

Left Ventricular Dysfunction in Outpatients with Frequent Ventricular Premature Complexes

Kyoung-Min Park, MD¹; Sung Il Im, MD¹; Sung Ho Lee, MD¹; Hye Bin Gwag, MD¹; Youngjun Park, MD¹; Seung-Jung Park, MD¹; June Soo Kim, MD¹; Young Keun On, MD¹

¹Division of Cardiology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Frequent ventricular premature complexes (VPCs) and VPC QRS duration are risk factors for left ventricular (LV) dysfunction. To determine which clinical characteristics and electrocardiographic features are associated with LV dysfunction (ejection fraction, <50%) and frequent VPCs, we retrospectively reviewed data from a single-center registry of all patients diagnosed with frequent VPCs at a Korean outpatient clinic.

We identified 412 consecutive outpatients (mean age, 54.7 ± 16.8 yr; 227 women [55.1%]) who were diagnosed with frequent VPCs and had no structural heart disease from January 2010 through December 2017. Available transthoracic echocardiograms and 24-hour Holter monitoring data were evaluated to correlate the occurrence of VPCs and symptoms.

Typical VPC-related symptoms (palpitations or dropped beats) were observed in 251 patients (61.1%). Electrocardiograms revealed VPCs with a left bundle branch block–like morphology in 327 patients (79.5%) and VPCs with an inferior axis in 353 (85.8%). Twenty-six patients (6.3%) were diagnosed with VPC-related LV dysfunction. The mean VPC burden did not differ significantly by LV functional status (11.06% ± 10.13% [normal] vs 14.41% ± 13.30% [impaired]; P=0.211). Patients with impaired LV function were more often men (P=0.027), had no typical VPC-related symptoms (P=0.006), and had significantly longer VPC QRS durations (mean, 157 ms vs 139 ms; P <0.01).

Our findings suggest that male sex, absence of typical VPC-related symptoms, and a VPC QRS duration >157 ms are associated with LV dysfunction in patients with frequent VPCs, findings that may be useful in predicting such dysfunction. (Tex Heart Inst J 2022;49(1):e207265)

Citation:

Park KM, Im SI, Lee SH, Gwag HB, Park Y, Park SJ, Kim JS, On YK. Left ventricular dysfunction in outpatients with frequent ventricular premature complexes. *Tex Heart Inst J* 2022; 49(1):e207265. doi: 10.14503/THIJ-20-7265

Key words:

Echocardiography; electrocardiography; electrocardiography, ambulatory; retrospective studies; sex distribution; ventricular dysfunction, left/epidemiology/physiopathology; ventricular premature complexes

Corresponding author:

Sung Il Im, MD,
Division of Cardiology,
Department of Internal
Medicine, Kosin Univer-
sity Gospel Hospital,
Kosin University
College of Medicine,
262 Gamcheon-ro,
Seo-Gu, Busan 49267,
ROK

E-mail:

sungils8932@
naver.com

© 2022 by the Texas Heart[®]
Institute, Houston

Ventricular premature complexes (VPCs) are frequently observed on 12-lead electrocardiograms (ECGs) in healthy individuals and patients with ischemic or structural heart disease.¹ According to a population-based study in the United States,^{1,2} more than 6% of middle-aged adults have VPCs, and the prevalence increases with age. Several clinical reports suggest that a VPC burden of >20% on a 24-hour Holter ECG is associated with left ventricular (LV) dysfunction and that radiofrequency (RF) ablation can restore normal LV function.^{1,3-6} Of note, LV function can remain normal in patients with severe symptoms and a high VPC burden, but be reduced in patients with fewer symptoms and a lower VPC burden. This suggests that VPC burden alone cannot explain VPC-induced LV dysfunction. Moreover, the risk factors for VPC-induced LV dysfunction in the healthy heart remain unclear. Several studies have demonstrated that a long VPC QRS duration (>153 ms) correlates with VPC-induced LV dysfunction.^{7,8} However, most studies have been performed in Western and inpatient populations. We sought to identify retrospectively the clinical and ECG characteristics of VPC-related LV dysfunction in a Korean outpatient population.

Patients and Methods

We retrospectively reviewed and extracted data from a single-center registry of all patients diagnosed with frequent VPCs at Samsung Medical Center's outpatient clinic, regardless of the reason for their visit. We included all patients who were diagnosed

with frequent VPCs in the absence of known structural heart disease from January 2010 through December 2017. The study was conducted in accordance with the Declaration of Helsinki, and its protocol was approved by our institutional ethics committee. All patients provided written informed consent.

