Ablation of Ventricular Arrhythmias in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

Arrhythmia-Free Survival After Endo-Epicardial Substrate Based Mapping and Ablation

Rong Bai, MD, FHRS*; Luigi Di Biase, MD, PhD, FHRS*; Kalyanam Shivkumar, MD; Prasant Mohanty, MBBS, MPH; Roderick Tung, MD; Pasquale Santangeli, MD; Luis Carlos Saenz, MD; Miguel Vacca, MD; Atul Verma, MD; Yariv Khaykin, MD; Sanghamitra Mohanty, MD; J. David Burkhardt, MD, FHRS; Richard Hongo, MD; Salwa Beheiry, RN; Antonio Dello Russo, MD; Gemma Pelargonio, MD; Pietro Santarelli, MD; Javier Sanchez, MD; Claudio Tondo, MD; Andrea Natale, MD, FHRS

Background—In patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy, freedom from ventricular arrhythmias (VAs) after endocardial ablation is limited. We compared the long-term freedom from recurrent VAs by using endocardial-alone ablation versus endo-epicardial substrate-based ablation.

Methods and Results—Forty-nine patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy undergoing ablation of ventricular tachycardia (VT) were divided into 2 groups: endocardial-alone ablation (group 1, n=23) and endo-epicardial ablation (group 2, n=26). All patients had an implantable cardioverter-defibrillator (ICD). Conventional and 3D mappings were used to determine the mechanism of induced VTs and to identify area of “scar” or “abnormal” myocardium. All critical sites responsible for VTs and points with “abnormal” potential were targeted for ablation from endocardium (group 1) or from both endocardium and epicardium (group 2). The procedural end point was noninducibility of sustained, monomorphic VT with isoproterenol. The presence of frequent premature ventricular contractions at the end of ablation was recorded. Patients were followed up by ECG, Holter, and ICD interrogation. After a follow-up of at least 3 years, freedom from VAs or ICD therapy was 52.2% (12/23) in group 1 and 84.6% (22/26) in group 2 (P=0.029), with 21.7% (5/23) and 69.2% (18/26) patients off antiarrhythmic drugs (P<0.001), respectively. Compared with patients with no premature ventricular contractions after ablation, patients with frequent premature ventricular contractions after ablation were more likely to have VA recurrence/ICD therapy [3/33 (9%) versus 12/16 (75%); log-rank P<0.001].

Conclusions—An endo-epicardial–based ablation strategy achieves higher long-term freedom from recurrent VAs off antiarrhythmic therapy in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy when compared with endocardial-alone ablation. The presence of ≥10 premature ventricular contractions per minute after ablation is associated with more VA recurrence. (Circ Arrhythm Electrophysiol. 2011;4:478-485.)

Key Words: arrhythmogenic right ventricular dysplasia ■ cardiomyopathy ■ ventricular tachycardia ■ ablation ■ epicardial ■ premature ventricular contraction

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is characterized by ventricular arrhythmias (VAs) or even sudden cardiac death secondary to fibro-fatty replacement of the right ventricular (RV) myocardium. It is a genetically determined myocardial disease in which the pathological lesions are believed to progress over time from the epicardium to the endocardium and with diffuse involvement of the RV and the left ventricle (LV) in rare cases.1,2
Patients having recurrent sustained VT while receiving optimal pharmacological therapy are candidates for catheter ablation. Even though the recent technological advances with electroanatomic and voltage mapping systems have significantly improved the outcomes, catheter ablation of ventricular tachycardia (VT) in ARVD/C patients is not considered curative and has not been supported by the guideline as a first-line therapy. However, only an endocardial approach was used in most of the cases previously reported. We hypothesized that the epicardial substrate may play an important role in the development of VT in patients with ARVD/C, and an ablation strategy including both endocardial and epicardial substrate modification may be necessary to achieve better outcome. This multicenter study compared the long-term freedom from VA in ARVD/C patients undergoing VT ablation by using either an endocardial-alone or an endo-epicardial–based approach. We also sought to identify the predictor to ablation failure and recurrence of VA.

