Intramural mapping of intramural septal ventricular arrhythmias

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Abstract

Background: Intramural ventricular arrhythmias (VAs) can originate in patients with or without structural heart disease. Electrogram (EGM) recordings from intramural sources of VA have not been described thoroughly.

Objective: We hypothesized that the presence of scar may be linked to the site of origin (SOO) of focal, intramural VAs.

Methods: In a series of 21 patients (age: 55 ± 11 years, 12 women, mean ejection fraction 43 ± 14%) in whom the SOO of intramural VAs was identified, we analyzed bipolar EGM characteristics at the SOO and compared the findings with the endocardial breakout site. The patients were from a pool of 86 patients with intramural VAs referred for ablation.

Results: In 16/21 patients intramural scarring was detected by cardiac magnetic resonance (CMR) imaging. In patients in whom the intramural SOO was reached, intramural bipolar EGMs showed a lower voltage and had broader EGMs compared to the endocardial breakout sites (0.97 ± 0.56 vs. 2.28 ± 0.15 mV, p = .001; and 122.3 ± 31.6 vs. 96.5 ± 26.3 ms, p < .01). All intramural sampled sites at the SOO had either low voltage or broad abnormal EGMs. The activation time was significantly earlier at the intramural SOO than at breakout sites (−36.2 ± 11.8 vs. −23.2 ± 9.1 ms, p < .0001).

Conclusions: Sites of origin of intramural VAs with scar by CMR display EGM characteristics of scarring, supporting that scar tissue localizes to the SOO of intramural outflow tract arrhythmias in some patients. Scarring identified by CMR may be helpful in planning ablation procedures in patients with suspected intramural VAs.

KEYWORDS
bipolar intramural electrograms, cardiac magnetic resonance imaging, intramural scarring, intramural ventricular arrhythmia
1 | INTRODUCTION

Most idiopathic ventricular arrhythmias (VAs) originate from the outflow tracts and can be targeted for ablation from either the right or the left ventricular outflow tract including the sinuses of Valsalva. A significant number of patients, however, have an intramural origin and ablation efforts from the outflow tract often fails to eliminate these arrhythmias. These intramural VAs are difficult to target and often are identified only after long ablation procedures in which the site of origin (SOO) was not found. Furthermore, intramural scar often is present in patients with intramural VAs, including frequent premature ventricular complexes (PVC). Because the SOO of intramural arrhythmias can be difficult to reach, the characteristics of intramural tissue at the SOO of intramural VAs are incompletely characterized. Yet, an approach to reach the intramural origin via proximal septal veins has been described. The purpose of this study was to describe the electrogram (EGM) characteristics of intramural VAs in which the SOO was reached with a bipolar mapping catheter and to determine if scar tissue was located at the SOO.

2 | METHODS

2.1 | Patients characteristics (Table 1)

The protocol was approved by the institutional review committee. The subjects of this retrospective study were 21 consecutive patients with frequent PVCs (age: 55 ± 11 years, sex: 12 women, ejection fraction: 43 ± 14%) in whom mapping of intramural VA SOO was successfully accomplished. The patients were drawn from a pool of 86 consecutive patients with intramural VAs.

The patients had failed to respond to a mean of 1.3 antiarrhythmic medications including beta-blockers and calcium channel blockers. Fifteen/21 patients (71%) had prior failed ablation procedures.

2.2 | Cardiac magnetic resonance imaging (CMR)

All but two patients underwent late gadolinium enhanced CMR studies before the ablation procedure. The studies were performed on a 1.5 Tesla magnetic resonance imaging scanner (Signa Excite CV/i, General Electric, Milwaukee, Wis. or 5 T Achieva Philips MR, Amsterdam, Netherlands) with a 4-CV/i, General Electric, Milwaukee, Wis. or 5 T Achieva Philips MR, on a 1.5 Tesla magnetic resonance imaging scanner (Signa Excite studies before the ablation procedure. The studies were performed. All but two patients underwent late gadolinium enhanced CMR procedures. Fifteen/21 patients (71%) had prior failed ablation medications including beta-blockers. Fifteen/21 patients (71%) had prior failed ablation procedures.