We included patients who were ≥ 19 years old; had frequent VPCs (≥ 2 monomorphic VPCs on a 12-lead ECG and a $>1\%$ burden or $>1,000$ beats on a 24-hour Holter ECG at enrollment); had at least two 24-hour Holter ECGs separated by at least 1-week intervals; had a full description of symptoms in the medical record; underwent transthoracic echocardiography (TTE) at baseline within 1 month before VPC suppression treatment and at follow-up after treatment; and had available 12-lead ECGs showing VPCs for use in measuring various characteristics.

We excluded patients who had a history of atrial fibrillation (AF), atrial flutter (AFL), atrial tachycardia (AT), nonsustained ventricular tachycardia (VT), or sustained VT, or evidence of any of these arrhythmias documented on a 12-lead or 24-hour Holter ECG; a history of myocardial infarction, structural heart disease, or heart valve replacement or repair; or any evidence of ischemic or structural heart disease based on information obtained from ECGs, coronary angiography, radio-nuclide evaluation, cardiac magnetic resonance (CMR), or cardiac catheterization.

A total of 650 patients initially met the inclusion criteria (Fig. 1). Of those, 32 were excluded because their medical records contained insufficient data. Another 206 patients were excluded because they had a history of atrial arrhythmias ($n=37$), episodes of sustained or nonsustained VT ($n=26$), coronary artery disease ($n=101$), valvular heart disease ($n=29$), LV noncompaction ($n=1$), cardiac sarcoidosis ($n=3$), arrhythmogenic right ventricular cardiomyopathy or dysplasia ($n=5$), myocarditis ($n=1$), and other major abnormalities on CMR ($n=3$). The remaining 412 patients were included in this study.

Available TTE and 24-hour Holter data were reviewed. Symptoms related to VPCs, as described in the medical records, were evaluated by a cardiologist. Palpitations and dropped beats were considered typical VPC-related symptoms. All other symptoms, including fatigue, dizziness, syncope, and shortness of breath, were considered atypical. Data from 24-hour Holter monitoring at enrollment were evaluated in detail to correlate the occurrence of VPCs and symptoms. Any patient who had palpitations or dropped beats during the VPCs documented on the 24-hour Holter ECG was considered to have typical VPC-related symptoms.

Echocardiographic Analysis

Transthoracic echocardiograms, which were obtained with patients in the left lateral decubitus position, were used to evaluate LV systolic function by the modified

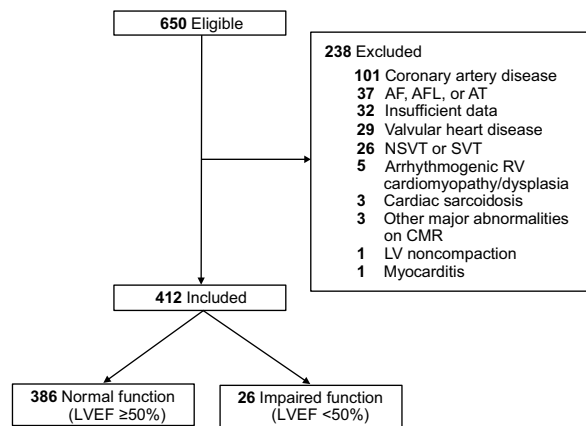


Fig. 1 Flow diagram shows selection of patients included in the study.

AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia; CMR = cardiac magnetic resonance; LV = left ventricular; LVEF = left ventricular ejection fraction; NSVT = nonsustained ventricular tachycardia; RV = right ventricular; SVT = sustained ventricular tachycardia

biplane Simpson method, as recommended by the American Society of Echocardiography.⁹ Normal LV systolic function was defined as an ejection fraction (EF) $\geq 50\%$, according to joint American College of Cardiology Foundation (ACCF) and American Heart Association (AHA) guidelines.¹⁰ Patients were classified into 2 groups according to their baseline LVEF (normal vs impaired). Normal LV function was defined as a baseline LVEF of $\geq 50\%$. Impaired LV function was defined as a baseline LVEF of $<50\%$ that improved by $\geq 10\%$ to the normal range after successful RF ablation or medical treatment. Patients in the impaired-function group underwent TTE again 3 to 6 months after treatment.