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Methods

Study Population

This is a prospective study including 49 consecutive patients with ARVD/C undergoing ablation of VTs at 7 centers in the United States, Italy, Colombia, and Canada. They were diagnosed with ARVD/C according to the Task Force Criteria. All patients had at least 1 episode of symptomatic, sustained, monomorphic VT with left bundle-branch block pattern documented by ECG or Holter, with or without syncope. They all had received an implantable cardioverter-defibrillator (ICD) before the ablation but still had recurrent VTs or multiple ICD therapies despite taking antiarrhythmic drugs (AAD), including sotalol, amiodarone, dofetilide, and β-blockers. The study population was divided into 2 groups, based on the ablation strategy chosen by the ablation physician: in 23 patients (group 1), ablation was performed by an endocardial-alone approach, whereas 26 patients (group 2) underwent an endo-epicardial–based ablation. Before the index procedure, 14 patients from group 2 had 1 failed endocardial ablation that had been performed at other centers, using only standard activation map of induced VT. They were referred to participating centers of the present study and did not overlap with the patients in group 1. The remaining patients from group 2 (n=12) underwent endo-epicardial ablation as their primary procedures. All patients signed an informed consent for catheter ablation of their VT.

Electrophysiology Study and Mapping

Patients were studied in the electrophysiology laboratory in the fasting state under conscious sedation. Venous access was obtained from the groin veins. One quadripolar catheter and 1 duo-decapolar catheter (St Jude Medical Inc, Minneapolis, MI) were placed in the RV and coronary sinus–right atrium, respectively. In patients in group 2, subxiphoid epicardial access was obtained by using fluoroscopic guidance as previously described. Programmed stimulation including burst ventricular pacing and ramp pacing with up to 3 ventricular extrastimuli were delivered from 2 different RV sites to induce VA. Intraoperative isoproterenol was also used (maximum dose 10 μg/min) when necessary. Induced VTs were compared with 12-lead ECGs of the clinical VT.

Endocardial mapping was performed in all patients; epicardial mapping was performed once the epicardial space was accessed in group 2 patients. Conventional mapping techniques included pace mapping, activation mapping, and entrainment mapping, which helped in understanding the mechanism of the arrhythmias and identifying potential critical sites. The 3D electroanatomic CARTO maps (Biosense Webster, Diamond Bar, CA), including the activation and voltage map, were obtained in sinus rhythm and/or during hemodynamically stable VT, using a 3.5-mm, open irrigated-tip catheter (Biosense Webster). Bipolar electrogram signals were filtered at 30 to 400 Hz and were displayed on a real-time recording system. A fill threshold <15 mm was used when CARTO map points were collected. Bipolar voltage definitions of abnormal and normal myocardium were based on values validated previously in both right and left ventricles. Epicardial regions with a bipolar electrogram amplitude >1.5 mV were defined as “normal,” and “scar” is defined as those area with an amplitude <0.5 mV. “Abnormal” myocardium was defined as a region with a bipolar electrogram amplitude between 0.5 and 1.5 mV. However, considering that overlying fat may result in voltage attenuation of the epicardial electrogram, the cutoff to define “normal” area of epicardium was set as a bipolar electrogram amplitude >1.0 mV, whereas the “scar” myocardium was defined as a bipolar electrogram amplitude <0.5 mV. In addition to voltage criteria, “abnormal” electrograms both in the endocardium and the epicardium included the fragmented or delayed recordings. The area of scar was measured using the “area calculation” software included in the CARTO system.

Ablation Strategy

In the index procedure, we intended to ablate not only the clinical VTs but all inducible, sustained, monomorphic VTs at the time of electrophysiology study. Ablation was typically performed with the 3.5-mm open irrigated-tip catheter. At each ablation point, radiofrequency energy was applied for 60 to 120 seconds with a power output starting at 30 W and titrating up to 45 W, with a maximum temperature limit of 41°C. In regions close to the phrenic nerve, high-output pacing (20 mA) was performed through the ablation catheter, and these locations were marked on the electroanatomic map.

