Impact of Nonischemic Scar Features on Local Ventricular Electrograms and Scar-Related Ventricular Tachycardia Circuits in Patients With Nonischemic Cardiomyopathy

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Background—The association of local electrogram features with scar morphology and distribution in nonischemic cardiomyopathy has not been investigated. We aimed to quantify the association of scar on late gadolinium-enhanced cardiac magnetic resonance with local electrograms and ventricular tachycardia circuit sites in patients with nonischemic cardiomyopathy.

Methods and Results—Fifteen patients with nonischemic cardiomyopathy underwent late gadolinium-enhanced cardiac magnetic resonance before ventricular tachycardia ablation. The transmural extent and intramural types (endocardial, midwall, epicardial, patchy, transmural) of scar were measured in late gadolinium-enhanced cardiac magnetic resonance short-axis planes. Electroanatomic map points were registered to late gadolinium-enhanced cardiac magnetic resonance images. Myocardial wall thickness, scar transmurality, and intramural scar types were independently associated with electrogram amplitude, duration, and deflections in linear mixed-effects multivariable models, clustered by patient. Fractionated and isolated potentials were more likely to be observed in regions with higher scar transmurality (P<0.0001 by ANOVA) and in regions with patchy scar (versus endocardial, midwall, epicardial scar; P<0.05 by ANOVA). Most ventricular tachycardia circuit sites were located in scar with >25% scar transmurality.

Conclusions—Electrogram features are associated with scar morphology and distribution in patients with nonischemic cardiomyopathy. Previous knowledge of electrogram image associations may optimize procedural strategies including the decision to obtain epicardial access. (Circ Arrhythm Electrophysiol. 2013;6:1139-1147.)

Key Words: tachycardia, ventricular
Methods

Study Patients

Our institutional review board approved the study protocol. All patients provided written informed consent. We enrolled 15 consecutive patients with monomorphic VT and NICM who consented to undergoing MRI before VT ablation. Patients with hypertrophic cardiomyopathy, arrhythmogenic right ventricular (RV) dysplasia, and renal dysfunction (glomerular filtration rate <60 mL/min per 1.73 m²) were excluded.

CMR Studies

CMR was performed with a 1.5-T CMR scanner (Avanto; Siemens, Erlangen, Germany). In 13 patients with ICD systems, potential risks were explained and CMR images were obtained using our established safety protocol.20 Short-axis spoiled gradient echo cine images were acquired with repetition time (TR) 40 ms, echo time (TE) 3.1 ms, flip angle 15°, average in-plane resolution 2.0×1.6 mm, and slice thickness 6 mm. Next, 0.2 mmol/kg intravenous gadopentetate dimeglumine was administered, and MR angiography images were acquired with TR 2.9 ms, TE 1.08 ms, flip angle 25°, average in-plane resolution 1.0×1.0 mm, and slice thickness 1.0 mm. Ten minutes after the injection of the contrast medium, LGE-CMR images were obtained in short axis with a segmented inversion recovery gradient echo turbo-fast low-angle shot sequence (TR 1 R-R interval, TE 1.04 ms, flip angle 25°, average in-plane resolution 1.3×1.3 mm, slice thickness 8 mm, and inversion time typically 240–360 ms). The inversion time was modified iteratively to obtain maximal nulling of the signal from normal ventricular myocardium.

CMR Image Analysis

QMass MR software (Medis, Leiden, the Netherlands) was used to measure scar transmurality and left ventricular (LV) wall thickness in short-axis image planes that did not include the mitral annulus. Candidate hyperenhanced regions were identified as scar if the mean intensity of the hyperenhanced region was >6 SDs above the mean intensity of remote normal myocardium.21,22 Scar transmurality and LV wall thickness were determined as previously described.4,16 Intramural scar types were recorded based on the classification of NICM scar in previous reports (endocardial, midwall, epicardial, patchy, transmural scar; Figure 1A).19 In contrast to the other scar types that exhibited cohesive areas of fibrosis, patchy scar regions were inhomogeneous with alternating areas of scar and viable tissue in close proximity and extending from endocardium to epicardium (Figure 1A).

Electrophysiological Study

In patients with ICD systems, tachyarrhythmia therapies were disabled before the procedure. Ventricular programmed stimulation to induce VT was performed using a quadripolar catheter at the RV apex.