Electrocardiographic Analysis

Initial 12-lead ECGs, if available, were analyzed for VPC morphology, VPC axis, and distribution of precordial R-wave transitions. The VPC morphology was classified as left bundle branch block (LBBB) or right bundle branch block (RBBB), according to joint recommendations by the AHA, ACCF, and Heart Rhythm Society.¹¹ The VPC axis was classified as superior or inferior based on the vector of the dominant VPC deflection in leads II, III, and aVF. Precordial R-wave transitions were classified as occurring before V_3 (at leads V_1 and V_2), at V_3 , or after V_3 (at leads V_4 to V_6).

Initial 12-lead ECGs, which were recorded at a sweep speed of 100 ms and before intake of antiarrhythmic drugs that affect the QRS interval, were analyzed off-line with a Muse Cardiology Information System and digital calipers to evaluate the following variables (Fig. 2):

- Sinus QRS duration: from QRS onset to terminal S wave

- VPC QRS duration: from VPC onset to terminal S wave
- Sinus VPC coupling interval: from onset of R wave of previous sinus beat to VPC onset
- Post-VPC coupling interval: from VPC onset to initiation of next sinus beat

Holter Monitoring

Before treatment of VPCs with RF ablation or antiarrhythmic drugs, 24-hour Holter monitoring was performed twice a month (at intervals of at least 1 week) to evaluate the mean VPC burden (number and percentage of VPCs daily). In the impaired-function group, Holter monitoring was repeated twice a month (at intervals of at least 1 week) for 6 months after treatment and then every 3 to 6 months or whenever VPC-related symptoms recurred.

Statistical Analysis

Data for continuous variables were reported as mean \pm SD, and differences between groups were evaluated with use of the Student *t* test or Wilcoxon rank-sum test. Data for categorical variables were reported as number and percentage, and differences between groups were evaluated with use of the Pearson χ^2 test or Fisher exact test. *P* values <0.05 were considered statistically significant. All statistical analyses were 2-tailed and were performed with use of SPSS version 18.0 (SPSS, an IBM company).

Results

Baseline Patient Characteristics

The study population was predominantly female ($n=227$; 55.1%) and had a mean age of 54.79 ± 16.88 years (Table I and Fig. 3). Most women were in the 4th to 6th decades of life (58.9%), whereas most men were in the 5th to 7th decades (58.6%). Left ventricular

systolic function was normal in 386 (93.7%) patients and impaired in 26 (6.3%) patients. Overall, the mean VPC burden on 24-hour Holter ECGs was $13.94\% \pm 12.72\%$ by percentage and $15,721 \pm 14,298$ by number. Of the 386 patients who had normal LV function, 308 (79.8%) were evaluated with use of CMR and 77 (19.9%) with use of coronary angiography. Of the 26 patients who had impaired LV function, 20 (77%) were evaluated with use of CMR and 6 (23.1%) with use of coronary angiography.

Echocardiographic Analysis

As shown by TTE analysis, impaired LV function was observed more frequently in men than in women ($P=0.027$). Use of β -blockers ($P<0.001$) and angiotensin II receptor blockers ($P=0.231$) was more frequent in the impaired-function group (Table I). Typical VPC-related symptoms (palpitations and dropped beats) occurred more frequently in the normal-function group ($P=0.007$). Women were significantly more likely than men to have typical VPC-related symptoms (odds ratio=1.83; 95% CI, 1.34–2.51; $P<0.01$).

Electrocardiographic Analysis

Overall, the VPC morphology was more frequently LBBB (327 patients [79.4%]) than RBBB (85 [20.6%]), and the VPC axis was more frequently inferior (353 [85.7%]) than superior (159 [14.3%]) (Table II). Precordial R-wave transitions occurred before V_3 in 107 patients (26.0%), at V_3 in 72 (17.5%), and after V_3 in 233 (56.6%).

Between LV function groups, the distributions of VPC morphology, VPC axis, and precordial R-wave transitions were similar (Table II). However, the mean sinus QRS duration (96.3 ± 13.7 vs 87.4 ± 11.1 ms; $P=0.04$) and VPC QRS duration (157.1 ± 10.5 vs 139.5 ± 13.3 ms; $P<0.01$) were longer in the impaired-function group. The number of patients with a daily VPC burden of 10,000 to 20,000 beats was greater in the impaired-function group ($P<0.001$); conversely,



Fig. 2 Sample 12-lead electrocardiogram shows the intervals used to evaluate the sinus QRS duration (A), ventricular premature complex (VPC) QRS duration (B), sinus VPC coupling interval (C), and post-VPC coupling interval (D).