In general, our targets for ablation were:

1. All points with “abnormal,” fractionated, or delayed electrograms regardless of the location within or around the scar area. In the epicardium, the end point was the elimination of these potentials. In the endocardium, when we targeted low-voltage potentials (bipolar voltage amplitude 0.5 to 1.5 mV), the end point was signal attenuation (bipolar voltage amplitude decreased to <0.5 mV), whereas when we targeted fragmented or delayed potentials with bipolar voltage amplitude 0.5 to 1.5 mV, the end point was the complete elimination of these potentials.

2. Points that were critical in the initiation or maintenance of a VA (eg, isthmus of a circuit or a focal firing). If no specific foci/isthmus could be determined as the mechanism of the target VTs or if the patient became hemodynamically unstable during the induced VTs, only substrate ablation was performed to abolish all “abnormal” potentials. The specific ablation techniques used in different groups are described below.

Group 1, endocardial-alone ablation: Radiofrequency energy was delivered at specific sites demonstrating “abnormal” voltage, isthmus of a circuit, or arthymogenic foci. Under CARTO guidance, linear ablation lines were created to modify the endocardial substrate and were designed to (1) connect scar/abnormal myocardium to valve continuity, (2) connect scar/abnormal myocardium to another scar, or (3) encircle the scar/abnormal region, depending on the scar location and size (Figure 1A and 1B).

Group 2, endo-epicardial ablation: An epicardial mapping and ablation was planned at the beginning of the procedure rather than as a complementary approach to an unsuccessful endocardial ablation. A coronary angiogram was performed to confirm the absence of a coronary artery at the ablation site, based on operator preference. At those specific sites suggestive of “abnormal” myocardium on both endocardial and epicardial mapping, radiofrequency energy was delivered from the endocardium and the opposite epicardial position to create transmural lesions. At target sites demonstrating an “abnormal” electrogram solely on the epicardial surface but not on the endocardial mapping, ablation was delivered only in the epicardial space. In certain cases, epicardial linear ablation was designed to encircle the entire scar/abnormal region and composed with sequential point lesions along the boundary and within the scar area, with a
goal to eliminate/isolate all the “abnormal” recordings (Figure 1C and 1D).

Programmed RV stimulation was repeated after completion of ablation. As before, up to 3 extrastimuli at 2 different RV sites were used to induce VT. If VT was still inducible, additional ablation was performed using the strategy described previously. If the ablated VTs or other sustained monomorphic VT could not be induced even with intravenous isoproterenol infusion (up to 10 \( \mu \)g/min), the procedure was considered successful. No further ablation was performed when the only inducible arrhythmias were polymorphic VT/ventricular fibrillation. After removing all the catheters from the ventricle, frequent spontaneous premature ventricular contractions (PVCs) \( \geq 10 \) bpm with/without isoproterenol provocation were recorded but not targeted for additional ablation. All patients received screening for pericardial effusion at the end of the procedure with echocardiography and fluoroscopy.

**Follow-Up**

The patients were followed up by their treating electrophysiologist. AADs were either discontinued after ablation or maintained for 3 additional months and subsequently stopped. Patients were routinely followed up in the outpatient clinic at 3, 6, and 12 months and then

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**Figure 1.** A and B, Bipolar voltage map of the right ventricular (RV) endocardium in a patient with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) from group 1 (A, left anterior oblique view; B, anteroposterior view). Regions in red represent scar (bipolar voltage <0.5 mV); purple regions represent normal myocardium (bipolar voltage >1.5 mV). Other colored regions represent abnormal myocardial regions (bipolar voltage between 0.5 and 1.0 mV). The scar is located in the superior anterior RV and proximal RV outflow tract. In this case, serial ablations were applied (red dots) inside scar region and to surround region of abnormal voltage. C and D, Endocardial (C, anteroposterior view) and epicardial (D, anteroposterior view) bipolar voltage map of the RV in a patient with ARVD/C from group 2. Definitions of endocardial scar or normal myocardium remained the same as in A and B. Epicardially, “normal” area was set as a bipolar electrogram amplitude >1.0 mV; “scar” myocardium was defined as a bipolar electrogram amplitude <0.5 mV. Electrograms (EGMs) of representative endocardial/epicardial mapping site are shown in the middle panel. In each EGM recording, in addition to ECG leads II, V3, and aVL, EGMs on proximal (M3–M4) and distal (M1–M2) ablation catheters are shown. The scar region was larger in the epicardium, and it was located in anterior and lateral RV, extending to the basal RV and tricuspid valve area. In addition to lesions (red dots) placed at opposite endocardial and epicardial sites with abnormal voltage, more radiofrequency applications were applied in the epicardium at sites demonstrating abnormal recordings.
Table 1. Baseline Characteristics of Study Subjects

