

# The RV<sub>1</sub>-V<sub>3</sub> transition ratio: A novel electrocardiographic criterion for the differentiation of right versus left outflow tract premature ventricular complexes



Michael Efremidis, MD,<sup>\*†</sup> Konstantinos Vlachos, MD,<sup>\*†</sup> Maria Kyriakopoulou, MD,<sup>‡§</sup> Panagiotis Mililis, MD,<sup>\*†</sup> Claire A. Martin, MD,<sup>||</sup> George Bazoukis, MD, PhD,<sup>†</sup> Stylianos Dragasis, MD,<sup>\*†</sup> Athanasia Megarisiotou, MD,<sup>\*†</sup> Philippe Unger, MD, PhD,<sup>§¶</sup> Antonio Frontera, MD,<sup>#</sup> Giuseppe Mascia, MD,<sup>\*\*</sup> Athanasios Saplaouras, MD,<sup>\*†</sup> Sotirios Xydonas, MD,<sup>†</sup> Kosmas Valkanas, Msc,<sup>\*</sup> Frédéric Sacher, MD,<sup>††</sup> Pierre Jaïs, MD,<sup>††</sup> Konstantinos P. Letsas, MD, PhD<sup>\*†</sup>

From the <sup>\*</sup>Onassis Cardiac Surgery Centre, Athens, Greece, <sup>†</sup>Arrhythmia Unit, Laboratory of Cardiac Electrophysiology, Second Cardiology Department, Evangelismos General Hospital of Athens, Athens, Greece, <sup>‡</sup>Department of Cardiology, Laboratory of Cardiac Electrophysiology, Centre Hospitalier de Luxembourg (CHL), Luxembourg City, Luxembourg, <sup>§</sup>Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Cardiology, Clinique Notre Dame de Grâce, Charleroi, Belgium, <sup>||</sup>Cardiology Department, Royal Papworth Hospital, Cambridge, United Kingdom, <sup>¶</sup>Department of Cardiology, CHU Saint Pierre Hospital, Brussels, Belgium, <sup>#</sup>Department of Arrhythmology, San Raffaele Hospital, Milan, Italy, <sup>\*\*</sup>Department of Internal Medicine, IRCCS Ospedale Policlinico San Martino, University of Genoa, Genoa, Italy, and <sup>††</sup>LIRYC, University of Bordeaux, CHU de Bordeaux, Service de Rhythmologie, Hôpital Cardiologique du Haut-Lévêque (Centre Hospitalier Universtaire de Bordeaux), Bordeaux, France.

**BACKGROUND** Several electrocardiographic (ECG) indices have been proposed to predict the origin of premature ventricular complexes (PVCs) with precordial transition in lead V<sub>3</sub>. However, the accuracy of these algorithms is limited.

**OBJECTIVES** We sought to evaluate a new ECG criterion differentiating the origin of outflow tract with precordial transition in lead V<sub>3</sub>.

**METHODS** We included in our study patients exhibiting outflow tract PVCs with precordial transition in lead V<sub>3</sub> referred for ablation. We analyzed a novel new ECG criterion, RV<sub>1</sub>-V<sub>3</sub> transition ratio, for distinguishing right from left idiopathic outflow tract PVCs with precordial transition in lead V<sub>3</sub>. The RV<sub>1</sub>-V<sub>3</sub> transition ratio was defined as  $(RV_1 + RV_2 + RV_3)_{PVC} / (RV_1 + RV_2 + RV_3)_{SR}$  (sinus rhythm).

**RESULTS** We included 58 patients in our study. The ratio was lower for right ventricular outflow tract origins than left ventricular outflow tract (LVOT) origins (median [interquartile range], 0.6953

[0.4818–1.0724] vs 1.5219 [1.1582–2.4313],  $P < .001$ ). Receiver operating characteristic analysis revealed an area under the curve of 0.856 for the ratio, and a cut-off value of  $\geq 0.9$  predicting LVOT origin with 94% sensitivity and 73% specificity. This ratio was superior to any previously proposed ECG criterion for differentiating right from left outflow tract PVCs.

**CONCLUSION** The RV<sub>1</sub>-V<sub>3</sub> transition ratio is a simple and accurate novel ECG criterion for distinguishing right from left idiopathic outflow tract PVCs with precordial transition in lead V<sub>3</sub>.

**KEYWORDS** Ablation; Electrocardiogram; Premature ventricular complexes; RV<sub>1</sub>-V<sub>3</sub> transition ratio; Ventricular outflow tract

(Heart Rhythm 0<sup>2</sup> 2021;2:521–528) © 2021 Heart Rhythm Society. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Address reprint requests and correspondence:** Dr Konstantinos Vlachos, Laboratory of Cardiac Electrophysiology, "Evangelismos" General Hospital of Athens, Ipsilantou 47, Athens, Greece 10676. E-mail address: [vlachos.konstantinos7@gmail.com](mailto:vlachos.konstantinos7@gmail.com).

## Introduction

Idiopathic outflow tract ventricular arrhythmias (OT-VAs), including monomorphic premature ventricular contractions (PVCs), nonsustained ventricular tachycardias (VT), and sustained monomorphic VT, commonly originate from neighboring anatomical structures at the outflow tract.<sup>1</sup>

### KEY FINDINGS

- The RV<sub>1</sub>-V<sub>3</sub> transition ratio is significantly lower for right ventricular outflow tract origins than left ventricular outflow tract (LVOT) origin premature ventricular contractions (PVCs).
- A cut-off value of  $\geq 0.9$  can predict LVOT origin PVCs with 94% sensitivity and 73% specificity.
- The RV<sub>1</sub>-V<sub>3</sub> transition ratio showed superiority when compared with already well-known electrocardiographic indices of V<sub>2</sub> transition ratio, V<sub>2</sub>S/V<sub>3</sub>R index, and V<sub>1</sub>-V<sub>3</sub> transition index.
- The use of RV<sub>1</sub>-V<sub>3</sub> transition ratio could increase the safety, shorten the procedural time, and limit the cost of the procedure by avoiding unnecessary arterial or venous punctures, angiography, and mapping.