TABLE I. Demographic, Clinical, and Echocardiographic Characteristics

Variable	Overall (N=412)	Normal Function (LVEF ≥50%) (n=386)	Impaired Function (LVEF <50%) (n=26)	P Value
Age (yr)	54.79 ± 16.88	54.42 ± 15.64	58.91 ± 14.68	0.101
Sex	—	—	—	0.027
Male	185 (44.9)	168 (43.5)	17 (65.4)	—
Female	227 (55.1)	218 (56.5)	9 (34.6)	—
Height (cm)	163.64 ± 56.05	163.63 ± 57.37	163.90 ± 11.57	0.202
Weight (kg)	61.75 ± 13.20	61.64 ± 13.16	64.05 ± 14.08	0.139
VPC burden (%/24 hr)	13.94 ± 12.72	11.06 ± 10.13	14.41 ± 13.30	0.211
VPC burden (n/24 hr)	15,721 ± 14,298	13,914 ± 12,941	16,528 ± 13,290	0.254
VPC frequency (n/24 hr)				
1,000–10,000	255 (61.8)	251 (65.0)	4 (15.4)	<0.001
10,001–20,000	109 (26.4)	91 (23.6)	18 (69.2)	<0.001
>20,000	48 (11.6)	44 (11.4)	4 (15.4)	0.526
Symptoms				
Chest pain	136 (33.0)	130 (33.7)	6 (23.1)	0.749
Dizziness	65 (15.8)	61 (15.8)	4 (15.4)	0.189
Dyspnea	90 (21.8)	84 (21.8)	6 (23.1)	0.881
Fatigue	6 (1.5)	6 (1.6)	0	>0.99
Palpitations or dropped beats	251 (61.0)	238 (61.7)	13 (50.0)	0.007
Syncope	23 (5.6)	21 (5.4)	2 (7.6)	0.278
Medical history				
Diabetes	32 (7.8)	30 (7.8)	2 (7.7)	>0.99
Dyslipidemia	12 (2.9)	11 (2.8)	1 (3.8)	0.249
Hypertension	94 (22.8)	88 (22.8)	6 (23.1)	0.417
Medications				
ACE inhibitor	8 (1.9)	6 (1.6)	2 (7.7)	0.125
Angiotensin II receptor blocker	21 (5.1)	18 (4.7)	3 (11.5)	0.231
β-blocker	67 (16.3)	54 (14.0)	13 (50.0)	<0.001
Calcium channel blocker	28 (6.8)	27 (7.0)	1 (3.8)	0.921
Antiarrhythmic agents	51 (12.4)	45 (11.7)	6 (23.1)	0.115
Type Ic				
Flecainide	31 (7.5)	31 (8.0)	0	<0.001
Propafenone	13 (3.2)	13 (3.4)	0	<0.001
Type III				
Amiodarone	7 (1.7)	1 (0.3)	6 (23.1)	<0.001
TTE variables				
LVEF (%)	47.0 ± 7.0	59.0 ± 6.0	35.0 ± 8.0	<0.001
LVEDD (mm)	52.5 ± 6.5	49.0 ± 5.0	56.0 ± 8.0	<0.001
LVESD (mm)	36.4 ± 7.1	31.0 ± 5.0	42.0 ± 9.0	<0.001
Functional imaging modes				
CMR	114 (27.7)	94 (24.4)	20 (77.0)	<0.001
Coronary angiography	83 (20.1)	77 (19.9)	6 (23.1)	0.687

ACE = angiotensin-converting enzyme; CMR = cardiac magnetic resonance; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic dimension; TTE = transthoracic echocardiography; VPC = ventricular premature complex

Data are presented as mean ± SD or as number and percentage. *P* < 0.05 was considered statistically significant for differences between LV function groups.

the number of patients with a daily VPC burden of <10,000 beats was greater in the normal-function group ($P < 0.001$). However, the 2 groups had similar proportions of patients with a VPC burden of >20,000 beats ($P = 0.526$) and similar mean percent VPC burdens ($11.06\% \pm 10.13\%$ vs $14.41\% \pm 13.30\%$; $P = 0.211$).

