Endocardial Ablation to Eliminate Epicardial Arrhythmia Substrate in Scar-Related Ventricular Tachycardia

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Objectives
We evaluated the feasibility and safety of epicardial substrate elimination with endocardial radiofrequency (RF) delivery in patients with scar-related ventricular tachycardia (VT).

Background
Epicardial RF delivery is limited by fat or associated with bleeding, extra-cardiac damages, coronary vessels and phrenic nerve injury. Alternative ablation approaches might be desirable.

Methods
Forty-six patients (18 ischemic cardiomyopathy [ICM], 13 nonischemic dilated cardiomyopathy [NICM], 15 arrhythmogenic right ventricular cardiomyopathy [ARVC]) with sustained VT underwent combined endo- and epicardial mapping. All patients received endocardial ablation targeting local abnormal ventricular activities in the endocardium (Endo-LAVA) and epicardium (Epi-LAVA), followed by epicardial ablation if needed.

Results
From a total of 173 endocardial ablations targeting Epi-LAVA at the facing site, 48 (28%) applications (ICM: 20 of 71 [28%], NICM: 3 of 39 [8%], ARVC: 25 of 63 [40%]) successfully eliminated the Epi-LAVA. Presence of Endo-LAVA, the most delayed and low bipolar amplitude of Epi-LAVA, low unipolar amplitude in the facing endocardium, and Epi-LAVA within a wall thinning area at computed tomography scan were associated with successful ablation. Endocardial ablation could abolish all Epi-LAVA in 4 ICM and 2 ARVC patients, whereas all patients with NICM required epicardial ablation. Endocardial ablation was able to eliminate Epi-LAVA at least partially in 15 (83%) ICM, 2 (13%) NICM, and 11 (73%) ARVC patients, contributing to a potential reduction in epicardial RF applications. Pericardial bleeding occurred in 4 patients with epicardial ablation.

Conclusions
Elimination of Epi-LAVA with endocardial RF delivery is feasible and might be used first to reduce the risk of epicardial ablation. (J Am Coll Cardiol 2014;63:1416–26) © 2014 by the American College of Cardiology Foundation

Since the first description of epicardial ventricular tachycardia (VT) ablation with percutaneous subxiphoid access in 1996 (1), epicardial mapping and ablation have been widely performed for the treatment of scar-related VT. Combined endo- and epicardial ablation has been used to achieve improved outcomes, not only in the setting of nonischemic dilated cardiomyopathy (NICM) (2,3) and arrhythmogenic right ventricular cardiomyopathy (ARVC) (4–6), but also in ischemic cardiomyopathy (ICM) (7,8). Regions of critically slow conduction necessary for re-entry can lie deep in the subendocardial layer or in the epicardial myocardium, and can be recorded as local abnormal ventricular activities (LAVA) from the pericardial space. Complete elimination of both endocardial (Endo-LAVA) and epicardial local abnormal ventricular activities (Epi-LAVA), if present, is associated with superior survival from recurrent VT during long-term follow-up (9).

Endocardial ablation is usually effective in eliminating most endocardial substrates, but epicardial lesions are
thought to be required for epicardial targets. Epicardial radiofrequency (RF) ablation has potential risks, however, such as pericardial bleeding and injury of coronary vessels or the phrenic nerve (10–12). Epicardial ablation, particularly if contact force is not directed toward the heart, can result in extra-cardiac damage such as pulmonary lesions (13). Furthermore, epicardial fat can significantly reduce ablation lesion depth (14). One-fourth of the epicardial surface is covered by >4 mm of fat, which is predominantly present at the left ventricular (LV) superior wall and right ventricular (RV) anterior wall (15). An epicardial fat layer >7 mm and substrate in close proximity to the coronary arteries are associated with epicardial ablation failure (15), highlighting the need for alternative ablation approaches.

The objective of this study was to evaluate the feasibility and safety of Epi-LAVA elimination with endocardial RF delivery in patients with scar-related VT as a result of ICM, NICM, and ARVC. The secondary objective was to assess variables that might be predictive of successful Epi-LAVA elimination endocardially, including clinical and electrophysiological parameters and anatomic information as assessed by contrast-enhanced multidetector computed tomography (MDCT).

