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Novel method for the prediction of para-Hisian premature ventricular complexes from the electrocardiogram

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Abstract

Background: Catheter ablation of para-Hisian (PH) premature ventricular complexes (PVCs) has a high risk of heart block. This study aimed to find the electrocardiographic (ECG) predictors of PH-PVCs.

Methods: We enrolled 47 patients who underwent an electrophysiologic study for catheter ablation of PVCs and analyzed the ECG characteristics, retrospectively.

Results: The PVC locations were the PH in 14, right ventricular (RV) outflow tract (OT) in 11, left ventricular (LV) OT in 16, LV septum in 5, and LV summit in 1. The QRS width of the PH-PVCs was significantly narrower than that of the rest of PVCs (140.9 ± 17.1 ms vs. 158.9 ± 19.4 ms, $P = 0.004$). Precordial transition of the PH-PVCs related to sinus rhythm was not helpful in predicting the location. Lead I had monophasic R waves in 100% and lead aVR QS waves in 100%. In aVL, 13 of 14 patients had monophasic R waves, and 1 had biphasic (rS) waves with an initial positive polarity. Among the study cohort, 15 patients had a QS in aVR and R in aVL, including 13 PH-PVCs and 2 PVCs coming from the RVOT septum and LVOT septum, respectively. The QS in aVR and monophasic R in aVL had a sensitivity of 92.8%, specificity of 93.9%, positive predictive value of 86.7%, and negative predictive value of 96.9% for localizing PH-PVCs.

Conclusions: A PVC morphology with a QS in aVR and monophasic R in aVL and QRS width <143 msec, could be used as a reliable parameter for predicting the PH location.

KEYWORDS
catheter ablation, electrocardiography, His bundle, ventricular premature complexes

1 | INTRODUCTION

Frequent premature ventricular complexes (PVCs) may cause a cardiomyopathy or worsen a preexisting cardiomyopathy. Most of the PVCs can be safely and effectively treated by radiofrequency catheter ablation (RFCA) which has become a first-line therapy in symptomatic patients or in those with a left ventricular (LV) dysfunction.[1] However, previous studies have reported that PVCs originate from the para-Hisian region (PH-PVC), where there is a high risk of heart block during RFCA.[2-8] Therefore, it is important to recognize

the PH location of PVCs before planning the RFCA. Several electrocardiographic (ECG) characteristics have been described, and some parameters are helpful to localize the PH-PVCs. However, no unique features for PH-PVCs are available. The purpose of our study was to find a more useful and simple method to determine if there were PH-PVCs based on PVC vectors of the surface ECG.

2 | METHODS

2.1 | Study population

We retrospectively analyzed ECGs of 47 patients who underwent a symptomatic PVC ablation at the ventricular outflow tract (OT) and/or ventricular septum between January 2009 and December 2012. A physical examination, echocardiography, cardiac computed tomography, and/or cardiac magnetic resonance imaging were used to reveal any structural heart disease. Before the ablation procedure, 24-hour ambulatory Holter monitoring was performed. All patients signed informed consent for the procedure and the study was approved by the research ethics committees of the institutions.

2.2 | Electrocardiographic analysis

The 12-lead ECGs of the clinical PVCs were analyzed focusing on the following characteristics: (a) QRS width, (b) transition site of the precordial R waves, and (c) deflection of the QRS complex in the limb leads and V1. The analysis of the QRS complex deflection was determined by the following criteria: capital letters (Q, R, and S) were used to refer to relatively high amplitudes (>0.5 mV), and lowercase letters (q, r, and s) to refer to relatively low amplitudes (<0.5 mV). The main QRS vectors of each lead were determined as positive, which had dominant R waves regardless of s waves, or as negative, which had dominant Q or S waves regardless of r waves. The amplitude ratio between R/r and S/s waves in the limb leads were also analyzed.