Recent reports state that left ventricular outflow tract (LVOT) PVCs/VT may represent more than 50% of idiopathic OT-VAs.<sup>2</sup> The electrocardiographic (ECG) characteristics of PVCs/VT originating from the outflow tract are similar owing to the anatomical proximity of the right ventricular outflow tract (RVOT) and LVOT; thus PVCs with inferior QRS axis and left bundle branch block morphology may originate from either the RVOT or the LVOT. Predicting the anatomical origin is crucial not only for improving mapping and catheter ablation techniques, but also for minimizing the risk of complications.<sup>3</sup> Currently, several ECG indices have been proposed to predict the origin of PVCs with precordial transition in lead V<sub>3</sub>.<sup>4-7</sup> However, the accuracy of these algorithms may be limited, not only because of the close proximity and complex overlay of the outflow tract structures, but also because QRS morphology can be influenced by several parameters: lead position, cardiac anatomy, cardiac rotation, ventricular hypertrophy, patients' breast size, chest wall deformities, patients' sex, body mass index, and preferential conduction across the ventricular OT septum.<sup>8,9</sup> In our study, we sought to evaluate a novel ECG discriminatory criterion of idiopathic outflow tract PVCs/VT with precordial transition zone in lead V<sub>3</sub>, independently of the ECG pattern. The sensitivity, specificity, and accuracy of the new criterion was evaluated and compared with previously described ECG indexes.

## Methods

### Study population

We prospectively analyzed patients with a left bundle branch block pattern ( $R/S \leq 1$  in lead V<sub>1</sub>) and inferior axis (positive polarity in all inferior leads) QRS morphology and precordial transition in lead V<sub>3</sub> (from  $R/S < 1$  to  $R/S > 1$ ) that were referred for first-time catheter ablation owing to symptomatic idiopathic OT-VAs between January 2018 and August 2020 at 4 high-volume European tertiary referral hospitals. Patients

with structural heart disease based on echocardiography, coronary angiography, or cardiac magnetic resonance imaging were excluded from our study. We also excluded patients with Brugada ECG pattern and patients with bundle branch block QRS morphology at baseline ECG. Prior to the study, all antiarrhythmic drugs were discontinued for more than 5 half-lives except amiodarone. The research reported in this article adhered to the Declaration of Helsinki, and the study was approved by the institutional review board; all patients provided written informed consent.

### ECG analysis of the VA morphology—Definition of the RV<sub>1</sub>-V<sub>3</sub> transition ratio

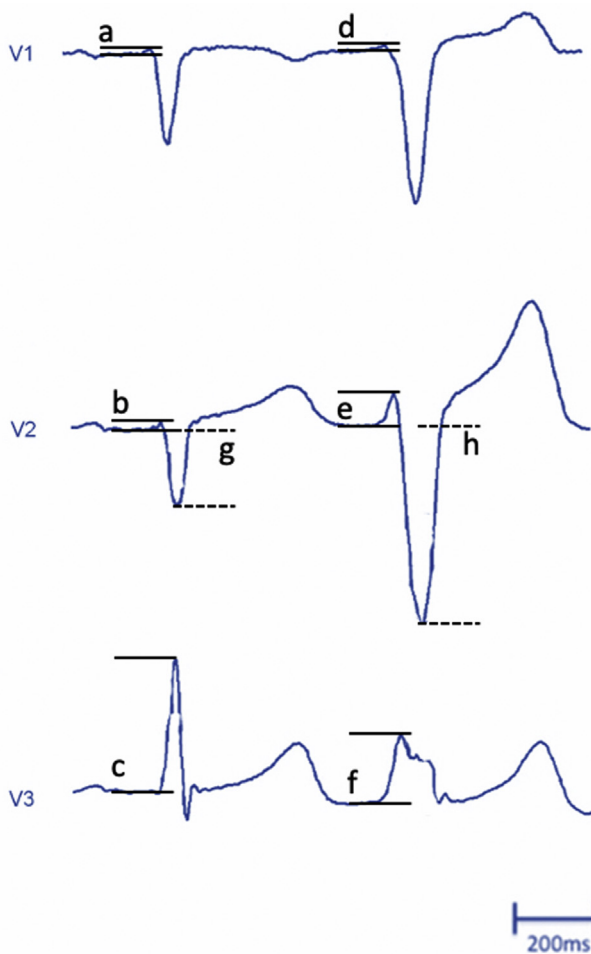
Sinus rhythm (SR) and VA ECG morphology were measured on the Prucka CardioLab recording system (GE Medical Systems, San Francisco, CA), with the recordings displayed at a sweep speed of 100 and 200 mm/s. Surface 12-lead ECGs were recorded during SR and during PVCs at a paper speed of 100 mm/s with limb and chest leads placed in a standard position. In particular, the electrodes of leads V<sub>1</sub> and V<sub>2</sub> were placed at the fourth intercostal space and the electrode of lead V<sub>3</sub> was placed midway between leads V<sub>2</sub> and V<sub>4</sub>. The QRS morphology during SR and PVCs was analyzed on the same 12-lead ECG using an electronic caliper on the recording system (Prucka CardioLab recording system). Measurements of R-wave amplitude in leads V<sub>1</sub>-V<sub>3</sub> and S-wave amplitude in leads V<sub>1</sub>-V<sub>3</sub> were performed manually by 2 different authors blinded to the PVC origin. The following measurements were assessed on the surface ECG of the first beat of VT or the PVCs: (1) QRS duration; (2) R-wave amplitude and the duration from the onset of QRS to the peak of QRS deflection in leads II, III, aVF; (3) R-wave ratio of leads III/II<sup>10</sup>; (4) Q-wave amplitude in leads aVL and aVR; (5) R- and S-wave amplitudes in leads V<sub>1</sub> to V<sub>3</sub>; (6) R-wave duration in leads V<sub>1</sub> to V<sub>3</sub>; (7) aVL/aVR Q wave ratio; (8) R/S ratio in leads V<sub>1</sub> to V<sub>3</sub>; (9) V<sub>2</sub>S/V<sub>3</sub>R index<sup>7</sup>; (10) V<sub>2</sub> transition ratio; (11) peak deflection index in the inferior leads<sup>11</sup>; (12) precordial transition in LBBB morphology. During the sinus beats, R- and S-wave amplitudes in lead V<sub>2</sub> were also measured on the surface ECG. The ECG data were measured with electronic calipers by 2 experienced investigators blinded to the site of the origin. If there were discrepancies between those results, they were adjudicated by a third investigator.

### PVC QRS duration

The PVC QRS duration (milliseconds) was defined as the interval measured from the earliest ventricular activation (or from the stimulation artifact) to the offset of the QRS complex in the precordial leads.

### Peak QRS duration

The peak QRS duration (milliseconds) was defined as the time from the QRS onset to the peak QRS deflection in the inferior leads.



