INTRODUCTION

Idiopathic ventricular premature depolarizations (VPDs) are usually considered a benign condition, even when the VPDs are frequent.\(^1,2\) However, the VPD burden is one of the main causes leading to left ventricular (LV) dysfunction.\(^3,4\) Previous several studies have described that a high burden of VPDs (>24%) is associated with LV cardiomyopathy (CMP) that resolves after successful VPD ablation.\(^4-8\) However, in 25%-30% of patients the status of the LV systolic function cannot be explained only by the VPD burden.\(^9\)
mechanisms underlying the development of VPD-induced CMP are not completely understood. In our experience, some VPD patients maintained normal ventricular function even with persistent ventricular bigeminy, while a significant number of patients had a depressed LV function, continuously, even with a lower VPD burden. Nishikawa et al reported that mild to severe interstitial fibrosis was observed by myocardial biopsy performed in patients with various arrhythmias. It could be that the extent of microscopic myocardial disease at baseline varies, which would not be detected by imaging studies in patients with idiopathic VPD-induced CMP. In this study, we sought to find the useful electrocardiographic (ECG) characteristics of patients with VPD-induced cardiomyopathy by analyzing and comparing the clinical and ECG parameters between patient groups with normal LV function and VPD-induced CMP after undergoing successful radiofrequency catheter ablation (RFCA).

## METHODS

### 2.1 Study population

A total of 282 patients underwent RFCA of VPDs at the Samsung Medical Center (SMC) from January 2008 to December 2016. All procedures were performed following the institutional guidelines of the University of Sungkyunkwan Health System and all patients provided written informed consent prior to participation as stipulated in the Declaration of Helsinki.

### 2.2 The inclusion criteria were as follows

All patients were enrolled based on the following criteria: (a) frequent VPDs (>10% or 10,000 VPDs/day); (b) no evidence of structural heart disease; (c) history of a successful VPD ablation (>80% suppression of the VPD burden); (d) baseline and follow-up transthoracic echocardiography (TTE), 24 hours Holter monitoring data; (e) no evidence of sustained ventricular tachycardia (VT); and (f) coupling interval ratio (CI/SCL); (f) post-VPD CI between sinus rhythm and VPD (QRSd) we examined the intracardiac electrograms (after catheters were in place) to evaluate any retrograde conduction. Assessment of the interobserver variability was performed for the measurements of the VPD QRSd and VPD coupling interval (CI; Figure 1A-C).

### 2.3 Assessment of the LV function

TTE was performed before the ablation procedure using the Simpson formula. For assessment of the LV EF, the second of three consecutive sinus beats was used to avoid any post-extra-systolic potentiation. An LV EF of <50% was considered abnormal. TTE with a quantitative assessment of the LV function was repeated 3-6 months post-ablation.

### 2.4 Follow-up

Patients were seen in an outpatient clinic 3, 6, and 12-48 months post-ablation. 24 hours Holter monitoring was performed prior to the ablation procedure to measure the VPD burden (% and numbers/day). Follow-up Holter monitoring was repeated 3-6 months post-ablation and again, later, if palpitations recurred. All anti-arrhythmic drug therapy was discontinued if the ablation was effective. β-Blockers (BB) and heart failure medications were continued initially and were discontinued if and when the LV function and dimensions normalized. No new medications were added after an effective ablation procedure.

### 2.5 ECG measurement

Sinus rhythm and the VPD ECG morphology were measured on the same 12-lead ECG with electric calipers on the Prucka Cardiolab recording system (GE Healthcare; Figure 1). A standard 12-lead ECG electrode placement was used. The lead gain was uniform with a paper speed of 100 mm/s. Additional clinical and electrophysiologic parameters were assessed by a detailed retrospective review. All electrocardiographic measurements were performed, blinded to the TTE outcomes, by one of the two authors (SII or KMP) using digital calipers at 100 mm/s, on the CardioLab® (version 6.5.4.1858; GE Medical Systems). To distinguish between the true J point and presence of retrograde p waves in the measurement of the VPD QRS duration (QRSd), we examined the intracardiac electrograms (after catheters were in place) to evaluate any retrograde conduction. Assessment of the interobserver variability was performed for the measurements of the VPD QRSd and VPD coupling interval (CI; Figure 1A-C).