2.3 | Electrophysiological study and ablation

The procedures were performed under a fasting state with light sedation after withdrawal from anti-arrhythmic drugs for a period equal to five times the half-lives of the drugs. The femoral veins were then accessed with four venous sheaths. Through these sheaths, three diagnostic quadripolar catheters were advanced into the right heart: one to the right atrial appendage (HRA), one to the His bundle (HB) recording area, and one to the right ventricular (RV) OT. The right internal jugular vein was cannulated with an 8 Fr sheath for the insertion of a decapolar coronary sinus catheter, which was advanced as far as possible into the anterior interventricular vein. Noninvasive arterial pressure measurements were obtained and monitored throughout the procedure. After completion of the catheterization, anticoagulation was achieved with boluses of heparin according to the activated clotting time, which was maintained at a level of more than 270 seconds throughout the procedure. The mapping and ablation were performed with a 7 Fr, 3.5 mm, nonirrigated ablation catheter (NaviStar, Biosense Webster Inc., Diamond Bar, CA, USA). The ablation catheter was introduced from the right femoral vein for RV mapping or from the right femoral artery for LV or cusp mapping. Spontaneous PVCs were initially mapped via three diagnostic catheters. Based on the activation time compared to the onset of the PVCs, detailed mapping with a 3-D mapping system (Carto 3: Biosense-Webster Inc.) was performed from the suspicious chamber. An activation map was used to identify the origin of the PVCs. In the case of a very low incidence of spontaneous PVCs, pace mapping was performed. PVCs that exhibited the earliest activation near the HB region with visible HB potentials recorded on the mapping catheter or within a distance of 5 mm from the His potential recording site on the 3-D mapping system were defined as PH-PVCs. For PH-PVCs, additional detailed mapping was performed on both the ventricular septum and in the OT, including the aortic coronary cusps. Elimination of the PVCs by ablation further supported the PH location of the PVCs.

Radiofrequency applications were delivered with a target temperature of 60°C and maximum power output of 40 W at sites exhibiting the earliest bipolar activity and/or a local unipolar QS pattern during the PVCs. When an acceleration or reduction in the incidence of PVCs was observed during the first 10 seconds of the application, the radiofrequency energy delivery was continued for 30-60 seconds. Otherwise, the radiofrequency delivery was terminated, and the catheter was repositioned.

2.4 | Statistical analysis

Continuous variables are expressed as the mean value ± standard deviation. Categorical variables are expressed as numbers and percentages. A receiver-operating characteristics curve analysis was performed to evaluate the optimal cutoff value of the PVC QRS width to differentiate PH-PVCs from PVCs originating from other sites. All statistical analyses were performed using the MedCalc software package, version 18.5 (MedCalc Software, Mariakerke, Belgium). A P value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Patient clinical characteristics

A total of 47 patients were enrolled. The mean age was 58.9 ± 15.1 years and 25 patients (53.2%) were male. Of those patients, 14 had PH-PVCs. A representative ECG and the intracardiac electrograms with fluoroscopic images of the successful ablation site for the PH-PVCs are shown in Figure 1. The successful ablation sites in the other PVC patients were located at the RVOT in 11, LVOT in 12, LV septum in 5, and LV summit in 5. There were no differences in the age (PH-PVC: 62.4 ± 15.1 vs. non-PH-PVC: 57.5 ± 15.0, P = 0.306) and sex (PH-PVC: 9 men, 64.3% vs. non-PH-PVC: 16 men, 48.4%, P = 0.358) between the two groups. Three PH-PVC patients had a reduced LV ejection fraction (EF). The remaining 11 PH-PVC patients had structurally normal hearts

