The Efficacy of Isochronal 3D Mapping-Based Ablation of Ventricular Arrhythmia

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Summary

Treatment of ventricular arrhythmias (VAs) commonly involves ablating sites showing electrograms with the earliest activity relative to the VA, but there is no threshold value for prematurity guaranteeing success. Ablation of sites with great prematurity can still result in failure.

We hypothesized that isochronal map area (ISCA), derived from isochrones indicating electrogram prematurity, could help identify ablation targets in VA patients, as well as predict outcome. Specifically, we hypothesized that smaller ISCA for a given prematurity value would indicate a shallower arrhythmogenic focus leading to a higher likelihood of successful ablation.

We studied ISCA in 29 patients (12 males, 57 [17-65] years old) undergoing VA ablation. The VAs originated from the right and left ventricles in 11 and 18 patients, respectively. The earliest activation site of the VAs, ECG morphology of sinus beats and premature ventricular complexes (PVCs), and ISCA of activation preceding PVCs were evaluated.

RF ablation at the site showing earliest prematurity resulted in VA elimination in 21 patients (success group). The 5-ms ISCA was smaller in the success group than in the failure group (0.2 [0.1-0.6] versus 1.0 [0.8-1.5] cm², respectively; P < 0.01). No significant difference was noted in prematurity itself (36 [30-45] versus 30 [29-33] ms, respectively; P = 0.07). The cut-off value of the 5 ms ISCA for successful RF ablation was 0.7 cm² with 87.5% sensitivity and 85.6% specificity.

Isochrones of activity preceding PVCs appear to contain information beyond prematurity values and may help dictate suitable areas for successful ablation of VAs. (Int Heart J 2017; 58: 495-499)

Key words: Ventricular tachycardia radiofrequency ablation, Activation map, Isochronal map

PVCs are among the most common cardiac arrhythmias encountered in clinical practice. Several studies have reported that a high burden of PVCs can lead to left ventricular (LV) systolic dysfunction.1,2 Thus, frequent idiopathic ventricular arrhythmias (VAs) are a target for catheter ablation. Ablation of sites with electrograms preceding the PVC on the 12-lead surface ECG by the longest period of time is expected to maximize the chances of successful elimination of PVCs, since they are likely to be closest to the ectopic focus. For purposes of this article, we will define the duration between a PVC and electrograms preceding it as prematurity. It would be useful if there were a threshold value of prematurity over which successful ablation was assured. Unfortunately, the range of prematurity values resulting in successful ablation overlaps with values for unsuccessful ablation sites,3–5 and therefore, better or additional criteria are needed.

We hypothesized that part of the reason that ablation of a site with great prematurity does not necessarily result in successful elimination of a focus is that intramural depth of the focus plays a role. A deeper focus may be more difficult to ablate, not only because of the ablative energy failing to reach the focus effectively, but because excitation reaching the endocardium will arrive at a larger area at the same precocity, so that the site ablated might not be directly above the focus. In contrast, a more superficial focus would produce a smaller excited area at the same precocity. We therefore tested whether what is called isochronal map area (ISCA) measurement could provide a new predictor for eliminating VAs, and whether more superficial sites of origin would have smaller ISCA (Figure 1). ISCA has been analyzed previously in patients with RVOT VAs,6–8 but no one has ever evaluated its ability to discriminate between multiple sites of VA origin as we have attempted to do here.

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Methods

Patient population: We conducted our prospective study on 29 patients (mean age, 54 ± 16 years, 13 males) with a total of 29 morphologies of idiopathic PVCs or ventricular tachycardia (VTs). Radiofrequency catheter ablation (RFCA) procedures were conducted between November 2013 and November 2015. No patient had structural heart disease. All patients provided written informed consent for mapping and ablation. The study was approved by the institutional review board.

