Catheter ablation of ventricular arrhythmias originating from the sinus of valsalva: the reminder from the mapping or ablation in the lower right ventricular outflow tract

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Abstract

Background Ventricular arrhythmias (VAs) originating from ventricular outflow tracts can possess a high similarity of QRS configuration resulting in an inaccurate localization, while the reminder of mapping or ablation in the lower right ventricular outflow tract (RVOT) commonly provide the preferred transformation strategy. Methods We retrospectively analyzed the total of 958 patients who were referred for radiofrequency (RF) ablation of VAs in our center. VAs with the sinus of valsalva (SoV) origins were enrolled. Results A total of 120 consecutive patients (mean age 45.0 ± 15.5 years) undergoing the ablation of VAs arising from the left-sided ventricular outflow tracts were included, with 55 (45.8%) female. All patients had a QRS morphology of the LBBB pattern and an inferior axis, with the mean earliest ventricular activation (EVA) of target site of 34.9 ± 8.8ms. 37 (30.8%), 60 (50.0%), and 23 (19.2%) patients obtained the successful RF ablation at the right sinus cusp (RCC), left sinus cusp (LCC), and the commissure of RCC and LCC (R-LCC), respectively. 62 (51.7%) target sites of SoV could record a high-frequency potential. Moreover, 25 (20.8%) patients were continuously recorded an early ventricular activation in the lower RVOT and achieved the elimination of VAs in SoV. Conclusions VAs originating from the SoV could show a low specificity of QRS morphology mimicking the RVOT-like ECG feature. An early ventricular activation mapped in the lower RVOT or RF ablation with poor response likely demonstrated the VAs originating from the SoV, especially the RCC.

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Conclusions

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Key words : catheter ablation; ventricular arrhythmias; sinus of valsalva; right ventricular outflow tract

1 | Introduction

Ventricular arrhythmias (VAs) originating from the sinus of valsalva (SoV) approximately account for 17% of the outflow-tract VAs in patients without overt structure heart disease [1]. Moreover, long-standing frequent VAs can result in the arrhythmia–induced cardiomyopathy irrespective of arrhythmic symptoms [2]. Radiofrequency (RF) ablation has been acknowledged as a safe and preferred therapy for eradicating the drug-refractory outflow-tract VAs[3-5], with a success rate of 80-95%[1, 3, 6]. Nevertheless, VAs origins arising from the right or left ventricular outflow tract sometimes can exhibit a similar QRS configuration of LBBB pattern with an inferior axis[4], especially VAs originating from the SoV could exhibit the trivial electrocardiographic difference from VAs arising from the lower RVOT. On the other hand, among the VAs with no or limited response to RF ablation in RVOT, VAs were commonly demonstrated and eliminated in the

SoV [7]. To the best of our knowledge, the anatomy of the lower RVOT and SoV is in close proximity[4]. Additionally, the preferential conduction pathways always have the effect on the atypical formation of the QRS morphology [8].

The purpose of this study sought to investigate the electrocardiographic and electrophysiologic characteristics of VAs originating from the SoV adjacent to the lower RVOT.

2 | Methods

2.1 |Patient Characteristics

Among the total of 958 patients who underwent the RF ablation of VAs between January 2014 and December 2019 in our center, 120 cases of VAs originating from the SoV were consecutively enrolled in this retrospective study. All patients had the drug-refractory palpitations or symptomatic discomforts. Transthoracic echocardiography or coronary angiography demonstrated the absence of the structural heart diseases (e.g., rheumatic cardiac disease, situs inversus, Tetralogy of Fallot, dilated or hypertrophic cardiomyopathy, dilated left ventricle [?]50 mm, severe coronary stenosis, etc.). Patients with the following characteristics were excluded (i.e., RF ablation history, aortic bivalve deformity, aortic valvular replacement, congenital heart diseases, and non-SoV origins). Before the procedure, each patient had a minimum discontinuance of five-lives of anti-arrhythmias (AADs). All patients gave the written informed consent. This study was approved by the institutional ethics committee at the Chinese Academy of Medical Sciences Fuwai hospital.

