Epicardial Substrate and Outcome With Epicardial Ablation of Ventricular Tachycardia in Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia

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Background—Efficacy of endocardial ventricular tachycardia (VT) ablation in arrhythmogenic right ventricular cardiomyopathy/dysplasia may be limited by epicardial VT, right ventricular thickening, or both. We sought to characterize the endocardial versus epicardial substrate, measure right ventricular free wall thickness, and determine epicardial ablation efficacy in patients with right ventricular cardiomyopathy/dysplasia.

Methods and Results—Thirteen consecutive patients (3 female; aged 43±15 years; range, 17 to 70 years) undergoing endocardial and epicardial sinus rhythm voltage mapping and epicardial VT ablation after failed endocardial VT ablation were included. In each patient, the low bipolar voltage area (<1.0 mV for epicardium and <1.5 mV for endocardium) was more extensive on the epicardium (95±47 versus 38±32 cm²; P<0.001) and was uniformly marked by multicomponent and late electrograms. The basal right ventricular thickness assessed by electroanatomic map was ≥10 mm in 6 of 13 patients compared with 5 to 10 mm in 4 reference patients without structural disease. Twenty-seven VTs were targeted on the epicardium with the use of activation, entrainment, or pace mapping with focal/linear ablation and targeting of late potentials. Epicardial VTs were targeted opposite normal endocardium in 10 patients (77%) and/or opposite ineffective endocardial ablation sites in 11 patients (85%). During 18±13 months, 10 of the 13 patients (77%) had no VT, with 2 patients having only a single VT at 2 and 38 months, respectively.

Conclusions—Patients with right ventricular cardiomyopathy/dysplasia and VT after endocardial ablation have a more extensive epicardial area of electrogram abnormalities and frequently have basal right ventricular wall thickening. Epicardial substrate and VT mapping identifies targets, and ablation results in VT control.

Key Words: ablation ■ cardiomyopathy ■ epicardium ■ arrhythmogenic right ventricular cardiomyopathy-dysplasia ■ ventricular tachycardia

In patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) and ventricular tachycardia (VT), sizable areas of endocardial free wall low voltage extending from the perivalvular region have been identified as the typical endocardial substrate.1 Ablation of ventricular arrhythmias in ARVC/D is successful in most cases by an endocardial approach.1–5 However, ablation success is not achieved uniformly, and many patients experience a late VT recurrence.3 In autopsy series, the epicardial substrate in patients with ARVC/D and VT may be more extensive than the endocardial.6 Areas of marked thickening and fibrosis, particularly on the endocardium, have been described.7,8 Protected VT circuits not amenable to endocardial ablation or opposite normal endocardium may need an epicardial approach for successful VT elimination by ablative therapy. The purpose of this study was to characterize the electroanatomic substrate and outcome in patients with ARVC/D and recurrent VT after endocardial ablative therapy undergoing simultaneous endocardial and epicardial mapping/ablation.

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Methods

Patient Population

Thirteen consecutive patients with ARVC/D undergoing simultaneous endocardial and epicardial catheter mapping and ablation for recurrent drug-refractory left bundle-branch block VTs after previous endocardial ablative therapy were included in the analysis. The risks of mapping/ablation were discussed in detail, and all patients gave written informed consent in accordance with the institutional guidelines of the University of Pennsylvania Health System. All patients fulfilled task force criteria for ARVC/D with evidence of right ventricular (RV) dilatation, segmental wall motion abnormalities, ECG abnormalities, and multiple left bundle-branch block VT morphologies9 (Table 1).
Endocardial Mapping