**Figure 1** The RV<sub>1</sub>-V<sub>3</sub> transition ratio  $[(RV1+RV2+RV3)_{PVC} / (RV1+RV2+RV3)_{SR}]$  was defined as the sum of R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during premature ventricular contraction divided by the sum of R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during sinus rhythm.

### RV<sub>1</sub>-V<sub>3</sub> transition ratio

The RV<sub>1</sub>-V<sub>3</sub> transition ratio  $[(RV1+RV2+RV3)_{PVC} / (RV1+RV2+RV3)_{SR}]$  was defined as the sum of R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during PVC divided by the sum of R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during SR (Figure 1).

### V<sub>2</sub> transition ratio

The V<sub>2</sub> transition ratio  $[V2(R/R+S)_{PVC} / V2(R/R+S)_{SR}]$  was calculated by computing the percentage R wave during PVC (R/R+S) divided by the percentage R wave during SR (R/R+S), in lead V<sub>2</sub>.<sup>5</sup>

### V<sub>1</sub>-V<sub>3</sub> transition index

The V<sub>1</sub>-V<sub>3</sub> transition index  $[(S_{PVC}/S_{SR})V1 + (S_{PVC}/S_{SR})V2] - [(R_{PVC}/R_{SR})V1 + (R_{PVC}/R_{SR})V2 + (R_{PVC}/R_{SR})V3]$  was defined as the sum of S-wave amplitude in leads V<sub>1</sub> and V<sub>2</sub> during PVCs divided by the S-wave amplitude during SR, respectively, minus the sum of R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during PVC divided by the R-wave amplitude during SR, respectively.<sup>6</sup>

### V<sub>2</sub>S/V<sub>3</sub>R index

The V<sub>2</sub>S/V<sub>3</sub>R index was defined as the S-wave amplitude in V<sub>2</sub> divided by the R-wave amplitude in V<sub>3</sub> during the VA.<sup>7</sup>

### Peak deflection index

The peak deflection index was defined as the inferior lead presenting the tallest R wave by dividing the time from the QRS onset to the peak QRS deflection by the total QRS duration.<sup>11</sup>

### Mapping and radiofrequency catheter ablation

The electrophysiological study and catheter ablation were performed under deep sedation with intravenous midazolam, fentanyl, and propofol and under local anesthesia with lidocaine 1%. In patients with PVCs, the 12-lead surface electrocardiogram (Prucka CardioLab recording system) of the clinical PVCs was recorded before sedation. Intravenous heparin was administered to maintain an activated clotting time >300 seconds in LVOT procedures. For mapping and pacing, a quadripolar catheter was positioned via the right femoral vein at the His-bundle region, and a decapolar navigation catheter (DECANAV®; Biosense-Webster, Irvine, CA) via the femoral vein in the coronary sinus or RVOT. The coronary sinus catheter was advanced into the great cardiac vein (GCV) as far as possible until the proximal electrode pair recorded an earlier ventricular activation than the most distal electrode pair during the VAs. Under the guidance of a 3-dimensional electroanatomic mapping system (CARTO 3), mapping and pacing were performed using an 8F open-tip irrigated radiofrequency (RF) catheter with tip-integrated CF sensor (ThermoCool SmartTouch®; Biosense-Webster Inc) introduced via the femoral vein for sites in the RVOT or the right femoral artery for the endocardial LVOT or aortic cusps. Bipolar and unipolar signals were filtered at 30–500 Hz and 0.05–500 Hz, respectively. When few PVCs were observed at the beginning of the electrophysiological study, induction of the VT or PVCs was attempted by burst pacing from the right ventricle with the addition of an isoproterenol infusion at a rate of 2–4 µg/min intravenously. Three activation maps were acquired, using the decapolar navigation catheter for the RVOT and also for indirect mapping of the epicardial LV summit via the GCV, and the ablation catheter for the LVOT including the aortic cusps. The target site for the PVC ablation was determined by the earliest bipolar electrogram preceding the QRS onset, the QS morphology of the unipolar electrogram during PVCs, and/or an excellent pace map (>95% 12-lead QRS matching). If PVCs or VT occurred infrequently, pace mapping was performed. Pace mapping was performed using the distal bipolar electrodes at a pacing cycle length of 500 ms and at the minimum stimulus amplitude required for consistent capture (up to a maximum output of 10 mA and pulse width of 2.0 ms). The score for the pace mapping was determined as the number of leads with an identical height of the R wave / depth of the S wave (R/S) ratio match (12 represented a perfect R/S ratio match in all 12 leads)

**Table 1** Electrocardiographic characteristics of right ventricular outflow tract and left ventricular outflow tract premature ventricular contractions

	RVOT	LVOT	<i>P</i> value
Age (y)	47.82 ± 11.87	46.28 ± 13.68	.496
Male (%)	45	58	.330
QRS duration (ms)	156.6 ± 19.4	138.3 ± 11	<.001
R-wave amplitude in lead V <sub>1</sub> (PVC) (mV)	0.12 ± 0.14	0.18 ± 0.15	.198
R-wave amplitude in lead V <sub>2</sub> (PVC) (mV)	0.27 ± 0.17	0.48 ± 0.27	.0017
R-wave amplitude in lead V <sub>3</sub> (PVC) (mV)	0.71 ± 0.24	1.15 ± 0.42	<.001
S-wave amplitude in lead V <sub>1</sub> (PVC) (mV)	1.2 ± 0.3	0.82 ± 0.36	<.001
S-wave amplitude in lead V <sub>2</sub> (PVC) (mV)	1.45 ± 0.48	1.23 ± 0.48	.091
S-wave amplitude in lead V <sub>3</sub> (PVC) (mV)	0.44 ± 0.27	0.56 ± 0.34	.186

LVOT = left ventricular outflow tract; PVC = premature ventricular contraction; RVOT = right ventricular outflow tract.

using automated pace-map algorithms integrated in a 3-D mapping system (PaSO software; Biosense Webster). The sites mapped with the earliest ventricular activation or exhibiting a perfect (12/12) or near-perfect (10–11/12) pace match were determined as the target site. When the earliest ventricular activation site was recorded at the LVOT, selective coronary angiography was performed to define the anatomical relationship between the aortic cusps, the coronary arteries, and the ablation catheter. RF ablation was performed in a power-control mode starting at 15 W in the GCV–anterior intraventricular vein, 30 W in the RVOT, and 30–40 W in the LVOT with an irrigation flow rate of 17–30 mL/min (normal saline 0.9%) and a temperature limit of 43°C. Ablation was performed at least 5 mm from the ostium of any coronary artery. When acceleration or reduction in the clinical PVC frequency was identified during the first 10 seconds of ablation, then RF was continued for 120 seconds more. Otherwise, the RF application was terminated, and the catheter was repositioned to another target site. The endpoint of the procedure was the elimination and noninducibility of clinical PVCs during a waiting time of 30 minutes after the last application. Absence of spontaneous or inducible PVCs or VT with isoproterenol infusion (2–4 µg/min) and burst pacing from the right ventricle of a cycle length up to 300 ms determined successful catheter ablation. Successful catheter ablation was defined as the absence of clinical PVCs with and without isoproterenol at the end of the procedure. Follow-up after the procedure included clinic visits with 12-lead ECGs and 24-hour ambulatory (Holter) monitoring. Successful catheter ablation was defined as no recurrence of any OT-VAs during >6 months of follow-up.