### 2.5.1 Durations (width) and intervals

During the clinical VPD, the following measurements were obtained during both sinus rhythm (SR) and VPDs: (a) sinus cycle length (SCL); (b) sinus QRS width; (c) VPD QRSd; (d) CI between sinus rhythm and VPDs; (e) coupling interval ratio (CI/SCL); (f) post-VPD CI between VPDs and sinus rhythm; (g) post-VPD CI ratio (post-VPD CI/ SCL);
The VPD QRSd was defined as the interval from the earliest ventricular activation to the offset of the QRS in any of the 12 leads. The CI was defined as the interval from the onset of the "q" or "R" wave of the previous sinus rhythm to the onset of the VPD QRS. The CI ratio was defined as the CI divided by the SCL. The post-VPD CI was defined as the interval from the VPD onset to the onset of the "q" or "R" wave of the next sinus rhythm. The post-VPD CI ratio was defined as the post-VPD CI divided by the SCL. The "qR" width was defined as the width from the initial onset of the "q" wave of the VPD to the highest peak of the "R" wave in the precordial and limb leads. The "Rs" width was defined as the width from the peak "R" at the highest amplitude, in the same lead as the qR interval, to the terminal s wave in the precordial and limb leads. The "r/ R" transition interval was defined as the interval from the peak point of the earliest "r/ R" to the peak point of the latest "r/ R" in the precordial and limb leads. The definition of an "r" wave was one with an amplitude of over 0.1 mV. If there was notching in the summit of the VPD, the dominant peak was measured.

2.5.2 | Parameters

The following parameters were obtained during normal SR and VPDs: (a) highest "RS" amplitude on the precordial and limb leads; (b) maximal "R" and "S" amplitude on the precordial and limb leads; (c) initial and terminal angles measured using the Pythagorean theorem from the isoelectric line to the peak of the "R" or "S" wave in the lead with the highest amplitude in the precordial and limb leads (Figure 1D).

The highest RS amplitude was defined as the highest amplitude from the peak "r/ R" to the peak "s/ S" in the precordial and limb leads. The maximum "R" amplitude was defined as the amplitude from the maximum peak "R" point to the isoelectric line in the precordial and limb leads. The angles were measured using the Pythagorean theorem in the lead with the highest "R" amplitude. If there was no "R" wave in either the precordial or limb leads, then the "S" wave was used instead of the "R." The initial angle was defined as the angle between the QRS onset to the peak "R" or "S" peak and the isoelectric line. The terminal angle was defined as the angle between the terminal point of the QRS to the peak "R" or "S" peak and the isoelectric line.

2.6 | Terminal signals

Terminal signals were defined as the terminal QRS delay marked by a notch followed by a discrete lower amplitude signal after the peak R wave in any precordial lead. If there were any potential-like terminal signals in the precordial leads, we considered as those patients with terminal signals (Figure 2).

2.7 | Statistical analysis

The Pearson's product moment correlation coefficient was calculated to quantify the inter-variability in the measurement of both the VPD QRSd and coupling interval. Differences in the baseline characteristics across the groups of interest were carried out first in a univariate fashion using a Fisher's exact test for categorical variables and the Kruskal-Wallis test for continuous variables. The percent of VPDs
over 24 hours was a priori included in the preliminary main effects model given its clinically plausible influence on the outcomes following ablation. For all continuous variables, the linear assumption was tested by plotting the coefficients versus quartiles as well as performing a lowess smoothed plot of the continuous variables against the logit of the dependent variables. A goodness of fit was assessed by calculating the area under the curve of the receiver operating table and using the Hosmer-Lemeshow test. All analyses were performed using SPSS Version 18.0 for Windows software (SPSS Inc). For all tests, a \( P < .05 \) was considered statistically significant.