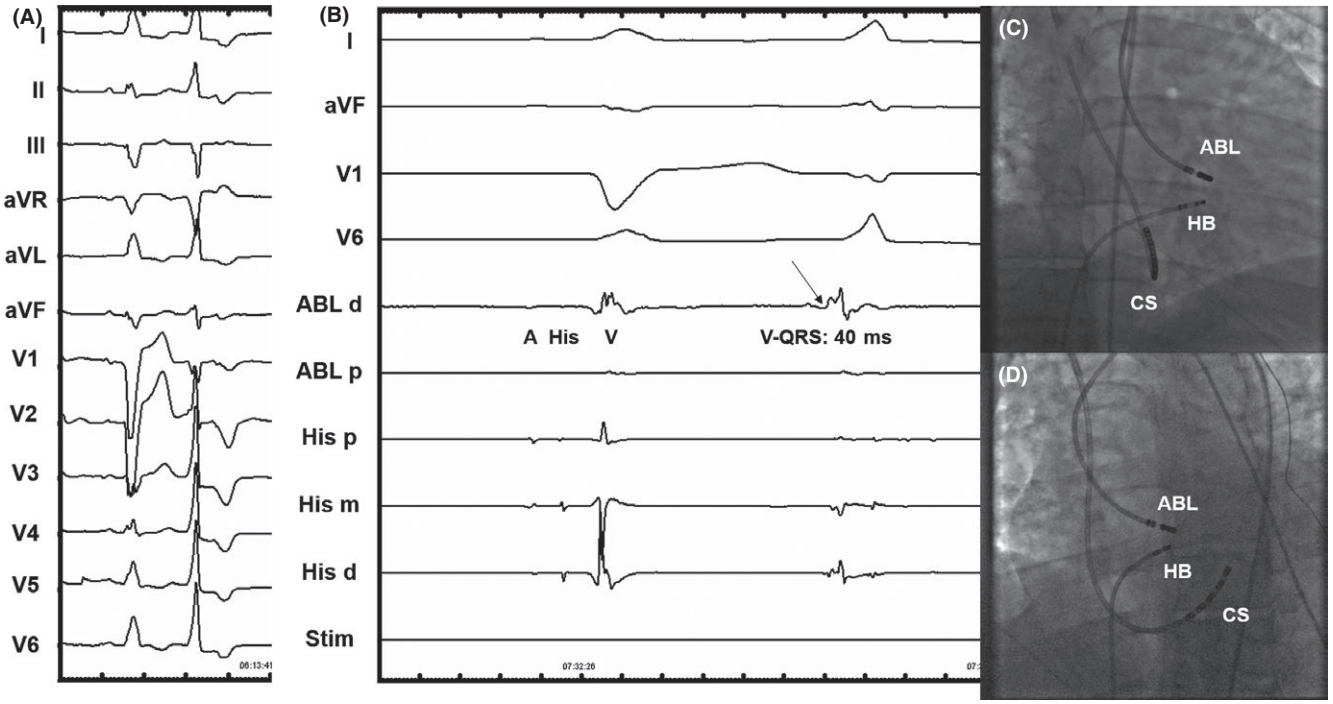

FIGURE 1 Example of the successful ablation of a para-Hisian PVC. (A) Left: Baseline 12-lead electrocardiogram (ECG) showing sinus rhythm with a left bundle branch block. Right: The 12-lead ECG of a PVC showing a polarity reversal between aVR and aVL. (B) The recording of the electrograms at the successful ablation site. During sinus rhythm, a far-field His bundle signal was observed in the distal ablation catheter recording. During the PVC, a local ventricular potential preceding the QRS onset by 40 ms was observed on the same catheter. (C, D) RAO and LAO fluoroscopic images of the catheter positions. The ablation catheter was positioned at the right coronary cusp toward the His bundle catheter. PVC: premature ventricular complex, ECG: electrocardiogram, ABL d, ablation catheter distal electrogram; ABL p, ablation catheter proximal electrogram; His p/m/d, His bundle recording catheter proximal/middle/distal electrogram; A, atrial potential; His, His bundle potential; V, ventricular potential; RAO, right anterior oblique; LAO, left anterior oblique; ABL, ablation catheter; HB, His bundle catheter; CS, coronary sinus catheter

TABLE 1 Baseline characteristics of patients

	PH-PVC (N = 14)	Others (N = 33)	*P* value
Male (%)	9 (64.3%)	16 (48.4%)	0.358
Age	62.4 ± 15.1	57.5 ± 15.0	0.306
PVC QRS width	140.9 ± 17.1	158.9 ± 19.4	0.004
PVC-induced cardiomyopathy with reduced LV EF	3 (21.4%)	0 (0%)	0.014
Successful ablation site	Right side (2)	RVOT (11)	
	Left side (3)	LVOT (12)	
	Both ventricular sides (2)	LV septum (5)	
	NCC-RCC junction (1)	LV summit (5)	
	NCC (1)		
	Unable to ablate (5)		

PVC, premature ventricular complexes; PH-PVC, PVCs originating from Para-Hisian region; others, idiopathic PVCs originating from ventricles except Para-Hisian region; LV, left ventricle; EF, ejection fraction; RVOT, right ventricle outflow tract; LVOT, LV outflow tract; NCC, non-coronary cusp; RCC, right coronary cusp.

with a normal LVEF. One PH-PVC patient experienced an out-of-hospital cardiac arrest of unknown etiology with a successful resuscitation. The baseline characteristics of the patients are summarized in Table 1.