Electrophysiological evaluation, mapping, and ablation: Antiarrhythmic drugs were discontinued a week before the study. No patients were on amiodarone. Electroanatomical mapping was performed using the CARTO3 navigation system (Biosense Webster, Diamond Bar, CA, USA) with a 3.5-mm irrigated tip catheter (Thermocool SF, Biosense Webster). During the procedure, a 12-lead surface ECG and intracardiac recording were displayed by an electrophysiological data acquisition system (CardioLab, GE Medical Systems, Milwaukee, WI, USA). The catheter was placed at multiple sites on the endocardial surface to record bipolar and unipolar electrograms. Bipolar electrogram signals (filtered at 16-500 Hz and displayed at 200 mm/s speeds on the CARTO system) were analyzed with regard to relation to the surface QRS and the presence of multiple components. Relevant ECG data known to differentiate between RV origin and LV origin, such as R wave duration and QRS morphology, was used to determine the origin of PVCs.\(^\text{1-14}\) Baseline 24-hour ambulatory electrocardiographic monitoring was performed to count the number of PVCs.

Detailed bipolar endocardial activation mapping was conducted during PVCs using the stable mode. Respiratory gating was not useful due to difficulty encountered when acquiring the points during PVC mapping. The minimum density of points required to conclude that the electroanatomic map of a given chamber was acceptable was a fill threshold of 15 mm (Figure 2). RF maximum power output of 40W was delivered at the earliest activated site after careful mapping. If the ablation site was close to the ostium of a coronary artery, RF application was delivered to an area greater than 5 mm from the ostium visualized by manual contrast injections. If PVCs could not be induced during the baseline state, the stimulation protocol was repeated during the administration of isoproterenol (1-3 µg/minute).

During the RF catheter ablation, when the VT or PVCs were not affected within 30 seconds of RF application, the RF discharge was terminated and the catheter was repositioned for a repeat attempt. When an acceleration or reduction in the VT or PVCs was observed during the first 30 seconds of the application, the RF delivery was continued up to 60 to 90 seconds. When PVCs were abolished after RF application, one or more drugs (such as isoproterenol, phenylephrine hydrochloride, and edrophonium chloride) were infused to provoke any concealed PVCs. All patients were monitored in hospital for 12 to 24 hours after the procedure and followed by office visits thereafter.

Statistical analysis: Data are expressed as the median and interquartile range. Welch’s unequal variances \(t\) test was used for comparisons between group means expressed as continuous variables. The chi-square test was used to evaluate differences in categorical variables between groups. A \(P\) value < 0.05 was considered statistically significant.

Results

Patient population: The baseline characteristics of the 29 patients with PVC or non-sustained VT are summarized in Table I. Ablation was successful in 21 of 29 patients (72.4%). For baseline clinical characteristics, there were no significant differences between the successful ablation group and the failed ablation group, although the frequency of PVCs (PVC counts/total heart beats) was higher in the successful ablation group with near significance (20.6% versus 11.2%, \(P = 0.06\)). The sites of successful ablation (21 patients) were mostly in the outflow tracts: in the RVOT in 8 and in the LVOT in 9 (1 in the right sinus of Valsalva, 5 in the left sinus of Valsalva, 2 below the aortic valve between the left and right coronary cusps, and
in the aortomitral continuity). Regarding the remaining 4 non-outflow tract sites, 2 were in the mitral annulus, 1 in the tricuspid annulus, and 1 in the LV septal endocardium. Of the 8 failed sites, 4 were in the LVOT (2 each in the right and left sinuses of Valsalva), 2 in the RVOT, 1 in the tricuspid annulus, and 1 in the mitral annulus. Of the 29 study patients, 8 had non-sustained VT (5 of whom were successfully ablated) and 3 had sustained VT (none of whom were successfully ablated).

**Surface ECG characteristics and mapping area:** Characteristics of the surface ECG in the two groups are shown in Table II. Baseline ECG in sinus rhythm did not show an LBBB pattern in any of the 29 patients (not shown in Table II). None of the parameters studied differed between the two groups. QRS widths in either sinus rhythm or PVCs were not different between the two groups (77 [69-85] versus 73 [70-85] ms, 139 [132-150] versus 142 [130-153] ms, respectively). There was no difference in the morphology of PVC, RBBB pattern, or LBBB pattern between the two groups.

