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Presence of fragmented QRS may be associated with complex ventricular arrhythmias in patients with essential hypertension

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ABSTRACT

Background: Ventricular arrhythmias (VAs) are frequent in hypertensive patients. Myocardial fibrosis is one of the components of left ventricular hypertrophy secondary to hypertension. Fragmented QRS (fQRS) on electrocardiography (ECG) has been shown to be a marker of myocardial fibrosis. In this study, we aimed to investigate the association between fQRS and complex VAs in patients with essential hypertension.

Methods: Two hundreds consecutive patients who were diagnosed with hypertension were included in the study. The control group consisted of 153 age and sex matched healthy individuals. ECG and transthoracic echocardiography were performed to all patients. fQRS was defined as additional R' wave or notching/splitting of S wave in two contiguous ECG leads. All patients underwent 24-hour Holter monitoring and VAs were classified using Lown's scoring system. Lown class ≥3 VAs were considered as complex VAs.

Results: There was no significant difference with respect to age (52 ± 8 vs 52 ± 6 years, $p = 0.836$) and gender distribution (female: 64% vs 63%, $p = 0.907$) between the groups. As compared to the healthy individuals, prevalence of fQRS (67% vs 9.2%, $p < 0.001$) and complex VAs (19% vs 0%, $p < 0.001$) were significantly higher in patients with hypertension. Furthermore, complex VAs (25.4% vs 6.1%, $p = 0.001$) were significantly higher in hypertensive patients with fQRS. In multiple logistic regression analysis, left ventricular ejection fraction (OR: 1.11, 95%CI: 1.025 to 1.183; $p = 0.006$), left ventricular mass index (OR: 1.04, 95%CI: 1.021 to 1.107; $p = 0.001$) and presence of fQRS (OR: 5.605, 95%CI: 1.427 to 22.019; $p = 0.014$) were independent predictors for complex VAs.

Conclusion: The presence of fQRS may be associated with complex VAs in patients with essential hypertension. Therefore, fQRS may be used in risk stratification of complex VAs and sudden cardiac death especially in hypertensive patients with left ventricular hypertrophy.

Introduction

Hypertension is one of the common cardiovascular diseases and may cause serious complications [1]. Left ventricular hypertrophy (LVH) is one of the most frequently seen target organ injuries in hypertensive patients. Contrary to physiologic LVH such as athlete's heart, LVH developed secondary to hypertension is associated with increased cardiovascular morbidity and mortality [2]. In the Framingham survey study, LVH was found to be related to increased cardiovascular morbidity and mortality [3]. Besides, in subjects with left ventricular hypertrophy, the presence of asymptomatic ventricular arrhythmias (VAs) was associated with higher mortality [4].

During the progress of LVH, myocytes undergo hypertrophy, and meanwhile exaggerated collagen accumulation occurs in interstitium which results in myocardial fibrosis [5]. Thus, contractile and connective tissue components of heart tissue increase and, areas of myocardial fibrosis due to accumulation of fibroblasts and collagen develop adjacent to areas with myocyte hypertrophy [6]. Increase in fibrotic areas may delay and impair homogeneity of electrical stimuli conduction [7]. These electrophysiologic alterations may predispose hypertensive patients to the development of VAs. In previous studies, the association between the development VAs and the severity of myocardial fibrosis has been demonstrated [8].

Fragmented QRS (fQRS) is a depolarization disorder which may be easily detected in 12 lead superficial electrocardiography (ECG) which

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displays a conduction delay caused by myocardial fibrotic tissue [9]. Fibrotic tissue slows down the electrical conduction and causes notching in QRS complex [10]. Possible association between the presence of fQRS and myocardial fibrosis in hypertensive patients has been previously reported [11]. In this study, we aimed to investigate the association between the presence of fQRS and complex VAs in patients with essential hypertension.

Methods

Study population

Consecutive adult patients with essential hypertension who referred to our cardiology outpatient clinic were included in this study between January 2010 and December 2011. The control group consisted of age and sex matched health individuals. The exclusion criteria included known or suspected coronary artery disease, rheumatic heart disease, cardiomyopathy, diabetes mellitus, pregnancy, malignancy, systemic or metabolic disease including hepatic and renal insufficiency, and atrial fibrillation. ECGs with typical bundle branch block, pace rhythm, or any kind of significant conducting abnormalities were also excluded from the study. Routinely obtained 12 lead ECG recordings were examined, and patients were divided into two groups as those with and without fQRS complexes. All patients provided a written or oral-witnessed informed consent, and the study protocol was approved by the local ethics committee of the hospital in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines.