3.2 | Electrocardiographic findings

The baseline ECGs in all patients were within normal range. The QRS width of the PVCs between the two groups significantly

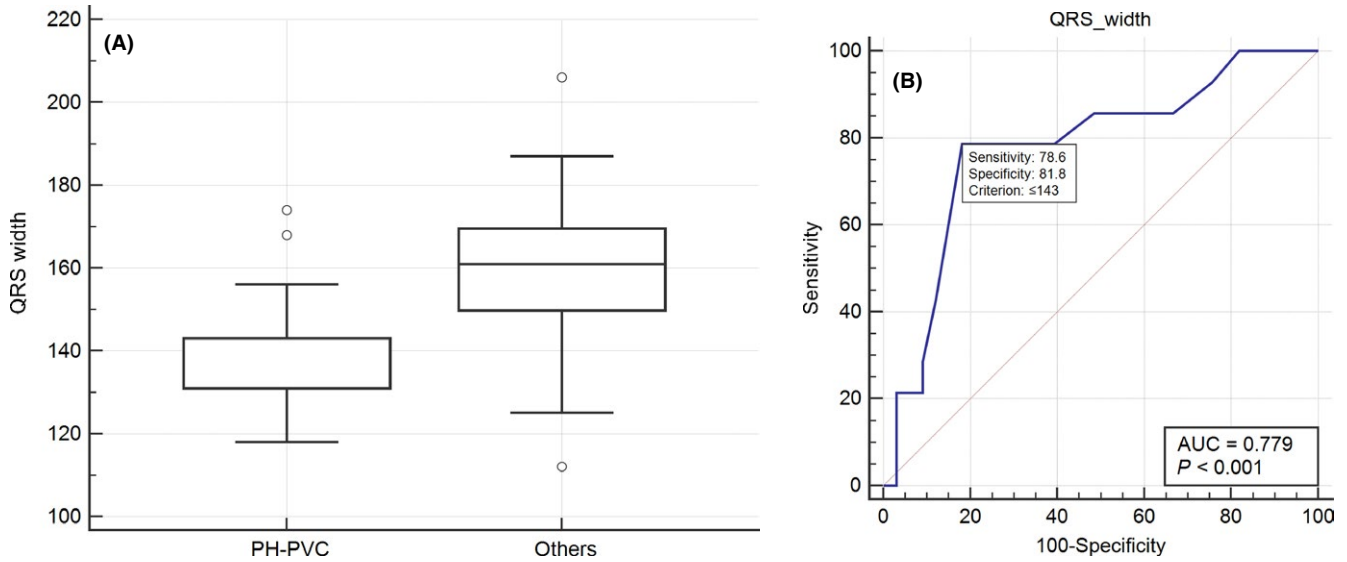

FIGURE 2 Comparison of the QRS width of para-Hisian (PH) premature ventricular complexes (PVCs) versus other PVCs. (A) The box and whisker plots of the two groups. (B) Receiver operating characteristics curve analysis of the QRS width in predicting PH-PVCs. The AUC (area under curve) is 0.779. A QRS width of 143 mm serves as the best cutoff value. It predicts PH-PVCs with a sensitivity of 78.6% and specificity of 81.8%

differed: PH-PVCs were significantly narrower than the non PH-PVCs (140.9 ± 17.1 ms vs. 158.9 ± 19.4 ms, $P = 0.004$). A QRS width cutoff value of 143 ms predicted PH-PVCs with a 78.6% sensitivity and 81.8% specificity (AUC 0.779, Youden index J 0.604, $P < 0.001$) (Figure 2A,B).

In the precordial leads for the PH-PVCs, lead V_1 had a left bundle branch block morphology without any initial positive deflections, except for in one patient. A precordial transition of the PVCs related to sinus rhythm was not helpful in identifying PH-PVCs (a precordial transition earlier than sinus rhythm was observed in seven patients, equal to sinus rhythm in six patients, and later than sinus rhythm in one).