Figure 1. Scar types in nonischemic cardiomyopathy and electrogram characteristics. A, Scar on late gadolinium enhanced cardiac magnetic resonance (LGE-CMR; red arrows) was divided into 14 types by intramural scar types (no scar, endocardial, midwall, epicardial, patchy, transmural) and scar transmurality (0%–25%, 26%–50%, 51%–75%, 76%–100%; top, right). B, Electrogram characteristics on electroanatomic map (EAM) were defined as electrogram parameters (bipolar and unipolar voltages, duration, deflection) and electrogram types (normal, fractionated electrogram, isolated potential). C, Mapping points on EAM were registered to the corresponding region on short-axis planes of LGE-CMR.
and outflow tract with up to triple extrastimuli at 3 basic cycle lengths. If the induced VT sustained without hemodynamic collapse, EAM was attempted during tachycardia. Otherwise, substrate mapping was performed during sinus rhythm or backup ventricular pacing.

3-Dimensional EAMs and Electrogram Characteristics
A 3-dimensional EAM system (CARTO; Biosense Webster, Inc, Diamond Bar, CA) was used to create endocardial voltage maps in left and right ventricles during sinus rhythm or backup ventricular pacing using a 3.5-mm-tip electrode with 2 mm interelectrode spacing (Thermocool; Biosense Webster, Inc) and Fill Threshold set at 15 mm. After administration of sufficient heparin to maintain an activated clotting time of >300 seconds, the mapping catheter was inserted into the left ventricle using a transeptal approach. The LV or RV shell reconstructed from the CMR angiogram was registered to the LV or RV EAMs using the landmark registration method as previously described.4 Registration accuracy was determined using statistical summation, which is the average distance of each EAM point to the closest surface point of the reconstructed image of the chamber. Local electrogram bipolar and unipolar voltage, duration, and deflection were measured (Figure 1B).4,12,16 Electroanatomic mapping was performed during sinus rhythm in all patients except 1 patient with complete heart block, in whom mapping was performed during RV pacing. Bipolar and unipolar electrograms were filtered at 10 to 400 Hz and 1 to 240 Hz, respectively, and recorded as the difference between the highest and lowest deflections of a stable contact signal. Electrogram duration and deflection were measured from the onset to the end of electrogram deflections at 400 mm/s speed manually. The number of deflections was counted as the summation of both negative and positive deflections in each electrogram. Fractionated potentials and isolated potentials on bipolar electrograms were identified based on previously published criteria: fractionated—voltage ≤0.5 mV, duration ≥133 ms, or amplitude/duration ratio <0.005; isolated potential—a potential separated from the ventricular electrogram by an isoelectric segment or a segment with low voltage noise (<0.05 mV) of ≥20 ms duration at a gain of 40 to 80 mm/mV.4,12 Two independent observers analyzed electrogram characteristics. Discrepancies were resolved by repeat review by a third observer and consensus among all reviewers. In accepting the electrogram in each EAM point, we confirmed that ≥2 consecutive electrograms had the same morphology to avoid electrogram artifact due to poor catheter contact.

Catheter Ablation of Scar-Related VT
Ablation targets were determined by pace mapping during sinus rhythm or backup pacing, or entrainment mapping during sustained monomorphic VT. Circuit sites of scar-related re-entrant VT were defined as exit, central pathway, or entrance sites by determination of the ratio of stimulus to QRS time over VT cycle length (%S-QRS/VT-CL: exit <30%, central pathway 30% to 70%, entrance >70%) at sites with 12/12 ECG morphology pace map match to clinical VT, or concealed entrainment and postspacing interval minus VT cycle length <30 ms identified during hemodynamically stable VT.14 If the VT was hemodynamically unstable, the %S-QRS/VT-CL was measured using the S-QRS interval during pacing with the same cycle length as the VT-CL. In addition, VT circuit sites were defined as sites meeting both of the following criteria: (1) ≥1/12 pace morphology match to the targeted clinical VT, and (2) where catheter ablation rendered the VT noninducible. Additional radiofrequency lesions targeted fractionated and isolated potentials within scar.1,3,5,14 Catheter ablation targeting scar or abnormal myocardium adjacent to scar was performed with maximum power of 50 W for 30 to 60 seconds at each site. When isolated potentials or VT circuit sites as defined above were adjacent (<1 cm) to a valve annulus or other region of electrically unexcitable scar, lesions were extended to the unexcitable area in the hope of dividing re-entry circuit paths as previously described.20 In such sites, linear RF ablation at 40 W was performed until unipolar pacing with an output of 10 mA at 2 ms failed to capture the myocardium. Complete success was defined as noninducibility of any VT. Partial success was defined as suppression of the clinical VT but inducibility of any other VT. In patients with ICD systems, devices were reprogrammed to original settings immediately after the procedure.