3 | RESULTS

Among a total of 180 patients with >10% VPDs/day (or >10 000 VPDs/day), 41 (23%) had an impaired LV function while the remaining 139 (77%) had a normal LV function and served as controls. Among the patients with an impaired LV function, 12 of 41 (29.2%) patients had failed prior attempts of ablation at referring institutions. An overall acute success rate, defined as no further appearance of clinical VPDs during a waiting period of at least 30 minutes after the ablation, was achieved in all cases (180; 100%). Among the patients with LV dysfunction, the rate for long-term success for ablation, defined as a reduction of at least 80% in the VPD burden as determined by the post-procedure Holter monitoring, was 82.9% (34/41), with second procedures (within our institution) required for success in seven (17%) of those patients. The median follow duration was 11.4 ± 7.5 months. Post-procedure Holter monitoring was performed at a median of 1.6 months after ablation.

3.1 | Baseline characteristics

There was no difference in both groups except age, gender, implanted cardiac defibrillator (ICD) implantation, use of BB, angiotensin-converting enzyme inhibitor (ACEI), and angiotensin receptor blocker (ARB; Table 1). There are older patients in Group A (Group A; mean age: 49.9 ± 15.3 years vs Group B; 55.4 ± 14.5 years; \( P = .05 \)). In Group B, male gender were enrolled more (A vs B; 48.2% vs 73.1%, \( P < .001 \)). BB, ACEI, and ARBs were used more often by the patients in Group B than those in Group A (\( P < .001 \)). The number of asymptomatic patients was significantly higher in Group B than in Group A (A vs B; 10% vs 41.4%, \( P < .001 \)). In Group A, there was a higher incidence of palpitations associated with VPDs than in Group B (A vs B; 87% vs 39%, \( P < .001 \)). The 24-hour VPD burden (%) (A vs B; 21.6 ± 15.1% vs 29.0 ± 13.9%, \( P = .01 \)) and absolute number of VPDs (A vs B; 23 754 ± 18 992 vs 34 979 ± 18 202, \( P = .005 \)) were significantly higher in Group B. Among 180 patients, 28.9% underwent cardiac MRI and 13% underwent coronary angiography.

3.2 | ECG measurements

The sinus QRS width (A vs B; 87 ± 16 milliseconds vs 94 ± 18 milliseconds, \( P = .02 \)) and VPD QRSd (A vs B; 137.2 ± 12.0 milliseconds vs 159.7 ± 5.3 milliseconds, \( P < .001 \)) were significantly wider in Group B (Tables 2 and 3). The adjusted ratio between normal SR and the VPD width was also significantly higher in Group B (R vs N; 1.7 ± 0.2 vs 1.6 ± 0.2, \( P = .03 \)). Within the VPD QRSd, the Rs intervals were prolonged significantly more in both the precordial (A vs B; 58.2 ± 14.7 milliseconds vs 78.0 ± 18.1 milliseconds, \( P < .001 \)) and limb (A vs B; 57.5 ± 16.3 milliseconds vs 76.7 ± 15.8 milliseconds, \( P < .001 \)) leads than the qR intervals in Group B as compared to Group A. Terminal peak angle was significantly higher in Group A than in Group B (precordial lead, \( P = .01 \); limb leads, \( P = .04 \)), although there was no significant difference in the initial angle between Groups A and B.

3.2.1 | Interobserver reliability of the ECG measurements

The correlation coefficient for the measurements of the VPD QRSd was 0.871, and that for the VPD coupling interval was 0.936.