**Methods**

**Patient selection.** This study enrolled consecutive patients who underwent combined endo- and epicardial mapping/ablation of scar-related sustained VT with a 3-dimensional (3D) electroanatomic mapping system between April 2009 and March 2013 at our center. All patients had episodes of repetitive sustained VT, resistant to antiarrhythmic drug therapy, requiring external cardioversion or therapy from an implantable cardioverter-defibrillator (ICD). Ischemic cardiomyopathy was diagnosed on the basis of significant coronary artery disease (>75% stenosis), documented myocardial infarction, and/or Q waves in the 12-lead electrocardiogram with regional wall motion abnormality. The diagnosis of NICM was based on a LV ejection fraction of <50% in the absence of coronary artery disease, documented myocardial infarction, or focal wall motion abnormality. Patients diagnosed as ARVC fulfilled 2010 task force criteria (16). We excluded other causes of sustained VT, such as cardiac sarcoidosis, congenital heart disease, long-lasting hypertensive heart disease, valvular heart disease, and toxin-related cardiomyopathy. Written informed consent was obtained from all patients.

**Electrophysiological study.** All anti-arrhythmic drugs except amiodarone were discontinued for at least 5 half-lives before ablation if the stability of arrhythmia allowed it. The ICD therapies were turned off, and the device was programmed to a surveillance-only mode. A 6-F steerable quadripolar or decapolar catheter (Xtrem, ELA Medical, Montrouge, France; or Dynamic, BARD Electrophysiology, Lowell, Massachusetts) was inserted from the right femoral vein and placed into the distal coronary sinus or at the RV apex. The LV endocardium was accessed by transseptal or retrograde transaortic approach. Pericardial access was obtained through a subxiphoid and anterior puncture under left lateral fluoroscopic guidance in all patients. The indications for epicardial access were previous failed endocardial ablation, minimal or no endocardial scar, suspected epicardial substrate on the basis of VT morphology (17,18), or the type of cardiomyopathy (NICM and ARVC). A steerable sheath (Agilis, St. Jude Medical, St. Paul, Minnesota) was introduced into the pericardial space. Continuous aspiration was then connected to the sheath.

Systemic heparinization was maintained throughout the procedure with a target activated clotting time ≥200 s after establishment of pericardial access and transseptal puncture. Both endo- and epicardial mapping were performed with a multipolar high-density mapping catheter (PentaRay, Biosense Webster, Diamond Bar, California) in all patients. Although PentaRay allows high-density mapping in both endo- and epicardium, it may produce mechanical ectopics when used endocardially. In this situation, we used a 4-mm-tip mapping catheter (Navistar-Thermocool, Biosense Webster) to complete mapping. Electrograms were filtered at 30 to 250 Hz (bipolar) and 1 to 240 Hz (unipolar). Electrophyslogic mapping was performed during sinus rhythm with Carto (Biosense Webster) or NavX (St. Jude Medical).

**MDCT image processing and registration.** Our strategy for MDCT image acquisition and registration with the 3D electroanatomic map is provided in the Online Appendix and is as previously described (19). Contrast-enhanced MDCT was performed on a 64-slice computed tomography scanner (SOMATOM Definition, Siemens Medical Solutions, Forchheim, Germany) 1 to 3 days before the procedure in 21 patients. Three-dimensional surface meshes of the endocardium, epicardium, coronary arteries, coronary sinus, and LV myocardial wall thinning (defined as areas with end-diastolic wall thickness <5 mm) were generated from MDCT data with CardioviZ3D software (INRIA, Sophia Antipolis, France). A cutoff of 5 mm for significant LV wall thinning was based on a previous report describing the reference values of wall thicknesses by MDCT in a healthy population (20). The MDCT data were imported into 3D navigation systems and integrated with the electroanatomic maps. Whether Epi-LAVA were located inside
or outside of the LV wall-thinning segmentation was assessed.

**Definition of LAVA and low-voltage zone.** As previously described (9,21), LAVA were defined as electrograms from poorly coupled surviving myocardial fibers with the following features: 1) sharp, high-frequency ventricular potentials distinct from the far-field ventricular electrogram; 2) occurring anytime during or, more frequently, after the far-field ventricular electrogram during sinus rhythm; and 3) sometimes displaying double or multiple high-frequency signals separated by very low-amplitude signals or an isoelectric interval. When LAVA occur within the QRS and are fused with the far-field ventricular potential, ventricular pacing with extrasystole is performed to differentiate them from the far-field ventricular potential. The LAVA are delayed and distinguished from the far-field potential by the

![Figure 1](image_url)

**Figure 1** Endocardial Ablation Eliminates Epicardial LAVA at Facing Site in Patient With ICM

(A) The multielectrode catheter (PentaRayNav) lying epicardially displayed local abnormal ventricular activities (LAVA) (*). Endocardial (Endo) ablation catheter placed at the facing site to the epicardial (Epi) PentaRayNav by a transseptal approach also showed abnormal sharp signals. (B) Endocardial ablation eliminated Epi-LAVA after increasing their delay. dist = distal; RF = radiofrequency.
pacing maneuver, because of poor coupling of the muscle bundle generating the LAVA signal.