Discussion

Our retrospective, single-center study produced several important findings. First, women were slightly more likely than men to have frequent VPCs. Second, LV function was impaired more often in men and in pa-

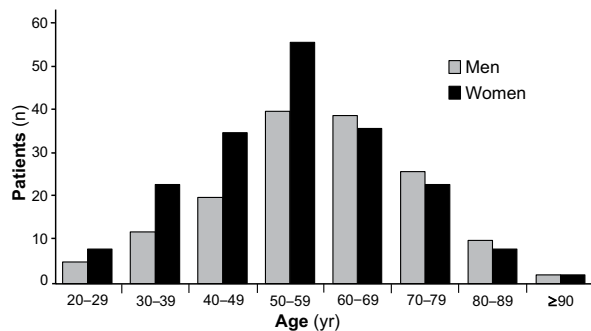


Fig. 3 Histogram shows the age distribution among patients with ventricular premature complexes.

tients with no history of typical VPC-related symptoms, and it was associated with significantly longer VPC QRS durations. Third, contrary to expectations, the VPC burden was higher in patients with impaired LV function.

Generally, VPCs are more prevalent among men than women and may be associated with age.^{1,2} It is reasonable to assume that the age-related increase in prevalence is cumulative. However, despite the normal age distribution in our study, we found that frequent VPCs occurred more often and a decade earlier in women than in men. Excluding patients with ischemic or valvular heart disease from our study may have reduced the numbers of men and older patients, which may explain the difference between our findings and those of others.

Left ventricular dysfunction occurred more frequently in men with no typical VPC-related symptoms. However, comparing the presence of typical VPC-related symptoms by sex revealed that women were more sensitive to VPCs. Many studies have revealed sex differences between patients with normal versus impaired LV function, including a higher incidence of LV dysfunction in men than in women.¹²⁻¹⁴ Being male is a major risk factor for coronary heart disease,¹⁵ and VPCs are observed more frequently in patients with ischemic heart disease.¹⁶ These associations may have affected the outcomes of previous studies. However, when ischemic

TABLE II. Electrocardiographic Characteristics

Variable	Overall (N=412)	Normal Function (LVEF ≥50%) (n=386)	Impaired Function (LVEF <50%) (n=26)	P Value
QRS morphology	—	—	—	0.541
RBBB	85 (20.6)	80 (20.7)	5 (19.2)	—
LBBB	327 (79.4)	306 (79.3)	21 (80.8)	—
Axis	—	—	—	>0.99
Inferior	353 (85.7)	331 (85.8)	22 (84.6)	—
Superior	59 (14.3)	55 (14.2)	4 (15.4)	—
R-wave transition	—	—	—	0.916
Before V ₃	107 (26.0)	102 (26.4)	5 (19.2)	—
At V ₃	72 (17.5)	67 (17.4)	5 (19.2)	—
After V ₃	233 (56.6)	217 (56.2)	16 (61.5)	—
ECG variables				
Sinus QRS duration (ms)	89.4 ± 11.1	87.4 ± 11.1	96.3 ± 13.7	0.04
VPC QRS duration (ms)	141.1 ± 14.7	139.5 ± 13.3	157.1 ± 10.5	<0.01
Sinus VPC coupling interval (ms)	513.3 ± 79.5	518.1 ± 81.9	539.3 ± 91.5	0.79
Post-VPC coupling interval (ms)	1,098 ± 319	1,118 ± 321	1,238 ± 510	0.62

ECG = electrocardiogram; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; RBBB = right bundle branch block; VPC = ventricular premature complex

Data are presented as number and percentage or as mean ± SD. $P < 0.05$ was considered statistically significant for differences between LV function groups.

factors are excluded, sex-based differences in sensitivity to VPCs may reasonably explain our results.

No association between asymptomatic VPCs and LV dysfunction has yet been identified. However, patients experiencing any arrhythmia-related symptoms might become anxious and thus more willingly seek medical advice. Consequently, symptomatic patients may be more likely to undergo an examination and routine ECG. As a result, their arrhythmias are more likely to be detected earlier and treated to reduce the VPC burden. In contrast, patients without symptoms may be less likely to visit a physician or to have their arrhythmias treated early and appropriately, before heart failure occurs.