The R and S wave ratio of the limb leads are shown in Table 2. Lead I and aVL for the PH-PVCs had a significantly larger R/S ratio than the non-PH-PVCs. The analysis of the PH-PVC QRS complex deflection showed the following results: the inferior leads exhibited a diverse polarity, lead II was positive in 85%, lead III was negative in 75%, and lead aVF was positive in 78%. However, lead I had monophasic positive (R) waves and lead aVR monophasic negative (QS) waves in all patients. In lead aVL, 13 of 14 patients had monophasic R waves and 1 patient had biphasic waves with an initial small positive polarity (rS pattern) (Figure 3). Therefore, 93% of the PH-PVC patients had QS waves in aVR with R waves in aVL. From a schematic viewpoint, the QS waves in aVR with R waves in aVL resulted in a shape in which the QRS peaks of two leads were in close contact with each other. That was thought to be a unique ECG pattern of PH-PVCs, and we referred to it as an "aVR-aVL polarity reversal."

Fifteen out of all 47 study patients had an aVR-aVL polarity reversal, 13 of which were PH-PVCs and 2 of which were PVCs coming from the RVOT septum and LVOT septum, close to the HB.

TABLE 2 Comparison of the limb lead R/S ratio between PH-PVCs and other idiopathic PVCs

	PH-PVC (N = 14)	Others (N = 33)	*P* value
Lead I	16.1 ± 25.7	2.15 ± 2.57	0.008
Lead II	10.0 ± 15.2	7.6 ± 10.4	0.548
Lead III	6.3 ± 22.4	10.0 ± 12.0	0.492
Lead aVR	0.0 ± 0.0	1.9 ± 6.8	0.301
Lead aVL	15.0 ± 15.1	5.3 ± 15.5	0.062
Lead aVF	6.3 ± 12.2	8.8 ± 11.7	0.521

The abbreviations are the same as those in Table 1.

Therefore, the aVR-aVL polarity reversal sign in idiopathic PVCs had a sensitivity of 92.8%, specificity of 93.9%, positive predictive value of 86.7%, and negative predictive value of 96.9% for localizing PH-PVCs (Table 3). However, those two PVCs coming from the RVOT and LVOT septum had QRS widths of 150 and 168 mm, respectively, which were above our cutoff criteria of the PH-PVC QRS width.

3.3 | Radiofrequency ablation results

In PH-PVCs, ablation was not attempted or failed in five patients due to a high risk of heart block, and a successful ablation was achieved from the septum or coronary cusps in nine patients: two patients on the right side, three on the left side, two on both sides, one on the non-coronary cusp (NCC), and one on the NCC-right coronary cusp junction. One patient had transient AV block during the ablation but completely recovered immediately.

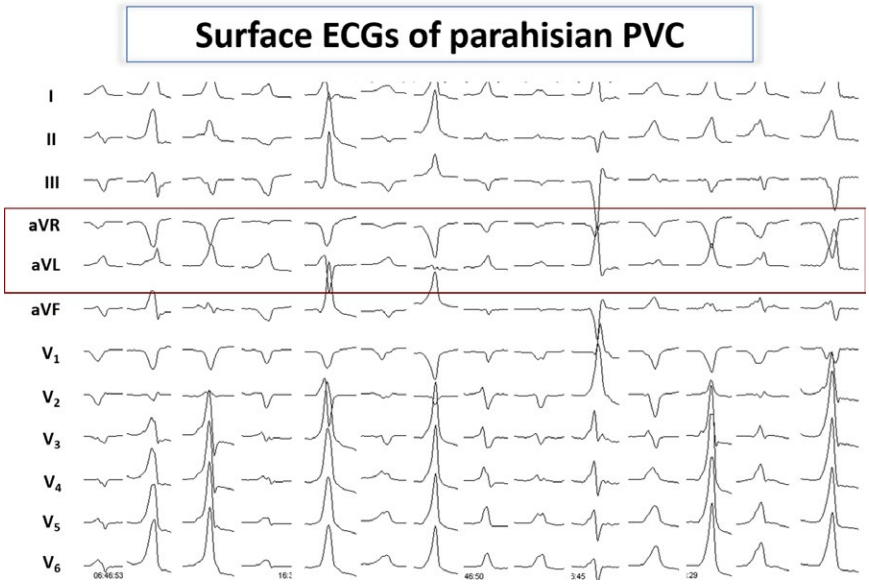

FIGURE 3 Representative 12-lead electrocardiographic (ECG) of the para-Hisian (PH) premature ventricular complexes (PVCs) in our study patients. Lead aVL had a predominant positive polarity and lead aVR a QS pattern, which we referred to as an "aVR-aVL polarity reversal sign." This characteristic ECG finding was observed in most of the PH-PVC patients

