Layered Activation of Epicardial Scar in Arrhythmogenic Right Ventricular Dysplasia
Possible Substrate for Confined Epicardial Circuits

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Background—Ventricular tachycardia ablation in arrhythmogenic right ventricular dysplasia (ARVD) is more successful when including epicardial ablation. Scarring may cause independent, layered epicardial activation and promote epicardially confined ventricular tachycardia circuits. We aimed to characterize transmural right ventricular activation in ARVD patients and to compare this with reference patients without structural heart disease.

Methods and Results—Eighteen ARVD patients underwent detailed endocardial and epicardial sinus rhythm electroanatomic mapping. Bipolar activation was annotated at the sharpest intrinsic deflection including late potentials and compared with 6 patients with normal hearts. Total scar area was larger on the epicardium (97±78 cm²) than the endocardium (57±44 cm²; \( P=0.04 \)), with significantly more isolated potentials. Total epicardial activation time was longer than endocardial (172±54 versus 99±27 ms; \( P<0.01 \)), and both were longer than in reference patients. Earliest endocardial site was the right ventricular anteroseptum in 17 of 18 ARVD patients versus 5 of 6 controls (\( P=0.446 \)), and latest endocardial site was in the outflow tract in 13 of 18 ARVD patients versus 4 of 6 controls and tricuspid annulus in 5 of 18 ARVD patients versus 2 of 6 controls (\( P=1.00 \)). In reference patients, epicardial activation directly opposite endocardial sites occurred in 5.2±1.9 ms, suggesting direct transmural activation. In contrast, ARVD patients had major activation delay to the epicardium with laminar central scar activation from the scar border, not by direct transmural spread from the endocardium.

Conclusions—Transmural right ventricular activation is modified by ARVD scarring with a delayed epicardial activation sequence suggestive of independent rather than direct transmural activation. This may predispose ventricular tachycardia circuits contained entirely within the epicardium in ARVD and explains observations on the need for direct epicardial ablation to eliminate ventricular tachycardia. (Circ Arrhythm Electrophysiol. 2012;5:796-803.)

Key Words: ablation ▪ cardiomyopathy ▪ catheter ablation ▪ electrophysiology ▪ tachycardia

Arrhythmogenic right ventricular dysplasia (ARVD) is a genetically determined cardiomyopathy characterized by cardiomyocyte loss with replacement of the myocardium by fibrofatty tissue. The altered myocardial architecture resulting from this process causes delayed and disordered electric propagation and predisposes to the development of reentrant ventricular tachycardia (VT). Although the left ventricle (LV) can be involved, the disease process predominantly affects the right ventricle (RV), and both pathological and electroanatomic studies show a disproportionate burden of disease on the epicardium compared with the endocardium. This is likely to have implications on the nature and location of the reentrant VT circuits seen in ARVD. In particular, confluent epicardial or intramural scarring may prevent transmural endocardial-to-epicardial activation during VT, precluding endocardial involvement, and establish the potential for all or major components of VT circuits to be confined entirely to the epicardium. We postulated that the compartmentalized activation of the epicardium induced by such confluent scarring would also alter the sinus rhythm right ventricular endocardial-to-epicardial activation sequence.

The purpose of this study was to define the pattern of activation of the RV endocardium and epicardium in patients without structural heart disease and to compare this with patients with anticipated extensive RV scarring caused by ARVD.

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Methods
The study population (group 1) consisted of 18 consecutive patients with ARVD (13 men; mean age, 43±15 years) who had detailed endocardial and epicardial electroanatomic mapping (EAM) performed. Patients were studied between 2007 and 2010 and met the Revised Task Force Criteria for ARVD as listed in Table 1. They had recurrent VT and multiple implantable cardioverter-defibrillator (ICD) therapies, despite antiarrhythmic drugs, and were undergoing catheter ablation. Thirteen of the 18 patients (72%) had undergone a prior ablation procedure. Patients had recurrent monomorphic VT documented either by 12-lead electrocardiograph or by stored ICD electrograms. The reference group...
Table 1. Task Force Criteria

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M indicates male; F, female.