### Statistical analysis

The data were analyzed using SPSS 26.0 (IBM, Armonk, NY). Continuous data are expressed as the mean ± standard deviation or median, interquartile range (IQR) as appropriate. Comparisons between groups were performed using Student *t* test or the Mann–Whitney *U* test for normally and non-normally distributed data, respectively. A receiver operating characteristic analysis was used to compare the accuracy among the different ECG criteria and to calculate the sensitivity, specificity, and area under the curve (AUC). A value of *P* < .05 was considered statistically significant.

### Follow-up

All patients underwent 24-hour monitoring the day after the procedure and were followed up as outpatients. Twenty-four-hour Holter was performed every 2 weeks during the first month, and every 3 months thereafter up to 12 months. ECG was performed if any relevant symptoms occurred during the follow-up period.

## Results

### Clinical and electrophysiological characteristics

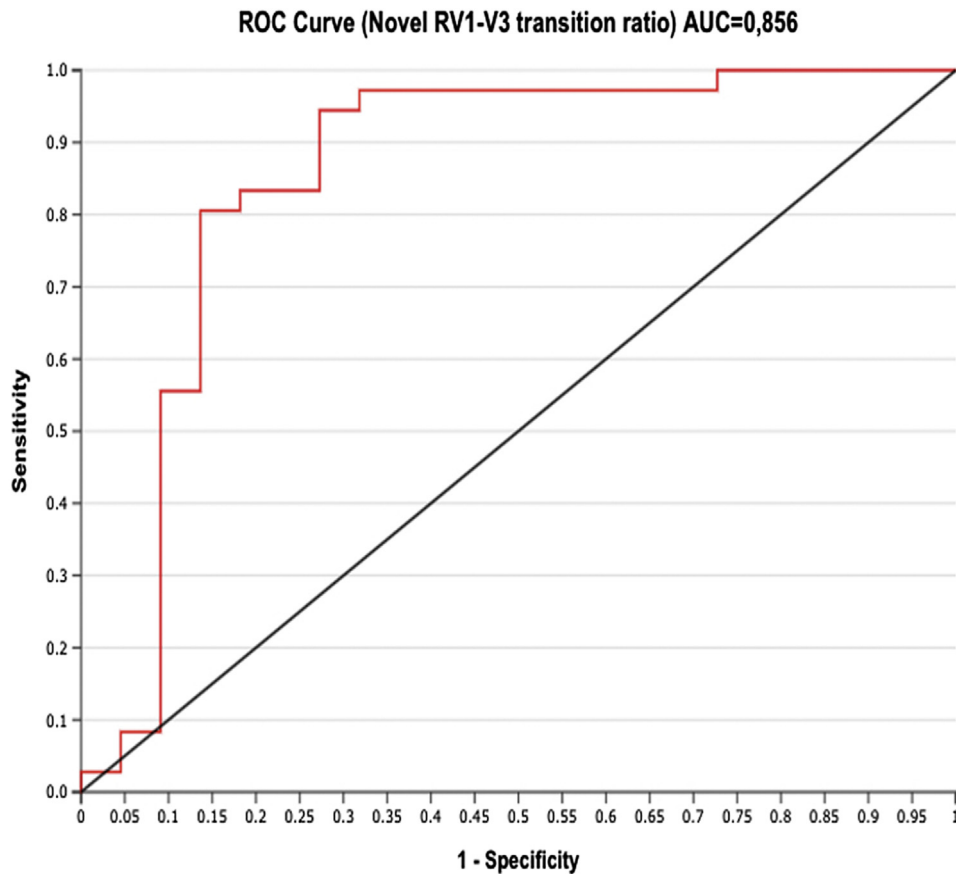
We studied 378 consecutive patients who underwent catheter ablation for symptomatic idiopathic OT-VAs between January 2018 and August 2020. We prospectively enrolled 58 patients (31 men; mean age 47 ± 13 years) with a left bundle branch block pattern (R/S ≤ 1 in lead V<sub>1</sub>) and inferior axis (positive polarity in all inferior leads) QRS morphology and precordial transition in lead V<sub>3</sub> (from R/S < 1 to R/S > 1). Based on activation, pace mapping, and successful ablation sites, 22 (38%) subjects exhibited RVOT origin and 36 (62%) subjects LVOT origin (Table 1). In the LVOT group, 7 cases of PVCs were successfully ablated at the left coronary cusp (LCC), 8 cases at the right coronary cusp (RCC), 10 cases at the commissure between the RCC and the LCC, 5 cases at the GCV near its continuation to the anterior intraventricular vein, 2 cases at the lateral wall of the mitral annulus, 2 cases at the LCC/GCV, 1 case at the LCC/LVOT (endocardially), and 1 case at the commissure between the non-coronary cusp and the RCC. No complications occurred during the procedure in either group.

### The novel ECG criterion: RV<sub>1</sub>-V<sub>3</sub> transition ratio

The RV<sub>1</sub>-V<sub>3</sub> transition ratio [(RV1+RV2+RV3)<sub>PVC</sub> / (RV1+RV2+RV3)<sub>SR</sub>] was significantly lower for RVOT origins than LVOT origins (median [IQR], 0.6953 [0.4818–1.0724] vs 1.5219 [1.1582–2.4313], *P* < .001) (Figure 2).

### Comparison of the RV<sub>1</sub>-V<sub>3</sub> transition ratio with previously described indices

The RV<sub>1</sub>-V<sub>3</sub> transition ratio was compared with 3 already known ECG indices: the V<sub>2</sub> transition ratio, the V<sub>2</sub>S/V<sub>3</sub>R index, and the V<sub>1</sub>-V<sub>3</sub> transition index. The novel ratio displayed an AUC of 0.856 with a cut-off value of ≥0.9 predicting an



**Figure 2** The RV<sub>1</sub>-V<sub>3</sub> transition ratio  $[(RV1+RV2+RV3)_{PVC} / (RV1+RV2+RV3)_{SR}]$  was significantly lower for right ventricular outflow tract origins than left ventricular outflow tract origins.