Registration of EAM Points to LGE-CMR Images
Short-axis LGE-CMR image planes were retrospectively registered to the endocardial EAM using previously validated custom software (Volley; Johns Hopkins University) based on the registration coordinates for EAM merged with the LV CMR angiograms.4,16 Each EAM point was superimposed onto the corresponding sector on short-axis LGE-CMR image planes (Figure 1C), and the electrogram characteristics corresponding to each image sector were recorded as continuous variables.

Statistical Analysis
Continuous variables are expressed as mean±SD, and categorical data as numbers or percentages. Comparisons of continuous variables were made using the 2-group Student t-test or the Wilcoxon rank-sum test based on the distribution of the values, and categorical variables were compared using the χ2 or Fisher exact test where appropriate. Comparisons of continuous variables regarding each electrogram parameter were made using ANOVA. Linear mixed-effects models, clustered by patient (independent correlation structure), were then used to examine the association of electrogram parameters as dependent variables with LV wall thickness, scar transmurality, and intramural scar types (endocardial, midwall, epicardial, patchy) as independent variables after adjusting for patient sex, age, and LV ejection fraction. Optimal threshold values for bipolar and unipolar voltage, duration, and deflection for any nonischemic scar were determined using receiver operating characteristic curves. The association of stimulus to QRS time (S-QRS) with scar transmurality was assessed by linear regression. Statistical analyses were performed using STATA software (version 10; StataCorp, College Station, TX).

Results

Patient Characteristics
A total of 23 patients with nonischemic scar-related VTs were screened. Of the initial 23, 8 patients (34.8%) were excluded because of refusals or screen failures, and the remaining 15 patients (aged 51±11 years; 3 women) were included in this study. Five patients had cardiac sarcoidosis and the other 10 patients had idiopathic dilated cardiomyopathy. Other baseline characteristics are summarized in Table 1. In addition to standard therapy for heart failure, antiarrhythmic drugs (amiodarone and sotalol) had been administered in 12 patients. Antiarrhythmic drugs were discontinued ≥3 days before VT ablation.

Analyzed Sectors on LGE-CMR and EAM Points
A total of 2522 image sectors in 113 short-axis LGE-CMR image planes and 1957 LV and 752 RV points on EAMs were reviewed. Of 2522 image sectors, 1988 (78.8%) were suitable for quantitative analysis. The remaining 21.2% of image sectors were excluded because of image susceptibility artifacts in patients with ICD systems. Low-voltage and dense-scar areas defined as <1.5 and <0.5 mV of bipolar voltage covered 8.4% and 1.6% of total LV endocardium on EAM. The mean surface registration error of the LV CMR angiogram with endocardial LV EAM was 2.7±0.4 mm. Ablation procedural details are summarized in Table I in the online-only Data Supplement. Ablation was not performed in 2 patients because of severe nausea and worsening of heart failure during the procedure, respectively. Figure 2 demonstrates the distribution and characteristics of LV
Men/women 12/3
Age, y 51±11

Gram duration and deflections were positively associated with scar in left ventricle in our patient cohort. The distribution (D) and characteristics (C) of scar in left ventricle were positively associated with scar transmurality (P<0.0001 by ANOVA for all intramural scar types; Figure 3C and 3D). Of all EAM points analyzed, 4.9% had fractionated electrograms and 3.3% had isolated potentials. There was a positive association between the incidence of fractionated and isolated potentials with scar transmurality (P<0.0001 by ANOVA for both; Figure 3E), and isolated potentials were more frequently observed in sectors with higher scar transmurality and patchy scar regions (P<0.05 by ANOVA).

Linear mixed-effects multivariable model results with electrogram parameters as dependent variables and LGE-CMR variables as independent variables, clustered by patient, are summarized in Table 2. LV wall thickness, scar transmurality, endocardial scar, and midwall scar were independently associated with electrogram parameters. Epicardial and patchy scar were also significantly associated with bipolar and unipolar voltage. Unlike epicardial scar, patchy scar was associated with electrogram deflections.