3.3 | Terminal signals

Potential-like signals were found at the terminal portion of the clinical VPDs in three patients in Group A (2.1%) and 22 in Group B (53.6%; \( P < .001 \)). Among the 22 patients in Group B, three had a past history of reversible CMP. Among the three patients in Group A, two had a borderline (EF = 50%) LV function (Figure 2).
| TABLE 1 | Baseline epidemiologic and clinical characteristics in patients with ventricular premature depolarization (VPD) according to left ventricular dysfunction |
|-------------------------------------------------|-------------------------------------------------|
| Demographics | Group A | Group B | P-value |
| Male sex, n (%) | 67 (48.2%) | 30 (73.1%) | <.001 |
| Age, years | 49.9 ± 15.3 | 55.4 ± 14.5 | .05 |
| BMI, kg/m² | 28.9 ± 5.6 | 28.2 ± 6.1 | .90 |
| BSA, m² | 2.01 ± 0.28 | 2.09 ± 0.31 | .16 |
| Medical history | | | |
| HTN, n (%) | 38 (27.3%) | 14 (34.1%) | .23 |
| DM, n (%) | 15 (10.8%) | 5 (12.1%) | .77 |
| ICD, n (%) | 0 (0%) | 5 (12.2%) | <.001 |
| Atrial fibrillation, n (%) | 12 (8.6%) | 6 (14.6%) | .33 |
| Medication history | | | |
| AAD, (%) | 24 (17.2%) | 10 (24.3%) | .24 |
| BB, n (%) | 77 (54.6%) | 33 (80.4%) | <.001 |
| CCB, n (%) | 23 (16.5%) | 4 (9.7%) | .45 |
| ACEI, n (%) | 16 (11.5%) | 12 (29.3%) | .005 |
| ARB, n (%) | 7 (5%) | 8 (19.5%) | .004 |
| Symptom history | | | |
| Asymptomatic | 14 (10%) | 17 (41.4%) | <.001 |
| Symptom, n (%) | 128 (92.1%) | 21 (51.2%) | <.001 |
| Palpitation, n (%) | 121 (87%) | 16 (39%) | <.001 |
| SOB, n (%) | 15 (10.8%) | 1 (2%) | .20 |
| Syncope, n (%) | 19 (13.7%) | 3 (7.3%) | .57 |
| Dizziness, n (%) | 22 (15.8%) | 1 (2.4%) | .05 |
| Fatigue, n (%) | 9 (6.4%) | 3 (7.3%) | .71 |
| Symptom duration, m | 64.2 ± 92.6 | 72.3 ± 95.9 | .73 |
| Holter monitoring | | | |
| VPD burden, % | 21.6 ± 15.1 | 29.0 ± 13.9 | .01 |
| VPD burden, n | 23 754 ± 18 992 | 34 979 ± 18 202 | .005 |
| NSVT, n (%) | 53 (38.1%) | 17 (41.4%) | .39 |
| Multifocal VPDs, n (%) | 12 (8%) | 5 (12%) | .56 |
| Echocardiography | | | |
| EF, % | 59.3 ± 6.5 | 36.5 ± 7.6 | <.001 |
| LVEDD, mm | 49 ± 6 | 54 ± 5 | <.001 |
| LVESD, mm | 31 ± 5 | 42 ± 6 | <.001 |
| Cardiac MRI, n (%) | | | |
| Performed | 39 (28%) | 13 (31.7%) | 0.67 |
| Abnormalb | 7 (5%) | 6 (14.6%) | 0.08 |

Abbreviations: AAD, anti-arrhythmic drug; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BB, β-blocker; BMI, body mass index; BSA, body surface area; CCB, calcium channel blocker; DM, diabetes mellitus; HTN, hypertension; ICD, implanted cardiac defibrillator; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LV, left ventricle; MRI, magnetic resonance imaging; RV, right ventricle; m, months; NSVT, non-sustained VT; SOB, shortness of breath; VPD, ventricular premature depolarization; Group A, normal EF; Group B, depressed EF.

aIncludes any class I or III anti-arrhythmic drugs.

bDefined as any area of delayed gadolinium enhancement or regional wall motion abnormality. The proportions presented are the number of abnormal exams over the number of subjects who underwent MRI.
ventricular dysfunction
ventricular premature depolarization (VPD) according to left

