasma glucose; HDL-C - high-density lipoprotein cholesterol; IVSD - interventricular septum end-diastolic diameter; LAD - left atrium diameter; LDL-C - low-density lipoprotein cholesterol; LVEDD - left ventricle end-diastolic diameter; LVESD - left ventricle end-systolic diameter; LVPWD - left ventricle posterior wall end-diastolic thickness; ND-CCB - non-dihydropyridine calcium channel-blocking agent; PVC - premature ventricular contraction; TSH - thyroid-stimulating hormone

7.6%, p<0.001). Moderate PVC was also higher in patients with fQRS (18.4% vs. 11.4%, p=0.012) when compared to the seldom PVC group.

In Table 2, we demonstrated the characteristics of the study population with respect to PVC frequency. There were no differences between the 3 groups with respect to gender, age, BMI, HTN, DM, smoking status, and family history of CAD. The EF was lower in groups 2 and 3 than in group 1 (p=0.007). Higher LVEDD measurements were present in group 3 than in groups 1 and 2 (p=0.003). The left atrium was larger in groups 2 and 3 than in group 1 (p=0.010). Creatinine was higher in group 3 than in group 1 (p=0.025), and eGFR was lower in group 3 than in group 1 (p=0.013). The percentage of patients with fQRS was significantly different between all 3 groups. While 65.9% of group 3 patients had fQRS, 46.2% and 26.2% of group 2 and group 1 patients had fQRS, respectively (p=0.001).

Table 2. Patient characteristics according to PVC frequency

	Group 1 (n=202) (PVC< 120/day)	Group 2 (n=39) (PVC 120-720/day)	Group 3 (n=41) (PVC≥ 720/day)	*P*
Gender, female, n (%)	119 (58.9)	23 (59.0)	21 (51.2)	0.653
Age, years	48.7±16.2	51±17.1	53.9±17.1	0.168
BMI, kg/m^2	27.1±6	27.1±5.1	28.2±5	0.596
Fragmented QRS, n (%)	53 (26.2)$^{\ddagger,\beta}$	18 (46.2)$^\beta$	27 (65.9)‡	0.001*
Hypertension, n (%)	62 (30.7)	13 (34.2)	16 (39.0)	0.563
Diabetes mellitus, n (%)	29 (%14.4)	6 (15.8)	5 (12.2)	0.896
Smoking, n (%)	49 (24.3)	12 (31.6)	8 (19.5)	0.453
Family history of CAD, n (%)	32 (15.8)	7 (18.4)	9 (22.5)	0.579
Ejection fraction, %	63.5±4‡	60.6±6.3‡	60.8±7.3	0.007*
LVEDD, mm	42.7±4.7‡	42.6±4.3	46.2±4.3‡	0.003*
LVESD, mm	27.6±4.8‡	29.3±4.1	30±4.2‡	0.039*
LVPWD, mm	9.8±1.8	9.5±2.9	10.7±2.2	0.089
IVSd, mm	9.7±2.1	9.7±2.3	10.3±1.9	0.475
LAD, mm	30.8±6‡	32.5±5.2	31.6±6‡	0.010*
BB, n (%)	35 (17.4)	10 (25.6)	13 (31.7)	0.085
ND-CCB, n (%)	14 (7.0)$^{\ddagger,\beta}$	8 (20.5)$^\beta$	8 (19.5)‡	0.006*
FPG, mg/dL	101.4±24.8	110.4±57.6	106.1±31.3	0.624
Creatinine, mg/dL	0.7±0.2‡	0.8±0.3	0.9±0.4‡	0.025*
eGFR, mL/min/1.73 m^2	102.4±27.2‡	93.8±29.0	86.2±25.0‡	0.013*
Total cholesterol, mg/dL	204.2±39.6	240.2±122.4	195±29.2	0.079
Triglyceride, mg/dL	115.9±57.4	140.1±63.3	113.5±58	0.197
LDL-C, mg/dL	128.8±36.4	134.3±34.2	117.5±27.6	0.267
HDL-C, mg/dL	52±12.7	47.2±8.4	53.7±11.5	0.262
Hemoglobin, g/dL	12.9±1.6	12.9±1.5	12.8±1.2	0.963
Leukocytes,10^3/mm^3	7.6±2.3	7.1±1.3	7.1±2.3	0.355
TSH, UI/mL	1.9±1.4	1.7±1	2.6±2	0.334
Potassium, mmol/L	4.4±0.3	4.5±0.5	4.4±0.4	0.551