2.2 | Pre-Procedural Preparation

Before the vessel puncture, two physicians identified the VAs with a QRS of left bundle branch block (LBBB) and an inferior axis. Upon a local anesthesia, an 8-F sheath was inserted into the right femoral vein or artery to construct the venous or arterial access. Intravenous heparin was administered to warrant the activated clotting time greater than 250s. When few VAs occurred at the beginning of the procedure, intravenous isoproterenol (3-5 ug/kg. min) or burst ventricular pacing (at an output of 0.5mA to 20mA) with a frequency of 500ms (not less than 300ms circle length) was used to induce the stable VAs. Patients without spontaneous and inducible VAs would be referred for a close follow-up or conservative treatment.

2.3 | Mapping and Catheter Ablation

The preliminary judgment about the site of origin were on the basis of surface 12-Lead ECG of VAs. An 8-F sheath was inserted into the right femoral vein if the VAs with the precordial V3 transition (or late to lead V3). Once the precordial transition of VAs localized at Lead V2 or much earlier with a tall R-wave, considering the probable left-sided origin, the right femoral artery would be inserted into an 8-F sheath. Mapping study used a 8-F (Interelectrode spacing 2-5-2 mm) irrigated ablation catheter (Navistar(r)Thermcool(r), Biosensewebster, Diamond, CA, USA) at an infusion speed of 2 ml/min (cold saline) to reconstruct the electroanatomic geometry of the right or left ventricular outflow tract, including the pulmonary sinus cusp (PSC), on the three-dimensional Carto system (Carto, Biosensewebster, Diamond, CA, USA). On the other hand, the mapping protocol was used to map the earliest activation timing of origin, and the site of earliest ventricular activation (EVA) timing preceding the onset of surface QRS was confirmed the target site of VAs focus. The site of EVA was tagged for the subsequent RF ablation. Meanwhile, the angiography of PSC or SoV was performed to distinguish the anatomic structure. Importantly, during the mapping in the RVOT, once the consecutively early ventricular activation was demonstrated at the proximal electrode of ablation catheter ($ABL\text{-}_p$) or the energy delivery in the distal electrode of ablation catheter ($ABL\text{-}_d$) at the RVOT could not diminish and eliminate the VAs with a short-time recovery, the mapping study would be transferred to SoV or left ventricular outflow tract (LVOT) via a retrograde artery technique to map the EVA. An electroanatomic geometry of SoV or LVOT was routinely reconstructed on the Carto system (Carto, Biosense Webster, Diamond, CA, USA). The angiography was performed to affiliate the navigation of the anatomic structure of SoV or LVOT. The purpose of the transformation strategy was to decrease the null energy delivery or local mapping for enhancing the mapping efficiency and avoiding the occurrence of procedure-related complications. Pacing mapping strategy was used to map the infrequent VAs which were inability to be induced stably even if administering the intravenous isoproterenol. Pacing QRS with at least 11 leads matching to the QRS morphology of VAs was considered to be the perfect match.

RF energy delivery was started with a 25-30 Watts (Infusion speed of cold saline at a 17 ml/min, Temperature-control model). The acceleration or decrement of the VAs frequency, the change of PVC coupling interval, or the alike QRS morphology resulting of discharge commonly was suggestive to the target site of origin. Thereby, RF application delivery time should extend to 60s or 90s for obtaining the sustained lesion. An additional discharge was at the physician's discretion according to the individual patient. The clinical VAs disappeared or were inability to induced by burst ventricular pacing, intravenous isoproterenol, or repeated valsalva maneuver more than 15 minutes after RF ablation was considered to achieve an acute successful end-point. All femoral artery punctures were used a manual compression for hemostasis at least 20 minutes at the end of the procedure.