Biochemical assessment

Venous blood samples were obtained from each patient following an overnight fasting and a 24-hour period of abstinence from alcohol and vigorous physical exercise for the determination of serum biochemical parameters. Routine serum biomarkers such as glucose, blood urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride, and complete blood count were calculated with standard laboratory methods (Beckmann Coulter aU5800 Autoanalyzer, Beckmann Coulter Inc., Brea, California, US).

Diagnosis of hypertension

For the new diagnosis of hypertension, office blood pressure measurements or 24-hour ambulatory blood pressure measurements were taken into consideration. During office measurements, the results of at least two measurements were taken into consideration. Blood pressure measurements were performed while the patients were sitting comfortably on a chair with their feet stepping on the floor using a sphygmomanometer with an appropriately sized cuff (wrapping at least 80% of the forearm). Before blood pressure measurements, the patients were rested for at least 10 min and they were withheld from smoking and consumption of tea or coffee before 30 min. In these measurements patients with persistent blood pressures ≥140/90 mm Hg were considered to be hypertensive. Among patients whose blood pressures values were monitored on an ambulatory basis, those with average 24 h, daytime, and nighttime blood pressures values were ≥130/80 mm Hg ≥ 135/85 mm Hg, and ≥120/70 mm Hg respectively were considered as hypertensive individuals. Patients who had diagnosed with hypertension previously and had been using antihypertensive drugs for at least two months were also considered as hypertensive.

Detection and definition of fQRS

The standard 12-lead ECGs were obtained at a paper speed of 25 mm/s and amplitude of 10 mm/mv (low-pass filter range: 100–150 Hz, AC filter: 60 Hz) from all patients using Nihon Kohden Cardiofax ECG-9132 device. fQRS was defined as the presence of an additional R wave (R′), notching of the R or S wave, or the presence of fragmentation (more than one R′) in two contiguous leads on ECGs [11] (Fig. 1). The ECGs were analyzed by 2 independent cardiologists blinded to the patient characteristics. The ECG and transthoracic echocardiography (TTE) were performed on the same day in all study population.

Echocardiographic evaluation

All patients underwent TTE performed by the same cardiologist using Vivid 5 echocardiography device (GE Vingmed Ultrasound AS, Horten, Norway), and 3.2 mHz adult probe with the patient in the left lateral decubitus position. In all patients, the left ventricular posterior wall thickness (PWT), interventricular septal thickness (IVST), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD) and left atrial diameter (LAD) were measured on the parasternal long-axis view. Left ventricular ejection fractions (LVEF) of the patients were calculated by using biplane Simpson's method. Left ventricular mass (LVM) was calculated based on Devereux formula [$LVM = 0.8\,(1.04\,(IVS + LVEDD + PW)^3 - (LVEDD)^3) + 0.6$], and body surface area was estimated using Mosteller formula [body surface area = (height (cm) × body weight (kg)/3600)$^{1/2}$]. Left ventricular mass was divided by body surface area to estimate left ventricular mass index (LVMI). Based on the recommendations of European Society of Cardiology, cut-off values of LVM indices for LVH were >115 g/m^2 for men, and >95 g/m^2 for women.

Detection and classification of ventricular arrhythmias

Frequency of VAs was investigated using 24-hour-Holter monitoring device (Sorin Group, ELA Medical, SpiderView recorders and SyneScope analysis program). All ventricular ectopic beats, couplets, triplets and ventricular tachycardia episodes were reviewed by two cardiologists and false positive events were excluded from the analyses. Rate and duration of each episode were noted. VAs were classified using Lown's scoring system [4]. Lown class 3 or higher VAs were considered as complex VAs.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 19.0. (IBM Corp. Armonk, NY). Descriptive statistics were reported as mean ± standard deviation for continuous variables with normal distribution or median (25^{th}–75^{th} percentiles) values for continuous variables without normal distribution and as frequency with percentages for the categorical variables. The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to test the normality of the distribution of continuous variables. Categorical variables were compared with Chi-square or Fisher exact tests. Student t-test or Mann-Whitney *U* test was used to compare continuous variables as appropriate. A logistic regression analysis was performed in order to identify any independent associates of VAs. In multiple logistic regression analysis, effect size was adjusted for variables with a univariate significance level of ≤0.1. Adjusted odds ratios (OR), along with their 95% confidence intervals (CI) were presented. A 2-tailed p value < 0.05 was considered statistically significant in all statistical analyses.