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imaging was performed using an inversion-recovery sequence (repetition time 6.7 ms, echo time 3.2 ms, in-plane spatial resolution 1.4 × 2.2 mm, slice thickness 8 mm) in the short axis and long axis of the left ventricle at matching cine-image slice locations. The inversion time (250–350 ms) was optimized to null the normal myocardium.

Using proprietary software (MUSIC), regions of interest were drawn to segment the myocardium, and the histogram of pixel intensities within the myocardium was analyzed. Thresholds for scar was set to >35% of the maximal signal intensity. Scar was registered to the electroanatomic map (Figure 1).

2.3 | Electrophysiology procedure mapping and ablation

After informed consent was obtained, multipolar catheters were placed in the right ventricle, and the His bundle position. Activation mapping was performed for frequent PVCs and pace-mapping for infrequent PVCs. For right-sided procedures, 3000 units of heparin initially were administered as a bolus followed by 1000 units every hour. For left-sided procedures, a 5000 unit bolus was administered after arterial access was obtained and the heparin dosage then was titrated to maintain an activated clotting time >250 s.

Mapping was performed in the right ventricular outflow tract, the left ventricular outflow tract including the sinuses of Valsalva, and the coronary venous system (CVS) using the ablation catheter. EGMs were filtered at 50 to 500 Hz. The intracardiac EGMs and leads V1, I, II, and III were displayed on an oscilloscope and displayed at a speed of 100 mm/s. The recordings were stored on optical disc (Workmate Claris™, Abbott Laboratories). An electroanatomical mapping system (CARTO, Biosense Webster) was used to guide mapping. A 3.5 mm open-irrigated-tip catheter (Thermocool Navistar, Biosense Webster) was used for mapping and ablation; an occlusive venogram of the CVS was performed to assess for the presence and location of septal veins (Figure 2). For mapping, of the CVS the ablating catheter was used first, followed by a smaller multipolar mapping catheter (Carmida, EP star, Map-it catheter, please see below for specific details of the catheters used). At the SOO the EGM characteristics were analyzed.

The local bipolar EGMs recorded by the distal electrode pair of the mapping catheter were categorized as normal or abnormal according to previously reported criteria which were adapted to the mapping and recording system used in this study. Accordingly, normal EGMs were defined as:

1. sharp biphasic or triphasic EGMs with an amplitude >1.5 mV and/or
2. an EGM duration of ≤69 ms.

The remaining EGMs were defined as abnormal (Figure 3). Sites with a potential separated from the ventricular EGM by an isoelectric
segment, and/or a segment with low amplitude noise (<0.05 mV) of >20 ms duration at a gain of 40–80 mm/mV were defined as isolated potentials\(^7\) (Figure 1).

Activation times and pace-maps were assessed. A pace-map was considered to match with the spontaneous arrhythmia in 10-12/12 leads. Otherwise, the map was classified as a non-matching pace-map. The SOO was identified when the earliest activation time was recorded at a site with a matching pace-map.

If the SOO was reached with the ablation catheter within the CVS, a coronary angiogram was performed before ablation to determine the distance of the ablation catheter to the coronary arteries (Figure 2). Provided the distance of the catheter to the closest coronary artery was ≥5 mm, radiofrequency energy was applied at a power of 15 Watts and was titrated to achieve an impedance drop of 10 Ohms. If the SOO was not reached with the ablation catheter but a septal vein was visualized on the venogram,
smaller mapping catheters were advanced instead to the targeted septal veins. The mapping catheters used included the Map-iT catheter (Access Point Technologies EP: 4 Fr, 10 electrodes, electrode spacing: 2.5-2 mm) the EP Star catheter (Balys Medical: 2Fr, 8 electrodes, electrode spacing: 5-5.5 mm) or Pathfinder (Pathfinder, CARDIMA, Inc.: 2.5 Fr, 16 electrodes, spacing 6-2.6 mm). To compare intramural and non-intramural mapping sites recorded with the same catheter, we compared EGM characteristics recorded with the 3.5 mm-tip-ablation catheter at the SOO and the breakout site.

2.4 | Follow-up

Patients were seen for routine follow-up at 3- and 12–48-months postablation. An echocardiogram was repeated 3–6 months post-ablation if the baseline ejection fraction had been abnormal. All antiarrhythmic drug therapy was discontinued if ablation was effective. Beta-blockers and heart failure medications were continued initially and were discontinued if and when LV function and dimensions normalized. No new medications were added after an effective ablation procedure.