A detailed electroanatomic map of the endocardial RV surface was performed during sinus rhythm in 11 patients and during RV pacing in 2 patients. A 4-mm standard tip catheter or 3.5-mm open irrigated tip catheter (Thermacool, Biosense Webster, Diamond Bar, Calif) was used, maintaining a fill threshold of 20 mm to ensure adequate sampling and representation of the entire endocardial surface area. The bipolar signals were filtered at 10 to 400 Hz and were displayed at 100-mm/s speed on the CARTO (Biosense Webster, Inc) system. The peak-to-peak signal amplitude of the bipolar electrogram was measured automatically and confirmed during manual review. The electrogram signals were displayed as color gradients on a 3-dimensional computerized bipolar voltage map. Tricuspid valvular sites were identified by the fluoroscopic catheter tip positions at the ventricular base with discrete bipolar recordings that demonstrated both atrial and ventricular signals of approximately equal amplitude. The pulmonic valve was carefully identified by passing the mapping catheter into the pulmonary artery and slowly withdrawing it until an RV electrogram was identified and RV capture was possible and confirmed with the use of direct visualization of the valve with intracardiac echocardiography (ICE, Acuson Inc). Valvular sites were given a “location only” tag to preclude their influence on the voltage map color. Careful attention was paid to record multiple endocardial electrograms around valvular structures. Intracavitary points were identified as abrupt indentations on the endocardial shell contour with associated sudden reductions in signal slew rate and were appropriately edited from the voltage maps.

Reference Values for Voltage Mapping and Area Assessment of Voltage Abnormalities

Reference values for identifying abnormal endocardial bipolar electrogram signal amplitude in the RV were defined according to previously established criteria. A signal amplitude of >1.5 mV was categorized as normal and was represented in the electroanatomic map (CARTO) by the color purple. Abnormal endocardium was represented by the nonpurple range of colors, with the most abnormal signal amplitude, arbitrarily defined as “dense scar” (consistent with signal amplitude <0.5 mV), represented by the color red. More rigid voltage cutoff criteria were used when bipolar signals on the RV epicardium were analyzed to limit the influence of epicardial fat and coronary vasculature. The reference value for defining abnormal electrograms in the epicardium was established recently on the basis of voltage maps in 8 patients with normal RVs and LVs. Normal epicardial electrograms were defined as >1.0 mV, which corresponds to 95% of the signals from normal epicardium recorded at a distance of at least 1 cm from the defined large-vessel coronary vasculature. This analysis, which defined normal epicardial electrogram amplitude, avoided the overrepresentation of smaller amplitude electrograms frequently associated with scarred regions.

Epicardial Mapping

Epicardial access was obtained with the techniques described by Sosa and colleagues. An inferior approach to the pericardial sac was used to prevent puncture or laceration of the dilated RV. An 8F sheath was introduced into the pericardial space, and the CARTO catheter was advanced through the sheath for mapping and ablation. A 4-mm standard tip catheter was used in 4 patients, and an open irrigated tip catheter was used for mapping the epicardium in detail in 9 patients. Detailed voltage mapping focused on the entire RV and extended over the left ventricular (LV) surface (Figure 1). The fill threshold for RV epicardial mapping was also maintained at ≤20 mm, and mapping over the RV was continued until all points were sampled. The epicardial boundaries of the RV were defined as being opposite the endocardial anatomic shell and were further limited by identifying a 0.5- to 1.0-cm margin from the anatomically defined large-vessel right and left anterior descending coronary anatomy with the use of coronary angiography, merged computed tomographic images, or both.

Figure 1. Endocardial vs epicardial bipolar voltage map (anterior view) in a patient with ARVC/D and VT not amenable to endocardial ablation. The area of the RV endocardial surface is traced (white broken lines) on the epicardial voltage map to approximate the location of the RV endocardial surface on the combined RV-LV epicardial voltage map shown on the right. Only a small basal RV region of low voltage was present on the endocardium in proximity to the tricuspid valve annulus (yellow arrows). Low voltage covered the entire epicardial free wall surface of the RV. Signals were not only low in amplitude but also multicomponent, fractionated, and late.
with the large coronary vasculature and associated fat. Dense scar was also arbitrarily defined as <0.5 mV for display purposes for the epicardial maps.