Results

A total of 200 hypertensive patients (female: 64%; mean age: 51.6 ± 8.3 years) and 153 controls (female: 63%; mean age: 51.7 ± 5.7 years) were included in this study. A total of 70 patients were excluded due to exclusion criteria described in the methods. fQRS was detected on ECG recordings of 134 (67%) hypertensive patients and 14 (9.2) controls. Demographic, laboratory and echocardiographic characteristics

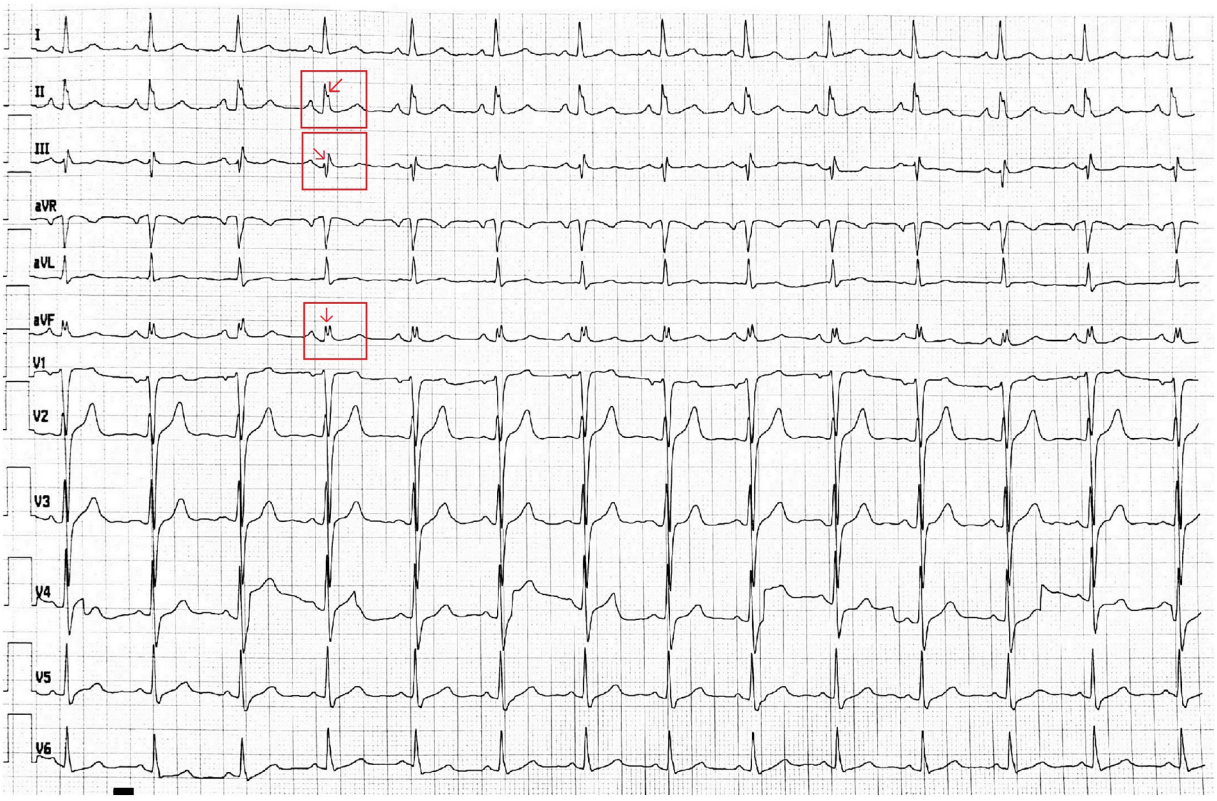

Fig. 1. An example electrocardiography revealing the presence of QRS fragmentation in contiguous leads II, III and aVF (arrows show the notching of the R waves).

