Pulmonary sinus cusp mapping and ablation: A new concept and approach for idiopathic right ventricular outflow tract arrhythmias

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BACKGROUND Right ventricular outflow tract (RVOT) ventricular arrhythmias (VAs) may originate from the pulmonary sinus cusps (PSCs) far more frequently than previously recognized.

OBJECTIVE The purpose of this study was to assess whether mapping and ablation in PSCs might be an appropriate first-choice treatment in unselected patients with idiopathic RVOT VAs.

METHODS Ninety consecutive patients with VAs of RVOT-type origin were prospectively enrolled at our institution between August 2015 and September 2016. Pulmonary valve (PV) and PSCs were precisely localized by pulmonary arteriography. Activation and pace-mapping were performed in the PSCs and RVOT region below the PV, and ablation was preferentially performed in PSCs.

RESULTS In 81 patients (90%), earliest activation of VAs was found in PSCs, and ablation resulted in elimination of VAs without any additional ablation in the RVOT region underneath the PV. The best pace-map was obtained at successful ablation sites in PSCs in 96.3% of patients. In the remaining 9 patients, final successful ablation sites were in the aortic coronary cusps in 5 and at the lowest and most posterior part of the RVOT in 4. During mean follow-up of 15.2 ± 9.5 months, single procedural success rate was 96.7%.

CONCLUSION In this single-center, prospective study, a strategy based on PSC mapping and ablation eliminated 90% (81/90) of unselected idiopathic RVOT-type VAs with favorable mid-term effectiveness.

KEYWORDS Ablation; Catheter; Mapping; Right ventricular outflow tract; Ventricular arrhythmia

Introduction

In structurally normal hearts, idiopathic ventricular tachycardia and premature ventricular contractions (PVCs) of left bundle branch block and inferior-axis morphology frequently originate from the right ventricular outflow tract (RVOT) region, and have been treated effectively with radiofrequency catheter ablation (RFCA). Ventricular arrhythmias (VAs) originating from the pulmonary sinus cusps (PSCs) have been recently reported and thought to be a specific entity mostly occurring in previous failed cases of ablation using conventional methods.1 We hypothesized that VAs originating from the PSCs are far more common than previously recognized. The present study was performed to assess whether mapping and ablation in PSCs would be appropriate as first-choice therapy in unselected patients with idiopathic RVOT VAs.

Methods

Study population

The study group prospectively enrolled 90 consecutive patients with symptomatic VAs of RVOT-type origin (left bundle branch block morphology, inferior frontal axis, and precordial lead transition zone ≥V3), and refractory to at least 1 antiarrhythmic agent. Patients with structural heart disease and polymorphic VAs were excluded from the study. All patients were treated with the so-called PSCs mapping and ablation strategy at our hospital between August 2015 and September 2016. All patients provided written informed consent before the procedure, and the study was approved by the institutional review board of Wuhan Asian Heart Hospital.

ECG analysis

Analysis of surface ECGs during VAs included QRS duration; QRS morphology on leads I, II, III, aVR, and aVL; R-wave amplitudes on leads II, III, and aVF; and the precordial R-wave transition zone (earliest lead with R>S).

Electrophysiological procedure

After withdrawal of antiarrhythmic drugs for 5 or more half-lives, all patients underwent electrophysiological evaluation. Both bipolar and unipolar electrograms were recorded by a Prucka system (GE Healthcare, Milwaukee, WI, USA) (filtered at 30–500 Hz and 0.05–500 Hz, respectively). Three-dimensional electromagnetic mapping (CARTO, Biosense Webster, Diamond Bar, CA) was performed in all patients. A 7Fr saline-irrigated ablation catheter was used for ablation.

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with a 3.5-mm distal electrode and 2-5-2 mm interelectrode spacing was used for mapping and ablation. Activation mapping and pace-mapping were combined to identify the origin of PVCs. Activation times were assigned based on the earliest rapid downstroke of the unipolar signal (fastest dV/dt) correlating with the first sharp peak of the bipolar electrogram. Pace-mapping was performed at a cycle length equal to the coupling interval of the PVCs and a stimulus amplitude of 1 mA greater than the late diastolic threshold. The deactivation rate of 17 to 20 mL/min for 60 to 120 seconds. The successful ablation site was defined as that rendering clinical VAs noninducible with isoproterenol after at least a 30-minute waiting period. All procedures were performed by 3 experienced operators.

**Follow-up**

All patients underwent 24-hour Holter monitoring the day after the procedure and were followed up in the cardiology outpatient.