LVOT origin with 94% sensitivity and 73% specificity (Figure 2). The RV<sub>1</sub>-V<sub>3</sub> transition ratio was significantly lower for RVOT origins than LVOT origins (median [IQR], 0.6953 [0.4818–1.0724] vs 1.5219 [1.1582–2.4313],  $P < .001$ ) (Figure 3). The V<sub>2</sub> transition ratio had an AUC of 0.818, with a cut-off value of  $\geq 0.60$  predicting LVOT origin with 81% sensitivity and 64% specificity. The V<sub>2</sub> transition ratio was significantly lower for RVOT origins than LVOT origins (median [IQR], 0.4392 [0.2587–0.7795] vs 1.2429 [0.6435–1.7757],  $P < .001$ ) (Figure 3). The V<sub>2</sub>S/V<sub>3</sub>R index had an AUC of 0.8283, with a cut-off value of  $\leq 1.5$  predicting LVOT origin with 75% sensitivity and 82% specificity. The V<sub>2</sub>S/V<sub>3</sub>R index was significantly higher for RVOT origins than LVOT origins (median [IQR], 2.1591 [1.7134–2.9135] vs 1.0426 [0.7290–1.5516],  $P < .001$ ) (Figure 3). The V<sub>1</sub>-V<sub>3</sub> transition index had an AUC of 0.8317, with a cut-off value of  $\leq -1.60$  predicting a LVOT origin with 60% sensitivity and 85% specificity. The V<sub>1</sub>-V<sub>3</sub> transition index was significantly higher for RVOT origins than LVOT origins (median [IQR], 1.5327 [-1.0075 to 3.4200] vs -2.1423 [-5.8776 to -0.3959],  $P < .001$ ) (Figure 3).

#### Accuracy and pitfalls of the RV<sub>1</sub>-V<sub>3</sub> transition ratio

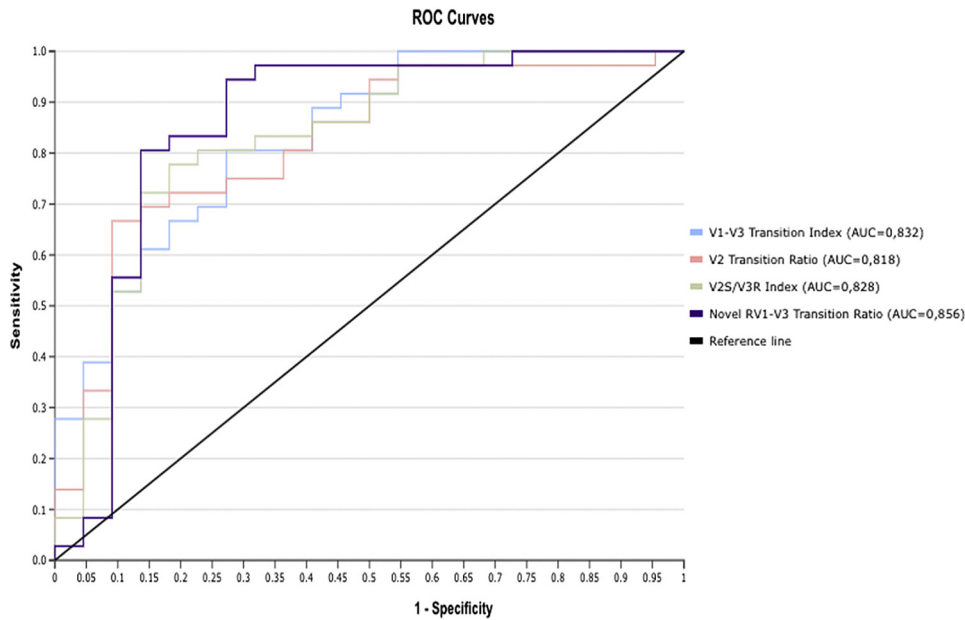
The RV<sub>1</sub>-V<sub>3</sub> transition ratio predicted an RVOT origin for idiopathic outflow tract PVCs with precordial transition in

lead V<sub>3</sub> with 88% accuracy (16 of 18 cases) and LVOT origin with 85% accuracy (34 of 40 cases). The ratio failed to determine the correct arrhythmia origin in 2 cases in the RVOT group including 1 PVC originating at the RCC (patient 27) and 1 PVC originating at the RCC-LCC commissure (patient 39). The new ECG index failed to determine the PVC origin in 6 cases in the LVOT group originating from the RVOT (patients 6, 14, 25, 47, 50 and 54).

#### Discussion

The main finding of our study is a novel ECG criterion allowing us to differentiate right from left outflow tract idiopathic PVCs with precordial transition zone in lead V<sub>3</sub>:

- (1) The RV<sub>1</sub>-V<sub>3</sub> transition ratio  $[(RV1+RV2+RV3)_{PVC} / (RV1+RV2+RV3)_{SR}]$ , defined as the sum of R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during PVC divided by the sum of R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during SR, exhibited a higher AUC 0.856 with a cut-off value of  $\geq 0.9$  predicting an LVOT origin with 94% sensitivity and 73% specificity.
- (2) The sensitivity, specificity, and accuracy of the RV<sub>1</sub>-V<sub>3</sub> transition ratio showed superiority when compared with already well-known ECG indices of V<sub>2</sub> transition ratio, V<sub>2</sub>S/V<sub>3</sub>R index, and V<sub>1</sub>-V<sub>3</sub> transition index.