of the study population were presented in Table 1. Age and gender distribution were similar between hypertensive patients and controls. As compared to the control group, prevalence of hyperlipidemia ($p = 0.009$), body mass index ($p < 0.001$), total cholesterol ($p = 0.038$) levels, systolic ($p < 0.001$) and diastolic ($p < 0.001$) blood pressures were significantly higher in hypertensive patients. Among echocardiographic parameters, aortic root diameter ($p = 0.018$), LAD ($p < 0.001$), LVEDD ($p < 0.001$), IVST ($p < 0.001$), PWT ($p < 0.001$), LVM ($p < 0.001$), LVMI ($p < 0.001$) and the prevalence of LVH ($p < 0.001$) were significantly higher in hypertensive patients (Table 1). The prevalence of fQRS formation was significantly higher in hypertensive patients than in the healthy controls (67% vs 9.2%, $p < 0.001$). Among hypertensive patients, the prevalence of fQRS formation was significantly higher in cases with LVH (80% vs 56%; $p < 0.001$).

Comparison of baseline characteristics of the hypertensive patients with and without fQRS was summarized in Table 2. LAD ($p = 0.006$), LVESD ($p = 0.037$), LVEDD ($p = 0.018$), IVST ($p = 0.002$), PWT ($p < 0.001$), LVM ($p < 0.001$), LVMI ($p < 0.001$) and the prevalence of LVH ($p < 0.001$) were significantly higher in hypertensive patients with fQRS (Table 2).

There were no Lown class 2 or higher VAs in the control group, while 27.5% of VAs were class ≥2 in the hypertensive patients. The prevalence of complex VAs (Lown class ≥3) was 19% in hypertensive group ($p < 0.001$). Lown class 4 VAs, characterized by couplet ventricular beats and non-sustained ventricular tachycardia episodes, were observed in 11.5% of the patients with hypertension (Table 3). Hypertensive patients with fQRS had significantly higher frequency of Lown class ≥2, ≥3 and ≥4 VAs as compared to the hypertensive patients without fQRS (all p values < 0.05) (Table 4). Among hypertensive patients, the prevalence of complex VAs was significantly higher in cases with LVH (32.6% vs 7.4%; $p < 0.001$).

Comparison of baseline characteristics of the hypertensive patients with and without complex VAs was summarized in Table 5. Age ($p = 0.031$), systolic blood pressure ($p = 0.031$), aortic root diameter ($p = 0.021$), LVEDD ($p = 0.019$), IVST ($p < 0.001$), PWT ($p < 0.001$), LVM ($p < 0.001$), LVMI ($p < 0.001$) and the prevalence of LVH ($p < 0.001$) were significantly higher in hypertensive patients with complex VAs. The prevalence of fQRS was significantly higher hypertensive patients with complex VAs (89.5% vs 61.7; $p = 0.001$) (Table 5).

Age, systolic blood pressure, total cholesterol level, aortic root diameter, LAD, LVEF, LVEDD, IVST, PWT, LVM, LVMI and the prevalence of LVH were considered as the potential predictors of complex VAs (all p values ≤ 0.1) in univariate analysis (Table 5). In multiple logistic regression analysis, LVEF (OR: 1.11, 95%CI: 1.025 to 1.183; $p = 0.006$), LVMI (OR: 1.04, 95%CI: 1.021 to 1.107; $p = 0.001$) and presence of fQRS (OR: 5.605, 95%CI: 1.427 to 22.019; $p = 0.014$) were independent predictors for complex VAs (Table 6).

Discussion

In this study, we have focused on the association between the presence of fQRS and complex VAs in patients with essential hypertension. The prevalence of fQRS formation was significantly higher in hypertensive patients than in the healthy controls. It was observed that LAD, LVESD, LVEDD, IVST, PWT, LVM, and LVMI were higher in the hypertensive patients with fQRS. Besides, LVH was more frequently observed in fQRS(+) group. Hypertensive patients with fQRS had significantly higher frequency of complex VAs as compared to the hypertensive patients without fQRS. The presence of fQRS was found to be independently associated with the complex VAs in hypertensive patients.