<table>
<thead>
<tr>
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<th>Group 1 (n=23)</th>
<th>Group 2 (n=26)</th>
<th>P</th>
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<tbody>
<tr>
<td>Age, y*</td>
<td>34±14</td>
<td>37±11</td>
<td>0.47</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>15 (65)</td>
<td>18 (69)</td>
<td>0.76</td>
</tr>
<tr>
<td>LV ejection fraction, %*</td>
<td>57±7</td>
<td>53±10</td>
<td>0.32</td>
</tr>
<tr>
<td>Failed AAD before index ablation, n (%)</td>
<td>11 (47.8)</td>
<td>13 (50)</td>
<td>1.00</td>
</tr>
<tr>
<td>Sotalol</td>
<td>17 (73.9)</td>
<td>18 (73.1)</td>
<td>0.72</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>1 (4.3)</td>
<td>2 (7.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>4 (17.4)</td>
<td>5 (19.2)</td>
<td>0.97</td>
</tr>
<tr>
<td>β-blocker</td>
<td>7 (30.4)</td>
<td>6 (23.1)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; AAD, antiarrhythmic drug.
*Numbers represent mean±standard deviation.

Table 2. Comparison of Procedural Parameters Between the 2 Groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=23)</th>
<th>Group 2 (n=26)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT targeted for ablation†</td>
<td>2 (1–4)</td>
<td>2 (1–5)</td>
<td>0.69</td>
</tr>
<tr>
<td>Cycle length of VTs, ms</td>
<td>262±62</td>
<td>287±57</td>
<td>0.85</td>
</tr>
<tr>
<td>Endocardial CARTO map points</td>
<td>316±127</td>
<td>356±143</td>
<td>0.87</td>
</tr>
<tr>
<td>Epicardial CARTO map points</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Endocardial scar area, cm²</td>
<td>10.9±6.4</td>
<td>9.8±7.0</td>
<td>0.51</td>
</tr>
<tr>
<td>Epicardial scar area, cm²</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Procedure time, h</td>
<td>3.9±1.1</td>
<td>5.3±1.2</td>
<td>0.008</td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
<td>51.3±20.2</td>
<td>65.9±13.1</td>
<td>0.015</td>
</tr>
<tr>
<td>Radiofrequency time, min</td>
<td>20.2±15.3</td>
<td>25.8±13.7</td>
<td>0.036</td>
</tr>
</tbody>
</table>

VT indicates ventricular tachycardia.
†Numbers represent median (range). The rest of the numbers represent mean±standard deviation.

Patients

Baseline clinical characteristics of the patients are summarized in Table 1. The demographics were comparable between the 2 groups. All the patients had recurrent VT refractory to AADs (median 2; range 1 to 4) and underwent an ICD implant before the index ablation procedure. No statistically significant bias was noted in the choice of procedure by physicians at the participating centers (Fleiss κ=0.667; 95% confidence interval, 0.48 to 0.87; P=0.001).

Electrophysiology Study, Mapping, and Ablation

During the electrophysiology study, a median of 2 VTs (range 1 to 4 in group 1; 1 to 5 in group 2) were induced and targeted for ablation. The procedure, fluoroscopy, and radiofrequency times were longer in group 2 (Table 2).

The CARTO map was successfully performed in all patients. Scar was identified in all patients with predominant locations at the lateral tricuspid annulus, RV outflow tract, anterior or apical RV wall, and inferior RV wall. In group 2 patients, the area of scar was larger in the epicardium (17.6±14.8 cm²) than that in the endocardium (9.8±7.0 cm²; Table 2; P=0.04; Figure 1C and 1D).