2.4 |Anatomic Computerized Tomography Image Measurements

Fifty results of cardiac computed tomography (CT) scans deriving from the patients who were excluded the diagnosis of aortic dissection were reviewed for studying the anatomic structure between the RVOT and SoV. The distance of the SoV from RVOT was quantified by two physicians using the cardiac CT angiography technique (Philips Brilliance iCT*256, Holland) with a method of retrospective cine ECG-gated multi-slice CT scan. After the injection of contrast agent, CT scan was achieved during the 75% of cardiac diastolic period. In the sagittal and coronal plane, the plane of SoV with the widest diameter close to the RVOT was used to measure the distance value, while the measurements were calibrated in the adjusted transverse plane.

2.5 | Data statistical analysis and follow-up

Continued variables are expressed as mean +- SD, while the categorical variables are expressed as number with percentage. Comparison of two or more groups would undergo the test of normality or homogeneity of variance. Continuous variables were analyzed with t -test or nonparametric t -test. Categorical variables were analyzed with the Fisher's test or Chi-square test. All patients were scheduled for the outpatient visit every 3 months to assess the ECG and 24-hour Holter monitoring. $P < 0.05$ was considered statistically significant.

3 | Results

3.1 | Study population characteristics

A total of 120 consecutive patients (55 female, mean age 45.0 +- 15.5 years) with monomorphic VAs originating from the SoV were included, with the mean symptomatic duration of 16.9 +- 12.5 months. Clinical VAs consisted of 109 premature ventricular contractions (PVCs), 6 PVCs with non-sustained ventricular tachycardias, and 5 ventricular tachycardias. 7 (30.8%), 60 (50.0%), and 23 (19.2%) patients were successfully ablated the VAs at the RCC, LCC, and R-LCC, respectively. Moreover, 25 (20.8%) patients had the electrophysiological phenomenon of early ventricular activation of ABL-p recording preceding that of ABL-d during the RVOT mapping, while RF ablation of RVOT with failure. 13 (10.8%) patients were mapped with an early ventricular activation in the PSC but with RF failure. Finally, the VAs were successfully ablated in SoV. Of the 60 patients with LCC origins, 3 patients underwent the successful RF ablation of VAs below the SoV corresponding to the site of LCC. Additionally, 163 patients with the following diseases (i.e., dilated left ventricle or cardiomyopathy diseases, severe coronary stenosis, RF ablation history, aortic bivalve deformity, aortic valvular replacement history, congenital heart diseases, non-SoV origins, etc.) were excluded. No complications occurred throughout the procedure. The process of inclusion and exclusion criteria is shown in **Figure 1** .

3.2 | Electrocardiographic and Electrophysiologic Characteristics

All patients had a QRS morphology of LBBB pattern and an inferior axis. The transition zone (TZ) index of VAs arising from the three sites of SoV had the certain extent of proportion of greater than zero. V2 transition ratios of LCC origin VAs were greater than that of VAs arising from the RCC and R-LCC (P¡0.05). R-wave duration index of VAs originating from the SoV in Lead V1 or V2 had no statistical difference (P >0.05), while the R/S-wave amplitude of RCC VAs in Lead V1 were significantly lower than the other sites of VAs (P¡0.05). The mean V2S/V3R index of RCC VAs obviously exceeded that of the other two sites of origin (P¡0.05). VAs with the RCC origins had more narrower R-wave deflection interval (mean internal 65.7 +- 18.6ms) in Lead V3 comparing with VAs arising from the LCC and the R-LCC (mean internal 83.3 +- 19.1ms and 80.9 +- 28.1ms, P¡0.05). VAs arising from LCC origins in Lead I had the lowest R-wave amplitude (P¡0.05). The ratio of the R-wave amplitude in Lead II and III (III/II ratio) and the ratio of the S-wave amplitude in Lead avL and avR (avL/avR ratio) had no statistical significance (P >0.05). On the other hand, 17 (45.9%) VAs originating from the RCC exhibited the maximum proportion of an early ventricular activation of ABL-p at the lower RVOT. The left-sided VAs seemed to show a high proportion of the recording rate of high-frequency potentials. In addition, there was no statistical significance found in the following characteristics (P >0.05) (i.e., QRS Duration, III/II R-wave amplitude ratio, avL/avR QS-wave amplitude, earliest ventricular activation, and RF application). The electrocardiographic and electrophysiologic parameters are summarized in**Table 1** .