LVH is one of the most important cardiovascular injuries caused by hypertension and associated with increased mortality and morbidity. The main reason for this association is myocardial fibrosis. LVM is increased in LVH secondary to hypertension and extracellular collagen tissue increases excessively relative to myocytes, resulting in myocardial fibrosis [12]. fQRS is a depolarization disorder that appears as a notch in the QRS complex on routine ECG recordings [13]. In our study, we found a significant and strong relationship between the

Table 1
Baseline characteristics of the study groups.

	Hypertension (n = 200)	Control (n = 153)	p value
Demographic parameters			
Age (years)	51.6 ± 8.3	51.7 ± 5.7	0.836
Gender, female, n (%)	128 (64)	97 (63)	0.907
Body mass index (kg/m^2)	32.2 ± 5.3	29.3 ± 4.3	<0.001
Hypertension duration (years)	7.5 ± 5.4	–	–
Hyperlipidemia, n (%)	83 (42)	43 (28)	0.009
Current smoker, n (%)	23 (12)	28 (18)	0.072
Systolic blood pressure (mm Hg)	145 ± 16	120 ± 14	<0.001
Diastolic blood pressure (mm Hg)	91 ± 11	78 ± 9	<0.001
Presence of fragmented QRS, n (%)	134 (67.0)	14 (9.2)	<0.001
Biochemical parameters			
Glucose (mg/dL)	93 ± 12	92 ± 9	0.181
BUN (mg/dL)	13.8 ± 7.3	11.8 ± 3.3	0.001
Creatinine (mg/dL)	0.73 ± 0.18	0.73 ± 0.16	0.940
Total cholesterol (mg/dL)	203 ± 36	195 ± 37	0.038
Triglyceride (mg/dL)	158 ± 80	147 ± 97	0.253
Low-density lipoprotein (mg/dL)	132 ± 30	126 ± 32	0.067
High-density lipoprotein (mg/dL)	46 ± 10	47 ± 13	0.412
Medications			
ACE inhibitors, n (%)	96 (48)	1 (7)	<0.001
Angiotensin receptor blockers, n (%)	70 (35)	0 (0)	<0.001
Calcium channel blockers, n (%)	**57 (28.5)**	0 (0)	<0.001
B-blockers, n (%)	44 (22)	**4 (2.6)**	<0.001
Diuretics, n (%)	122 (31)	0 (0)	<0.001
Echocardiographic parameters			
Aortic root diameter (cm)	3.0 ± 0.4	2.9 ± 0.4	0.018
Left atrial diameter (cm)	3.6 ± 0.5	3.1 ± 0.4	<0.001
LV ejection fraction (%)	67 ± 6	67 ± 5	0.821
LV end-diastolic diameter (cm)	4.4 ± 0.5	4.5 ± 0.5	0.243
LV end-systolic diameter (cm)	2.8 ± 0.4	3.0 ± 0.4	<0.001
Interventricular septal thickness (cm)	1.27 ± 0.18	1.01 ± 0.11	<0.001
Posterior wall thickness (cm)	1.20 ± 0.16	0.92 ± 0.13	<0.001
Left ventricular mass (gr)	203.9 ± 51.5	147.1 ± 35.6	<0.001
Left ventricular mass index (gr/m^2)	107 ± 25	79 ± 17	<0.001
Left ventricular hypertrophy, n (%)	92 (46)	3 (2)	<0.001

BUN: blood urea nitrogen, LV: left ventricle, VAs: ventricular arrhythmias.

Table 2
Comparison of baseline characteristics of hypertensive patients with and without fragmented QRS complexes.