Complications

There were no major complications associated with the procedure in all patients. A groin hematoma was noted in 2 patients in group 1 and 1 patient in group 2. No patient in group 2 had symptomatic pericardial effusion/tamponade after ablation or at the time of discharge.

Follow-Up

No patient died or underwent heart transplantation during the follow-up period. After a follow-up of at least 3 years (1224±310 days for group 1 and 1175±112 days for group 2), freedom from VA or appropriate ICD therapy was 52.2% (12/23) in group 1 and 84.6% (22/26) in group 2, respectively (Table 3). Among these patients, 5 from group 1 (5/23, 21.7%) and 18 from group 2 (18/26, 69.2%) were off AADs (P<0.001). Of the 4 patients who had recurrence of VA in group 1, 1 patient had an ICD shock 2 weeks after the procedure, 1 had a VT treated with antitachycardia pacing at 6-month follow-up, and 2 had an ICD shock after 1 year when discontinuing AADs. The Kaplan-Meier curve showed significant difference of arrhythmia/ICD therapy-free survival between the 2 groups (log-rank P=0.029, Figure 2).

Of the 26 patients in group 2, 14 (54%) had prior VT ablation from the endocardium at other centers before the index procedure. We performed a subanalysis to examine if patients with prior endocardial ablation had significantly different success rates compared with those undergoing their
first procedure. The event-free survival at the end of follow-up was 86% among patients with previous endocardial ablation and was 83% for those undergoing endo-epicardial ablation as the first procedure (log-rank \(P = 0.884\)).

At the end of the procedure, more patients in group 1 presented with frequent PVCs than in group 2 (12/23 versus 4/26, \(P = 0.006\); Table 3). More VA recurrence/ICD therapy was seen in patients who had frequent PVCs after ablation (12/16, 75%) compared with patients in whom PVCs were absent (3/33, 9%; log-rank \(P < 0.001\); Table 3). In the overall study population (Figure 3A) or in each separate group (Figure 3B and 3C), patients who had no PVC after isoproterenol challenge at the end of the procedure had higher VA/ICD therapy-free survival.

**Discussion**

The main findings of this study are (1) compared with an endocardial-alone ablation strategy, an endo-epicardial–based approach increases long-term arrhythmia-free survival in patients with ARVD/C; (2) endo-epicardial ablation is more likely to result in discontinuation of AAD; and (3) at the end of the VT ablation procedure, the presence of frequent PVCs was associated with more VA recurrence at follow-up.

ARVD/C is a genetic, heterogeneous disorder characterized by an autosomal dominant pattern of inheritance and by histopathologic changes of the myocardium that are believed to continue progressing. The disease process usually begins in the subepicardium and progresses to the subendocardium and rarely from RV to LV.\(^{15,16}\) The clinical presentation of ARVD/C is variable and is thought to be related to the temporal progression of the pathological lesions. Accordingly, ARVD/C patients are classified into 4 clinicopathological stages: concealed phase or silent phase, overt arrhythmic phase, global RV dysfunctional phase, and biventricular pump failure phase.\(^{17}\) However, mostly commonly, patients with ARVD/C come to clinical attention because of the development of symptomatic VA with RV origin, usually at the age of 30 to 40 years and precipitated by exercise. This subgroup of ARVD/C patients mostly remained in the second stage of the disease and constituted the majority who seek treatment for their arrhythmias rather than heart failure. At this time, the disease is characterized by segmental or global RV pathological changes with residual normal myocardium located in the endocardium, rarely associated with histological evidence of LV involvement.\(^{15–19}\) The regional (between “normal” and “scar/abnormal” areas) and transmural (between epicardium, midlayer myocardium, and endocardium) electrophysiological heterogeneities provide the arrhythmogenic substrates, which are the targets of ablation in ARVD/C patients.\(^{20}\) In light of this, one would expect that a combined endo-epicardial ablation approach would achieve higher freedom from recurrent arrhythmias.