2.5 | Statistical analysis

Continuous variables were expressed as mean ± standard deviation. Discrete variables were compared using the Fisher exact test or by Chi-square analysis as appropriate, and continuous variables were
compared using two-group t-test. A p-value < 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Mapping

All the patients had intramural origins that were reached by placing a catheter with bipolar recording capabilities into a proximal septal vein. At this location, the earliest activation time was recorded }

### TABLE 1 Patient characteristics

| Variables              | Patients (N) |
|------------------------|--------------|
| Age (y)                | 55 ± 11      |
| Gender (male/female)   | 9/12         |
| Left Ventricular EF (%)| 43 ± 14      |
| PVC burden (%)         | 25 ± 13      |
| Prior failed ablation (n) | 15          |

### Comorbidities

- Hypertension: 9
- COPD: 0
- Diabetes: 2
- Atrial fibrillation: 5
- CKD: 1
- HLP: 7
- CVA: 0
- CAD: 3

### Medications

- Beta blockers: 18
- ACE inhibitors: 4
- Ca-blockers: 1
- Amiodarone: 4
- Class IC AA: 2
- Class III AAs: 2

### Procedure time (min) | 337 ± 80
### RF time (min)    | 30 ± 18
### Successful ablation (n) | 19
### PVC burden post ablation (%) | 1 ± 2
### EF post ablation (%) | 53 ± 4

### Abbreviations: AA, antiarrhythmic medications; Ca-blockers, calcium channel blockers; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive lung disease; CVA, cerebrovascular accident; EF, ejection fraction; HLP, hyperlipidemia; PVC, premature ventricular complexes.

3.2 | Imaging

There was evidence of scarring in the basal septum in 16/21 patients (76%). The scar was intramural in all patients without involving the endocardial myocardium. The SOO could be reached with the ablation catheter in 13/21 patients. In the remaining 8 patients, a smaller catheter was required to identify the SOO. The SOO was at a distance of 4.1 ± 2.4 mm from the registered scar if the SOO was reached with the ablation catheter (n = 8, Figure 1A,B).

3.3 | Electrograms at the SOO

At the SOO there was a matching pace-map in 19/21 patients compared to no matching pace-maps when pacing was performed at the break-out site of the targeted VA (p < .0001). The sinus rhythm EGM amplitude at the intramural recording site was lower compared to breakout sites (0.97 ± 0.56 vs. 2.28 ± 0.15 mV, p = .001, Table 2). The sinus rhythm EGM duration at the SOO was broader compared to the EGM duration at the breakout site (122.3 ± 31.6 vs. 96.5 ± 26.3 ms, p < .01). In the presence of scarring, provided that the SOO was reached with the mapping/ablation catheter, the bipolar voltage was lower compared to the bipolar voltage of the breakout site (0.61 ± 37 vs. 1.39 ± 0.84 mV, p = .03). The EGM duration at the SOO in the presence of scarring was longer in the presence of scarring compared to breakout sites (137 ± 41 vs. 92 ± 34, p < .04).

The difference in bipolar EGM voltage and duration at the SOO compared to the breakout site persisted when comparing EGM characteristics recorded with the same catheter (i.e., the 3.5 mm-tip ablation catheter): 0.85 ± 0.42 vs. 1.97 ± 1.56 mV, p = .02, and 123.9 ± 33.3 vs. 93.7 ± 27.3 ms, p = .03, respectively. In two patients there were isolated potentials (Figure 1B) at the SOO. The activation time at the SOO was significantly earlier than at the breakout site −36.2 ± 11.8 ms vs. −23.2 ± 9.1 ms (p < .0001). Catheter ablation was acutely successful in 19/21 patients. In one patient, although an intramural origin of one of his VA was

### TABLE 2 Electrogram characteristics at mapping sites

| Variables | SOO | Breakout site | p-value |
|-----------|-----|---------------|---------|
| No of sites | 21 | 21            |         |
| Local activation time | −36.2 ± 11.8 | −23.2 ± 9.1 | <0.0001 |
| EGM amplitude (mV) | 0.97 ± 0.56 | 2.28 ± 0.15 | 0.001   |
| EGM duration (ms) | 122.3 ± 31.6 | 96.5 ± 26.3 | 0.007   |

Abbreviations: EGM, electrogram; SOO, site of origin.
identified and eliminated, the patient had multiple PVC morphologies and his PVC burden decreased from 24% to 5% during follow-up. In one patient the SOO was too close to a coronary artery for safe ablation at the SOO.