We employed the following voltage criteria: a peak-to-peak bipolar amplitude of <1.5 mV defined the bipolar low-voltage zone \((22)\); and a unipolar amplitude of <8.3 mV in the LV and <5.5 mV in the RV defined the low unipolar voltage zone \((23,24)\).

**RF ablation.** After completion of endo- and epicardial mapping, VT inducibility was tested by programmed ventricular stimulation from the RV apex at a basic drive cycle length of 600 and 400 ms with up to triple extrastimuli decrementally to 200 ms or ventricular refractoriness. When hemodynamically tolerated VT was inducible, ablation was guided by conventional activation and entrainment mapping \((25)\). The critical sites of VT were defined as the sites where pre-systolic or mid-diastolic electrograms were present and either RF ablation or mechanical manipulation by the catheter terminated the VT, followed by noninducibility of the VT that was reproducibly inducible before. After termination of VT, further ablation targeting LAVA during sinus rhythm was performed. In patients with noninducible or poorly tolerated VT, ablation of LAVA was performed in sinus rhythm. Radiofrequency energy was delivered with a 3.5-mm open-irrigation catheter (NaviStar-Thermocool, Biosense Webster) with a power of 30 to 50 W endocardially. When ablating epicardially or in the RV endocardium, power ranged from 25 to 35 W.

If LAVA were detected on both the endo- and epicardium, our strategy was always to start ablation endocardially, aiming at elimination of both Endo- and Epi-LAVA. If LAVA were detected epicardially in the absence of Endo-LAVA, endocardial ablation was performed at the facing site aiming to abolish the potentials transmurally. During endocardial ablation at the facing site of Epi-LAVA, careful monitoring of transmural response and elimination of Epi-LAVA was possible with a multipolar high-density mapping catheter (PentaRay, Biosense Webster), which was placed at Epi-LAVA sites and stabilized by a steerable sheath (Agilis, St. Jude Medical) (Fig. 1). This strategy was repeated at adjacent sites as needed to achieve complete Epi-LAVA elimination. After endocardial ablation, epicardial mapping of areas previously displaying LAVA was performed and used to guide further ablation as indicated by Epi-LAVA persistence. Remapping allowed us to classify patients as having complete or incomplete Epi-LAVA elimination after endocardial ablation.

The goal and ideal procedural endpoint was complete elimination of all identified LAVA. Induction of VT was repeated with programmed stimulation with the same protocol as pre-ablation. In hemodynamically unstable patients, VT inducibility was not retested post-ablation.

**Follow-up.** After ablation, ICD therapies were reprogrammed with active VT and ventricular fibrillation zones. Patients were monitored at least 48 h in-hospital before discharge. Patients were followed every 3 months to assess VT recurrences. Recurrence of VT after hospital discharge was assessed by ICD interrogation at each visit and by careful interview, electrocardiogram, and a Holter monitoring for the patients without ICD. Any sustained VT during follow-up, whether symptomatic or treated by ICD or not, was considered a recurrence of VT.

**Statistical analysis.** Categorical variables were expressed as numbers and percentages, and were compared with Pearson chi-square test or Fisher exact test, as appropriate. Continuous data for normally distributed variables were expressed as mean ± SD and compared by Student \(t\) test. Non-normally distributed variables were expressed as median (25th, 75th percentiles) and compared with Mann-Whitney \(U\) test or Kruskal-Wallis test. No corrections were made for multiple observations within individuals. Statistical calculations were performed with SPSS (version 21.0, IBM, SPSS, Chicago, Illinois). All tests were 2-tailed, and a \(p\) value of <0.05 was considered statistically significant.

**Results**

**Study population.** During the study period, a total of 51 patients (20 ICM, 15 NICM, 16 ARVC) underwent combined endo- and epicardial mapping with a 3D navigation system. The 46 (18 ICM, 13 NICM, 15 ARVC) patients who demonstrated evidence of Epi-LAVA comprised this study cohort (Table 1). Four patients had previously failed ablation (range 1 to 3). No patient had previous cardiac surgery. Percutaneous access was obtained percutaneously in all. For LV endocardial access (ICM and NICM patients), a retrograde approach was used in 7 patients, and a transseptal approach was used in 24 patients.