**Table 3. Prevalence of PVC and Recurrence of VA in the 2 Groups**

<table>
<thead>
<tr>
<th>Presence of Frequent PVCs With/Without Isoproterenol</th>
<th>Absence of PVCs With Isoproterenol</th>
</tr>
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<tbody>
<tr>
<td>Group 1, n=23</td>
<td>Group 2, n=26</td>
</tr>
<tr>
<td>Total, n</td>
<td>No VA Recurrence/ICD Therapy, n (%)</td>
</tr>
<tr>
<td></td>
<td>VA Recurrence/ICD Therapy, n (%)</td>
</tr>
<tr>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>(25)</td>
</tr>
<tr>
<td></td>
<td>3 (75)</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>(25)</td>
</tr>
<tr>
<td></td>
<td>4 (25)</td>
</tr>
<tr>
<td>Total, n</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>(25)</td>
</tr>
<tr>
<td></td>
<td>4 (75)</td>
</tr>
</tbody>
</table>

PVC indicates premature ventricular contraction; VA, ventricular arrhythmia; and ICD, implantable cardioverter-defibrillator.
Radiofrequency ablation of VA has traditionally only been used in medically refractory ARVD/C cases because of the possibility of perforation of the thin RV wall and the progressive nature of the disease. With the currently available techniques, catheter ablation has become a therapeutic option in ARVD/C patients with recurrent VA, because AADs have not clearly proven to be effective and ICD implantation is not curative. However, most of the procedures in the published series were performed by use of an endocardial approach, and the ablation success rate was not satisfactory. Epicardial ablation has been recently applied in ARVD/C patients and associated with better arrhythmia control, but, under most circumstances, this technique was used as a complementary approach to previous single or multiple failed endocardial-alone ablations. Of note, the initial experience on nonpharmacologic therapy of refractory VT in ARVD/C came from surgeons who either made epicardial incisions or placed surgical ablation at the site of origin of VT, which successfully prevented the recurrence of arrhythmias. Several mechanisms may explain the uniform outcome of endocardial-alone ablation and the necessity of performing endo-epicardial–based ablation in ARVD/C patients. First, parts of the RV wall may have become thickened in some ARVD/C patients, and radiofrequency energy delivered from the endocardium alone is unable to achieve transmural lesions. In this aspect, the endo-epicardial ablation is more likely to create full-thickness permanent myocardial necrosis and eliminate the arrhythmogenic sources, including intramural phase 2 reentry. Second, the specific target of ablation, based on endocardial mapping (ie, exit of a reentry circuit or a focal pattern activation), could be just the breakout site of a reentry circuit that is located in the epicardium. Therefore, the tachycardia can only be abolished by radiofrequency ablation in the epicardial space. Furthermore, it has been noted that the epicardial scar/abnormal region identified by 3D voltage mapping often extends beyond the site of the endocardial scar/abnormal areas, suggesting that parts of the epicardial arrhythmogenic substrate would never be targeted and modified by extensive endocardial-alone ablation. Our approach used in group 2 patients included linear ablation encircling the epicardial scar/abnormal area and abolition of any delayed, split, and fragmented “abnormal” electrograms. In this way, potential arrhythmogenic sources localized within this zone were isolated or abolished, and possible reentrant circuits located in the scar border zone were also eliminated. A similar technique was recently reported by Bakir et al, who used cryo energy in a surgical ablation procedure in an

Figure 3. Ventricular arrhythmia (VA)/ICD therapy–free survival by the presence of frequent premature ventricular contractions (PVCs) in the entire study population (A) and in group 1 (B) or group 2 (C). Regardless of the ablation approach, the presence of frequent PVCs at the end of ablation was associated with more VA recurrence.
ARVD/C patient with incessant VT despite 3 endocardial ablations, and by Garcia et al., who reported their experience on epicardial ablation in patients with previously failed endocardial procedures.

It has been recognized that the fat tissue in the pericardial space may influence the human epicardial bipolar electrogram recordings by which an ablation target is determined. However, the fat pad will only decrease the amplitude of the electrogram if it is overlying an area of normal myocardium; it will not cause the electrogram to be delayed, split, or fragmental, which are characteristics of diseased myocardium. Looking at the amplitude, timing, and morphology of the epicardial electrogram, we were able to accurately detect the boundary of “abnormal/scar” region and distinguish it from normal myocardium. This is consistent with the findings during LV epicardial mapping.