**PSC mapping and ablation strategy**

For this study, the RVOT region below the pulmonary valve (PV) was mapped first in 6 cross-sectional segments: posterior septal, midseptal, anterior septal, posterior free wall, mid–free wall, and anterior free wall. In all patients, activation and pace-mapping were subsequently performed in the PSCs. Right ventriculography and/or pulmonary arteriography were performed using a pigtail catheter to locate the position of the PV and to determine the precise location of the 3 PSCs, namely, left cusp (LC), anterior cusp (AC), and right cusp (RC). The LC is situated relatively left and at the lowest level; the AC in the superior and anterior position, and the RC in the superior and relatively right position. The location of PVC origin was identified as the successful ablation site according to fluoroscopic views in the right anterior oblique and left anterior oblique projections. Detailed mapping in 3 individual PSCs was achieved using a reversed U curve of the ablation catheter. An 8.5Fr long sheath (St Jude Medical, St Paul, MN) was used to facilitate and stabilize the mapping catheter.

An automated pace-mapping software (PaSo module, CARTO) was used in this study. Initially, the template from clinically documented VAs was acquired. The pacing beats and the selected template were automatically compared, and the correlation index was scored between 0 and 1. The values of the correlation index in each lead and an average correlation value for the entire ECG were calculated and displayed on the electroanatomic map. The PaSo criteria of a good pace-mapping included both the mean correlation index of 12 lead ≥0.95, and at least 11 of 12 individual leads met the ≥0.95 matches between the paced and spontaneous VAs QRS complexes. The following parameters were measured and assessed: shortest perpendicular distance from the lowest PSCs bottom (LC) to the superior tricuspid valve; correlation index of pace-mapping in PSCs and RVOT region below the PV; earliest local activation time in PSCs and RVOT region below the PV; shortest perpendicular distance between ideal ablation sites (with earliest activation and good pace-mapping) in RVOT region below the PV and the final successful ablation site in PSCs.

In this study, ablation was preferentially performed at the ideal target in the PSCs (with the earliest activation and good pace-mapping). Unless necessary, the RVOT region below the PV was not targeted in any patients. Ablation was performed using power of 30 to 35 W (32.4 ± 4.7 W) and irradiation rate of 17 to 20 mL/min for 60 to 120 seconds. The successful ablation site was defined as that rendering clinical VAs noninducible with isoproterenol after at least a 30-minute waiting period. All procedures were performed by 3 experienced operators.

![Figure 1: Top left: Right ventricular angiography showing the location of the ablation catheter. Top right: Anatomic CARTO map of the right ventricle and RVOT in the posteroanterior view. Yellow tag represents the location of His. Note that the target site was at the posterior and inferior ends of the RVOT, just above the tricuspid annulus. Bottom: Simultaneous recordings of 12-lead ECG and the ablation catheter (ABLd). Local activation of the ablation catheter precedes QRS onset by 32 ms during the premature ventricular contraction. RVOT = right ventricular outflow tract.](image)
Clinic ECGs and 24-hour Holter monitoring were performed every 2 months for the first year and every 6 months thereafter. Transthoracic echocardiography was performed the day after the procedure and at the 3-month follow-up visit. Enhanced coronary artery computed tomographic scan or angiography was performed 6 months after the procedure.

Statistical analysis
All continuous variables are expressed as mean ± SD, and statistical differences were evaluated using the Student t test or the Mann–Whitney U test, depending on data distribution. The χ² test was used for analysis of categorical variables. P <.05 was considered significant. Statistical testing was performed using with SAS software version 9.2 (SAS Institute, Cary, NC).

Results
Clinical characteristics
Frequent PVCs or short runs of ventricular tachycardia occurred spontaneously in 78 patients. Isoproterenol infusion
was administered to provoke VAs in the remaining 12 patients. One female patient with dextrocardia and situs inversus presented with frequent RVOT-type PVCs and no other heart disease. Baseline patient characteristics was listed in Table 1.

### Electrophysiological mapping and RFCA

Right ventriculography and/or pulmonary arteriography were performed in all 90 patients to determine the precise location of the PSCs, PV, and ablation catheter. The measured shortest perpendicular distance from the lowest PSC bottom (LC) to the superior tricuspid valve was 1.87 ± 0.64 cm (range 1.4–2.5 cm).