	Hypertension and fQRS (+) (n = 134)	Hypertension and fQRS (−) (n = 66)	p value
Demographic parameters			
Age (years)	52.2 ± 7.9	50.3 ± 9.1	0.131
Gender, female, n (%)	85 (63.4)	43 (65.2)	0.812
Body mass index (kg/m^2)	32.3 ± 5.2	32 ± 5.5	0.627
Hypertension duration (years)	7.6 ± 5.2	7.2 ± 5.7	0.635
Hyperlipidemia, n (%)	50 (37.3)	33 (50)	0.087
Current smoker, n (%)	15 (11.2)	8 (12.1)	0.847
Systolic blood pressure (mm Hg)	147.6 ± 16	141.1 ± 16.3	0.008
Diastolic blood pressure (mm Hg)	92.4 ± 10.9	89.4 ± 11.2	0.071
Complex ventricular arrhythmia, n (%)	34 (25.4)	4 (6.1)	0.001
Biochemical parameters			
Glucose (mg/dL)	93.6 ± 10.5	93.5 ± 8.3	0.968
BUN (mg/dL)	13.7 ± 4.2	13.9 ± 11.2	0.854
Creatinine (mg/dL)	0.74 ± 0.18	0.70 ± 0.16	0.094
Total cholesterol (mg/dL)	204.3 ± 37.6	199.9 ± 32.7	0.421
Triglyceride (mg/dL)	157.4 ± 84.2	157.7 ± 70.3	0.985
Low-density lipoprotein (mg/dL)	131.6 ± 31.4	133.5 ± 27.3	0.665
High-density lipoprotein (mg/dL)	46.7 ± 10.8	45.1 ± 9.3	0.275
Echocardiographic parameters			
Aortic root diameter (cm)	3.02 ± 0.41	2.97 ± 0.43	0.385
Left atrial diameter (cm)	3.70 ± 0.48	3.51 ± 0.39	0.006
LV ejection fraction (%)	66.7 ± 6.0	68.5 ± 6.0	0.056
LV end-diastolic diameter (cm)	4.47 ± 0.47	4.29 ± 0.51	0.018
LV end-systolic diameter (cm)	2.81 ± 0.41	2.68 ± 0.41	0.037
Interventricular septal thickness (cm)	1.29 ± 0.16	1.21 ± 0.21	0.002
Posterior wall thickness (cm)	1.23 ± 0.13	1.13 ± 0.18	<0.001
Left ventricular mass (gr)	215.5 ± 49.9	180.6 ± 47.1	<0.001
Left ventricular mass index (gr/m^2)	112.8 ± 23.3	96.1 ± 24.7	<0.001
Left ventricular hypertrophy, n (%)	74 (55.2)	18 (27.3)	<0.001

BUN: blood urea nitrogen, fQRS: fragmented QRS, LV: left ventricle, VAs: ventricular arrhythmias.

presence of fQRS and LVH parameters in hypertensive patients. These fibrotic areas decrease the conduction speed of the electrical stimulation, which causes notching in the QRS complex. In previous studies, there was evidence that the presence of fQRS may demonstrate myocardial fibrosis in hypertensive patients [11,14,15]. Increased LAD was measured in hypertensive individuals with fQRS complexes in this study. This condition may be related to impaired diastolic functions. Indeed, higher incidence of impaired diastolic functions has been previously demonstrated in hypertensive patients with established fQRS [16].

In hypertensive heart disease, components of cardiac tissue change during remodelling process. The foremost change among them is increase in collagen synthesis, while its degradation decreases. This condition induces accumulation of collagen in myocardium [12]. As a result of these pathological processes mediated by mechanical, neurohormonal factors and cytokines, myocardial fibrosis develops [17]. This process is a key factor in the development of many clinical conditions including left ventricular dysfunction, arrhytmias and sudden cardiac death [18–20].

Arrhythmia is a common problem in hypertensive patients. They may be present in a wide spectrum ranging from premature beats, ventricular tachycardia and sudden cardiac death [21]. In our study, we observed higher frequency of VA in hypertensive patients when compared with healthy individuals. One of the most important parameters in the pathogenesis of VA is LVH and myocardial fibrosis. Extensive fibrous tissue formed during development of LVH leads to electrical heterogeneity which predisposes to the formation of arrhytmias [22–24].

In a subgroup analysis of original Framingham Heart Study subjects, the presence of asymptomatic VAs was significantly associated with higher mortality rates in subjects with LVH [4]. Reduced coronary vascular reserve, silent myocardial ischemia, abnormal membrane properties of hypertrophied myocytes and electrophysiologic disturbances due to increased fibrous tissue or altered collagen content have been considered as possible mechanisms for arrhythmogenesis [25–28].