(group 2) consisted of 6 consecutive patients (3 men; mean age, 44±16 years) with no structural heart disease who had endocardial and epicardial EAM performed during catheter ablation of idiopathic ventricular arrhythmias. All patients provided written informed consent for electrophysiological study and catheter ablation in accordance with the University of Pennsylvania Health System’s institutional guidelines.

Preprocedural Imaging

All patients underwent transthoracic echocardiography to exclude intracardiac thrombus. Cardiac magnetic resonance (CMR) imaging was performed to define further the arrhythmogenic ventricular substrate in some of the patients. Contrast-enhanced CMR was performed on a clinical 1.5-T scanner (Avanto; Siemens, Erlangen, Germany) using a standard protocol that included assessment of delayed gadolinium enhancement. To reduce the risk of radiofrequency-related heating of the intracardiac lead in patients with ICDs a nonbalanced echo sequence (TurboFLASH) was used for cine imaging to reduce energy deposition and device artifacts. All devices were interrogated prescanning and postscanning, with no change in pacing threshold, lead, or battery data observed.

Endocardial Electroanatomic Mapping

Patients were studied in the postabsorptive state under conscious sedation or general anesthesia after preoperative echocardiography excluded intracardiac thrombus. Antiarrhythmic drugs were stopped >5 half lives preoperatively. An intracardiac echocardiography catheter (ACUSON Acuvue; Siemens, Mountain View, CA) was deployed in the RV where it was used to assess ventricular function and scarring, confirm catheter contact, and monitor lesion formation during ablation. The CARTO (XP and 3) system (Biosense Webster, Diamond Bar, CA) was used for EAM in conjunction with a standard open-irrigated catheter (Navistar Thermocoool; Biosense Webster), which has a 3.5-mm tip electrode, a 2-mm ring electrode, and a 1-mm interelectrode spacing. Bipolar electrograms were filtered at 30 to 400 Hz, displayed at 200 mm/s sweep speed, and stored for offline annotation and analysis. Unipolar electrograms were filtered at 1 to 240 Hz. Annular points were tagged, and mapping density was sufficient to allow for complete surface geometry reconstruction with a fill threshold of <15 mm. Normal bipolar endocardial RV electrogram voltage was defined as ≥1.5 mV, whereas dense scar was taken to be <0.5 mV. When endocardial bipolar voltage was unremarkable, we examined the unipolar electrograms with their wider field of view for evidence of deeper subjacent substrate. Normal RV free wall unipolar electrograms were defined as having peak-to-peak amplitude ≥5.5 mV.

Fractionated potentials were defined in a standard fashion as electrograms with multiple deflections from baseline with an amplitude ≤0.5 mV and duration ≥133 ms or an amplitude:duration <0.005. Standard criteria were also used to define isolated late potentials (ILP), as electrograms displaying an additional signal separated from the initial ventricular electrogram by a >20-ms isoelectric interval, with the second component usually (but not invariably) occurring after the end of the surface QRS complex had been inscribed.

Epicardial EAM

Percutaneous pericardial access was obtained using a Tuohy needle via a subxiphoid approach as described by Sosa et al. An open-irrigated EAM catheter was used to perform high-density mapping of the epicardium, particularly concentrating on the RV epicardium. As previously described, to optimize the distinction between epicardial fat and fibrosis, we defined epicardial scar zones to be those areas with bipolar signal amplitude of <1.0 mV and containing prolonged (>80 ms) electrograms or ILP.

Activation Mapping

Local sinus rhythm activation was annotated at the onset of the highest frequency deflection of the bipolar electrogram by 2 independent investigators. The latest, split component of ILP was taken to represent local activation, and this was annotated (Figure 1). For fractionated signals, reference was also made to the steepest negative components of the tip and ring unipolar electrograms and to the activation times of the immediately adjacent regions. Endocardial and epicardial virtual geometries were superimposed to determine the site of epicardial breakout relative to the underlying endocardium.