The extent of abnormal endocardial and epicardial bipolar voltage signals was estimated by measuring contiguous areas of abnormal electrograms by using the “area calculation” algorithm included in the CARTO system (Table 2). To further limit the influence of epicardial fat and small-vessel coronary vasculature on the low-voltage region for all area measurements of abnormal electrograms from the RV epicardium, the contiguous low-voltage electrograms had to demonstrate not only a low amplitude but also signals with discrete late potentials (recorded after the QRS) and/or demonstrate broad multicomponent or split signals within the boundary of the defined contiguous low-voltage abnormality (Figure 2). Electrograms included in the area analysis were recorded at least 0.5 cm from the anatomically defined major trunk of the right coronary artery.

Table 2. Substrate Characterization

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sinus Rhythm RV Points</th>
<th>Abnormal Bipolar RV Voltage Area, cm²</th>
<th>Endocardial-Epicardial Distance, mm</th>
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</thead>
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<tr>
<td></td>
<td>Endocardial Epicardial</td>
<td>Endocardial Epicardial</td>
<td>Basal RV Mid Free Wall RV Opposing RF Lesions</td>
</tr>
<tr>
<td>1</td>
<td>154 332</td>
<td>43.4 72.1</td>
<td>7 7 7</td>
</tr>
<tr>
<td>2</td>
<td>267 260</td>
<td>53.8 141.7</td>
<td>15 8 9</td>
</tr>
<tr>
<td>3</td>
<td>183 195</td>
<td>40.2 78.4</td>
<td>7 8 7</td>
</tr>
<tr>
<td>4</td>
<td>297 260</td>
<td>31.3 82.8</td>
<td>7 8 7</td>
</tr>
<tr>
<td>5</td>
<td>318 316</td>
<td>136.3 187.7</td>
<td>11 8 6</td>
</tr>
<tr>
<td>6</td>
<td>326 431</td>
<td>34.4 178.6</td>
<td>12 7 11</td>
</tr>
<tr>
<td>7</td>
<td>458 415</td>
<td>34.8 51.6</td>
<td>23 7 12</td>
</tr>
<tr>
<td>8</td>
<td>355 443</td>
<td>17.0 90.8</td>
<td>15 7 13</td>
</tr>
<tr>
<td>9</td>
<td>590 527</td>
<td>43.5 67.5</td>
<td>20 8 16</td>
</tr>
<tr>
<td>10</td>
<td>386 695</td>
<td>12.2 106</td>
<td>6 7 ...</td>
</tr>
<tr>
<td>11</td>
<td>185 311</td>
<td>13.2 28.3</td>
<td>9 5 4</td>
</tr>
<tr>
<td>12</td>
<td>552 356</td>
<td>26.4 73.7</td>
<td>7 5 ...</td>
</tr>
<tr>
<td>13</td>
<td>319 605</td>
<td>6.1 77.8</td>
<td>5 5 6</td>
</tr>
</tbody>
</table>

Mean±SD 337±134 396±145 37.8±32.8 95.2±47.1 11.1±5.6 6.9±1.2 8.9±3.6

Opposing RF lesions indicates sites ablated at endocardial/epicardial sites directly opposite from each other.

Figure 2. Epicardial bipolar voltage map in the anterior view showing a diffuse area of low-amplitude signals indicating consistent signal amplitude <0.5 mV. To define area of abnormal epicardial voltage for comparison with endocardial voltage map, the majority of signals in low-voltage area were also multicomponent, wide, and/or late (arrows).
RV Wall Thickness
Simultaneous overlapping electroanatomic maps from both the epicardial and endocardial surfaces were used to assess the RV wall thickness of the RV base and free wall (Table 2). The shortest anatomic distance between directly opposite endocardial and epicardial points was measured with the software incorporated in the CARTO system. The measurement of the wall thickness was assessed at the basal RV near the lateral tricuspid valve annulus and mid RV free wall. The demonstration of RV pacing ensured that the catheter tip was in contact with the endocardial and epicardial surfaces at the basal sites where measurements were made. Measurements at the RV mid free wall did not require the demonstration of pacing and attempted to define the closest anatomic point on the basis of visual inspection of the electroanatomic map. An overlay of endocardial and epicardial maps allowed for the measurement of the distance between the epicardial and the opposite endocardial point as an approximation to the local RV wall thickness (Figure 3). Measurements of the wall thickness at the tricuspid valve annulus and mid RV free wall from 4 patients without RV or LV structural heart disease undergoing ablation of idiopathic focal LV VT served as reference values for assessment of normal RV thickness. Intracardiac echo assessment was used to corroborate increases in observed thickness suggested by the electroanatomic maps in the region of the tricuspid valve annulus when noted.