3.3 | Subgroup Analysis of Patients with SoV Origins

25 (20.8%) patients displayed an early ventricular activation recorded by the ABL-p ahead of that of ABL-d (mean early timing 16.6 +- 5.2ms) during the RVOT mapping (**Figure 2: A, B, and C**). All these patients had a QRS morphology of LBBB pattern and a tall R-wave in inferior leads, while 5 patients with RCC origins and 1 patient with the R-LCC origin in Lead III had an S-wave. Lead I dominantly displayed an R-wave morphology of short or "M" pattern R-wave, except that 2 PVCs originating from LCC had a terminal S-wave. The mean EVA of the lower RVOT was 32.3 +- 8.8ms, but RF ablation without success. After the transformation to SoV, 17 (68%), 3 (12%), and 5 (20%) patients obtained the successful RF ablation of VAs in the RCC, LCC, and R-LCC of SoV, respectively. On the other hand, the R-wave amplitude of Lead I, Transition Zone, and EVA were above that of group A (0.3 +- 0.2 *vs*0.1 +- 0.1mV; P¡0.001, 2.6 +- 0.6 *vs* 1.9 +- 1.0 ; P¡0.01, and 38.6 +- 8.6 *vs* 34.1 +- 8.8ms ; P¡0.05, respectively). Moreover, the value of R-wave duration index, R/S amplitude index, R-wave deflection interval (V_3) in group B were significantly greater than those of them in group A (all P¡0.05).The detailed data are summarized in **Table 2** .

3.4 | Anatomic results of the RVOT and SoV

RCC localized close proximality to the lower RVOT, while the R-LCC and LCC localizing at a relatively high level corresponding to the lower RVOT (**Figure 3**). Cardiac CT angiography scan found that the mean closest distance of RCC from the anterior RVOT was 1.9 +- 0.4 mm, while RCC had the majority of proportion adjacent to the RVOT, including the upper RVOT and lower RVOT. The mean distance of LCC from the PSC was 1.7 +- 0.4 mm. Moreover, the RCC localized at the level of RVOT, and LCC corresponded to the level of PSC at most of the time (**Figure 4 C**). Furthermore, 12 (10%) patients had a cardiac rotation resulting in the variant anatomy of RCC or LCC. Of the 12 patients, 7 patients displayed the RCC corresponding to the PSC over the RVOT (with a mean closest distance of 1.6 +- 0.3 mm) (**Figure 4 A**) and 5 patients with the LCC corresponding to the RVOT (mean closest distance of 1.8 +- 0.5 mm) (**Figure 4 B**). The sectional anatomy of CT angiography is shown in **Figure 4** .

4 | Discussion

4.1 | Main findings

VAs originating from the SoV could show a low specificity of QRS morphology reducing the accuracy of the localization of site of origin. An early ventricular activation mapped in the lower RVOT or RF ablation with poor response likely demonstrated the VAs originating from the SoV, especially the RCC. The high-frequency potentials recorded in SoV could be preferentially chosen as the target of RF ablation.

4.2 | Electrocardiographic Characteristics and Predictive Algorithms

To the best of our knowledge, VAs originating from the SoV and RVOT always have the demonstrated electrocardiographic differences. Yamada et al[1] reported that a III/II ratio of >0.9 predicted a LCC origin (with 80.0% positive predictive accuracy and 100% negative predictive accuracy), while the VAs with a LCC origin had a greater III/II ratio than those of with a RCC origin. Ouyang et al [4] found that R-wave duration index [?]0.5 and R/S-wave amplitude [?]0.3 in Lead V1 and V2 could efficiently suggest the VAs with the SoV origin. Yoshida et al[9] found that the cardiac rotation-corrected transitional zone (TZ) index <0 was the useful marker for differentiating RVOT origin from SoV origins. Nevertheless, in the present study we found that the conventional ECG algorithms seemed to exist the limitation on the preprocedural localization of VA origins. First, the R-wave duration index in VAs with the RCC origins were lower than 0.5, especially the 25 patients with an early ventricular activation of ABL-p in the lower RVOT. On the other hand, the III/II ratio in the group B patients (**Table 2, group B**) could not reach the value of 0.9; the Transition Zone Index of left sided VAs were not always less than zero. Moreover, this phenomenon actually accounted for a certain percentage of the total cases contrast to the findings reported by Yoshida et al [9].