We have detected that the presence of fQRS was one of the independent predictors of complex VAs in the hypertensive patients. The

Table 3
Prevalence of ventricular arrhythmias among study population.

	Hypertension (n = 200)	Control (n = 153)	p value
Lown class (n, %)			
Class 0	60 (30)	87 (57)	<0.001
Class 1a	78 (39)	61 (40)	
Class 1b	7 (3.5)	5 (3.3)	
Class 2	17 (8.5)	0 (0)	
Class 3	15 (7.5)	0 (0)	
Class 4a	16 (8.0)	0 (0)	
Class 4b	7 (3.5)	0 (0)	
≥Lown class 2 (n, %)	55 (27.5)	0 (0)	<0.001
≥Lown class 3 (n, %)	38 (19.0)	0 (0)	<0.001
≥Lown class 4 (n, %)	23 (11.5)	0 (0)	<0.001

Table 4
Prevalence of ventricular arrhythmias among of hypertensive patients with and without fragmented QRS complexes.

	Hypertension and fQRS (+) (n = 134)	Hypertension and fQRS (−) (n = 66)	p value
Lown class (n, %)			
Class 0	31 (23.1)	29 (43.9)	0.003
Class 1a	49 (36.6)	29 (43.9)	
Class 1b	5 (3.7)	2 (3)	
Class 2	15 (11.2)	2 (3)	
Class 3	13 (9.7)	2 (3)	
Class 4a	14 (10.4)	2 (3)	
Class 4b	7 (5.2)	0 (0)	
≥Lown class 2 (n, %)	49 (36.6)	6 (9.1)	<0.001
≥Lown class 3 (n, %)	34 (25.4)	4 (6.1)	0.001
≥Lown class 4 (n, %)	21 (15.7)	2 (3)	0.008

fQRS: fragmented QRS.

frequency of complex VAs in hypertensive patients with fQRS was significantly higher as compared to other hypertensive cases without fQRS. Presence of fQRS has been reported to be an indicator for myocardial fibrosis in hypertensive patients [11]. Since myocardial fibrosis may trigger arrhytmias by inducing electrical heterogeneity, there may be a relationship between VAs and myocardial fibrosis in hypertensive patients [8].

In this study, LVEF and LVMI were other independent predictors of complex VAs in the hypertensive patients. In parallel with the development of LVH in hypertensive patients, LVEF also increases. Nearly 1 mm increase in cardiac wall thickness causes 3.43% increase in LVEF [29]. During this increase, longitudinal and circumferential shortening of myocardium may be impaired. This myocardial dysfunction may predispose to the development of VAs.

Table 5
Baseline characteristics of the patients with and without complex ventricular arrhythmias.

	Complex VAs (+) (n = 38)	Complex VAs (−) (n = 162)	p value
Demographic parameters			
Age (years)	54.2 ± 8.2	50.9 ± 8.3	0.031
Gender, female, n (%)	21 (55.3)	107 (66)	0.213
Body mass index (kg/m^2)	31.7 ± 4.9	32.4 ± 5.4	0.454
Hypertension duration (years)	8.4 ± 5.6	7.2 ± 5.3	0.221
Hyperlipidemia, n (%)	17 (44.7)	66 (44.7)	0.653
Current smoker, n (%)	5 (13.2)	18 (11.1)	0.722
Systolic blood pressure (mm Hg)	150 ± 15	144 ± 16	0.031
Diastolic blood pressure (mm Hg)	92 ± 10	91 ± 11	0.508
Presence of fragmented QRS, n (%)	34 (89.5)	100 (61.7)	0.001
Biochemical parameters			
Glucose (mg/dL)	93.2 ± 11.3	93.6 ± 9.4	0.838
BUN (mg/dL)	14.2 ± 4.1	13.6 ± 7.8	0.668
Creatinine (mg/dL)	0.76 ± 0.18	0.72 ± 0.17	0.271
Total cholesterol (mg/dL)	193 ± 31	205 ± 36	0.074
Triglyceride (mg/dL)	158 ± 79	157 ± 80	0.928
Low-density lipoprotein (mg/dL)	125 ± 25	133 ± 30	0.166
High-density lipoprotein (mg/dL)	44 ± 8	46 ± 10	0.144
Echocardiographic parameters			
Aortic root diameter (cm)	3.1 ± 0.4	2.9 ± 0.4	0.021
Left atrial diameter (cm)	3.7 ± 0.5	3.6 ± 0.4	0.066
LV ejection fraction (%)	69.1 ± 6.5	66.9 ± 6.3	0.067
LV end-diastolic diameter (cm)	4.5 ± 0.4	4.3 ± 0.5	0.019
LV end-systolic diameter (cm)	2.7 ± 0.4	2.8 ± 0.4	0.862
Interventricular septal thickness (cm)	1.37 ± 0.12	1.24 ± 0.18	<0.001
Posterior wall thickness (cm)	1.30 ± 0.11	1.17 ± 0.15	<0.001
Left ventricular mass (gr)	240.9 ± 41.5	195.3 ± 49.9	<0.001
Left ventricular mass index (gr/m^2)	125.8 ± 20.9	102.9 ± 23.9	<0.001
Left ventricular hypertrophy, n (%)	30 (78.9)	62 (38.3)	<0.001