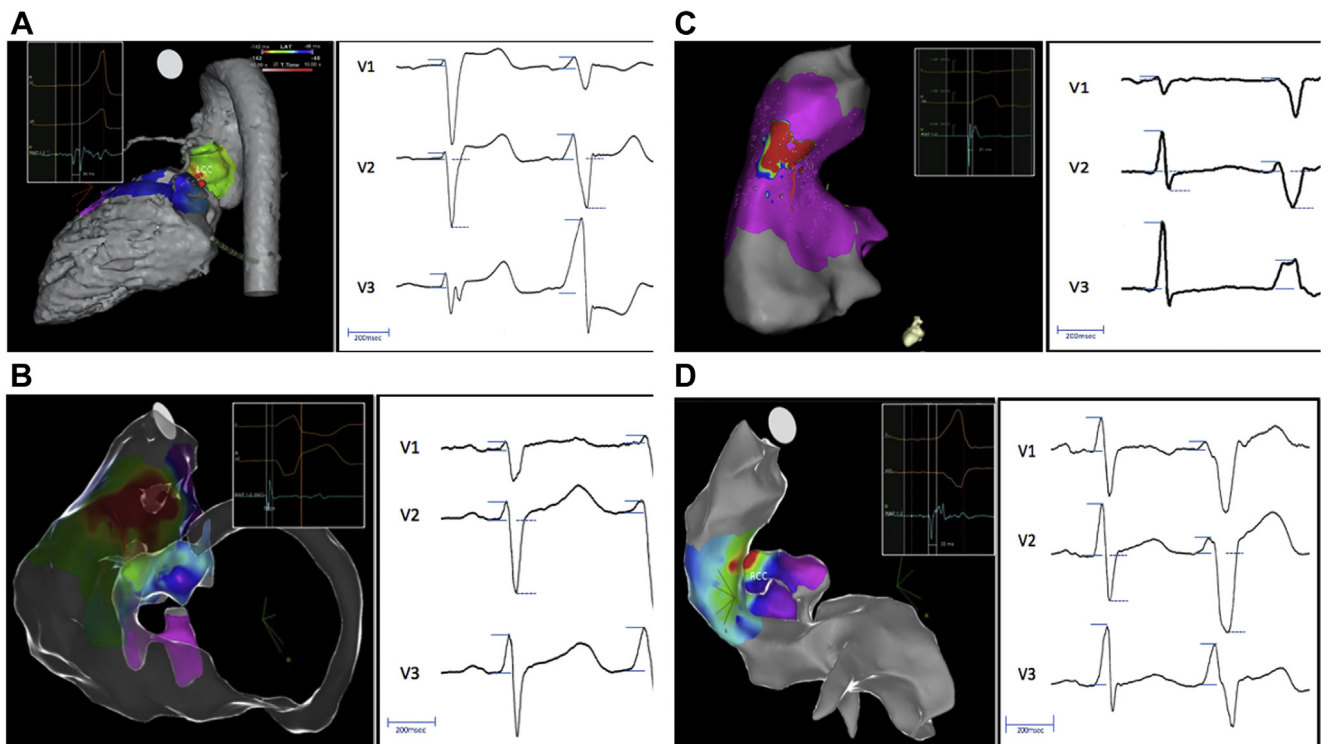


**Figure 3** The RV<sub>1</sub>-V<sub>3</sub> transition ratio was compared with 3 already known electrocardiography indices: the V<sub>2</sub> transition ratio, the V<sub>2</sub>S/V<sub>3</sub>R index, and the V<sub>1</sub>-V<sub>3</sub> transition index. The novel ratio displayed an area under the curve (AUC) of 0.856 with a cut-off value of  $\geq 0.9$  predicting a left ventricular outflow tract (LVOT) origin with 94% sensitivity and 73% specificity. The RV<sub>1</sub>-V<sub>3</sub> transition ratio was significantly lower for right ventricular outflow tract (RVOT) origins than LVOT origins (median [interquartile range (IQR)], 0.6953 [0.4818–1.0724] vs 1.5219 [1.1582–2.4313],  $P < .001$ ). The V<sub>2</sub> transition ratio had an AUC of 0.818, with a cut-off value of  $\geq 0.60$  predicting LVOT origin with 81% sensitivity and 64% specificity. The V<sub>2</sub> transition ratio was significantly lower for RVOT origins than LVOT origins (median [IQR], 0.4392 [0.2587–0.7795] vs 1.2429 [0.6435–1.7757],  $P < .001$ ). The V<sub>2</sub>S/V<sub>3</sub>R index had an AUC of 0.8283, with a cut-off value of  $\leq 1.5$  predicting LVOT origin with 75% sensitivity and 82% specificity. The V<sub>2</sub>S/V<sub>3</sub>R index was significantly higher for RVOT origins than LVOT origins (median [IQR], 2.1591 [1.7134–2.9135] vs 1.0426 [0.7290–1.5516],  $P < .001$ ). The V<sub>1</sub>-V<sub>3</sub> transition index had an AUC of 0.8317, with a cut-off value of  $\leq -1.60$  predicting an LVOT origin with 60% sensitivity and 85% specificity. The V<sub>1</sub>-V<sub>3</sub> transition index was significantly higher for RVOT origins than LVOT origins (median [IQR], 1.5327, [-1.0075 to 3.4200] vs -2.1423 [-5.8776 to -0.3959],  $P < .001$ ).

Accurate prediction of PVC origin before the catheter ablation procedure is important because different anatomical approaches may be required for mapping, depending on the PVCs/VT site of origin. Moreover, knowledge of the anatomic relation between the RVOT and LVOT is also crucial for the accurate diagnosis of the origin of the PVC.<sup>12–15</sup> Anatomically, the aortic cusps occupy a central location within the heart, with the RVOT located anterior and leftward of the aortic root, while the anteriorly situated RVOT passes slightly superior to and leftward of the aortic cusp.<sup>16</sup> The more distal posterior RVOT wall is immediately adjacent to the RCC and a portion of the LCC. The intimate nature of these 2 structures explains why previous ECG algorithms fail in a significant number of cases to distinguish the origin of outflow tract PVCs. PVCs from the RCC usually exhibit a transition at or before lead V<sub>3</sub>, while PVCs from the RVOT have a typical precordial transition at lead V<sub>3</sub> or later. Sometimes the successful site to eliminate a PVC from the posterior wall of the RVOT is in the RCC. Preferential conduction of the PVCs/VT from the aortic cusps to the RVOT may constitute a logical explanation for the underestimation of LVOT involvement in OT-VAs.<sup>14</sup>