Statistical Analysis

Continuous data are presented as mean±1 sd after being assessed for a normal distribution by inspection of histograms, Q–Q plots, and a 1-sided Kolmogorov–Smirnov test. Baseline and mapping data were analyzed by the Fisher exact test and paired and unpaired Student t test as appropriate. A 2-tailed P value of <0.05 was considered to be statistically significant.
Results

Baseline Characteristics
The baseline characteristics of the 2 groups are compared in Table 2. There were no significant differences between the 2 groups in terms of age, sex, LV size and systolic function, antiarrhythmic drug use, or sinus rhythm mean QRS complex duration. ICDs were present in 15 of 18 (83%) ARVD patients and in none of the 6 control patients. Contrast-enhanced CMR was performed in 10 of 18 ARVD patients and showed regional RV wall motion abnormalities in 9 and delayed RV enhancement in 7. No CMR abnormalities were seen in the control patients. No adverse events related to CMR scanning occurred in patients with ICD. The mean RV ejection fraction was 33±8% in the ARVD patients compared with 42±2% in the control group (P=0.02).

Electroanatomic Substrate Mapping
Endocardial RV point sampling was greater in the ARVD patients (294±110 points) than the control patients (113±33 points; P<0.01). Likewise, epicardial point sampling was also greater in the ARVD group (506±126 points versus 258±50 points; P<0.01). The results of electroanatomic voltage mapping are presented in Table 3. The most common sites of endocardial scarring in group 1 patients were the infundibulum (15/18) and the basal peritricuspid region (15/18). No significant endocardial or epicardial scarring was seen in the control patients. In the ARVD patients, total scar area was greater on the epicardium than the endocardium (98±79 cm² versus 57±44 cm²; P=0.048) and was often arranged in confluent sheets. The basal lateral free wall and peritricuspid region were involved with epicardial scarring in all ARVD patients, and the infundibulum was involved in 16 of 18 patients.

In the ARVD group, a similar proportion of endocardial and epicardial electrograms were fractionated (3.6±3.1% versus 3.1±4.4%; P=0.727); however, isolated potentials were significantly more prevalent on the epicardium than the endocardium (16±8.1% versus 9.2±7.6%; P=0.017).

Table 2. Baseline Characteristics

<table>
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<tr>
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<th>Group 1 ARVD (n=18)</th>
<th>Group 2 Control (n=6)</th>
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<tr>
<td>Age, yr</td>
<td>42.5±15</td>
<td>43.8±16</td>
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<td>Sex, men (%)</td>
<td>13 (72)</td>
<td>3 (50)</td>
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<td>LV ejection fraction, %</td>
<td>53±13</td>
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<td>LV diastolic dimension, mm</td>
<td>45±9</td>
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<td>RV ejection fraction, %</td>
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<td>Amiodarone use preablation</td>
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<td>0.54</td>
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<td>ICD present</td>
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<tr>
<td>QRS duration, ms</td>
<td>101±28</td>
<td>93±15</td>
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<td>Right bundle branch block</td>
<td>3</td>
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ARVD indicates arrhythmogenic right ventricle dysplasia; LV, left ventricle; RV, right ventricular; ICD, implantable cardioverter-defibrillator.