TABLE 2
Comparison of ECG parameters in patients with ventricular premature depolarization (VPD) according to left ventricular dysfunction

|                        | Group A | Group B | P-value |
|------------------------|---------|---------|---------|
| SCL, ms                | 814 ± 159 | 885 ± 176 | .06     |
| Sinus QRS width, ms    | 87 ± 16  | 94 ± 18  | .02     |
| VPD QRS width, ms      | 137.2 ± 12.0 | 159.7 ± 5.3 | <.001   |
| VPD/sinus QRS ratio    | 1.6 ± 0.2 | 1.7 ± 0.2 | .02     |
| CI, ms                 | 503.3 ± 72.5 | 519.0 ± 75.5 | .39     |
| CI ratio               | 59 ± 11  | 61 ± 15  | .31     |
| VPD CI, ms             | 1085 ± 253 | 1141 ± 257 | .53     |
| VPD CI ratio           | 134 ± 24 | 130 ± 20 | .72     |
| Highest R amp (pre), mV| 2.5 ± 0.7 | 2.5 ± 1.4 | .58     |
| Highest R amp (limb), mV| 1.7 ± 0.6 | 1.9 ± 0.7 | .06     |
| VPD notch duration, ms | 29.0 ± 10.4 | 37.6 ± 26.6 | .45     |
| Terminal potential, n (%)| 3 (2.1%) | 22 (53.6%) | <.001   |
| Sites of origin (RV), n (%)|         |         |         |
| RVOT/RCC/PA            | 60 (43.1%) | 9 (21.9%) | .09     |
| Other RV               | 5 (3.6%)  | 1 (2.4%)  | .87     |
| LCC/AMC/RLJ/AIV        | 51 (36.7%) | 16 (39%)  | .16     |
| Other LV               | 26 (18.7%) | 12 (29.3%)| .04     |
| Multifocal VPDs, n (%) | 12 (8.6%) | 5 (12.2%) | .56     |

*VPD site (1)*

|                        | Group A | Group B | P-value |
|------------------------|---------|---------|---------|
| Septal                 | 100 (71.9%) | 20 (48.8%) | .14     |
| Non-septal             | 35 (25.2%) | 14 (34.1%)|         |

*VPD site (2)*

|                        | Group A | Group B | P-value |
|------------------------|---------|---------|---------|
| Outflow tract          | 97 (69.7%) | 19 (46.3%) | .08     |
| Non-outflow tract      | 38 (27.3%) | 15 (36.6%)|         |

Abbreviations: CI, coupling interval; EF, ejection fraction; ms, msec; NSR, normal sinus rhythm; pre, precordial; VPD, ventricular premature depolarization; TI, transition interval; Group A, normal EF; Group B, depressed EF. Subjects with multiple PVC morphologies were excluded.

TABLE 3
Comparison of ECG parameters in patients with ventricular premature depolarization (VPD) according to left ventricular dysfunction

|                        | Group A N = 139 | Group B N = 41 | P-value |
|------------------------|-----------------|----------------|---------|
| qR width (pre), ms     | 79.3 ± 16.3     | 84.0 ± 21.4    | .06     |
| qR width (limb), ms    | 79.5 ± 16.2     | 85.4 ± 16.7    | .07     |
| Rs width (pre), ms     | 58.2 ± 14.7     | 78.0 ± 18.1    | <.001   |
| Rs width (limb), ms    | 57.5 ± 16.3     | 76.7 ± 15.8    | <.001   |
| r/R TI (pre-NSR), ms   | 19.6 ± 11.7     | 22.9 ± 11.6    | .18     |
| r/R TI (limb-NSR), ms  | 20.6 ± 11.3     | 20.2 ± 22.2    | .71     |
| r/R TI (pre-VPD), ms   | 44.8 ± 19.4     | 45.6 ± 22.9    | .63     |
| r/R TI (limb-VPD), ms  | 30.6 ± 13.8     | 30.7 ± 26.4    | .82     |
| Transition ratio (pre lead), ms | 1.9 ± 1.3 | 2.8 ± 2.6 | .08     |
| Transition ratio (limb), ms | 2.2 ± 1.8 | 2.2 ± 2.1 | .51     |
| Initial peak angle (pre), ° | 47.0° | 50.0° | .16     |
| Initial peak angle (limb), ° | 41.0° | 41.0° | .87     |
| Terminal peak angle (pre), ° | 51.5° | 46.0° | .01     |
| Terminal peak angle (limb), ° | 56.0° | 51.5° | .04     |

Abbreviations: EF, ejection fraction; ms, msec; NSR, normal sinus rhythm; pre, precordial; VPD, ventricular premature depolarization; TI, transition interval; Group A, normal EF; Group B, depressed EF. P-value between irreversible and reversible CMP.