Several ECG indices have been proposed for differentiating PVCs originating from the RVOT vs LVOT. Cheng and colleagues<sup>5</sup> retrospectively examined 31 patients with outflow tract PVCs/VT and V<sub>3</sub> transition and proposed a surface ECG algorithm using the R-wave deflection interval

in lead V<sub>3</sub> combined with a R-wave amplitude index in lead V<sub>1</sub>.<sup>5</sup> They prospectively applied the algorithm in a population consisting of 12 patients with idiopathic outflow tract PVCs/VT with transitional lead at V<sub>3</sub> and managed to identify the correct site of origin in 11 of them (accuracy 91.7%), using the thresholds for R-wave deflection interval of  $> 80$  ms in lead V<sub>3</sub> and the R-wave amplitude index  $> 0.3$  in lead V<sub>1</sub> for LVOT PVCs/VT (100% sensitivity and 83.3% specificity). Similarly, Betensky and colleagues<sup>4</sup> retrospectively analyzed the ECGs of 40 patients with outflow tract PVCs/VT and precordial transition in lead V<sub>3</sub> and proposed an ECG criterion for distinguishing PVCs/VT originating from the left or right outflow tract.<sup>4</sup> This new criterion, also called “V<sub>2</sub> transition ratio,” was prospectively evaluated in 21 patients with idiopathic outflow tract PVCs/VT and precordial transition in lead V<sub>3</sub>. In cases where the PVC transition occurred at or earlier than the SR transition and the V<sub>2</sub> transition ratio was  $\geq 0.60$ , an LVOT origin was predicted with a sensitivity of 95% and specificity of 100%. Yoshida and colleagues<sup>7</sup> reported high rates of sensitivity (89%) and specificity (94%) with the use of the V<sub>2</sub>S/V<sub>3</sub>R index in a population of 207 patients with idiopathic outflow tract PVCs/VT, using a cut-off value of  $< 1.5$  for the prediction of LVOT origin. However, it must be noted that the V<sub>2</sub>S/V<sub>3</sub>R index exhibited lower accuracy for the subgroup of patients with precordial transition in lead V<sub>3</sub> (94% sensitivity and 78% specificity in 77 patients, 37% of the study



**Figure 4** **A:** An electroanatomical map in posteroanterior (PA) projection with clipped view showing the positions of the left coronary cusp (LCC) and endocardial left ventricular outflow tract (LVOT) regions. Activation mapping delineates the site of origin of premature ventricular contraction (PVC) at the LCC. Surface electrocardiogram (12 leads), distal bipolar (MAP 1–2), intracardiac electrograms recorded from the early site are shown. Local activation precedes QRS by 30 ms. Our novel RV<sub>1</sub>-V<sub>3</sub> transition ratio was 4.07 ( $\geq 0.9$ ), predicting an LVOT origin. V<sub>2</sub> transition ratio was 4.18, predicting an LVOT origin; V<sub>2</sub>S/V<sub>3</sub>R index was 0.61 predicting an LVOT origin; and V<sub>1</sub>-V<sub>3</sub> transition index was -9.6, predicting an LVOT origin. **B:** An electroanatomical map in left anterior oblique projection with clipped view showing the positions of the LCC, great cardiac vein (GCV), and right ventricular outflow tract (RVOT) regions. Activation mapping delineates the site of origin of the PVC at the right coronary cusp (RCC)-LCC. Surface electrocardiogram (12 leads), distal bipolar (MAP 1–2), intracardiac electrograms recorded from the earliest site are shown. Local activation precedes QRS by 20 ms. We successfully ablated the PVC targeting the RCC-LCC region and adding a lesion endocardially on the LVOT facing the earliest site of activation in the RCC-LCC. Our novel RV<sub>1</sub>-V<sub>3</sub> transition ratio was 1.03 ( $\geq 0.9$ ), predicting an RVOT origin. V<sub>2</sub> transition ratio was 0.55, predicting an RVOT origin; V<sub>2</sub>S/V<sub>3</sub>R index was 2.16, predicting an RVOT origin; and V<sub>1</sub>-V<sub>3</sub> transition index was -0.53, predicting an RVOT origin. **C:** An electroanatomical map in anteroposterior projection with clipped view showing the RVOT region. Activation mapping delineates the site of origin of the PVC at the anterior RVOT region. Surface electrocardiogram (12 leads), distal bipolar (MAP 1–2), intracardiac electrograms recorded from the earliest site are shown. Local activation precedes QRS by 21 ms and the unipolar signal delineates a QS pattern. We successfully ablated the PVC targeting the site of earliest activation on the bipolar EGM at the anterior part of the RVOT. Our novel RV<sub>1</sub>-V<sub>3</sub> transition ratio was 0.48 ( $< 0.9$ ), predicting an RVOT origin; V<sub>2</sub> transition ratio was 0.37, predicting an RVOT origin; V<sub>2</sub>S/V<sub>3</sub>R index was 0.8, predicting an LVOT origin; and V<sub>1</sub>-V<sub>3</sub> transition index was 3.47, predicting an RVOT origin. **D:** An electroanatomical map in PA projection with clipped view showing the positions of the RCC, LCC, GCV, and endocardial LVOT regions. Activation mapping delineates the site of origin of the PVC at RCC. Surface electrocardiogram (12 leads), distal bipolar (MAP 1–2), intracardiac electrograms recorded from the earliest site are shown. Local activation precedes QRS by 33 ms. We successfully ablated the PVC, targeting the RCC region and adding a lesion endocardially in the LVOT facing the earliest site of activation in the RCC. There was no prematurity in the RVOT region. Our novel RV<sub>1</sub>-V<sub>3</sub> transition ratio was 0.49 ( $< 0.9$ ), predicting an RVOT origin. V<sub>2</sub> transition ratio was 0.35; predicting an RVOT origin; V<sub>2</sub>S/V<sub>3</sub>R index was 1.97, predicting an RVOT origin; and V<sub>1</sub>-V<sub>3</sub> transition index was 1.63, predicting an RVOT origin.

population). Recently, Di and colleagues<sup>6</sup> published the results of their retrospective evaluation of the ECGs of 147 patients with idiopathic outflow tract PVCs/VT and precordial transition in lead V<sub>3</sub>. Their novel “V<sub>1</sub>-V<sub>3</sub> transition index” predicted an RVOT origin with a 93% sensitivity and 86% specificity with a cut-off value of  $> -1.60$ . Interestingly enough, only 29 patients in this retrospective cohort suffered from LVOT PVCs/VT. Prospective evaluation of the algorithm in 37 patients exhibited 95% accuracy in RVOT PVCs/VT and 75% accuracy in LVOT PVCs/VT.