*significant differences
$^{\ddagger,\beta}$significant difference between groups
BB - beta-blocking agent; BMI - body mass index; eGFR - estimated glomerular filtration rate; FPG - fasting plasma glucose; HDL-C - high-density lipoprotein cholesterol; IVSd - interventricular septum end-diastolic; LAD - left atrium diameter; LDL-C - low-density lipoprotein cholesterol; LVEDD - left ventricle end-diastolic diameter; LVESD - left ventricle end-systolic diameter; LVPWD - left ventricular posterior wall end-diastolic thickness; ND-CCB - non-dihydropyridine calcium channel-blocking agent; TSH - thyroid-stimulating hormone

Table 3. Univariate and multivariate analyses for predictors of frequent premature ventricular contraction

Variable	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age ≥65 years	2.47 (1.21-5.05)	0.013	4.24 (2.08-8.64)	0.001
GFR≤60 mL/min/1.73m^2	1.98 (0.50-7.86)	0.328		
Diabetes mellitus	0.81 (0.29-2.21)	0.679		
Family history	1.49 (0.66-3.38)	0.334		
Male gender	1.36 (0.70-2.65)	0.357		
CCB	2.39 (0.98-5.81)	0.054		
fQRS	4.61 (2.28-9.32)	<0.001	2.11 (1.00-4.45)	0.05

CCB - calcium channel blocker; CI - confidence interval; fQRS - fragmented QRS; GFR - glomerular filtration rate; OR - odds ratio

Table 4. Patient characteristics according to presence of fragmented QRS when hypertension, diabetes mellitus, and left ventricular hypertrophy are excluded

	fQRS (-) (n=122)	fQRS (+) (n=49)	P
Gender, male, n (%)	37 (30.3)	21 (42.9)	0.118
Age, years	39.1±15.6	44.7±17.5	0.045‡*
BMI, kg/m^2	25.1±5.8	25.4±4.8	0.757
Smoking, n (%)	34 (27.9)	13 (27.1)	0.918
Family history of CAD, n (%)	14 (11.5)	6 (12.5)	0.852
Ejection fraction, %	63.7±3.0	63.2±4.8	0.588
LVEDD, mm	41.7±4.1	43.0±4.9	0.133
LVESD, mm	27.1±3.4	28.0±3.5	0.324
LVPWD, mm	8.8±1.4	8.9±1.0	0.720
IVSd, mm	8.3±1.1	8.8±1.0	0.100
FPG, mg/dL	89.9±11.2	92.6±10.1	0.318
Creatinine, mg/dL	0.77±0.45	0.81±0.41	0.288
Total cholesterol, mg/dL	190.1±32.1	243.9±138.2	0.028*
Triglyceride, mg/dL	105.8±53.3	127.6±87.8	0.517‡
LDL-C, mg/dL	120.9±33.1	126.8±21.6	0.480
HDL-C, mg/dL	54.8±12.3	54.7±13.1	0.976
Hemoglobin, g/dL	13.0±1.5	13.1±1.5	0.715
TSH, UI/mL	1.77±1.04	2.08±0.96	0.073‡*
Frequent PVCs, n (%)	7 (5.7)	14 (28.6)	<0.001*