Table 3. RV Endocardial and Epicardial Substrate Characteristics

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<th>Group 1 ARVD (n=18)</th>
<th>Group 2 Control (n=6)</th>
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<td>RV endocardial mapping points</td>
<td>362±161</td>
<td>124±45</td>
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<td>Epicardial mapping points</td>
<td>506±126</td>
<td>290±79</td>
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<td>RV endocardial EAM SA, cm²</td>
<td>233±38</td>
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<td>RV endocardial EAM volume, cm³</td>
<td>222±50</td>
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<td>RV bipolar scar (&lt;1.5 mV) SA, cm²</td>
<td>57±44</td>
<td>7.6±14</td>
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<td>RV scar percentage of RV SA</td>
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<td>3.2±6.1</td>
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<td>RV mean bipolar voltage, mV</td>
<td>2.7±0.9</td>
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<td>RV unipolar scar (&lt;5.5 mV) SA, cm²</td>
<td>122±57</td>
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<td>RV mean unipolar voltage, mV</td>
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<td>RV epicardial scar (&lt;1.0 mV) SA, cm²</td>
<td>98±79</td>
<td>0.6±1.3</td>
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RV indicates right ventricle; ARVD, arrhythmogenic right ventricular dysplasia; EAM, electroanatomic mapping; SA, surface area.
A periannular, patchy distribution of endocardial ILPs was the most common pattern seen (in 14/18 patients), whereas a minority had isolated anterior or inferior RV ILPs. In contrast, on the epicardium, large networks and clusters of ILPs across all regions were seen in all ARVD patients (Figure 2). The epicardium overlying the inferior RV displayed ILPs in 9 of 18 patients, whereas the same was seen in 7 of 18 anterior walls. The epicardium overlying the infundibulum, the lateral RV free wall, and the lateral tricuspid annulus harbored ILPs in 16 of 18, 15 of 18, and 12 of 18 patients, respectively. Both isolated and fractionated electrograms were rare in the control patients (0.3% and 0.1% of signals, respectively).

**Endocardial RV Activation**

Total endocardial RV activation was longer in the ARVD group compared with the control patients and accounted for a greater proportion of QRS duration (Figure 3). The earliest endocardial breakout occurred on the anteroseptal RV wall in 17 of 18 (94%) ARVD patients and 5 of 6 (83%) control patients ($P=0.446$). Endocardial RV breakthrough occurred $5\pm13$ ms before QRS onset in the ARVD patients and $1\pm7$ ms in group 2 ($P=0.148$). The latest endocardial activation occurred in the infundibulum in 13 of 18 (72%) ARVD patients and in 4 of 6 (67%) control patients. The inferior tricuspid annulus was activated last in the remaining 28% of the ARVD patients and 33% of the control patients ($P=1.00$).

**Epicardial RV Activation**

Similar to the endocardium, ARVD patients had longer total epicardial activation time than the control patients (Figure 3). A substantial portion of epicardial activation occurred after the end of the surface QRS because of the very late timing of most epicardial ILPs (Figures 1–3). Epicardial activation breakout occurred over the anteroseptal RV in all group 2 patients; however, 1 patient also had a simultaneous second breakout overlying the inferoseptal RV. The ARVD patients had epicardial breakthrough over the anteroseptal RV in 14 of 18 patients, whereas the anterior LV was the earliest epicardial site in the remaining 4 patients. Of these 4 patients, 3 had complete right bundle branch block and 1 had

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**Figure 2.** Electroanatomic maps depicting endocardial (ENDO) activation, epicardial (EPI) activation, and epicardial bipolar voltage of the right ventricle of a control patient are displayed (A). From a breakout in the anteroseptal region, activation can be seen to smoothly progress back toward the infundibulum and inferior tricuspid annulus. No evidence of endocardial (not shown) or epicardial scarring was seen in the control patients, with low-voltage red areas on the epicardium displaying otherwise normal electrograms indicating epicardial fat. B, The same electroanatomic maps in a 27-year-old man with arrhythmogenic right ventricular dysplasia (ARVD). Confluent epicardial scarring is seen on the right with low voltage and large clusters of isolated potentials (black dots), and they were much less frequent on the endocardium. Although activation breakouts were in a similar region to the control patient, wavefront propagation is significantly altered by the sheets of scarring, particularly on the epicardium, where very delayed activation into the scar is seen.
partial right bundle branch block. Epicardial breakout time was not significantly different between the groups (6.3 ± 12 ms after QRS onset for group 1 versus 3.2 ± 8.2 ms for group 2; \( P = 0.493 \)).