Electrophysiological Study and VT Ablation
The 12-lead ECG morphology of all spontaneous VTs was analyzed to approximate site of origin. The VT QRS complex of all inducible arrhythmias were also recorded and analyzed with the use of the Prucka Cardiolab recording system (Houston, Tex).1,11 The programmed ventricular stimulation protocol included up to triple extrastimuli from at least 2 ventricular sites with at least 2 drive cycle lengths. For hemodynamically tolerated VT, activation and entrainment mapping were used for tachycardia localization. The defined “site of origin” demonstrated presystolic activity and entrainment with concealed fusion and a return cycle length within 30 ms of the VT cycle length. Termination with focal radiofrequency energy application was associated with these criteria and confirmed the origin of the tachycardia.

For VTs that were not mappable, the site of origin was approximated by using pace mapping to reproduce the VT QRS complex and identify sites with a long stimulus to QRS interval1,11 (Figure 4). Limited activation and entrainment information was used to corroborate the pace map information when possible. Radiofrequency ablation was guided on the basis of all mapping data including the location of the best pace map, the location of valvular anatomic boundaries, and detailed characterization of the substrate defined by voltage mapping, including definition of all signals with discrete late potentials and definition of discrete higher voltage channels in sinus rhythm in the low-voltage region.1,11 Characteristically, linear lesions were placed through the site of the best pace map and transected the abnormal myocardium, extending from the valve annulus to normal myocardium (≥1.5 mV in the endocardium and 1.0 mV in the epicardium). Linear lesions always avoided large marginal right coronary vessels and the right coronary artery by at least 1 cm. The epicardial ablation strategy included targeting late
patients in whom an epicardial VT was targeted on the basis of history of prior endocardial ablation in all patients (Table 3). In the 12 of the 13 patients, endocardial ablation was performed before fluid accumulation was confirmed on transthoracic echocardiography. Within 24 hours after the absence of continued pericardial drainage or within 72 hours of the first documented absence of pericardial effusion, a closed irrigation catheter was inserted in the pericardial space and activated for 15 minutes. The effusion was routinely administered intrapericardially in the last 10 patients.

At the end of the ablation procedure, 2 mg/kg of triamcinolone was administered intrapericardially (Acuson Inc) and continuous intracardiac echocardiography (Acuson Inc) was used to monitor the achievement of a maximum temperature of 45°C and a maximum impedance drop of 12 to 15 Ohms. Finally, in 9 patients, open irrigated ablation targeted a maximum temperature of 42°C and a maximum impedance drop of 12 to 15 Ohms; with an output of 20 to 50 W.

The amount of fluid in the epicardial space associated with the open irrigated catheter mapping and ablation was monitored with intracardiac echocardiography (Acuson Inc) and continuous intracardiac blood pressure monitoring for evidence of hypotension. The fluid was withdrawn from the space with the use of either repeated manual withdrawal or a closed vacuum bottle connected to the side port of the 8F sheath once >100 to 150 mL was introduced in the pericardial space or fluid became visible by intracardiac echocardiography, which was routinely deployed. A totally “dry” pericardial space made catheter manipulation more difficult, and therefore a small amount of fluid was ideal to allow mapping and did not seem to interfere with energy delivery.