‡Mann-Whitney U test
*significant differences
BMI - body mass index; CAD - coronary artery disease; FPG - fasting plasma glucose; HDL-C - high-density lipoprotein cholesterol; IVSD - interventricular septum end-diastolic thickness; LDL-C - low-density lipoprotein cholesterol; LVEDD - left ventricle end-diastolic diameter; LVESD - left ventricle end-systolic diameter; LVPWD - left ventricle posterior wall end-diastolic thickness; PVC - premature ventricular contraction; TSH - thyroid-stimulating hormone

In the multinomial regression analysis, only age (odds ratio: 4.24, 95% confidence interval 2.08-8.64, p=0.001) and fQRS (odds ratio: 2.11, 95% confidence interval 1.00-4.45, p=0.05) were found as predictors of frequent PVCs on the HMs in this study (Table 3).

Table 5. Univariate analyses for risk factors of frequent premature ventricular contractions in patients without hypertension, diabetes, and left ventricular hypertrophy

Variable	OR (95% CI)	P
Age ≥45 years	1.93 (0.77-4.85)	0.159
Male gender	1.03 (0.39-2.71)	0.952
fQRS	6.57 (2.45-17.56)	<0.001
Smoking	0.58 (0.18-1.82)	0.351
Family history	1.95 (0.58-6.53)	0.276
Total cholesterol ≥200 mg/dL	1.31 (0.23-7.25)	0.753

CI - confidence interval; fQRS - fragmented QRS; OR - odds ratio

In Table 4, we show the baseline characteristics of the patients without hypertension, diabetes, and left ventricular hypertrophy. Fragmented QRS was also more prevalent in patients with frequent PVCs in these groups. While 7 (5.7%) of the 112 patients without fQRS had frequent PVCs, 14 (28.6%) of the 49 patients with fQRS had frequent PVCs. In this group, only fQRS was associated with frequent PVCs, as shown by univariate analysis (Table 5).

Discussion

The main finding of the present study is that the presence of fQRS on surface ECG is related to frequent PVCs in patients without overt structural heart disease. We also found that patients with frequent PVCs have lower EF values and higher LV and LA dimensions. To our knowledge, this is the first study demonstrating the association between fQRS and PVC frequency.

Fragmentation of QRS complex can easily be detected by the naked eye, and growing evidence corroborates its role in various areas of cardiac manifestations. First of all, it was found to be associated with increased cardiac mortality and morbidity in patients with CAD (20), acute coronary syndromes (13, 21), and ischemic and nonischemic cardiomyopathy (22, 23). Secondly, fQRS was found to be associated with ventricular arrhythmias in various conditions, such as ischemic and nonischemic cardiomyopathy (23), hypertrophic cardiomyopathy (15), Brugada syndrome (24), acquired long QT syndrome (25), and arrhythmogenic right ventricular dysplasia (26, 27). Additionally, fQRS was found to be associated with the response to cardiac resynchronization therapy (28) and shock delivery from implanted devices (29).

Although the main causative mechanism of fQRS formation is not fully understood yet, myocardial fibrosis and/or ischemia is generally accepted as being responsible for fQRS formation through the altered homogeneity of myocardial electrical activity (30, 31). Really, studies with cardiac magnetic resonance imaging (MRI) (31, 32) and myocardial single-photon emission tomography (SPECT) (33) showed that fQRS was associated with myocardial scars and had higher sensitivity and specificity for detecting myocardial scars than Q wave. Myocardial scarring or fibrosis is not only developed by myocardial infarction or isch-