In addition, although VAs in the group B (**Table 2**) were confirmed the SoV origins, the conventional ECG algorithms could not exhibit the ideal properties of localization for these group of VAs possessing the feature of early ventricular activation recorded by ABL-p at the lower RVOT (**Figure 2: A, B, and C**). Of interest, the electrocardiographic characteristics of these VAs were more likely to be the RVOT VAs (e.g., Transition zone, Transition zone index, V2S/V3R index, R-wave deflection interval of lead V3, III/II ratio). Therefore, in our perspective, once an early ventricular activation was mapped at the lower RVOT or the EVA in RVOT but with RF failure, the preferred mapping region should be considered to transfer to the SoV, especially the RCC or R-LCC region, irrespective of the morphology of QRS complex.

4.3 | Anatomic consideration

Anatomically, the aortic root situates at the center of heart and localizes posteriorly adjacent to RVOT [10], while the ventricular septum connects the RVOT and SoV[5]. The aorta is joint to the left ventricular ostium with the membranous attachments, including the most anterior attachment of RCC and the lateral and posterolateral attachment of LCC[11]. Moreover, the RVOT gradually rises from the anteroinferior level to the superior leftward site of SoV, while the lower RVOT spatially is in close proximity to the RCC[4], R-LCC [12], and corresponds to the anteroinferior division of LCC (**Figure 3: B, C, D, E, and F**). Similar to the aforementioned anatomic findings, the CT scan in the present study found that RCC was most frequently apposition to the lower RVOT, while LCC was mostly apposition to the upper RVOT or the lower pulmonary trunk beyond the PSC (**Figure 4: A, B, and C**). But sporadically, RCC straddled the PSC apposition to the pulmonary trunk and LCC descended to the RVOT straddling on the PSC (**Figure 4: A and B, respectively**).

In addition, the histological distribution of the left ventricular myocardium (i.e., RCC with the relatively more myocardial attachment compared to LCC) extending into SoV resulted in the diverse electrocardiographic and electrophysiologic presentation of VAs originating from the SoV [11]. Although our research did not reproduce the aforementioned findings, the recording rate of reversal potential in RCC and the high-frequency potentials recorded in LCC corresponded to the specific pathology nature between left ventricular and SoV. Hereby, the structural complexity based on the histological and anatomic morphology commonly generated the trivial variation of QRS configuration of VAs arising from the SoV.

4.4 | Preferential Conduction of VAs

The ECG prediction algorithms differentiating the VAs originating from the RVOT or SoV are not invariably accurate [13]. Theoretically, the preferential transmural conduction of anisotropic myocardium could result in the differences of surface potentials[14]. Moreover, Stavros et al[15] developed that the basal septum existed an obvious preferential conduction. Yasuhiro et al[16] found that the change of preferential conduction exits resulted in the QRS morphology shift during the RF application, and the site of EVA did not mean the very site of origin. Thereafter, the preferential conduction and multiple exits were further demonstrated the existing between the LVOT and RVOT[17]. Yamada et al [8]validated that approximately 25% VAs patients with SoV origins exhibited the preferential conduction of breakout sites resulting in the RVOT-like

QRS morphology. Storey et al [18]reported a case of VT origin originating from the SoV indicating two breakout sites of early ventricular activation in RVOT and the ventricular septum respectively. Similar to the above-mentioned findings, in the present study 25 (20.8%) patients with SoV origins were mapped an early ventricular activation in the lower RVOT (**Figure 1**), while VAs with RF failure in RVOT were successfully eliminated at the SoV. In addition, 13 (10.8%) patients with an early ventricular activation in the PSC finally achieved the successful ablation at the SoV and 3 patients had a successful ablation below the SoV. Therefore, it was reasonably believed that parts of VAs with the SoV origins (i.e., RCC, LCC, and L-R commissure) could show the preferential conduction or distinct exits mimicking the so-called VAs arising from the RVOT.