The optimal thresholds for identification of nonischemic scar based on bipolar and unipolar voltage, electrogram duration, and deflection by receiver operating characteristic curves, and associated sensitivity and specificity measures were <1.78 mV (sensitivity 79.2%, specificity 88.6%) for bipolar voltage, <5.64 mV (69.5%, 86.6%) for unipolar voltage, >101 ms (80.3%, 83.7%) for electrogram duration, and >9 (80.5%, 79.9%) for electrogram deflection (Figure I in the online-only Data Supplement). Figure II in the online-only Data Supplement provides optimal thresholds for nonischemic scar identification by intramural scar type.

Comparison of Ablation Sites of Scar-Related VT and Scar on LGE-CMR
A total of 98 LV and 78 RV radiofrequency applications were made. Of all lesions in LV endocardium, 22.5%, 37.8%, 18.4%, and 10.2% were delivered to areas with 1% to 25%, 26% to 50%, 51% to 75%, and 76% to 100% scar transmurality, respectively (Figure IIIA in the online-only Data Supplement). Endocardial scar was more frequently targeted than other intramural scar types. Scar regions in the lateral left ventricle (42 sites; 42.9%) and septal right ventricle (40 sites; 39.6%) were more likely to be targeted for ablation (Figure IIIB and IIIC in the online-only Data Supplement). Additionally, 11.2% of lesions were delivered to regions without scar on LGE-CMR. Of 11 LV sites without scar on LGE-CMR, 9 were ablated adjacent to scar on LGE-CMR to target abnormal electrograms, guided by pace mapping as well as substrate modification strategies. The remaining 2 sites with normal electrograms were ablated in the same patient to create a linear lesion set connecting 2 islands of scar in close proximity (<1 cm). No adverse effects (effusion, decreased ejection fraction, or increased heart failure) were observed in these patients. A total of 20 sites of scar-related re-entrant VT in the left (N=12) and right ventricles (N=8) were identified (Figure 4A). Of all VT circuit sites, 5 sites (4 in left ventricle, 1 in right ventricle) were identified as exit sites by both entrainment and pace mapping. The mean VT cycle length was significantly longer in VTs that enabled entrainment mapping, compared with those where only pace mapping was used (464±64 versus 314±72 ms; P<0.001 by

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>VT (N=15)</th>
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</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>51±11</td>
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<tr>
<td>BMI, kg/m²</td>
<td>29.4±6.6</td>
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<tr>
<td>Idiopathic/sarcoidosis</td>
<td>10/5</td>
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<tr>
<td>Epicardial ablation (patients)</td>
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<tr>
<td>Use of antiarrhythmic drug: amiodarone/sotalol/mexiletine/flecainide/β-blocker</td>
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<tr>
<td>MRI with in situ ICD</td>
<td>13</td>
</tr>
<tr>
<td>LV end-diastolic volume, mL</td>
<td>154.0±28.5</td>
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<tr>
<td>LV end-systolic volume, mL</td>
<td>99.0±21.1</td>
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<td>LV stroke volume, mL/beat</td>
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<tr>
<td>LV ejection fraction, %</td>
<td>40.6±9.1</td>
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</tbody>
</table>

Values are expressed as mean±SD or number. BMI indicates body mass index; ICD, implantable cardioverter defibrillator; LV, left ventricular; and VT, ventricular tachycardia.

**Comparison of Scar on LGE-CMR and Electrogram Characteristics**

Univariate comparisons of local electrogram and scar features revealed that voltage amplitude was negatively associated with scar transmurality (P<0.0001 by ANOVA for all intramural scar types; Figure 3A and 3B) and that electrogram duration and deflections were positively associated with scar transmurality (P<0.0001 by ANOVA for all intramural scar types; Figure 3C and 3D). Of all EAM points analyzed, 4.9% had fractionated electrograms and 3.3% had isolated potentials. There was a positive association between the incidence of fractionated and isolated potentials with scar transmurality (P<0.0001 by ANOVA for both; Figure 3E), and isolated potentials were more frequently observed in sectors with higher scar transmurality and patchy scar regions (P<0.05 by ANOVA).

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**Figure 2. Scar characteristics in patients with nonischemic ventricular tachycardia.** The distribution (A) and characteristics (B–D) of scar in left ventricle in our patient cohort.
VT circuit sites were more likely to be identified within endocardial scar (50% in LV and RV septum, respectively; Figure 4B). The mean scar transmurality of VT circuit sites was 39.6±20.7%, and most VT circuit sites were identified in scar with >25% scar transmurality (83.3% in left ventricle, 100% in right ventricle; Figure 4C). In addition, most VT circuit sites were identified in basal (50.0%; 10 sites) and mid regions (35.0%; 7 sites).