In 5 cases the final successful ablation site was at the aortic coronary cusps (3 right coronary cusp, 2 anterior wall between left and right coronary cusps). In another 4 cases, elimination of the VAs could only be achieved at the most posterior and inferior ends of the RVOT just above the tricuspid annulus (1 at the septal aspect and 3 at the lateral aspect of this region) (Figure 1).

For the remaining 81 patients, RFCA in the PSCs resulted in elimination of VAs without any additional ablation in the RVOT region below the PV. In these patients, when first mapping in the RVOT region below the PV, earliest activation was at the posteroseptal region in 33, midseptal in 18, anteroseptal in 11, anterior free wall in 7, middle free wall in 6, and posterior free wall in 6. The earliest bipolar electrogram preceded the onset of the QRS complex by 25.4 ± 12.6 ms. At these sites, the presence of QS wave in the unipolar electrogram was found in 58% of patients (47/81). Using the PaSo module to compare the pacing beats and the VAs template, the highest correlation index in the RVOT region below the PV was 0.934 ± 0.426. When subsequently mapping in the PSCs, the earliest activation of VAs was identified at the RC in 19 patients (23.5%), LC in 24 (29.6%), and AC in 38 (46.9%) (Figure 2). On bipolar recording, the target potential in PSCs preceded QRS complex onset by 35.7 ± 12.7 ms, which was greater than that for the RVOT region below the PV (25.4 ± 12.6 ms). The mean difference in the time of earliest activation between the PSC and the RVOT region below the PV was 10.6 ± 5.4 ms. All of the unipolar recordings at the target sites in PSCs showed QS morphology, a finding that was less common in the RVOT region below the PV (Figure 3). In 56.8% of patients (46/81), a blunt far-field activation followed by a sharp near-field potential was observed at the target sites in PSCs during sinus rhythm. The relationship between the 2 signals was reversed during the VAs. The recording of the earliest sharp potential could predict successful ablation in 100% of patients (46/46). These sharp potential all became diminished after ablation. In 43.2% of patients (35/81) at the successful target sites in PSCs, the sharp potential was not recorded. At 11 sites where the initial ablation attempt was not successful, only 1 (9.1%) could record this characteristic sharp potential. While mapping in the RVOT region below the PV, this sharp potential was observed in only 8.6% of patients (7/81), but we did not attempt any ablation there. Pace-mapping was obtained in all 81 patients in PSCs (mean lowest pacing output 7.2 ± 3.3 mA). Good pace-mapping (≥11 of 12 matches between the paced and spontaneous VAs QRS complexes) could be obtained at successful ablation sites in PSCs in 96.3% of patients (78/81). The mean correlation index was 0.978 ± 0.214, which was

| Table 2 | Comparison of mapping parameters between PSCs and RVOT region below the PV |
|-----------------|-----------------------------|-----------------------------|-----------------------------|
|                | PSCs | RVOT region below the PV | P value |
| Highest correlation index of pace-mapping | 0.978 ± 0.214 | 0.934 ± 0.426 | .023 |
| Earliest activation time (ms) | 35.7 ± 12.7 | 25.4 ± 12.6 | .035 |
| Presence of QS wave in the unipolar electrogram | 100% | 58% | .014 |
| Incidence of near-field sharp potential at the best mapping sites | 56.8% | 8.6% | <.001 |

Values are given as mean ± SD or %, unless otherwise indicated.
PSC = pulmonary sinus cusp; PV = pulmonary valve; RVOT = right ventricular outflow tract.
higher than that of the RVOT region below the PV. The mean difference of the highest correlation index between the PSCs and the RVOT region below the PV was 0.045 ± 0.326. The major differences of mapping parameters are listed in Table 2. The mean distance from ideal ablation sites (with earliest activation and best pace-mapping) in the RVOT region below the PV to final successful ablation sites in the PSCs was 14.5 ± 9.6 mm (range 4–26 mm) (Figure 4). Interestingly, there were 19 VAs with earliest activation at the RVOT free wall below the PV, which could all be eliminated by ablation in the RC.

Of these successful ablation sites, 72 were at the bottom of the PSCs, including the patient with dextrocardia and situs inversus (Figure 5); the remaining 9 were located 3.8 ± 2.2 mm beyond the PSC bottoms. The number of radiofrequency (RF) lesions ranged from 2 to 8 (mean 4.3 ± 2.7) in these patients. After the initial ablation attempts, the VAs were either diminished or remained in the same morphology (at 11 ablation sites). The change of VA QRS morphology after the initial failed ablation was not observed in any patient.