At the end of the ablation procedure, 2 mg/kg of triamcinolone was subsequently administered intrapericardially in the last 10 patients. A pigtail catheter was left in place in the pericardial sac and removed within 24 hours after the absence of continued pericardial drainage or fluid accumulation was confirmed on transthoracic echocardiography. In 12 of the 13 patients, endocardial ablation was performed before attempted epicardial mapping/ablation at the index procedure despite a history of prior endocardial ablation in all patients (Table 3). In the patients in whom an epicardial VT was targeted on the basis of activation or pace mapping directly opposite ineffective endocardial ablation lesions, the closest endocardial to epicardial anatomic distance was also documented with the use of the electroanatomic mapping system software (Table 2).

### Results

#### Patient Population

There were 10 men and 3 women with a mean age of 43 ± 15 years. All patients presented with recurrent VTs (symptomatic tolerated VT, implantable defibrillator shocks, or both) after prior endocardial ablative therapy (Table 4). The 13 consecutive patients undergoing epicardial ablation were from a larger group of 33 patients with ARVC/D who had undergone endocardial ablation for recurrent VT. A mean of 2 (range, 1 to 4) endocardial ablation procedures had been performed (Table 3), including 3 with procedures at other institutions, and all patients had failed at least 1 antiarrhythmic drug (range, 1 to 4; Table 4). All patients had evidence of multiple left bundle-branch block VTs during prior ablation procedures, with a mean of 3 distinct inducible VT morphologies (range, 2 to 6). None of the patients had a known family history of ARVC/D. On transthoracic echocardiography, all patients had evidence of abnormal RV function, RV dilatation, and segmental wall motion abnormalities. Two of the 11 patients had mild LV dysfunction with LV ejection fractions of 40% and 45%, respectively, and I had severe LV dysfunction (ejection fraction, 15%).

#### Endocardial and Epicardial Electroanatomic Substrate

The entire surface of the RV endocardium and epicardium was sampled in detail to characterize the anatomic substrate...
in each of the 13 patients. An average of 337±134 sites (range, 154 to 590 per patient) was mapped on the endocardial RV surface. Epicardial RV/LV voltage map points were obtained from an average of 517±194 epicardial sites (range, 218 to 892 per patient) with the focus on the RV epicardium (range, 195 to 695 RV epicardial sites per patient; Table 2).

The endocardial electrogram abnormalities always involved the perivalvular region of the tricuspid valve and extended for a variable distance toward the RV free wall. In 6 patients, there was also involvement of the peripulmonic area. In only 1 patient, the endocardial scar extended to include the RV apex.

The area of low-voltage electrogram abnormality was greater on the epicardium at 95±47 cm² (range, 28 to 188 cm²) than on the endocardium at 38±33 cm² (range, 6 to 136 cm²) (P<0.001) (Table 2). The area of abnormal epicardial electrograms matched the areas of endocardial abnormalities but extended farther over the surface of the RV beyond the area subtended by the endocardial abnormalities and represented a larger area in all patients (Figures 1 and 5). In all patients, the low-voltage electrogram abnormalities that were included in the area measurement always displayed signals that were wide (>80 ms), multicomponent, or late (Figure 2).

Areas of the epicardium that did not demonstrate these abnormal signal characteristics but only showed low-voltage signals were not included in the area calculation to avoid an overestimation of the region of low voltage due to fat and not altered substrate.

### RV Wall Thickness in Patients With ARVC/D

The mean basal RV wall thickness in proximity to the tricuspid valve in our patient population was 11.1±5.6 mm. Notably, 6 of the 13 patients had a wall thickness >10 mm in the tricuspid valve annulus region, a frequent site of origin for VT in the setting of ARVC/D and recurrent VT (Table 2). The measurements contrasted with the 5-, 6-, 8-, and 10-mm RV thickness measurements in the tricuspid valve annulus region for the 4 reference patients (Figure 3). These measurements were consistent with the intracardiac echocardiographic assessment that also identified thickening of the peritricuspid RV.

The mean mid RV free wall thickness (Table 2) was 6.9±1.2 mm and was significantly less than the basal wall thickness (P=0.016). Specifically, the 6 patients with an increase in RV thickness to >10 mm at the base did not have a similar increase at the RV free wall (Table 2). The RV free wall thickness in the 4 reference patients was 3, 3, 4, and 2 mm and was only modestly less than the thickness noted for the study population.