Isolated potentials were observed in 3 (15.0%) of 20 VT circuit sites. S-QRS ($R=0.482, P=0.047$ by Spearman correlation test) and $\%S/QRS/VL-CT (R=0.500, P=0.046$ by Spearman correlation test) were associated with scar transmurality (Figure 4D). Slow conduction defined by >40 ms of S-QRS delay (12.2% of sites) was confined to regions with >75% scar transmurality or patchy scar. In addition, all VT circuit sites demonstrated <30% of $\%S/QRS/VL-CL$ and were identified as VT exit sites. Figure 5 provides an example of concealed entrainment during VT, and sinus rhythm local electrograms, from a successful ablation site highlighted on electroanatomic mapping and LGE-CMR.

**Comparison of Patient Characteristics Between Complete and Partial Success of VT Ablation**

Table 3 summarizes the characteristics of patients with complete versus partial success. Of 13 patients with re-entrant VT ablation, complete success was achieved in 7 and partial success attained in the remaining patients. Patients with complete success were younger (median age of patients with complete success: 40 years [interquartile range (IQR), 39–46] versus median age for partial success: 56 years [IQR, 54–62]; Wilcoxon rank-sum test; $P=0.003$) and had less extensive low-voltage areas in the right ventricle (complete success: 12.7 cm$^2$ [IQR, 2.6–22] versus partial success: 45 cm$^2$ [IQR, 25.3–75]; Wilcoxon rank-sum test; $P=0.049$).

Additionally, the presence of patchy scar was associated
with partial success (complete success: 0 sector [IQR, 0–0.5] versus partial success: 3.8 sectors [IQR, 1.3–7.5]; Wilcoxon rank-sum test; \( P = 0.028 \)).

**Discussion**

The main findings of this study are that (1) LV wall thickness, scar transmurality, intramural location, and type are independently associated with local electrogram bipolar and unipolar voltage, duration, and deflections; (2) most VT exit sites are located in scar regions with >25% scar transmurality; (3) sites with evidence of slow conduction are associated with >75% transmurality or patchy scar on LGE-CMR; and (4) the presence of extensive regions with patchy scar is associated with incomplete success of VT ablation.

**Nonischemic Scar and Electrogram Characteristics**

The VT substrate in NICM exhibits more complicated morphology and distribution patterns compared with the substrate in ischemic cardiomyopathy.\(^\text{19}\) We noted a preponderance for basal scar distribution, consistent with previous reports using voltage mapping in patients with NICM.\(^\text{8–15}\) Previous reports have shown associations between ischemic scar on LGE-CMR and local electrograms on EAM.\(^\text{3–8}\) However, to the best of our knowledge, aside from a single case report,\(^\text{16}\)

![Figure 4. Associations between scar on late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR) and ventricular tachycardia (VT) circuit sites of scar-related VT. A total of 20 VT circuit sites were identified in left (12 sites) and right ventricles (8 sites) endocardially. A, The VT circuit sites in left and right ventricles were more frequently observed in lateral and inferior LV and septal RV regions, respectively. The VT circuit sites were more frequently observed in regions with endocardial scar (B) and 25% to 75% scar transmurality (C) in LV and RV septum. D, S-QRS (R=0.482; \( P=0.047 \)) and %S-QRS/VT-CL (R=0.500; \( P=0.046 \)) were significantly associated with scar transmurality. The VT circuit sites with \( >40 \text{ ms of S-QRS} \) were associated with 75% scar transmurality and patchy scar.](image-url)
no clinical studies have previously examined the association of nonischemic scar on LGE-CMR with local electrograms. Psaltis et al\textsuperscript{25} demonstrated negative associations between the extent of scar on LGE-CMR and bipolar and unipolar voltage measures in 12 sheep with NICM induced by doxorubicin coronary infusions. Our results confirm Psaltis et al’s findings regarding voltage measures in the sheep model. In addition, the present study demonstrated a positive association between scar transmurality and electrogram duration and deflections, which suggests the existence of slow conduction in regions with higher scar transmurality regardless of intramural scar distribution. Isolated potentials were associated with regions with higher scar transmurality or patchy scar.