The latest epicardial RV activation was seen overlying the inferior tricuspid annulus in 5 of 6 and the infundibulum in 1 of 6 control patients. In the ARVD group, when annotating the second component of ILPs, the latest activation site was determined by the location of the dense scar sheets containing the longest coupled ILPs. This was overlying the inferior tricuspid annulus in 9 of 18 patients, the infundibulum in 7 of 18, and the mid-RV free wall in 2 of 18. These regions usually contained networks or clusters of ILPs that were activated in 1 of 3 patterns. In 2 patients, broad sweeping wavefronts propagated from one end of the cluster to another. In 3 patients, a branching pattern of activation activated the scar from one end. In the remaining 13 patients, a collision of wavefronts was observed that activated epicardial scarring from its periphery and progressed inward to its center (Figure 4).

**Figure 3.** A, An endocardial (ENDO) activation map from a 44-year-old man with arrhythmogenic right ventricular dysplasia (ARVD) demonstrating smooth endocardial wavefront propagation from the apical anteroseptum to the base within 86 ms. The epicardial (EPI) shell of the same patient has had isolated potentials annotated (B), and this shows progressive, late activation from the midinferior ventricle (RV) toward the epicardial infundibulum. This occurs much later than corresponding endocardial activation and with a discordant vector suggestive of independent epicardial activation rather than multisite transmural conduction breakthrough from the endocardium. Overall, both endocardial and epicardial total activation time (TAT) was significantly longer in the ARVD patients than the control patients, despite similar QRS duration (C). In ARVD patients, however, epicardial TAT was almost twice as long as endocardial TAT. The mean activation delay between corresponding endocardial and opposite epicardial points and the delay between latest activating endocardial and epicardial points were both significantly greater in ARVD patients (D).

**Relationship Between Endocardial and Epicardial RV Activation**

Activation at directly opposite endocardial and epicardial points was compared at the infundibulum, the lateral free RV wall, the anterior wall, the inferior wall, the apex, and the inferolateral tricuspid annulus. In control patients, mean activation at the respective opposite epicardial site occurred with significantly shorter delay than in the ARVD patients (Figure 3D). Latest epicardial RV activation occurred within 20 ms after latest RV endocardial activation in all control patients. By comparison, in the ARVD patients, a 4-fold delay elapsed between the last recorded endocardial activation and the latest epicardial RV sites, which were generally located within a cluster of late-coupled epicardial isolated potentials (Figure 3D).

**VT Characteristics**

During these combined endocardial and epicardial procedures, 28 VTs were induced and targeted for ablation in these 18 patients, 1.6 VTs per patient. Of these, only 9 (32%)
were mappable, mainly because of short cycle length causing hemodynamic instability. Using a combination of limited entrainment data, and activation and pace mapping, it was found that 22 of these 28 VTs (79%) had significant putative components of their circuits on the epicardium. Extensive epicardial ablation rendered 20 of these putative epicardial VTs (91%) noninducible by the end of the procedure.

**Discussion**

This is the first study to examine the transmural RV activation pattern both in a group of control patients without structural heart disease and in patients with ARVD. The main findings are as follows:

1. Sinus rhythm endocardial RV activation in the absence of structural heart disease progresses smoothly from the earliest breakthrough in the apical anteroseptal endocardium toward the basal regions.
2. Reference patients without structural heart disease also show evidence of epicardial RV activation in a similar sequence to the endocardium with relative activation timing suggestive of direct transmural endocardial-to-epicardial depolarization.
3. Endocardial RV activation in ARVD is altered by extensive fibrosis that characterizes this disease such that it takes proportionately longer but occurs in an overall similar sequence because of the largely periannular endocardial substrate distribution.
4. Epicardial RV activation is altered and activated in a delayed fashion, with a pattern that often appears independent of subjacent endocardial activation, suggesting that the dense confluent fibrosis characteristic of ARVD may potentially compartmentalize the endocardium from the epicardium.