5 | Conclusions

VAs originating from the SoV could show a low specificity of QRS morphology mimicking the RVOT-like ECG feature. An early ventricular activation mapped in the lower RVOT or RF ablation with poor response likely demonstrated the VAs originating from the SoV, especially the RCC.

6 | Limitations

The limited sample size of the present study reduced their generalizability of the elucidation of the SoV VAs. First, the majority of VAs originating from the LCC in the present study were just mapped the SoV which avoided the findings of other preferential conductions, including the other conduction exits, at the RVOT or PSC. On the other hand, owning to consider the relatively-unstable catheter-touch, pace mapping just was applicated on the limited cases resulting in the reduction of evidence between site of origin and RF target. Third, the judgement of target site of origin depending on angiography of SoV might exist some extent of bias from the real anatomy. Hereby, the further electrophysiological trials from the high-density mapping and the assistance of multiple mapping catheter were warranted to improve the above-mentioned shortness.

7 | Acknowledgement

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8 | Author contributions(I) Conception and design: Zhong-Jing Cao, Jian Ma, Xiao-Gang Guo; (II) Administrative support: Shu Zhang, Jian Ma; (III) Provision of study materials or patients: Jian Ma; (IV) Collection and assembly of data: Zhong-Jing Cao; (V) Data analysis and interpretation: Zhong-Jing Cao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Figure Legends

Figure 1 Flowchart of Inclusion and Exclusion

VAs, ventricular arrhythmias; ABL-p, the proximal electrode of ablation catheter; ABL-d, the distal electrode of ablation catheter; RVOT, right ventricular outflow tract; RF, radiofrequency; EVA, earliest ventricular activation; PSC, pulmonary sinus cusp

Figure 2 Mapping Catheter in the RVOT and Successful RF Target

A, B, and C represent the surface ECG and intracardiac electrograms and mapping in the RVOT, including the lower RVOT region. When mapping in the RVOT, the ventricular activation timing of ABL-$_{p}$recording continuously preceded that of the ABL-$_{d}$recording. $\Delta V_{ABL\text{-}p\text{-}ABL\text{-}d}$ represents the difference value.

D, E, and F represent the surface ECG and intracardiac electrograms of target sites. V-QRS represents the earliest ventricular activation timing. The arrows showed the deviations of the recording ventricular activation timing of ABL. RCC, right coronary cusp; LCC, left coronary cusp; RCC-LCC, the commissure of the right coronary cusp and left coronary cusp

Figure 3 Three-dimensional Reconstruction of Cardiac CT Angiography

The cardiac three-dimensional reconstruction showed the different positional relationship of the RVOT and SOV. RCC, right coronary cusp; LCC, left coronary cusp; NCC, non-coronary cusp; PSC, pulmonary sinus cusp; RV, right ventricle; LV, left ventricle; RVOT, right ventricular out-flow tract; RCA, right coronary artery; LAD, left anterior descending; LCX, left circumflex artery; AP, anteroposterior position; PA, posteroanterior position; RL, right lateral position; LL, left lateral position; RAO, right anterior oblique; LAO, left anterior oblique.

Figure 4 The position relationship between RVOT and SOV in Cardiac CT Angiography.

A: RCC is adjacent to the RVOT and PSC, while LCC rotated to the posterosuperior position. B: RCC is close to the RVOT away from the PSC, while LCC rotated to adjoin the RVOT. C: RCC and LCC are adjacent to the RVOT and PSC with a 1:1 matching anatomy. The red arrows direct the closest distance between the SOV and RVOT or PSC in figure A, B, and C. The coronal and sagittal plane are used to calibrate the SOV (i.e., RCC and LCC) adjusting to the widest diameter plane.

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