Impact of earliest activation site location in the septal right ventricular outflow tract for identification of left vs right outflow tract origin of idiopathic ventricular arrhythmias

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BACKGROUND The earliest activation site (EAS) location in the septal right ventricular outflow tract (RVOT) could be an additional mapping data predictor of left ventricular outflow tract (LVOT) vs RVOT origin of idiopathic ventricular arrhythmias (VAs).

OBJECTIVE The purpose of this study was to assess the impact of EAS location in predicting LVOT vs RVOT origin.

METHODS Macroscopic and histologic study was performed in 12 postmortem hearts. Electroanatomic maps (EAMs) from 37 patients with outflow tract (OT) VA with the EAS in the septal RVOT were analyzed. Pulmonary valve (PV) was defined by voltage scanning after validation of voltage thresholds by image integration. EAM measurements were correlated with those of macroscopic/histologic study.

RESULTS A cutoff value of 1.9 mV discriminated between subvalvular and supravalvular positions (90% sensitivity, 96% specificity). EAS $\geq$1 cm below PV excluded RVOT site of origin (SOO). According to anatomic findings (distance PV–left coronary cusp = 5 $\pm$ 3 vs PV–right coronary cusp = 11 $\pm$ 5 mm), EAS–PV distance was significantly shorter in VAs arising from left coronary cusp than from the other LVOT locations (4.2 $\pm$ 5.4 mm vs 9.2 $\pm$ 7 mm; P = .034). The 10-ms isochronal longitudinal/perpendicular diameter ratio was higher in the RVOT vs the LVOT SOO group (1.97 $\pm$ 1.2 vs 0.79 $\pm$ 0.49; P = .001). An algorithm based on EAS–PV distance and the 10-ms isochronal longitudinal/perpendicular diameter ratio predicted LVOT SOO with 91% sensitivity and 100% specificity.

CONCLUSION An algorithm based on the EAS–PV distance and the 10-ms isochronal longitudinal/perpendicular diameter ratio accurately predicts LVOT vs RVOT SOO in outflow tract VAs with EAS in the septal RVOT.

KEYWORDS Site of origin; Right ventricular outflow tract; Pulmonary valve; Idiopathic ventricular tachycardia; Left ventricular outflow tract

ABBREVIATIONS **CS** = coronary sinus; **EAM** = electroanatomic map; **EAS** = earliest activation site; **EG** = electrogram; **LCC** = left coronary cusp; **LVOT** = left ventricular outflow tract; **NCC** = noncoronary cusp; **OT** = outflow tract; **PV** = pulmonary valve; **PVC** = premature ventricular complex; **RCC** = right coronary cusp; **RV** = right ventricle; **RVOT** = right ventricular outflow tract; **SOO** = site of origin; **VA** = ventricular arrhythmia

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Introduction

Idiopathic ventricular arrhythmias (VAs) arising from the right ventricular outflow tract (RVOT) or left ventricular outflow tract (LVOT) are becoming a frequent target for catheter ablation.[1]

The outflow tract (OT) regions have complex 3-dimensional anatomic relationships, which make recognition of the VA origin particularly challenging. Different ECG algorithms have been proposed to predict LVOT vs RVOT origin of OT VAs.[2–9] However, their accuracy has been questioned recently, especially when the transition in the precordial leads occurs in V_3[10] and/or the maximum electrogram (EG) precocity is located in the septal RVOT.[11] Herczku et al[11] recently described different activation patterns in the septal RVOT in VAs arising from OT regions depending on right vs left origin. However, despite the

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high sensitivity and specificity found for these activation patterns, they resulted from a detailed electroanatomic map (EAM) of the septal RVOT in a small series of patients, in which not all of the possible locations were well represented.

On the other hand, in normally positioned hearts, the RVOT is located anterior and leftward relative to the aortic root, and the pulmonary valve (PV) is positioned approximately 1–2 cm superior to the aortic valve.[12] Therefore, the posterior (septal) aspect of the RVOT is essentially in continuity with the anterior portion of the aortic root. In addition, it should be noted that 3 common sources of VA—right coronary cusp (RCC), part of the left coronary cusp (LCC), and commissure between LCC and RCC—are directly posterior to the septal RVOT.[13] Despite this anatomic proximity, the RVOT and LVOT are supposed to have no muscular fibers connecting them; therefore, impulse propagation should occur through fibers connecting both ventricles transseptally. We hypothesized that if this were the case, the EAS location in the septal RVOT should differ depending on the site of origin (SOO) of the VA (left vs right OT), being located in a lower position in those cases originating in the LVOT. This could be useful for predicting LVOT vs RVOT SOO of OT VAs.