### Outcome of Epicardial VT Mapping and Ablation

All patients underwent RV epicardial VT ablation. A mean of 2 (range, 1 to 4) VTs was targeted and eliminated with ablation targeting the epicardial surface after failed attempts from the endocardium.

<table>
<thead>
<tr>
<th>Patient</th>
<th>No. of VTs in 2 Months Prior</th>
<th>Antiarrhythmic Drugs Failed</th>
<th>VT (Cycle Length) Inducible After Epicardial Ablation</th>
<th>Antiarrhythmic Drugs at Discharge</th>
<th>VT in Follow-Up</th>
<th>Follow-Up, mo</th>
<th>Antiarrhythmic Drugs at Follow-Up</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>Sotalol/propafenone</td>
<td>+ No</td>
<td>BB</td>
<td>None</td>
<td>41</td>
<td>BB</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>Quinidine/sotalol/propafenone</td>
<td>+</td>
<td>LBRI 280 ms</td>
<td>BB</td>
<td>1 VT: 38 mo</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>&gt;100</td>
<td>Sotalol/lidocaine/mexilinite/ sotalol+mexilinite</td>
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<td>25</td>
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<tr>
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<td>4</td>
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<td>24</td>
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<tr>
<td>5</td>
<td>26</td>
<td>Amiodarone/sotalol/lidocaine</td>
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<td>LBJL 410 ms</td>
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<td>BB</td>
<td>1 VT: 2 mo</td>
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<tr>
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<tr>
<td>Mean</td>
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BB indicates β-blocker; N/A, not applicable (transplant at 2 mo); LBRI, left bundle right inferior axis morphology; LBJL, left bundle left inferior axis morphology.
Of note, all 13 patients had undergone 1 to 4 prior endocardial ablation procedures at 0.3 to 102 months before the index procedure (Table 3). In at least 1 of the prior endocardial ablation procedures, 3-dimensional electroanatomic mapping had been used, and in 11 of 13 patients, irrigated radiofrequency ablation had been used. During the index procedure, 12 of the 13 patients had additional endocardial ablation with irrigated catheters to attempt to eliminate all VT before proceeding to the epicardium. A mean of 35±26 endocardial ablation lesions was applied at the index procedure (Table 3). In 5 of the 13 patients, additional morphologically distinct VTs were eliminated with the endocardial ablations at the time of the index procedure (Table 3).

Epicardial VT ablation targets were determined primarily by pace mapping and identification/ablation of surrounding late potentials (Table 3). In 8 of the 13 patients, at least 1 of the epicardial VTs was targeted on the basis of activation/entrainment mapping, with 7 of these VTs terminating with radiofrequency energy application. An average of 37±21 epicardial radiofrequency lesions was applied per patient (Table 3). Epicardial VT targets identified on the basis of pace mapping, activation/entrainment mapping, or both were beyond the extent of the endocardial voltage abnormality in 10 of the 13 patients. However, in 11 of the 13 patients, at least 1 VT origin and epicardial target were also directly opposite the endocardial voltage abnormality and site of unsuccessful ablation (Figures 4 and 6). The closest distance between opposite endocardial and epicardial ablation sites ranged from 4 to 16 mm (Table 2). These sites were noted in 4 patients in an area of thickened (>10 mm) myocardium at the inferior basal RV (Table 2). No complications were noted as a result of the epicardial mapping and ablation.

At the end of the procedure, 11 of the 13 patients (85%) had no inducible monomorphic VT, and 12 of the 13 patients (92%) had elimination of all targeted VT. One patient had inducible rapid (cycle length, 280 ms) VT at the end of the procedure that was not targeted for additional ablation. Finally, 1 patient had persistent inducible VT that matched...
the clinical arrhythmia on the basis of analysis of the rate and the electrogram morphology during spontaneous VT from the ICD device. The latter patient (patient 5) had an RV volume of 470 mL and LV ejection fraction of 10% to 15% and was designated an ablation failure. Ten of the 12 patients who underwent repeat programmed stimulation before hospital discharge had no inducible monomorphic VT. The remaining 2 patients had rapid (<300 ms cycle length) VT induced that had not been previously identified or targeted for ablation. Two patients underwent a repeat epicardial ablation for recurrent symptomatic ventricular depolarizations and non-sustained VT.