Optimal Thresholds for Scar Identification

Psaltis et al\textsuperscript{25} suggested optimal thresholds of 7.5 mV for unipolar voltage (sensitivity 77%, specificity 76%) and 2.7 mV for bipolar voltage (sensitivity 54%, specificity 76%) for scar identification in their sheep model of NICM. In contrast, Hutchinson et al\textsuperscript{11} suggested a unipolar voltage threshold of 8.27 mV for detection of scar on endocardial EAM of patients with NICM. Our study is unique in determination of optimal thresholds for identification of nonischemic scar not only for bipolar and unipolar voltage but also for electrogram duration and deflections. Surprisingly, sensitivity and specificity profiles for scar identification using bipolar voltage were relatively high. Although the performance of these thresholds is expected to decline with prospective testing, our study suggests that, contrary to previous belief, midwall, epicardial, and patchy scar can be detected by endocardial voltage mapping and electrogram duration and deflections.\textsuperscript{11,17}

Scar Characteristics on LGE-CMR and VT Circuit Sites of Scar-Related Re-entrant VT

Previous reports have revealed the electrogram characteristics of VT circuit sites necessary for VT initiation and maintenance in patients with ischemic cardiomyopathy\textsuperscript{1–5} and NICM.\textsuperscript{8–18} In this study, a significant association was observed between circuit site location and regions with 26% to 75% scar transmurality. Sites in regions with >75% scar transmurality and patchy scar demonstrated >40 ms of S-QRS, suggesting slow conduction. Additionally, the presence of patchy scar was associated with partial success of VT ablation. In such patients, slow conduction sites may be located epicardially. Consequently, LV endocardial mapping may be limited in the detection of slow conduction sites because of the predilection of nonischemic scar for the midwall and epicardium.

Clinical Implications

Because of atypical nonischemic scar distribution patterns, low-voltage areas on endocardial electroanatomic mapping are smaller in patients with nonischemic scar–related VTs compared with patients with ischemic scar–related VTs. In fact, \( \approx 50\% \) of nonischemic scar was located in the midwall and epicardial LV myocardium, and 75% of scar had <50% scar transmurality in this study population. In addition, \( \approx 20\% \)
of the myocardial sectors on LGE-CMR in patients with nonischemic scar–related VTs contained scar in contrast to 40% of CMR sectors on LGE-CMR in patients with ischemic scar–related VTs. Based on our findings, endocardial mapping may identify VT exit sites where the target VTs can be eliminated by ablation. Endocardial sites that exhibit slow conduction correspond to areas with scar transmurality >75% or patchy scar. In addition, if VT circuits within the interventricular septum are suspected in patients with NICM, the RV septum should be mapped. In this study, most ablations were performed using an endocardial approach and successfully suppressed the targeted VTs. However, central VT circuit sites were not identified. It is possible that central circuit sites are predominantly in the midwall or epicardium in this population; therefore, if an endocardial approach fails, epicardial access seems warranted.

Limitations
The main limitation of this study is the relatively small sample size. Additionally, because the targeted VT was successfully ablated in the majority of patients using an endocardial approach, epicardial mapping was only performed in a subset of patients. Some VT substrates may have been epicardial and missed by endocardial mapping. Further studies will be necessary to confirm our results in larger cohorts with epicardial mapping. In 2 patients, ablations were performed adjacent to scar on LGE-CMR to target the sites with abnormal electrograms or to create a linear lesion set connecting two islands of scar in close proximity. Data regarding the safety and efficacy of this approach are limited. In this study, 16.9% of the sectors on short-axis LGE-CMR images were excluded because of MRI susceptibility artifacts from ICD generators. Results may also be limited by a possibility for positional errors when registering EAM points to LGE-CMR images. It is important to emphasize that these results are based on endocardial voltage mapping and the specific LGE-CMR image acquisition parameters specified in the Methods section. Therefore, the results are not generalizable to epicardial mapping and other image acquisition protocols. Measurement of electrogram duration and deflections may differ depending on the criteria for analysis. We measured electrogram duration and deflections according to the criteria by Tung et al. Interobserver reliability analysis was not formally performed. However, disagreements among the 3 observers were rare. Finally, electrogram parameters can be affected by mapping catheter contact and orientation.