Previous studies have shown that a VPC burden of >20% is an important risk factor for VPC-induced cardiomyopathy.^{6,12,17-20} However, most of them included only inpatients undergoing RF ablation for suppression of a high daily VPC burden, which may have introduced selection bias. In our study, the VPC burden did not differ on the basis of LV function. Furthermore, the mean VPC burden was <20% in approximately 70% of patients with impaired LV function.

In 2 studies of the effect of VPC QRS duration on the development of cardiomyopathy,^{7,21} investigators concluded that wider VPCs on ECGs are associated with frequent VPC with LV dysfunction, independently of VPC burden. However, both studies included patients who underwent successful VPC ablation. Meanwhile, despite many attempts to differentiate between normal and impaired LV function in patients with frequent VPCs, the exact mechanism or mechanisms underlying VPC-induced LV dysfunction remain unknown. Our study included 6 patients whose LV dysfunction was partially reversible and 5 whose dysfunction was irreversible despite successful VPC suppression. Their CMR results revealed no cause of the irreversibility other than LV dilation and wider VPC QRS duration.

Our findings in a Korean outpatient population suggest that sex, presence of symptoms, and VPC QRS duration—in addition to VPC burden alone—may be useful predictors of LV dysfunction in patients with frequent VPCs. Clinically, our findings also suggest that aggressive outpatient monitoring is appropriate for asymptomatic men who ignore arrhythmias and do not seek medical care, or who have a VPC QRS duration >150 ms despite a daily VPC burden of <20%.

Study Limitations

Our study had several limitations. First, it was a retrospective, single-center study and so may have been influenced by confounding factors. Second, our use of surface ECGs to characterize and interpret VPC may have been limited by factors such as ECG lead position, cardiac rotation, and respiratory variation. However, the agreement of our results with those of others suggests that these limitations were minor. Third, monitoring

of the VPC burden may have been too brief to enable full analysis of the relationship between VPC burden and LV dysfunction, especially in patients with a low VPC burden. Although we tried to examine at least two 24-hour Holter recordings obtained at least one week apart, we acknowledge daily variations in VPC burden. Fourth, not all patients in the study population underwent examinations necessary to evaluate underlying cardiac diseases. Therefore, we could not always determine whether any improvement in ventricular function after RF ablation or medical treatment was dependent on improvement in other underlying cardiac diseases undetected by TTE. However, we were able to examine CMR data for most patients (77%) in the impaired-function group even though their LV function returned to normal after treatment. Finally, we could not monitor the progression of LV dysfunction in the normal-function group beyond 5 years. Yet, despite these limitations and to our knowledge, this is the first study of the clinical and ECG characteristics of VPCs in an Asian outpatient population. We strove to include individuals with healthy hearts and exclude patients with tachyarrhythmias (except for idiopathic VPCs) that could have caused LV dysfunction. In addition, we strove to reduce selection bias by including only outpatients from our clinic, unlike previous studies that included only inpatients who planned to undergo catheter ablation to reduce high VPC burdens.

Conclusion

We found that male sex, lack of typical VPC-related symptoms, and a VPC QRS duration >157 ms were associated with LV dysfunction in an outpatient population with frequent VPCs, findings that may be useful in predicting such dysfunction.

Acknowledgments

We thank all the members of the electrophysiology laboratories at the Heart Vascular Stroke Institute, Samsung Medical Center, and Kangbuk Samsung Hospital in Seoul and at Kosin University Gospel Hospital in Busan for their assistance and support with data collection.

Published: 28 February 2022

References

1. Cheriath P, He F, Peters I, Li X, Alagona P Jr, Wu C, et al. Relation of atrial and/or ventricular premature complexes on a two-minute rhythm strip to the risk of sudden cardiac death (the Atherosclerosis Risk In Communities [ARIC] study). *Am J Cardiol* 2011;107(2):151-5.
2. Simpson RJ Jr, Cascio WE, Schreiner PJ, Crow RS, Rautaharju PM, Heiss G. Prevalence of premature ventricular contractions in a population of African American and white men and women: the Atherosclerosis Risk In Communities (ARIC) study. *Am Heart J* 2002;143(3):535-40.