During a mean follow-up of 18.3 ± 12.7 months (range, 5 to 41 months) from the last ablation procedure (Table 4), 10 of the 13 patients (77%) have been free of sustained VT. Of the 3 patients with VT recurrence, the patient with ablation failure underwent heart transplantation at 2 months, 1 patient (patient 2) had a single episode of VT at month 38 of follow-up that was terminated by antitachycardia pacing, and 1 additional patient (patient 7) had a single episode of...
sustained VT during the extremes of exercise that did not recur during an additional 14 months of follow-up without the need for antiarrhythmic drug therapy. Only 3 patients are being treated with antiarrhythmic drugs: 2 for symptomatic premature ventricular contractions and 1 for ECG-documented recurrent atrial arrhythmias (Table 4). No patient is being treated with amiodarone.

Discussion

The present study provides a detailed characterization of the electroanatomic substrate of the RV endocardial and epicardial surfaces in patients with ARVC/D presenting with recurrent ventricular arrhythmias despite endocardial ablation. The results provide a definitive understanding of the anatomic basis for the failure of endocardial ablation in selected patients with this syndrome.1–5 In this setting, the epicardial area of abnormal electrograms was consistently and dramatically larger. The origin of VT defined by activation/entrainment mapping and suggested by the detailed substrate mapping observations and targeted for ablation was also frequently noted beyond the endocardial defined scar. Frequent and dramatic late potentials were recorded, and pace mapping that matched the targeted VT with long stimulus to QRS intervals was observed on the epicardium frequently well beyond the endocardial boundary of abnormal voltage (Figure 4). Furthermore, significant thickening of the RV in the periannular area was identified in nearly half of the patients. The epicardium in proximity to the tricuspid annulus at the acute angle of the RV was also identified as a common epicardial site of origin of the VT (Figure 4). This epicardial RV region was noted to be >1 cm from the infarctive RV endocardial ablation lesions in 4 of the patients. This thickening probably contributed to the inefficacy of endocardial ablation. It is also important to note that the thick endocardial scar identified in this region may also act as an effective insulator for radiofrequency delivery, preventing penetration toward the epicardium even without overall RV thickening. This endocardial fibrosis may make endocardial ablation ineffective even with the use of irrigated catheters (Table 3).1

The study results should have been somewhat anticipated given that the findings from autopsy series identified a more extensive epicardial than endocardial substrate for VT and an occasional unanticipated increase in RV endocardial wall thickness and fibrosis in the setting of ARVC/D.6–8 Nevertheless, this report confirms the clinical importance of these pathological observations and supports original observations made by Fontaine and colleagues13 on the importance of the epicardial substrate in this disease process.

This study also demonstrates the feasibility of a simultaneous endocardial/epicardial substrate-based ablation approach to facilitate arrhythmia control and further improve on the optimistic reports of aggressive endocardial ablation alone.1,4,5 Importantly, if the electrogram abnormality on the epicardial surface is more extensive than that noted with endocardial mapping, one will underestimate the substrate, and even with aggressive substrate ablation in appropriate endocardial areas, the VT will not be eliminated. These data not only provide an explanation for the lack of uniform success of endocardial ablation but also emphasize the importance of targeting the epicardium to further optimize long-term clinical outcome. Importantly, noninducibility of VT was accompanied by arrhythmia control without the need for antiarrhythmic drug therapy in most of the study group.