**ECG characteristics for PSC VAs**

RC VAs had a higher R-wave amplitude in lead I and more common notching of the R wave in the inferior leads. Because of heterogeneous QRS morphology, there were no discrete ECG findings that could distinguish between VAs in the LC and AC.

**Follow-up**

VAs recurred in 3 patients after ablation in the PSCs, and 2 underwent successful repeated ablation in the same PSCs 3 months after the index procedure. All the remaining 87 patients had freedom from VAs after a single procedure during 15.2 ± 9.5 months of follow-up. The single procedural success rate was 96.7%. No complications occurred during the ablation procedure or follow-up. Worsening of tricuspid or pulmonic regurgitation and new onset of coronary artery stenosis were not found in any patient in this group.

**Discussion**

**Major findings**

Traditionally, most idiopathic RVOT VAs have been thought to originate from below the PV. Although there have been reports of VAs mapped and ablated within the PA, supravalvular arrhythmia foci have been considered uncommon. The report by Liao et al provided detailed information on anatomic, ECG, and electrophysiological characteristics of VAs successfully eliminated via ablation from PSCs. Their cohort of 24 patients was derived as a special category of patients with idiopathic RVOT VAs from a larger series of 244 patients presenting with left bundle inferior-axis VAs.

To our knowledge, this is the first prospective study analyzing the incidence of idiopathic RVOT VAs of PSC origin. In this study using pulmonary arteriography, ablation within the PSCs effectively eliminated 90% (81/90) of unselected idiopathic RVOT-type VAs with favorable outcomes beyond 1 year. The latter findings would argue for a conceptual revisit of the paradigm of treatment of idiopathic RVOT VAs in favor of PSC mapping and ablation as a possible preferential choice.

**Anatomic considerations**

The distal RVOT is formed by the junction of the muscular infundibulum and the pulmonic valve. The semilunar valvular leaflets attach at the sinotubular junction, which separates the PSCs from the tubular component of the pulmonary trunk. Thus, the PSC wall is supported throughout its circumference by the muscular right ventricular (RV) infundibulum. The RV musculature can extend distally into the PSCs in a sleevelike manner, and the presence of ventricular myocardial extensions beyond the pulmonic ventriculoarterial junction were documented by Gami et al in 74% of 602 autopsy specimens from subjects without clinical VAs. In their study, myocardial extensions were noted above the pulmonary RC in 60%, LC in 52%, and AC in 45% of their cases. Liu et al showed the in vivo presence of myocardial extension beyond the PV in 92% of controls and 88% of patients with RVOT VAs. In their study, by using intracardiac echocardiography, 46% of RVOT arrhythmia foci were localized beyond the valve in the pulmonary artery. Because there is no fluoroscopic landmark for identifying the PV, we can deduce that many of the successful target sites traditionally localized to the RVOT region were, in fact, beyond the valve in the pulmonary artery. Myocardial extension into the PSCs in humans may be ubiquitous, resembling the pulmonary vein myocardial sleeves in patients with atrial fibrillation. These ventricular myocardium extensions may serve as the true origins of presumed RVOT VAs.

**Mapping and ablation in PSCs**

The RVOT is routinely mapped by catheter advancement in the anterograde direction (from RV to PA). Liao et al
provided an important new technique to facilitate catheter mapping of PSCs. As in this study, the PSCs were engaged retrogradely by passing the ablation catheter through the pulmonic valve and withdrawing the D-curved loop, using pulmonary arterial angiography as an important tool to guide catheter positioning into the respective PSCs.

The potential at the successful ablation sites in the PSC was earlier than at the earliest activation sites in the RVOT region below the PV. A sharp late potential was often evident in the PSC target site during sinus rhythm and became the early potential during VAs. The sharp potential diminished after ablation, whereas most of the local electrograms at the earliest sites in the RVOT region below the PV exhibited a single component electrogram. These findings may indicate that the sharp potential recorded in the PSCs reflects the near-field activation of the myocardial extension into the PSC.

Although good pace-mapping match could be obtained from multiple sites under the PV in patients with RVOT VAs, the probability of obtaining the best pace-mapping would increase with decreasing distance of the pacing site from the site of VA origin. Liao et al. considered that only one-half of the patients had a pace-map match from the successful PSC ablation sites. However, in our series, pace-mapping and activation mapping were highly correlated. Once the earliest activation site in the PSCs was identified, pace-mapping at this site produced an excellent pace-mapping match in most patients (96.3%), which was better than that of the RVOT region below the PV.