emia-patients may also have low-grade myocardial fibrosis that is undetectable by MRI or SPECT; indeed, a previous study showed the presence of fQRS in patients without detected myocardial fibrosis (34). Indeed, a substantial proportion of patients in our study had fQRS, although they did not have overt structural heart disease. This finding suggests that many patients without overt structural heart disease may have subclinical myocardial fibrosis, which makes them more prone to increased risk of future CV events. Very recently, the role of inflammation in fQRS formation was introduced in studies, and it was found that patients with inflammatory diseases are more likely to have fQRS (35, 36). As an example, cardiac MRI showed increased myocardial fibrosis despite the absence of cardiovascular disease in patients with rheumatoid arthritis (37). Experimental studies showed that tumor necrosis factor-α (TNF-α), which is a strong inflammatory marker, is associated with myocardial fibrosis (38). Additionally, C-reactive protein (CRP) may directly induce cardiac fibrosis via the inflammation of cardiac cells (39). Systemic inflammation has an important role in the occurrence of rhythm disorders and conduction abnormalities, and this was attributed to myocardial inflammation, focal fibrosis, or ischemia in the conduction system (40).

Myocardial scar is a known cause of ventricular arrhythmias, and the most common ventricular arrhythmia is PVC, which almost everyone has in his lifetime. At the beginning, frequent PVCs without an underlying structural heart disease were accepted as having no clinical importance (4), but later studies established contradictory findings (5, 6). Some recent studies showed that some PVCs may trigger ventricular tachycardia (VT) and/or fibrillations in apparently normal hearts (41), and in these patients, PVC ablation may effectively and safely reduce future VT (42). In addition to being responsible for triggering VT, frequent PVCs may also cause LV dysfunction by itself, which is termed PVC cardiomyopathy, and this may resolve after PVC elimination by catheter ablation (9-11, 43). In a very recent study, it was found that frequent PVCs were associated with declining of the EF in 4 years of follow-up (7). Similar to this study, EF was significantly lower in patients with frequent PVCs in our study, although it was in the normal range. Interestingly, EF values within groups in our study and the study mentioned above were nearly identical. Our study also demonstrated that patients with frequent PVCs had larger LV diameters, which were compatible with EF values. In a recent study, it was shown that fQRS was also associated with systolic and diastolic dysfunction (44). Diastolic dysfunction in subjects with normal systolic functions was also attributed to the underlying myocardial fibrosis (45). Our study is not a follow-up study; so, we can not claim that PVC causes EF reduction. We only found that frequent PVCs in patients with apparently normal hearts are associated with reduced EF and increased LV dimensions when compared to patients without frequent PVCs. This finding suggests that patients with frequent PVCs must be followed up, even if they are asymptomatic, to detect LV dysfunction.

Hypertension and DM are major risk factors for CVD, and LVH is accepted as target organ damage; thus, we also compared patients without HTN, DM, and LVH to exclude the possible role of subclinical CVD in these patients. We can suggest that the pretest probability of CAD in these patients is very low, because they have no chest pain and are predominantly female and relatively young (mean age 44.7 in fQRS and 39.1 in non-fQRS patients). We found that fQRS was associated with frequent PVCs, even in this group.

Finally, most of the PVCs in normal hearts originate from the right ventricular outflow tract (RVOT), and in a recent electrophysiological study, it was shown that fragmentations on the ECG due to local voltage potentials on the RVOT are associated with RVOT PVCs (46).

Study limitations

Firstly, this is a retrospective study with a relatively small number of patients; prospective follow-up studies are needed to clarify the clinical importance of fQRS in patients with frequent PVCs. Secondly, cardiac MRI to delineate the presence of myocardial fibrosis in patients with frequent PVCs may be useful, but obtaining these techniques in a retrospective study is impossible, because they have no regular indication for managing these patients. Thirdly, most of the patients were not evaluated with stress tests to exclude asymptomatic CAD. Lastly, we did not have inflammatory markers (like CRP, TNF-α, or interleukins) and markers of early atherosclerosis (like carotid intima-media thickness), which may strengthen our findings.

Conclusion

In conclusion, fQRS is independently associated with frequent PVCs. Patients with fQRS and palpitation should be monitored for measuring PVC burden, and in the case of frequent PVCs, patients should be followed for future arrhythmic events and LV dysfunction and should be treated conveniently.

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