TABLE 3 Frequency of QS waves in aVR and R waves in aVL among the ECGs of the idiopathic PVCs

QS in aVR and R in aVL	PH-PVC	Others	Number
(+)	13	2	15
(–)	1	31	32
	14	41	47

The QS wave in aVR and R wave in aVL had a sensitivity of 92.8%, specificity of 93.9%, positive predictive value of 86.7%, and negative predictive value of 96.9% for predicting PH-PVCs in our idiopathic PVC patient cohort. The abbreviations are the same as those in Table 1.

For the non PH-PVCs, the successful ablation sites were as follows: RVOT in 11, LVOT in 12, LV septum in 5, and LV summit in 5. The detailed ablation sites of the non PH-PVCs are summarized in Table 1.

4 | DISCUSSION

4.1 | Main findings

In this study, we analyzed the surface ECGs in 14 PH-PVC patients and compared those with the non-PH-PVCs. The main findings were as follows: (a) The QRS width of the PH-PVCs was narrower than that of the non PH-PVCs. A cutoff value of the QRS width of 143 ms predicted PH-PVCs with a 78.6% sensitivity and 85.4% specificity. (b) All PH-PVC patients had monophasic R waves in lead I and QS waves in lead aVR. In comparison to the non PH-PVCs, the R/S ratio of leads I and aVL was significantly larger for PH-PVCs. (c) An analysis of the QRS deflection of the PH-PVCs revealed a characteristic "aVR-aVL polarity reversal." This sign had a 92.8% sensitivity and 95.1% specificity in predicting PH-PVCs in this study cohort of PVCs. A narrow QRS width and a negative aVR polarity with a positive I/aVL polarity is a natural result of ventricular activation initiated near the HB region, that is similar to normal ventricular activation.

4.2 | Previous studies regarding the ECG characteristics of PH-PVCs

Yamauchi et al[2] firstly described the ECG characteristics of PH-PVCs as following: (a) a monophasic tall R wave present in lead I; (b) a relatively small R wave present in the inferior leads, especially a smaller R wave in lead III than in lead II; (c) an R wave present in lead aVL; (d) a relatively narrow QRS duration in the inferior leads; (e) a QS pattern in lead V1; (f) an early precordial transitional zone in leads V2-V3; and (g) a relatively tall R wave in V5 and V6. From our study cohort, we did not identify any specific ECG characteristics in the precordial leads for PH-PVCs. Yamada et al[4] and Ban et al[6] had also reported the ECG characteristics of PH-PVCs in which lead I/aVL exhibited predominantly a positive polarity and the precordial transition was not helpful in differentiating PH-PVCs. The mean QRS width of the PH-PVC reported by Yamada et al[4] was 146 ± 25 ms, which was similar to our results. However, Ban et al reported a mean QRS width of 114 ± 12 ms, which was narrower than our results.

4.3 | A comparison to the ECG characteristics of the other PVCs

Considering the representative ECG characteristics of the other PVCs, the PH-PVCs could be easily distinguished according to our study findings. QS waves in lead V1 and a predominant positive polarity in lead aVL were more frequent in the PH-PVCs than RVOT or LVOT PVCs. Posterior RVOT PVCs would exhibit a superior axis. PVCs originating from the left and right coronary cusps, mitral annulus, and aorto-mitral continuity had a more positive initial polarity in lead V1 and predominantly negative polarity in lead aVL. However,