4 DISCUSSION

4.1 Main findings of the study

It is increasingly recognized that idiopathic VPDs may cause LV dysfunction that is reversible after a successful ablation.9 Recent studies suggest that a VPD frequency of more than 24% during 24-hour Holter monitoring is a risk factor for VPD-induced CMP.3,4,7,12 However, 20%-25% of the VPD patients did not meet this cutoff value in those studies. In fact, many patients maintained a normal LV function even with a high VPD burden. Inversely, some patients have reduced ventricular function with a lower VPD burden. One study to date has examined the longitudinal impact of VPD burden on the LV function, and a subclinical deterioration in the LV function was found with a high burden of VPDs over 5 years.13 Finally, the paradigms of VPD-induced CMP could not be explained with the VPD burden alone. Recently, some authors have questioned the pre-existence of occult structural heart disease as one of the mechanisms of VPD-induced CMP.13,14

Interestingly, in this study, the number of asymptomatic patients was significantly higher in Group B than in Group A (A vs B; 10% vs 41.4%, P < .001). This finding is consistent with previous study that a lack of symptoms could be associated with a greater risk of VPC-induced cardiomyopathy.15,16

In this study, we examined the clinical and electrocardiographic features in patients with VPD-induced CMP compared with normal control patients. The VPD QRS duration of the CMP patients was significantly more prolonged than that of the normal patients, even after adjusting for the sites of origin of the VPDs, LV dimension, and body surface area. Among the ECG parameters, Rs width was significantly wider in Group B. Furthermore, only terminal peak angle was significantly lower in Group B. We also found abnormal distorted potential-like signals within the Rs segment of the VPD, and were found predominantly more often in patients with LV dysfunction than in the normal control patients. From these results, we could infer carefully that Rs segment of VPD is more important to identify the presence of occult myocardial disease in the patients with VPD-induced CMP than qR segment.
Several investigators have found potential contributing factors to explain the ventricular arrhythmias from endomyocardial biopsies or autopsies.\textsuperscript{17–19} Lemery et al\textsuperscript{20} described the clinical, laboratory, and electrophysiological features in idiopathic VT patients who had no clinical evidence of heart disease. This group reported that minor structural cardiac abnormalities were found in more than 30% of these patients. Nishikawa et al also mentioned that the advanced histopathologic findings, including myocyte hypertrophy, degeneration, interstitial fibrosis, and disarrangement of muscle bundles were observed in patients with idiopathic VT.\textsuperscript{10} Most imaging studies have not found any significant abnormalities in this patient population to corroborate the evidence of occult structural heart disease. However, current imaging technology might not be sensitive enough to identify all occult structural abnormalities that may predispose a patient to increased manifest CMP when the system is stressed. Some papers described that the VPD QRS\textsubscript{d} was significantly wider in patients with VPD-induced CMP than in normal controls.\textsuperscript{15,21} The wider VPD QRS\textsubscript{d} means a prolongation of the myocardial cell-to-cell conduction time and this finding may be indirect evidence of abnormal myocardial cells, such as those that are hypertrophied or fibrotic.