The study results suggest that the threshold for considering epicardial substrate mapping and VT ablation in this setting should probably be lowered despite recent reports of good arrhythmia control with endocardial ablation alone.4,5 Patients with limited endocardial ablation, those with late VT termination with radiofrequency delivery, and certainly those with persistent VT despite aggressive endocardial ablation should be considered for an epicardial approach. Surface ECG criteria identifying a QS complex in lead V2 or leads III and aVF during VT may also prove to be helpful in identifying patients who should be considered for an epicardial approach with the initial procedure.14 Although no complications were noted in this series, caution should be employed in gaining epicardial access to avoid puncture or laceration of the markedly dilated RV in patients with ARVC/D. An inferior approach may help to reduce this risk.

Limitations

The areas of electrogram abnormalities from both the epicardium and the endocardium were not corroborated by pathological analysis in our study population. To avoid overestimating the extent of low voltage on the epicardium, we (1) ignored signals that were immediately adjacent to the anatomically defined right coronary artery, (2) used a lowervoltage cutoff of 1.0 mV for the epicardium, and (3) required that the majority of signals recorded in the defined epicardial low-voltage area had to be fractionated, split, or late in addition to being low in amplitude. This effort should have minimized the effect of fat and large-vessel coronary vasculature on the area of epicardial bipolar voltage abnormality.

Of note, an analysis of genetic testing was not performed routinely in the study population, and the need for epicardial ablation as it relates to genetically defined abnormalities cannot be reported.15 Importantly, very-long-term follow-up after VT ablation was not available for all patients, and this may overestimate the long-term efficacy of combined epicardial/endocardial mapping and ablation in patients with ARVC/D and VT. In addition, 1 patient did not have an ICD, and it is possible that asymptomatic episodes of VT may have occurred and were not recognized. Importantly, this study assessed the outcome of epicardial ablation after endocardial ablation, and the efficacy of ablation of the epicardium alone cannot be addressed. Finally, RV thickness assessed by electroanatomic mapping may be influenced by epicardial fat and may overestimate the true endocardial to epicardial myocardial distance.

Conclusions

In patients with ARVC/D and recurrent VT after endocardial ablation, there is a more extensive area of epicardial than endocardial electrogram abnormality and occasional basal RV thickening. A simultaneous combined epicardial and endocardial approach for VT mapping and ablation is feasible and results in elimination of recurrent VT.
Disclosures

Dr Marchlinski has a research grant from and has been on the advisory board of Biosense Webster Inc. The other authors report no conflicts.

References


CLINICAL PERSPECTIVE

Myocardial involvement in arrhythmogenic right ventricular cardiomyopathy/dysplasia appears to progress from epicardial to endocardium. Catheter ablation of ventricular tachycardia (VT) from the endocardium may be limited by epicardial VT substrate/circuits, right ventricular thickening, or both. Percutaneous epicardial mapping and ablation were performed in 13 consecutive patients with right ventricular cardiomyopathy/dysplasia after failed endocardial VT ablation. Low-voltage areas consistent with scar were more extensive on the epicardium than the endocardium and uniformly included wide, split, and late electrograms consistent with abnormal conduction. Transmural thickness at the base of the right ventricle was >10 mm in 6 of the 13 patients. Twenty-seven distinct VTs were targeted for ablation from the epicardium; epicardial ablation sites were often opposite endocardial sites with normal voltage or where ablation had been ineffective. During follow-up, 77% of patients were free of VT. These findings suggest that failed endocardial ablation of VT in patients with right ventricular cardiomyopathy/dysplasia is often due to epicardial VT origins. Percutaneous epicardial mapping and ablation can improve outcomes in these patients.
Epicardial Substrate and Outcome With Epicardial Ablation of Ventricular Tachycardia in Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia
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In the article, “Epicardial Substrate and Outcome With Epicardial Ablation of Ventricular Tachycardia in Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia” by Garcia et al, which appeared in the August 4, 2009 issue of the journal (Circulation. 2009;120:366–375), the Universitat Autonoma de Barcelona, Departament de Medicina, Barcelona, Spain should have been listed as an affiliation of the second author, Victor Bazan.

The online version of the article has been corrected. The authors regret the error.

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