BUN: blood urea nitrogen, LV: left ventricle, VAs: ventricular arrhythmias.

Table 6
Multivariate regression analysis showing independent predictors of complex ventricular arrhythmias.

	OR	95% CI	p value
Age	1.033	0.973–1.097	0.286
Systolic blood pressure	1.016	0.991–1.043	0.215
Total cholesterol	0.991	0.979–1.003	0.148
Aortic root diameter	2.093	0.594–7.375	0.250
Left atrial diameter	0.646	0.242–1.715	0.383
LV ejection fraction	1.110	1.025–1.183	0.006
LV end-diastolic diameter	5.287	0.001–1980.22	0.692
Interventricular septal thickness	6.969	0.001–1.176	0.857
Posterior wall thickness	8.525	0.001–8.633	0.362
Left ventricular mass	0.973	0.876–1.082	0.617
Left ventricular mass index	1.043	1.021–1.107	0.001
Left ventricular hypertrophy	1.111	0.229–5.396	0.896
Presence of fragmented QRS	5.605	1.427–22.019	0.014

CI: confidence interval; LV: left ventricle, OR: odds ratio.

Systemic hypertension is one of the most important causes of pathological LVH and current evidence indicates that hypertensive patients with LVH are at increased risk of VAs and sudden cardiac death [30]. This evidence has led to speculation that these arrhythmias may be the cause of sudden cardiac death in these patients [31,32]. Soonafter, Saadeh et al. have studied the relationships between QT dispersion, LVH, complex VAs and sudden cardiac death over long-term follow-up in hypertensive patients. They reported that only LVH and high grade VAs were predictors of sudden cardiac death in patients with essential hypertension [33].

Several invasive and noninvasive tests for risk stratification of sudden cardiac death have been studied, mostly in the context of structural heart disease such as coronary artery disease, cardiomyopathy, and heart failure. fQRS caused by myocardial scar has been associated with increased mortality and arrhythmic events in patients with coronary artery disease [34,35]. Similarly, the presence of fQRS may be associated with increased arrhythmic events and sudden cardiac death in patients with essential hypertension. Therefore, the utility of fQRS in risk stratification of sudden cardiac death and guiding patients selection for device therapy needs to be explored in further studies especially in hypertensive patients with structural heart disease.

Limitations

The primary limitation was that our study was a nonrandomized and single center study with a relatively small number of patients. Secondly, only the patients with a QRS duration <120 ms were included in the study. The third was the lack of demonstration of myocardial fibrosis using advanced imaging techniques or histopathological examinations. Besides, 24-hour Holter recordings may not be adequate to detect VAs. Techniques allowing recordings for longer periods may determine the accurate frequency of arrhytmias in these patients. Although patients with known or suspected coronary artery disease were excluded in this study, several patients with subtle coronary artery disease might be underdiagnosed.

Conclusion

The presence of fQRS may be associated with complex VAs in patients with essential hypertension. Therefore, fQRS may be used in risk stratification of complex VAs and sudden cardiac death especially in hypertensive patients with LVH.

Competing interests

All of the authors have no conflict of interest.

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