Conclusions
Strong associations were found between scar characteristics on LGE-CMR and bipolar and unipolar voltage, duration, and deflections on endocardial EAM. These associations suggest that application of optimal thresholds to electrogram parameters may improve the detection of nonischemic midwall, epicardial, and patchy scar. Additionally, VT circuit sites are likely to reside in areas with >25% scar transmurality on LGE-CMR.

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Disclosures
Dr Nazarian is on the MRI advisory board to Medtronic Inc and is a scientific advisor to and principal investigator for research support to Johns Hopkins from Biosense Webster Inc. Dr Halperin has received research grant and consultant fees from Zoll Circulation Inc and has ownership interests in IMRiCOR Medical Systems Inc. Dr Berger has received research grants from St Jude Medical Inc and Medtronic Inc and consultant fees from Boston Scientific Corp and Cameron Health Inc. The Johns Hopkins University Conflict of Interest Committee manages all commercial arrangements. The other authors have no conflicts to report.

References
2. Stevenson WG, Sager PT, Nutterson PD, Saxon LA, Middlekauff HR, Wiener I. Relation of pace mapping QRS configuration and conduction

**CLINICAL PERSPECTIVE**

Radiofrequency catheter ablation can be used for treatment of monomorphic ventricular tachycardia (VT) in patients with implantable defibrillators and nonischemic cardiomyopathy (NICM). However, identification of appropriate targets for ablation can be challenging because of hemodynamic instability during VT and the presence of midmyocardial and epicardial scar substrates in NICM. We sought to quantify the association of VT substrate sites with late gadolinium-enhanced cardiac magnetic resonance (LGE-CMR) image characteristics to gain insights regarding the anatomy of tissues and critical sites that support nonischemic VT. Left ventricular wall thickness, scar transmurality, and intramural scar location on LGE-CMR were associated with local intracardiac bipolar and unipolar electrogram amplitudes, duration, and deflections. Optimal thresholds for identification of nonischemic scar were <1.78 mV for bipolar voltage, <5.64 mV for unipolar voltage, >101 ms for electrogram duration, and >9 for electrogram deflections. Fractionated and isolated potentials were more likely to be observed in regions with higher scar transmurality and patchy scar. Circuit sites for maintenance of postinfarct VT were associated with >25% scar transmurality, and slow conduction sites were associated with >75% transmurality or patchy scar. Previous knowledge of LGE-CMR and VT substrate associations may optimize procedural strategies by reducing the time devoted to electrogram mapping and guiding the decision to obtain epicardial access.
Impact of Nonischemic Scar Features on Local Ventricular Electrograms and Scar-Related Ventricular Tachycardia Circuits in Patients With Nonischemic Cardiomyopathy


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### Supplemental Table 1: Results of EAM and Catheter Ablation

<table>
<thead>
<tr>
<th>VT Patients (N=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mapping in LV / RV / Both</td>
</tr>
<tr>
<td>Analyzed EAM Points in LV / RV</td>
</tr>
<tr>
<td>Mean LV Volume [ml]</td>
</tr>
<tr>
<td>Low Voltage Area in LV [CM²] (% for LV Endocardium)</td>
</tr>
<tr>
<td>Dense Scar in LV [CM²] (% for LV Endocardium)</td>
</tr>
<tr>
<td>Mean RV Volume [ml]</td>
</tr>
<tr>
<td>Low Voltage Area in RV [CM²] (% for LV Endocardium)</td>
</tr>
<tr>
<td>Dense Scar in RV [CM²] (% for LV Endocardium)</td>
</tr>
<tr>
<td>Surface Registration Error [mm]</td>
</tr>
<tr>
<td>Number of Induced VT</td>
</tr>
<tr>
<td>Number of RF Application</td>
</tr>
<tr>
<td>Critical Sites of VT or PVC Origin</td>
</tr>
<tr>
<td>11/12 or 12/12 Pace Map</td>
</tr>
<tr>
<td>PPI-VTCL &lt;30ms</td>
</tr>
<tr>
<td>Concealed Entrainment</td>
</tr>
<tr>
<td>Successful Ablation / Modification</td>
</tr>
<tr>
<td>Procedure Time</td>
</tr>
</tbody>
</table>
Fluoroscopy Time    75±25
Ablation Time       20±15

Values are shown as number (%). Low voltage areas and dense scar on EAM were defined as areas with <1.5mV and <0.5mV of bipolar voltages, respectively.