We also found nonspecific distorted abnormal potential-like signals at later portions of the VPDs, predominantly in patients with CMP. Several previous reports have described the epsilon potential that occurs frequently in lead V\textsubscript{1,2} during sinus rhythm. This potential has been viewed as indirect evidence of RV myocardial dysplasia\textsuperscript{22–27} and Brugada syndrome.\textsuperscript{28} And Moulton et al found a useful ECG marker for the left ventricular structure and function.\textsuperscript{29} They explained that a broadly notched VPD with a long duration was a useful marker for a dilated globally hypokinetic left ventricle. They described the mechanisms of this distorted VPD as dilation of the T-tubule system due to altered microanatomy and as an abnormality in the cell-to-cell communication by desmosomes. Even though 61% of the patients had coronary artery disease, it was a meaningful result in that the prolonged VPD QRS duration and notch on the ECG were important as indirect evidence of the myocardial status. Aizawa Y et al also reported that tachycardia-dependent augmentation of “notched J waves” in a general patient population without ventricular fibrillation or cardiac arrest was augmented at shorter RR intervals, but not at prolonged RR intervals. Mechanically, conduction delay is most likely responsible for this change.\textsuperscript{20} However, we do not know the meaning of these signals in our study and could not perform myocardial biopsy to confirm the results in the tissue. However, the signals occurred more frequently in CMP patients than in normal patients. These findings may suggest some occult microscopic myocardial disease in the myocardium. If the occult microscopic myocardial disease was distributed diffusely, a myocardial conduction delay would occur globally and the VPD QRS\textsubscript{d} would be significantly wider than normal. Whatever the mechanisms of these signals, a delayed slow potential or dyssynchrony, these results suggest a new direction for the electrophysiological and pathophysiological mechanisms that lead to VPD-induced CMP.

### 4.2 Study limitations

There were some limitations in this study. First, this study was a single-center, retrospective study derived from a real-world practice with inherent limitations and we could not assess quantitative analysis of dyssynchrony by echocardiography. Hence the results of our study should be considered as hypothesis generating, and future prospective studies are warranted to confirm our results. Second, in our study, among all enrolled patients, 36% of the patients underwent cardiac MRI while 13% underwent CAG to rule out any structural heart disease. Therefore, we could not rule out with certainty the existence of minimal structural heart disease that could be detected by using TTE. Third, the accurate measurement of the LV dysfunction may have been compromised by frequent VPDs, particularly in patients with incessant ventricular bigeminy, who never have two simultaneous sinus beats.

### 5 CONCLUSION

In patients with idiopathic VPDs, the presence of wider VPD QRS duration and potential-like signals at the terminal portion of VPD may be indirect evidence of the pre-existence of occult microscopic myocardial disease with reversible CMP.

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### CONFLICT OF INTERESTS

The authors declare no conflict of interests for this article.