Even though reentry is the main mechanism of VT in ARVD/C, enhanced automaticity that occurs during exercise and triggered activity from inflammatory myocytes may also contribute to the development of VA. When a reentrant circuit was present, PVCs associated with trigger activity could initiate sustained reentry tachycardia. In addition, after all existing reentrant circuits are ablated, enhanced automaticity could initiate focal tachycardia. On the other hand, because of the progressive nature of ARVD/C, new reentrant circuits may become manifested. This could explain why the presence of frequent PVCs after VT ablation was associated with higher recurrence of arrhythmia in ARVD/C patients. Whether these PVCs should be targeted for ablation to further improve procedure success remains unclear and warrants additional studies.

Study Limitations
This was not a randomized study, but consecutive patients were enrolled in different centers. There could have been potential biases in selecting the ablation strategy for the patients. However, our subgroup analysis showed no inter-center differences in choice of procedure and no outcome differences between patients with and without previous endocardial ablation within group 2. This made it less likely that nonrandomization bias had significant influence on our results. Given the small number of events, we could not perform multivariable Cox analysis with the current population, which might not have sufficient power to show independent predictor(s). Biopsy and genetic testing were not available in all patients, but ARVD/C was diagnosed according to the consensus document criteria.

Conclusion
Epicardial scar and abnormality play an important role in the development of VAs in ARVD/C. An ablation strategy based on substrate modification with simultaneous endocardial and epicardial radiofrequency energy delivery is associated with improved arrhythmia-free survival and higher probability of AAD discontinuation. This approach should be considered as the initial strategy of VT ablation in patients with ARVD/C. The presence of ≥10 PVCs per minute after ablation is associated with more VA recurrence.

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Disclosures
Preliminary results of this study were presented as an abstract at the European Cardiology Society Scientific Session 2010 and the American Heart Association Scientific Session 2010 by Dr Di Biase. Dr Di Biase is a consultant for Hansen Medical and Biosense Webster. Dr Natale received speaker honorariums from Boston Scientific, Biosense Webster, St Jude Medical, Biotronik, and Life Watch.

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CLINICAL PERSPECTIVE

Long-term freedom from ventricular arrhythmia is limited after endocardial ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Percutaneous epicardial ablation of ventricular tachycardia in this population has been reported, but in most cases it was performed after a failed endocardial ablation. Our prospective study demonstrated that a combination of endocardial and epicardial ablation as “first-line” strategy can achieve higher long-term success rate with a greater number of patients discontinuing antiarrhythmic drugs. We compared 2 strategies of ventricular tachycardia ablation in a cohort of arrhythmogenic right ventricular cardiomyopathy/dysplasia patients: endocardial-alone ablation (n = 23) and or endo-epicardial ablation (n = 26). After a follow-up of at least 3 years, freedom from ventricular arrhythmia or appropriate implantable cardioverter-defibrillator therapy was 52% (12/23) in the endocardial-alone group and 85% (22/26) in the endo-epicardial group. Of interest, the presence of frequent premature ventricular contractions with/without isoproterenol provocation at the end of procedure was associated with higher arrhythmia recurrence. Whether ablation of these premature ventricular contractions will add more benefit needs further evaluation.
Ablation of Ventricular Arrhythmias in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy: Arrhythmia-Free Survival After Endo-Epicardial Substrate Based Mapping and Ablation

Rong Bai, Luigi Di Biase, Kalyanam Shivkumar, Prasant Mohanty, Roderick Tung, Pasquale Santangeli, Luis Carlos Saenz, Miguel Vacca, Atul Verma, Yariv Khaykin, Sanghamitra Mohanty, J. David Burkhardt, Richard Hongo, Salwa Beheiry, Antonio Dello Russo, Michela Casella, Gemma Pelargonio, Pietro Santarelli, Javier Sanchez, Claudio Tondo and Andrea Natale

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