RF=radiofrequency; PPI-VTCL=post pacing interval-VT cycle length. See abbreviations in Table 1.
Supplemental Figure 1 – Receiver Operating Characteristics Curves for Nonischemic Scar Identification Using EGM parameters – The figure illustrates receiver operating characteristics curves for the scar identification on EAMs regarding each EGM parameter (bipolar and unipolar voltages, duration and deflections). The optimal thresholds for bipolar and unipolar voltage, duration and deflection to identify nonischemic scar regardless of intramural scar types are shown with specificity and sensitivity, respectively.

(A) Bipolar Voltage
Bipolar: ≤1.78mV (79.2%, 88.8%)
AUC: 0.902

(B) Unipolar Voltage
Unipolar: ≤5.64mV (69.5%, 89.6%)
AUC: 0.846

(C) EGM Duration
Duration: >101 ms (80.3%, 83.7%)
AUC: 0.871

(D) EGM Deflection
Deflection: >9 (80.5%, 79.3%)
AUC: 0.863
**Supplemental Figure 2 – Receiver Operating Characteristics Curves for Nonischemic Scar Identification Using EGM parameters by scar intramural location** – The figure illustrates receiver operating characteristics curves for the scar identification on EAMs regarding each EGM parameter by scar intramural location (endocardial, mid wall, epicardial and patchy scar). The optimal thresholds for bipolar and unipolar voltage, duration and deflection to identify nonischemic scar for each intramural scar type is shown with specificity and sensitivity, respectively.

<table>
<thead>
<tr>
<th></th>
<th>Bipolar Voltage</th>
<th>Unipolar Voltage</th>
<th>Duration</th>
<th>Deflection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endocardial Scar</strong></td>
<td>AUC: 0.959</td>
<td>AUC: 0.933</td>
<td>AUC: 0.699</td>
<td>AUC: 0.811</td>
</tr>
<tr>
<td>Bipolar: ≤1.55mV</td>
<td>(Sensitivity: 91.8%, Specificity: 90.8%)</td>
<td>Unipolar: ≤5.25mV</td>
<td>(Sensitivity: 68.1%, Specificity: 90.9%)</td>
<td>Duration: &gt;162ms</td>
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<tr>
<td><strong>MidWall Scar</strong></td>
<td>AUC: 0.963</td>
<td>AUC: 0.962</td>
<td>AUC: 0.860</td>
<td>AUC: 0.845</td>
</tr>
<tr>
<td>Bipolar: ≤1.78mV</td>
<td>(Sensitivity: 93.2%, Specificity: 89.6%)</td>
<td>Unipolar: ≤6.64mV</td>
<td>(Sensitivity: 93.1%, Specificity: 88.3%)</td>
<td>Duration: &gt;108ms</td>
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<tr>
<td><strong>Epicardial Scar</strong></td>
<td>AUC: 0.914</td>
<td>AUC: 0.941</td>
<td>AUC: 0.894</td>
<td>AUC: 0.822</td>
</tr>
<tr>
<td>Bipolar: ≤1.90mV</td>
<td>(Sensitivity: 82.5%, Specificity: 82.7%)</td>
<td>Unipolar: ≤6.48mV</td>
<td>(Sensitivity: 97.3%, Specificity: 79.8%)</td>
<td>Duration: &gt;108ms</td>
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<tr>
<td><strong>Patchy Scar</strong></td>
<td>AUC: 0.909</td>
<td>AUC: 0.945</td>
<td>AUC: 0.891</td>
<td>AUC: 0.907</td>
</tr>
<tr>
<td>Bipolar: ≤1.72mV</td>
<td>(Sensitivity: 77.7%, Specificity: 90.7%)</td>
<td>Unipolar: ≤5.64mV</td>
<td>(Sensitivity: 89.6%, Specificity: 88.5%)</td>
<td>Duration: &gt;161ms</td>
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The figure illustrates receiver operating characteristics curves for the scar identification on EAMs regarding each EGM parameter by scar intramural location (endocardial, mid wall, epicardial and patchy scar). The optimal thresholds for bipolar and unipolar voltage, duration and deflection to identify nonischemic scar for each intramural scar type is shown with specificity and sensitivity, respectively.
Supplemental Figure 3 – Associations between Septal Scar on LGE-CMR and Ablation Sites

The figure illustrates the association of ablation sites and critical VT sites with scar transmurality. (A) Ablation sites were observed in regions with scar or adjacent to scar. Ablation sites in LV (B) and RV (C) were more frequently observed in LV lateral and RV septal regions, respectively.