Figure 5  Fluoroscopy, electroanatomic map, surface ECG, and intracardiac recordings from a patient with dextrocardia of complete situs inversus and frequent PVCs. A, B: Ablation catheter (ABLd) at the successful ablation site in the left anterior oblique (LAO) and right anterior oblique (RAO) projections. Note the right position of the cardiac apex due to complete situs inversus. The ablation catheter is located at the corresponding position of the left cusp (LC) in normal heart. C: Shortest perpendicular distance measured from the successful ablation site (pink tag) in the LC to the ideal mapping site in the right ventricular outflow tract below the pulmonic valve (blue tag) was 13 mm. D: Twelve-lead ECG in which limb and precordial leads were recorded in mirror-image fashion. At the target site, 2 components were recorded in sinus rhythm, with the sharp near-field component (red arrows) following the blunt far-field component. A reversed relationship between both components during PVCs was present. PVC = premature ventricular contraction.
Variations in QRS morphology of VAs after the initial catheter ablation in the RVOT VAs was not rare and often required more RF applications for final cure. However, in the present study, QRS morphology change after ablation did not occur in any patients. Certain distances from the ideal ablation sites in the RVOT region below the PV to the final successful ablation sites in the PSCs were always found. We hypothesized that there might exist a preferential conduction pathway between the origin in the PSCs and the exit sites in the RVOT. During VAs, activation would have conducted from the PSCs to the RVOT through this pathway. The RVOT exit site may be narrow in some patients, which may account for the complete elimination of VAs by only a single RF application in the RVOT below the PV. However, when the exit site is broad or alternative pathways exist, insufficient ablation might result in a change in VA QRS morphology.

A free-wall site of origin has been reported in 20%–30% of patients with RVOT VAs. Wider QRS duration and notching of the R wave in the inferior leads was associated with RVOT free-wall origin. Ablation in the free wall of the RVOT carried higher risk for cardiac tamponade than in the septal region. In the present series, 19 cases had the ECG features and earliest activation at the RVOT free wall. All of these VAs could be safely eliminated by ablation in the RC. Anatomically, the RC attaches to the free lateral wall of pulmonary conus in the RV. Because the orientation of the ablation catheter was downward when ablating in the bottom of the RC instead of pushing against the free wall of the RVOT using the conventional method, the former method may replace the latter because of safety considerations.

**New concept in ablation of idiopathic RVOT VAs**

The RVOT region is defined superiorly by the PV and inferiorly by the superior margin of the RV inflow tract (tricuspid valve). The conventional electrophysiological description of the RVOT has consisted of the opposing planar septal and free wall, which were further divided into anterior, medial, and posterior regions. Most RVOT VAs were thought to originate from myocardium within the first 1–2 cm beneath the PV. In the present study, mapping and ablation in the PSCs resulted in successful results in most unselected cases, thereby confirming that the junction of the muscular infundibulum and the pulmonary trunk (PSCs) might be the true origin and ideal ablation site for RVOT VAs. Apart from the 5.6% of patients (5/90) in whom the VA origin was located in the left ventricular outflow tract, the only exceptions in which VAs in the PSCs could not be eliminated were 4 cases (4.4%) in whom the final successful ablation site was at the junction of the RVOT and tricuspid annulus. We deduce that only the boundary between 2 anatomic structures, that is, either the distal part (PSCs) or inferior end (RVOT and tricuspid annulus junction) of the RVOT, was the true origin of so-called RVOT VAs. The region between the 2 parts, which is the focus of conventional mapping and ablation, might actually be the exit or the preferential insertion of the conduction pathway.

**Study limitations**

The present study had several limitations. First, intracardiac echocardiography was not used to further identify catheter location. Second, we did not systematically map closely related structures, such as aortic sinuses, left ventricular outflow tract, and coronary venous system. Third, it may be argued that at least in some patients, PSC ablation simply provides means to ablate the RVOT apex with greater catheter stability and contact rather than by eliminating an arrhythmic source within the cusp per se. Although this possibility cannot be ruled out with the available information, the preferential application of PSC ablation in these patients would still provide a new, reliable, and more efficient methodology. Most importantly, a randomized, prospective study to compare the PSC mapping strategy and conventional mapping in RVOT regions is warranted to confirm the true benefit of the new method reported in this study.

**Conclusion**

In the present single-center, prospective study, RVOT-type VAs could be located and eliminated in PSCs in most unselected patients, suggesting that mapping and ablation in PSCs...
with a reversed U curve would be considered the preferential choice in these patients.

References