Although some data exist on the normal sequence of ventricular activation in patients with and without structural and conduction system disease, these data are generally focused on the LV and concentrate on the endocardium using contact or noncontact mapping and on the epicardium using electrocardiographic imaging. No studies have performed simultaneous contact mapping of the ventricular endocardium and epicardium to examine the sequence and relationship of activation of the 2 surfaces, and there have not been any data describing the effect of structural disease on this relationship. Although existing studies have largely examined ventricular activation from the perspective of dyssynchrony resulting from intraventricular conduction delay (and its potential treatment with biventricular pacing), this activation sequence is also important in understanding the mechanism and location of VTs in various nonischemic cardiomyopathies. Compared with the postinfarct context, these are generally characterized by a typical basal, periannular substrate distribution, with a disproportionate burden of epicardial-to-endocardial scar. This epicardial substrate preponderance would be expected to increase the prevalence of VT circuits exiting on the epicardium, but it may...
also predispose the creation of VT circuits confined entirely to the epicardium with only passive endocardial activation.\(^{17}\) In the latter situation, the endocardium behaves as a separate chamber, and this is in contrast to its role in transmural VT circuits that may have entrance, exit, and central isthmus in either the endocardium, epicardium, or the intramural ventricle. The sorts of VT circuits established are likely to depend on the location and degree of transmural scar and on the thickness of the ventricle, and this is likely to be different in the RV and LV.

A unique opportunity to understand the 3-dimensional substrate underlying VT in nonischemic cardiomyopathies is presented by patients with ARVD. Patients requiring ablation for VT in this context generally have significantly more epicardial scar than endocardial scar but may also have substantial intramural fibrosis, which would increase the likelihood of conduction block to the endocardium and independent activation of the epicardium in VT by circuits unable to traverse the intramural RV. In sinus rhythm, the footprint of such a schema would be the independent, laminar activation of the endocardium and epicardium.

Control group data from this study suggest that normal human RV activation occurs in an apex-to-base fashion, from its initial breakout at the myocardial arborization of the distal right bundle branch toward the infundibulum and basal annuli. A similar sequence occurs on the epicardium, and this is consistent with the results obtained by Wyndham et al.\(^{18}\) with surgical mapping of intact hearts with coronary disease but without prior myocardial infarction. In that study, a constant anterior RV epicardial breakout was also seen and latest activation was again heterogeneous in precise location but generally in the basal regions of the RV. We observed a near simultaneous activation (delayed by only 5.2±1.9 ms) at sequential fiducial points along the course of activation of the endocardium and epicardium. This suggests that progressive transmural activation of the epicardium from subjacent endocardial points (rather than independent epicardial laminar activation) is occurring, as the absence of a Purkinje network on human epicardium would be expected to slow conduction relative to the endocardium to a significantly greater extent than that observed. The finding that the very latest epicardial site is activated within a mean of only 16 ms of the completion of endocardial activation further supports this hypothesis.

By comparison, the normal pattern of RV activation during sinus rhythm is greatly altered in ARVD by the location and extent of the scarring process, and significant uncoupling of the endocardial and epicardial activation timing and pattern suggests the presence of significant intramural or transmural substrate. Although RV free wall was seen on CMR, the resolution of this modality at present is insufficient to be certain about the exact transmural scar distribution. Of note, both the degree and nature of scarring was heterogeneous in these patients, as not only was there a larger epicardial scar area but also it contained a greater number of fractionated and isolated potentials, and ILPs here had longer coupling intervals of the isolated electrogram component compared with those on the endocardium. The isolated component of ILPs is very likely to represent local activation occurring beneath the catheter tip, and annotating this component generated 2 main results. First, local epicardial activation occurs significantly later than the subjacent endocardium in ARVD, and second, it occurs in atypical patterns that are likely to be related to scar geometry. In particular, the majority of patients exhibited a reverse centripetal pattern of activation of a confluent epicardial scar region from the periphery progressing to collision in the center. Such a pattern essentially excludes the possibility of direct sinus rhythm transmural endocardial-to-epicardial RV activation in these patients. This independent layered activation of the epicardium in sinus rhythm is likely to predispose the existence of VT circuits partly or even completely confined to the epicardium as the intramural fibrotic process provides a limited number of possible breakthrough sites to the endocardium that are insufficient to short circuit the reentrant VTs seen.