In our study, we prospectively compared the RV<sub>1</sub>-V<sub>3</sub> transition ratio with the V<sub>2</sub> transition ratio, the V<sub>2</sub>S/V<sub>3</sub>R index, and the V<sub>1</sub>-V<sub>3</sub> transition index in a population of 58 consecutive patients suffering from OT-VAs with precordial

transition in lead V<sub>3</sub>. The novel ratio exhibited a higher AUC 0.856 with a cut-off value of  $\geq 0.9$  predicting an LVOT origin with 94% sensitivity and 73% specificity (Figure 4). Our population sample exclusively included PVCs/VT with inferior axis and precordial transition in lead V<sub>3</sub> and was larger in its prospective evaluation than those in the cohorts reported by Cheng and colleagues,<sup>5</sup> Betensky and colleagues,<sup>4</sup> and Di and colleagues.<sup>6</sup> Another important point is that while the V<sub>2</sub> transition ratio uses data from only 1 lead (V<sub>2</sub>) and the V<sub>2</sub>S/V<sub>3</sub>R index takes into account the S-wave amplitude in lead V<sub>2</sub> and the R-wave amplitude in lead V<sub>3</sub> only during PVC, our RV<sub>1</sub>-V<sub>3</sub> transition ratio encompasses the R-wave amplitude in leads V<sub>1</sub>, V<sub>2</sub>, and V<sub>3</sub> during SR and PVCs. Furthermore, although the V<sub>1</sub>-V<sub>3</sub> transition index also takes

into account multiple leads in SR and PVC, it failed to exhibit high rates of sensitivity in our patient cohort, when compared with our RV<sub>1</sub>-V<sub>3</sub> transition ratio.

The RV<sub>1</sub>-V<sub>3</sub> transition ratio is a novel ECG criterion that accurately and simply differentiates left from right idiopathic OT-VAs with precordial transition in lead V<sub>3</sub>. The systematic calculation of this index before ablation could lead to more efficient and safer ablation procedures by reducing procedural and radiation time, radiation dose, and the possibility of complications. This new ECG index should be further validated in external cohorts.

### Limitations

Our study has the following limitations. First, this is a multicenter study with a small number of patients. Secondly, the RV<sub>1</sub>-V<sub>3</sub> transition ratio was tested only in patients with idiopathic outflow tract PVCs and precordial transition zone in lead V<sub>3</sub>. Thirdly, RF ablation at the site of earliest activity failed in some cases to eliminate ectopy and additional lesions had to be applied in close vicinity. Thus, it could be disputed whether the final ablation spot was the original source of the ectopy. Finally, our study did not include patients with underlying bundle branch block or structural heart disease, restricting the use of our algorithm in these clinical settings.

### Conclusion

The RV<sub>1</sub>-V<sub>3</sub> transition ratio is an accurate ECG diagnostic tool for the prediction of the outflow tract PVC origin in patients with transition zone in lead V<sub>3</sub>. The use of this index could increase the safety, shorten the procedural time, and limit the cost of the procedure by avoiding unnecessary arterial or venous punctures, angiography, and mapping.

### Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Disclosures

Dr Maria Kyriakopoulou received an ESC Training Grant from the European Society of Cardiology. Dr Stylianos Dragas received Training Grants from the Hellenic Society of Cardiology and the Hellenic Rhythmology Society.

### Authorship

All authors attest they meet the current ICMJE criteria for authorship.

### Patient Consent

All patients provided written informed consent.

### Ethics Statement

The research reported in this article adhered to the Declaration of Helsinki, and the study was approved by the institutional review board.

### References

- Anderson RD, Kumar S, Parameswaran R, et al. Differentiating right- and left-sided outflow tract ventricular arrhythmias: classical ECG signatures and prediction algorithms. *Circ Arrhythm Electrophysiol* 2019;12:e007392.
- Letsas KP, Dragasis S, Bazoukis G, et al. The aortic cusps are the predominant successful ablation site of idiopathic outflow-tract ventricular arrhythmias. *J Electrocardiol* 2020;61:63–65.
- Yamada T. Idiopathic ventricular arrhythmias: relevance to the anatomy, diagnosis and treatment. *J Cardiol* 2016;68:463–471.
- Betensky BP, Park RE, Marchlinski FE, et al. The V(2) transition ratio: a new electrocardiographic criterion for distinguishing left from right ventricular outflow tract tachycardia origin. *J Am Coll Cardiol* 2011;57:2255–2262.
- Cheng Z, Cheng K, Deng H, et al. The R-wave deflection interval in lead V3 combining with R-wave amplitude index in lead V1: a new surface ECG algorithm for distinguishing left from right ventricular outflow tract tachycardia origin in patients with transitional lead at V3. *Int J Cardiol* 2013;168:1342–1348.
- Di C, Wan Z, Tse G, et al. The V(1)-V(3) transition index as a novel electrocardiographic criterion for differentiating left from right ventricular outflow tract ventricular arrhythmias. *J Interv Card Electrophysiol* 2019;56:37–43.
- Yoshida N, Yamada T, McElderry HT, et al. A novel electrocardiographic criterion for differentiating a left from right ventricular outflow tract tachycardia origin: the V2S/V3R index. *J Cardiovasc Electrophysiol* 2014;25:747–753.
- Yamada T, Murakami Y, Yoshida N, et al. Preferential conduction across the ventricular outflow septum in ventricular arrhythmias originating from the aortic sinus cusp. *J Am Coll Cardiol* 2007;50:884–891.
- Shirai Y, Liang JJ, Garcia FC, et al. QRS morphology shift following catheter ablation of idiopathic outflow tract ventricular arrhythmias: prevalence, mapping features, and ablation outcomes. *J Cardiovasc Electrophysiol* 2018;29:1664–1671.
- Yang Y, Saenz LC, Varosy PD, et al. Using the initial vector from surface electrocardiogram to distinguish the site of outflow tract tachycardia. *Pacing Clin Electrophysiol* 2007;30:891–898.
- Hachiya H, Hirao K, Sasaki T, et al. Novel ECG predictor of difficult cases of outflow tract ventricular tachycardia: peak deflection index on an inferior lead. *Circ J* 2010;74:256–261.
- Lin CY, Chung FP, Lin YJ, et al. Radiofrequency catheter ablation of ventricular arrhythmias originating from the continuum between the aortic sinus of Valsalva and the left ventricular summit: electrocardiographic characteristics and correlative anatomy. *Heart Rhythm* 2016;13:111–121.
- Suleiman M, Asirvatham SJ. Ablation above the semilunar valves: when, why, and how? Part II. *Heart Rhythm* 2008;5:1625–1630.
- Yamada T, McElderry HT, Doppalapudi H, et al. Idiopathic ventricular arrhythmias originating from the left ventricular summit: anatomic concepts relevant to ablation. *Circ Arrhythm Electrophysiol* 2010;3:616–623.
- Suleiman M, Asirvatham SJ. Ablation above the semilunar valves: when, why, and how? Part I. *Heart Rhythm* 2008;5:1485–1492.
- Tzeis S, Asvestas D, Yen Ho S, Vardas P. Electrocardiographic landmarks of idiopathic ventricular arrhythmia origins. *Heart* 2019;105:1109–1116.