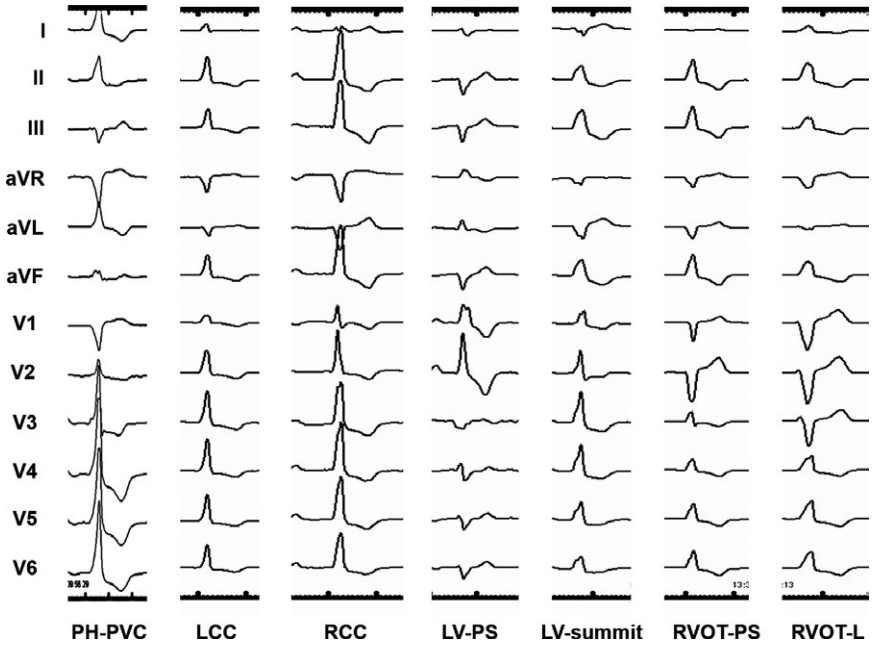

FIGURE 4 Representative 12-lead electrocardiographic (ECG) of the premature ventricular complexes (PVCs) according to the site of origin. From the left, a PVC from the para-Hisian region (PH-PVC), left coronary cusp (LCC), right coronary cusp region (RCC), left ventricular (LV) posteroseptum region, LV summit, right ventricular outflow tract (RVOT) posteroseptum (PS), and RVOT lateral wall (L) region. The average QRS width increases from left to right

the PVCs originating from the NCC or junction of the NCC-RCC could be one of the origins of PH-PVCs.[5] Therefore, careful mapping of the aortic sinus, especially the NCC, should be added during RFCA of PH-PVCs to accurately identify the site of origin.[4]

In lead aVR, a predominant negative polarity was observed in most of the OT PVCs. Therefore, it is not helpful to distinguish PH-PVCs by using the aVR lead alone even though the R/S ratio of aVR was lower than that in the other limb leads in our study (Table 2). However, together with a predominant positive polarity of lead aVL, the predominant negative polarity of lead aVR resulted in a distinctive ECG pattern of PH-PVCs as an aVR-aVL polarity reversal sign.

For comparison of the QRS width according to the site of origin, we classified non-PH-PVC patients into subgroups including the RVOT (11 patients), LVOT (12 patients), LV septum (5 patients), and LV summit (5 patients) and analyzed them. The mean QRS widths of the PVCs according to each origin were as follows: PH-PVCs 140.9 ± 17.1 ms, LVOT PVCs 149.0 ± 19.9 ms, LV septum PVCs 155.6 ± 6.0 ms, RVOT PVCs 167.0 ± 21.3 ms, and LV summit PVCs 168.4 ± 11.8 ms. The QRS width was found to increase with the distance from the PH/septum region and the difference between each origin was statistically significant despite the small number of patients (*P* value 0.005 using an ANOVA and Scheffe test). Therefore, the QRS width was one of the useful criteria for PVC/VT localization. Representative ECGs of the PVCs according to each site of origin are shown in Figure 4.

4.4 | Study limitations

Our study had some limitations. First, this study was a retrospective analysis with a small number of patients. Second, ablation was not attempted or failed in 5 out of 14 patients. That was a relatively higher failure rate (35.7%) than the previous reports.[2,4,6] It may also have affected the definition of the PH-PVCs in our study. Third, we did not perform a more detailed localization of the PH-PVCs such as of the RV origin/NCC-RCC origin or above/below the HB region.[4,9] We could not do any additional analyses with our study cohort, but those classifications might have produced different results if they had been applied in our study.

5 | CONCLUSION

The PH-PVCs had a narrower QRS width and aVR-aVL polarity reversal, which referred to a predominantly negative QS polarity in aVR and predominantly positive polarity in aVL, like the normal QRS vector during sinus rhythm, and had a high sensitivity and specificity in predicting PH-PVCs. Therefore, it can be used as a reliable ECG pattern to predict PH location of PVCs. The prediction of PH-PVCs before planning the RFCA may help to avoid possible complications and to plan accordingly.

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CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

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