3. Chugh SS, Shen WK, Luria DM, Smith HC. First evidence of premature ventricular complex–induced cardiomyopathy: a potentially reversible cause of heart failure. *J Cardiovasc Electrophysiol* 2000;11(3):328-9.
4. Ataklte F, Erqou S, Laukkanen J, Kaptoge S. Meta-analysis of ventricular premature complexes and their relation to cardiac mortality in general populations. *Am J Cardiol* 2013;112(8):1263-70.
5. Bogun F, Crawford T, Reich S, Koelling TM, Armstrong W, Good E, et al. Radiofrequency ablation of frequent, idiopathic premature ventricular complexes: comparison with a control group without intervention. *Heart Rhythm* 2007;4(7):863-7.
6. Baman TS, Lange DC, Ilg KJ, Gupta SK, Liu TY, Alguire C, et al. Relationship between burden of premature ventricular complexes and left ventricular function. *Heart Rhythm* 2010;7(7):865-9.
7. Deyell MW, Park KM, Han Y, Frankel DS, Dixit S, Cooper JM, et al. Predictors of recovery of left ventricular dysfunction after ablation of frequent ventricular premature depolarizations. *Heart Rhythm* 2012;9(9):1465-72.
8. Carballeira Pol L, Deyell MW, Frankel DS, Benhayon D, Squara F, Chik W, et al. Ventricular premature depolarization QRS duration as a new marker of risk for the development of ventricular premature depolarization–induced cardiomyopathy. *Heart Rhythm* 2014;11(2):299-306.
9. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18(12):1440-63.
10. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;128(16):1810-52.
11. Hancock EW, Deal BJ, Mirvis DM, Okin P, Kligfield P, Gettes LS, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part V: electrocardiogram changes associated with cardiac chamber hypertrophy: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009;53(11):992-1002.
12. Del Carpio Munoz F, Syed FF, Noheria A, Cha YM, Friedman PA, Hammill SC, et al. Characteristics of premature ventricular complexes as correlates of reduced left ventricular systolic function: study of the burden, duration, coupling interval, morphology and site of origin of PVCs. *J Cardiovasc Electrophysiol* 2011;22(7):791-8.
13. Yokokawa M, Kim HM, Good E, Crawford T, Chugh A, Pelosi F Jr, et al. Impact of QRS duration of frequent premature ventricular complexes on the development of cardiomyopathy. *Heart Rhythm* 2012;9(9):1460-4.
14. Ban JE, Park HC, Park JS, Nagamoto Y, Choi JI, Lim HE, et al. Electrocardiographic and electrophysiological characteristics of premature ventricular complexes associated with left ventricular dysfunction in patients without structural heart disease. *Europace* 2013;15(5):735-41.
15. Wilson PW, D’Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998;97(18):1837-47.
16. Kostis JB, Byington R, Friedman LM, Goldstein S, Furberg C. Prognostic significance of ventricular ectopic activity in survivors of acute myocardial infarction. *J Am Coll Cardiol* 1987;10(2):231-42.
17. Hasdemir C, Ulucan C, Yavuzgil O, Yuksel A, Kartal Y, Simsek E, et al. Tachycardia-induced cardiomyopathy in patients with idiopathic ventricular arrhythmias: the incidence, clinical and electrophysiologic characteristics, and the predictors. *J Cardiovasc Electrophysiol* 2011;22(6):663-8.
18. Kanei Y, Friedman M, Ogawa N, Hanon S, Lam P, Schweitzer P. Frequent premature ventricular complexes originating from the right ventricular outflow tract are associated with left ventricular dysfunction. *Ann Noninvasive Electrocardiol* 2008;13(1):81-5.
19. Takemoto M, Yoshimura H, Ohba Y, Matsumoto Y, Yamamoto U, Mohri M, et al. Radiofrequency catheter ablation of premature ventricular complexes from right ventricular outflow tract improves left ventricular dilation and clinical status in patients without structural heart disease. *J Am Coll Cardiol* 2005;45(8):1259-65.
20. Niwano S, Wakisaka Y, Niwano H, Fukaya H, Kurokawa S, Kiryu M, et al. Prognostic significance of frequent premature ventricular contractions originating from the ventricular outflow tract in patients with normal left ventricular function. *Heart* 2009;95(15):1230-7.
21. Hasdemir C, Yuksel A, Camli D, Kartal Y, Simsek E, Musayev O, et al. Late gadolinium enhancement CMR in patients with tachycardia-induced cardiomyopathy caused by idiopathic ventricular arrhythmias. *Pacing Clin Electrophysiol* 2012;35(4):465-70.