The transitional zone was divided into 6 groups. Transitional zones serve as clues for where to map. However, in one patient in whom the transitional zone was in V1 suggesting a left sided focus, activation was earlier in the RVOT than in the LVOT, so the activation mapping was performed in the RVOT. The mapping sites are shown in Table II in detail. The PVCs of 5 patients whose transitional zone was in V1 were successfully ablated: in the aortomitral continuity (n = 1), RVOT (n = 1), LCC (n = 1), and mitral annulus (n = 2). One patient whose transitional zone was in V1 in the failure group was not cured by ablation of the earliest activation site in the LV, but ablation of a CS distal site diminished the amplitude of the PVC.

There were 3 patients whose PVC transitional zone was in V1-2. Of these 3, one was successfully ablated in the LV septum, but in the other 2, the site of origin could not be determined.

Ablation was successful in 4 of the 6 patients whose transitional zone was in V2-3, in one in whom the transitional zone was in the RVOT, and in 3 in whom the transitional zone was in the LCC. The remaining two were successfully ablated in the RVOT after LVOT mapping and ablation failed.

Eight of the 10 patients who showed transitional zones in V3-4 were successfully ablated: in the RVOT (n = 3), LCC-RCC junctional zone (n = 2), tricuspid annulus (n = 1), RCC (n = 1), and LCC (n = 1). The origin of the remaining two failures appeared to be in the RVOT (n = 1) and RCC (n = 1), but ablation was not attempted.

Three of the 4 patients who showed transitional zones in V4-5 and V5-6 were ablated in the RVOT (n = 3), but the PVCs of one patient who received ablation in the RVOT remained.

There was no difference in the success rate between LV mapping and RV mapping (66.7% versus 81.8%; P = 0.37).

**Activation mapping:** Mapping data at the estimated earliest activation sites are shown in Table III. The number of points mapped and the intracardiac electrogram prematurity at the estimated earliest site were not different between the two groups (42 [31-57] versus 40 [26-73] points, P = 1.0; 36 [30-45] versus 30 [29-33] ms, P = 0.07). The diameter of the major and the minor axis of the 5-ms isochronal map area was shorter in

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<th>Table I. Characteristics of Successful Ablation Group and Failure Ablation Group After RF Application at Estimated Site of Origin of PVCs</th>
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<td>All patients (n = 29)</td>
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</tr>
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<td>Male</td>
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BMI indicates body mass index; HTN, hypertension; DM, diabetes mellitus; DLP, dyslipidemia; BNP, brain natriuretic peptide; PVC, premature ventricular complex; EF, ejection fraction; LVDD, left ventricular end-diastolic diameter; and LVDDs, left ventricular end-systolic diameter.

<table>
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<th>PVC morphology, RBBB/LBBB</th>
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<td>Success (n = 21)</td>
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<tr>
<td>PVC transitional zone</td>
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The cut-off level of ISCA of 5 ms at the successful RF ablation groups (1.23 [1.14-1.95] versus 1.43 [1.33-2.21], P = 0.14).

The successful earliest activation time preceding the QRS onset of the VA is approximately 30-100 ms is observed at successful ablation sites. The successful earliest activation time preceding the QRS onset of the VAs is difficult to determine during the procedure in these cases. Therefore, it is important to construct maps of activation times preceding the QRS onset of the VAs and to identify the earliest site of activation.

**Isochronal mapping:** Herczku, et al.\(^{(16)}\) reported that the 10-ms isochronal map area of RVOT could predict whether the site of origin was in the RVOT or LVOT in patients with outflow tract VAs with V3 transition and septal earliest activation. Acosta, et al.\(^{(15)}\) reported that both the distance between the earliest activation site of RVOT and the pulmonary vein and the 10-ms isochronal longitudinal/perpendicular diameter ratio could predict whether the site of origin was in the LVOT or RVOT in outflow tract VAs with earliest activation site in the septal RVOT. These studies reported that RVOT origin and LVOT origin could be discriminated by mapping only the RVOT. In contrast, there are few studies of successful ablation in the LVOT and non-outflow tract sites of origin. In our study, we analyzed the relationship between successful ablation and isochronal mapping area.