**Clinical Implications**

In the presence of the type of dense fibrosis seen in ARVD, successful endocardial ablation of such VT may be less likely given the poor transmural penetration of current ablation energy sources.\(^{19}\) This is particularly likely to be a limitation when burning in the thickened, densely scarred RVs seen in this condition. Though no randomized comparisons are available, the incorporation of epicardial mapping appears to be associated with better outcomes for ARVD-related VT ablation\(^{20}\) than does endocardial ablation alone. This is likely to be related to the increased ability to directly ablate the substrate for confined epicardial VT circuits when approaching these with a transpericardial, rather than a transmural, strategy.

**Limitations**

In this study, the endocardial and epicardial activation sequence have been determined in only the RV in ARVD patients with advanced scarring undergoing VT ablation, many of whom had undergone prior ablation, which could alter activation. These results cannot be extrapolated to the thinner walled LV nor to other disease states. Greater mapping density in the ARVD patients may also have affected the comparison with reference patients. Inaccuracies in determining local activation may have affected the results, including those related to the size of the mapping bipole, the orientation of the catheter shaft, and the difficulty in absolutely distinguishing far-field activation from local activation in fractionated signals. We could not map the midmural substrate by either EAM or imaging, and our conclusions about intramural activation are surmised from examining the endocardial and epicardial activation alone. Also, currently available technology does not allow for the ability to directly record simultaneous contact activation from opposite endocardial and epicardial points, and this may introduce some error into the analysis. Likewise, in the present study, we did not record epicardial activation times while pacing from directly subjacent endocardial points.

Finally, to date the detailed characterization of the entire VT circuit in this setting has not been performed and correlated with the observations noted in the present study. Unfortunately VTs are frequently poorly tolerated in this setting, particularly after general anesthesia is used during epicardial mapping, thus making such complete circuit characterization not possible at this point. Importantly, we have previously reported on successful ablation on epicardial sites directly opposite
normal endocardium or directly opposite sites of ineffective endocardial ablation consistent with our observations of the epicardium being likely to be effectively compartmentalized from the endocardium.  

Conclusions

Normal human RV activation progresses smoothly from apex to base on both the endocardium and epicardium, with likely direct transmural epicardial activation. RV activation in ARVD is modified by the presence of confluent scar with a delayed epicardial activation sequence, suggestive of possible independent rather than direct transmural activation. This may predispose VT circuits contained entirely within the epicardium in ARVD and explains observations on the need for direct epicardial ablation to successfully eliminate VT.

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Disclosures

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References


CLINICAL PERSPECTIVE

Arrhythmogenic right ventricular dysplasia (ARVD) is an important cause of scar-related ventricular tachycardia (VT). Multiple studies have shown the limited effectiveness of endocardial catheter ablation of VT in ARVD, but several centers, including our own, have reported significantly improved success rates when incorporating epicardial mapping and ablation into these procedures. Thick layers of confluent scarring may effectively separate the endocardium and epicardium of the right ventricle in ARVD. We examined the transmural sinus rhythm activation sequences of 18 ARVD patients undergoing VT ablation and compared them with 6 control patients with no structural disease. Epicardial scar burden was around 2-fold greater than endocardial scar in ARVD and contained networks of isolated potentials, which were activated in stereotypical patterns. In control patients, activation timing and sequences suggested a direct transmural spread of activation from the endocardium to the overlying epicardium. Annotating the isolated potentials in ARVD patients shows significant delay to epicardial activation with central scar activation from its periphery rather than direct transmural spread from the endocardium. This scar-induced independent epicardial activation suggests the possibility that some VT circuits may be confined entirely to the epicardium and explains the need for direct epicardial ablation to eliminate VT in ARVD.
Layered Activation of Epicardial Scar in Arrhythmogenic Right Ventricular Dysplasia: Possible Substrate for Confined Epicardial Circuits
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