Methods

To test these assumptions, we first performed macroscopic and histologic study in postmortem hearts to analyze the anatomic relationships between RVOT, LVOT, and related structures. Second, EAMs of idiopathic VAs with maximum EG precocity in the septal RVOT were analyzed to assess the impact of EAS location in the septal RVOT for predicting LVOT vs RVOT SOO. Furthermore, in order to define EAS location according to its distance from PV level, we also analyzed the ability of EAM to localize the PV annulus by color-coded voltage map adjustment.

Patient sample

Thirty-seven consecutive patients with drug-refractory OT premature ventricular complexes (PVCs) who underwent radiofrequency ablation were prospectively included. Preprocedural contrast-enhanced computed tomography or contrast-enhanced cardiac magnetic resonance was performed whenever possible. Precordial ECG transition during PVC and the presence of intraventricular conduction disturbances were not considered inclusion/exclusion criteria. Only patients with an EAS during PVC activation mapping in the septal RVOT were included. Patients with arrhythmogenic right ventricular (RV) cardiomyopathy were excluded. The remaining patients with structural heart disease were not excluded. Written informed consent was obtained from all included participants. The study was approved by the local ethics committee.

Macroscopic and histologic study in postmortem hearts

Twelve fixed hearts from patients who died of noncardiac causes (9 male, mean age 69 ± 8 years) were examined. The hearts were immediately fixed with 7% neutral formaldehyde to prevent shrinkage of the myocardium. After macroscopic study, the isolated OTs were sagittally cut at 3-mm intervals along each isolated PV and aortic root. The 3-mm-thick segments were the thinnest possible for histologic processing, and a total of 4 paraffin blocks were obtained from each heart. Serial sagittal sections 10 μm thick were cut from each block containing the outflow tracts; these sections were stained with Masson trichrome. Measurements were made on the endocardial surface from serial sagittal sectional light microscopy images at ∼1-mm intervals. We measured the infundibulum length of the RVOT at the level of RCC and LCC (Figures 1B–E).

Electrophysiologic study

EAM was performed using the CARTO navigation system (Biosense Webster, Diamond Bar, CA) with a 3.5-mm irrigated tip catheter (NaviStar, Biosense Webster). Antiarrhythmic drugs and beta-blockers were withdrawn for 5 half-lives before the procedure. No patient received isoproterenol during mapping. During the procedure, 12-surface ECG and intracardiac recordings were displayed by an electrophysiology data acquisition system (Bard LabSystem, CR Bard Inc, Lowell, MA; or EP-Tracer, CardioTek, Maastricht, The Netherlands).

Electroanatomic mapping

Definition of PV by voltage mapping

A detailed endocardial voltage map (166.2 ± 77.4 points) of the RV was performed in 5 patients during sinus rhythm. In order to obtain an accurate EAM for image fusion purposes, the higher density of points were taken in the RV inflow tract (tricuspid annulus), apex, and RVOT. Each point was acquired, accepted, and integrated to build the EAM when the variability in cycle length, local activation time stability, and maximum beat-to-beat difference of the spatial location of the catheter tip were $<2\%$, <3 ms, and <4 mm, respectively.[14] Thereafter, these EAMs were merged with preacquired contrast-enhanced computed tomography or contrast-enhanced cardiac magnetic resonance images. Fusion was considered to be accurate in each case when the average distance between mapping points and computed tomographic surface was <3 mm.[15] Once the image integration was complete, at least 10 mapping points were taken below and above the PV level as defined by the lower limit of PV sinuses. Bipolar EG amplitude of the mapping points obtained above and below the PV level were compared in order to obtain a voltage cutoff value to delineate PV annulus by voltage map adjustment of the lower and upper thresholds.

In order to apply the cutoff value obtained from sinus rhythm maps to activation maps, variability of bipolar voltage between sinus beats and PVCs was assessed. Bipolar voltage of 50 PVCs EGs was compared with the bipolar voltage of the immediately previous sinus beat signal. Bipolar voltage was measured using the voltage caliper tool of the CARTO system.