**Discussion**

**Main findings:** There are two main findings of the present study; 1) intracardiac electrogram prematurity varies in patients with ventricular arrhythmias (VAs), showing an overlap between successful and unsuccessful ablation sites, and 2) a smaller 5-ms isochronal area of estimated earliest activation of VAs was able to predict successful ablation with high sensitivity and specificity. To the best of our knowledge, this is the first study to examine the relationship between the isochronal mapping area and successful VA ablation.

**Surface ECG and activation mapping:** The ECG features of PVCs are important clues for identifying ablation sites. Several reports provide guidelines for identifying mapping sites based on PVC morphological criteria.\(^{(9,14)}\) However, we found in several cases that one could not strictly define the site of origin of PVC if only the transitional zone and PVC morphology were used. Therefore, intracardiac mapping data are necessary to increase the accuracy in identifying the actual site of PVC origin.

On the other hand, in some LVOT VAs,\(^{(16)}\) especially those arising from above the aortic cusp, a local electrogram whose earliest activation precedes the QRS onset of the VA was able to predict successful ablation with high sensitivity and specificity. To the best of our knowledge, this is the first study to examine the relationship between the isochronal mapping area and successful VA ablation.

![Figure 3](image_url) The 5-ms isochronal map area differed significantly between the successful ablation group and failed ablation group. The horizontal dashed line at 0.7 cm\(^2\) shows the cut-off value for successful ablation producing 87.5% sensitivity and 85.6% specificity.
We estimated the 5-ms and 10-ms isochronal areas of earliest activation in this study. Several studies have looked at the 10-ms isochronal area, but we found the 10-ms isochronal area was overly large, because it included sites with lower precocity relative to the earliest onset of PVC. Instead, we found that the 5-ms isochronal area was more accurate for detecting suitable ablation sites for VAs, and in fact, a smaller 5-ms isochronal map area was able to predict successful ablation sites of VAs in this study with statistical significance.

In the case of PVC origin of RVOT, the 10-ms isochronal map area in the RVOT was 2.5 (1.3-3.3) cm², about double a previous study where this area was 1.2 (0.4-2.1) cm². The larger size of the early activated area in our study is likely due to the administration of isoproterenol which causes an increase in conduction velocity, as was suggested by the authors of a previous study. This would be a further benefit in employing a 5-ms isochronal area as opposed to a 10-ms one in that the effects of higher conduction velocity would be reduced.

In ablation procedures, the time spent mapping should be minimized. Some cases are difficult to map, because for whatever reason, spontaneous PVC frequency decreases during the procedure. Azegami, et al reported that activation mapping and pace mapping were highly correlated techniques. They found that a smaller 10-ms isochronal mapping area was accompanied by a better pacemapping score. Thus, pace mapping may be a useful substitute for assessing suitable ablation sites when PVC frequency is too low to construct isochronal maps in a suitable amount of time.

**Limitations:** The small sample size was our main limitation. The cut-off value we found should be evaluated in a large population. This study did not include patients with structural heart disease, limiting the applicability of our results to a wider population of patients with VAs in whom structural or functional changes in myocardial tissue likely affect conduction velocity.

Our study did not include cases of PVCs arising via the Purkinje network and via preferential pathways. In such cases, there is the risk that only the exit sites of PVCs will be ablated. Our technique utilizing the isochronal map for VAs is mainly suitable for PVCs arising from uniformly conductive tissue, ie, ordinary cardiac muscle.

**Conclusions:** The area of 5-ms isochronal maps can be used to predict the success of ablation of PVCs with high accuracy. This approach may help minimize the number of energy applications for ablating PVCs.

**DISCLOSURE**

No authors have conflicts of interest to declare.

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