3.4 | Outcomes

The mean ejection fraction improved from 43 ± 14 to 53 ± 4% in these patients. The PVC burden at 3 months decreased from 26.1 ± 13.3 to 1.2 ± 2% (p < .0001).

4 | DISCUSSION

4.1 | Main findings

Sites of origin of intramural VAs often are located close to sites of intramural scarring. The bipolar EGM characteristics at the SOO reflect the presence of scarring with reduced EGM amplitude and broader EGMs. EGM characteristics and imaging support that the SOO of intramural VAs often is associated with intramural scarring.

4.2 | Mapping of intramural arrhythmias

Intraoperative mapping with endocardial and epicardial electrodes has been used in the past to characterize intramural substrates.10,11 Direct mapping of intramural septal arrhythmias has been first described in a series of patients by Yokokawa et al. by placing a multipolar catheter into septal veins1 allowing to target intramural VA based on the mapping data. Others have subsequently confirmed these data.12,13 Briceno et al.3 reported on unipolar mapping with an insulated wire placed in a septal vein when mapping intramural VTs. The EGMs were recorded by the distal tip of the wire that had a length of 15 mm versus the proximal end that was connected in a unipolar manner to the skin. In the present study, EGMs were recorded in a bipolar manner with closely spaced electrodes located in the septal veins. This permitted us to map the area immediately adjacent to the intramurally placed electrodes in contradistinction to unipolar recordings where farfield EGMs originating from a distance to the recording electrodes are displayed. Furthermore, CMRs were obtained in all but two patients allowing for correlation of the scar location relative to placement of the recording catheters. More recently, Pothineni et al. reported in a case series on integration of bipolar mapping data from endocardium, epicardium, and the intramural CVS generating 3-dimensional activation maps of intramural VAs.14 The principle of this approach is employed when electroanatomic activation mapping is performed in multiple chambers for a single arrhythmia. For focal VAs, the most important factor for procedural success is to identify and localize the SOO that allows to target intramural VA origins.1,15 In the study by Pothineni, data on tissue characterization with bipolar recordings or with CMR was not provided. Other methods of direct intramural mapping include the use of a needle catheter that allows to extend a needle intramurally from the tip of the ablation catheter.16

4.3 | Imaging and the SOO

Imaging data of scar located in the intramural septum have been used to clarify the substrate for intramural VAs.17-20 It is well known that in patients with structural heart disease critical sites of ventricular tachycardia are located within scar tissue.21 Similarly we demonstrated that in patients with prior infarction, premature ventricular complexes are also confined to scar tissue and can share the exit site of VT.22 Less is known about intramural scarring and intramural VAs. We reported that in the presence of scarring and frequent PVCs, in most patients, the scar is adjacent to the origin of PVCs.2 Direct proof that a PVC is originating from an intramural scar has been lacking. In this study, the EGM characteristics at the SOO of VAs were compatible with scarring around the catheter placed intramyocardially via a septal vein. Image registration provided further support that the catheter was in close proximity to the scarring found on CMR. These data support the use of CMR for targeting VAs, especially if an intramural source is suspected.

4.4 | Limitations

This is a small case series of patients in which different multipolar catheters were used with different electrode sizes and electrode spacing. This limits the ability to identify cut-off values that have been validated with other multipolar catheters. Patients with prior procedures were included in this series and scar possibly might have been caused by prior ablation procedures. However, all scarring detected by CMR was located in the intramural septum and not related to prior ablation procedures. Therefore, these patients were not excluded.

5 | CONCLUSIONS

The EGM characteristics at the SOO of intramural VAs and the location of scar identified by CMR both indicate that the SOO of intramural VAs is closely associated with scar. Imaging with CMR may be beneficial in patients with frequent PVCs and may improve procedural planning.

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CONFLICT OF INTERESTS
The authors declare that there are no conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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