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### REFERENCES

1. Gaitha F, Giustetto C, Di Donna P, Richiardi E, Libero L, Brusin MC, et al. Long-term follow-up of right ventricular monomorphic extrasystoles. J Am Coll Cardiol. 2001;38:364–70.
2. Conti CR. Ventricular arrhythmias: a general cardiologist’s assessment of therapies in 2005. Clin Cardiol. 2005;28:314–6.
3. Baman TS, Lange DC, Ilg KJ, Gupta SK, Liu T-Y, Alguire C, et al. Long-term follow-up of right ventricular monomorphic extrasystoles. J Am Coll Cardiol. 2001;38:364–70.
4. Efremidis M, Letsas KP, Sideris A, Kardaras F. Reversal of premature ventricular complex-induced cardiomyopathy following successful radiofrequency catheter ablation. Europace. 2008;10:769–70.
5. Sarrazin J-F, Labounty T, Kuhnke M, Crawford T, Armstrong WF, Desjardins B, et al. Impact of radiofrequency ablation of frequent post-infarction premature ventricular complexes on left ventricular ejection fraction. Heart Rhythm. 2009;6:1543–9.
6. Grimm W, Menz V, Hoffmann J, Maisch B. Reversal of tachycardia induced cardiomyopathy following ablation of repetitive...
monomorphic right ventricular outflow tract tachycardia. Pacing Clin Electrophysiol. 2001;24:166–71.
7. 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;4:863–7.
8. Lee Y-H, Zhong LI, Roger VL, Asivatham SJ, Shen W-K, Slusser JP, et al. Frequency, origin, and outcome of repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract. Circulation. 2005;112:1092–7.
9. Nishikawa T, Ishiyama S, Sakomura Y, Nakazawa M, Momma K, Hiroe M, et al. Histopathologic aspects of endomyocardial biopsy in pediatric patients with idiopathic ventricular tachycardia. Pediatr Int. 1999;41:534–7.
10. Mountantonakis SE, Frankel DS, Gerstenfeld EP, Dixit S, Lin D, Hutchinson MD, et al. Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract. Circulation. 2011;22:791–8.
11. 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;95:1230–7.
12. Wilber DJ. Ventricular ectopic beats: not so benign. Heart. 2009;95:1209–10.
13. 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 electrophysiological characteristics, and the predictors. J Cardiovas Electrophysiol. 2011;22:663–8.
14. Yokokawa M, Kim HM, Good E, Chugh A, Pelosi F, Algvere C, et al. Relation of symptoms and symptom duration to premature ventricular complex-induced cardiomyopathy. Heart Rhythm. 2012;9:92–5.
15. Sugrue DD, Holmes DR, Gersh BJ, Edwards WD, McLaran CJ, Wood DL, et al. Cardiac histologic findings in patients with life-threatening ventricular arrhythmias of unknown origin. J Am Coll Cardiol. 1984;4:952–7.
16. Strain JE, Grose RM, Factor SM, Fisher JD. Results of endomyocardial biopsy in patients with spontaneous ventricular tachycardia but without apparent structural heart disease. Circulation. 1983;68:1171–81.
17. Vignola PA, Aonuma K, Swayne PS, Rozanski JJ, Blankstein RL, Benson J, et al. Lymphocytic myocarditis presenting as unexplained ventricular arrhythmias: diagnosis with endomyocardial biopsy and response to immunosuppression. J Am Coll Cardiol. 1984;4:812–9.
18. Lemery R, Brugada P, Bella PD, Dugernier T, van den Dool A, Wellens HJ. Nonischemic ventricular tachycardia. Clinical course and long-term follow-up in patients without clinically overt heart disease. Circulation. 1989;79:990–9.
19. Del carpio munoz F, Syed FF, Noheria A, Cha Y-M, 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;22:791–8.
20. Nasir K, Bomma C, Tandri H, Roguin A, Dalal D, Prakasa K, et al. Electrocardiographic features of arrhythmogenic right ventricular dysplasia/cardio-myopathy according to disease severity: a need to broaden diagnostic criteria. Circulation. 2004;110:1527–34.
21. Kies P, Bootsm M, Bax JJ, Zeppenfeld K, van ERVEN L, Wijffels MC, et al. Serial reevaluation for ARVD/C is indicated in patients presenting with left bundle branch block ventricular tachycardia and minor ECG abnormalities. J Cardiovasc Electrophysiol. 2006;17:586–93.
22. Peters S, Trummel M, Koehler B, Westermann KU. The value of different electrocardiographic depolarization criteria in the diagnosis of arrhythmogenic right ventricular dysplasia/cardio-myopathy. J Electrocardiol. 2007;40:34–7.
23. You CC, Tseng YT, Hsieh MH. An epsilon wave in arrhythmogenic right ventricular cardiomyopathy/dysplasia. Int J Cardiol. 2007;119:e63–e64.
24. Yerra L, Caskey D, Modi K, Reddy P. Arrhythmogenic right ventricular dysplasia/cardio-myopathy: clinical profile of four patients and review. South Med J. 2008;101:309–16.
25. Wu S, Wang P, Hou Y, Yang P, Xiao Y, Zhan X. Epsilon wave in arrhythmogenic right ventricular dysplasia/cardio-myopathy. Pacing Clin Electrophysiol. 2009;32:59–63.
26. Ozeke O, Cavus UY, Atar I, Ozin B, Ilkay E. Epsilon-like electrocardiographic pattern in a patient with Brugada syndrome. Ann Noninvasive Electrocardiol. 2009;14:305–8.
27. Moutlon KP, Medcalf T, Lazzara R. Premature ventricular complex morphology. A marker for left ventricular structure and function. Circulation. 1990;81:1245–51.
28. Aizawa Y, Sato M, Kitazawa H, Aizawa Y, Takatsuki S, Oda E, et al. Tachycardia-dependent augmentation of “notched J waves” in a general patient population without ventricular fibrillation or cardiac arrest: not a repolarization but a depolarization abnormality? Heart Rhythm. 2015;12:376–83.

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