**Prevalence of abnormal regions.** Endo- and epicardium were mapped with 420 ± 271 and 572 ± 379 points/map, respectively. In ICM and NICM, the locations of epicardial low-voltage regions (bipolar voltage <1.5 mV) with presence of Epi-LAVA were the following: the apex in 15 (13 ICM, 2 NICM); anterior in 13 (10 ICM, 3 NICM); inferior in 15 (8 ICM, 7 NICM); and lateral in 18 (5 ICM, 13 NICM). In ARVC, epicardial low-voltage regions with Epi-LAVA were identified apically in 3, anteriorly in 9, inferiorly in 9, and laterally in 11. An endocardial low-voltage area was identified in all (100%) patients with ICM, 9 (69%) patients with NICM, and 13 (87%) patients with ARVC. The endo- and epicardial bipolar low-voltage area was 80.2 (62.9, 124.3) cm\(^2\) and 77.7 (45.4, 111.4) cm\(^2\) in ICM; 11.7 (3.2, 29.6) cm\(^2\) and 45.2 (39.2, 53.6) cm\(^2\) in NICM; and 32.5 (11.1, 55.7) cm\(^2\) and 110.6 (55.0, 139.0) cm\(^2\) in ARVC. Contrast-enhanced MDCT was performed in 21 patients (12 ICM and 9 NICM). A wall thinning region was identified in all ICM and 7 NICM patients. In all patients, high-resolution wall thinning segmentation was successfully integrated with 3D electroanatomic mapping, and its location corresponded to the electrophysiological scar.
Endocardial ablation at the facing site of Epi-LAVA.
There was no significant artifactual interference on the multielectrode catheter placed on the epicardium during ablation from the endocardial site, which enabled monitoring of the transmural response in the target Epi-LAVA (Fig. 1). A total of 173 endocardial ablations of Epi-LAVA monitored by multielectrode catheter during the RF energy delivery were analyzed. Of these, 79 (46%) were targeted from sites with no Endo-LAVA. Among 173 Epi-LAVA sites, 48 (28%) applications successfully eliminated the facing Epi-LAVA. Successful ablation was most frequently achieved in ARVC (25 of 63 applications [40%]), followed by ICM (20 of 71 applications [28%]). In NICM, only 3 of 39 applications (8%) successfully eliminated the Epi-LAVA at the facing site. Figure 2 shows Epi-LAVA and VT re-entry circuit eliminated by ablation at the facing endocardial site in a patient with ARVC. In total, 39 VTs (18 in ICM, 9 in NICM, 12 in ARVC) were hemodynamically tolerated and mapped with conventional activation and entrainment mapping approaches. Of these, 23 (7 in ICM, 7 in NICM, 9 in ARVC) VTs had the critical site of VT re-entrant circuit identified in the epicardium. Endocardial ablation at the facing site of the epicardial critical isthmus was performed, leading to successful termination of 5 VTs (2 [28%] ICM, 0 [0%] NICM, 3 [33%] ARVC).

Table 2 shows predictors of successful Epi-LAVA elimination endocardially. There were no significant differences in RF time, average temperature, average impedance, and power between successful and unsuccessful ablation. Endo-LAVA at the ablation site was more frequently present in the success site (32 of 48 [67%] vs. 62 of 125 [50%], p = 0.044). The most delayed Epi-LAVA were more frequently eliminated; that is, the duration from the onset of ventricular electrogram to the end of Epi-LAVA (electrogram-duration) was significantly longer in the successful site than unsuccessful sites (143 [116, 186] ms vs. 110 [86, 140] ms, p < 0.001). Bipolar amplitude of Epi-LAVA was significantly lower at successful ablation sites (0.26 [0.21, 0.34] mV vs. 0.71 [0.34, 1.24] mV, p < 0.001). Bipolar and unipolar amplitude of the facing endocardial ablation site was also lower at successful ablation sites (0.35 [0.21, 0.61] mV vs. 0.54 [0.22, 1.03] mV, p = 0.041; and 2.52 [2.02, 2.96] mV vs. 4.51 [3.38, 5.51] mV, p < 0.001, respectively).

The relationship between the impact of endocardial ablation on Epi-LAVA at the facing site and LV wall thinning seen on MDCT was assessed in 95 RF applications in the 21 patients. Of these, 72 (76%) Epi-LAVA (ICM: 59 of 67 [88%], NICM: 13 of 28 [46%]) were located within the wall thinning area, and the remaining 23 were outside. None of the 23 Epi-LAVA outside the wall thinning segmentation could be eliminated transmurally from the endocardium, whereas 23 (32%) of 72 Epi-LAVA within the wall thinning could be eliminated (p = 0.002).

Overall outcome of endocardial ablation of Epi-LAVA.
In 4 of 18 patients with ICM and 2 of 15 patients with ARVC, endocardial ablation could abolish all Epi-LAVA. These patients achieved complete elimination of both Endo- and Epi-LAVA with only endocardial ablation. By contrast, all patients with NICM required epicardial ablation. Incomplete Epi-LAVA elimination after endocardial ablation occurred in 22 patients (11 ICM, 2 NICM, 9 ARVC). Therefore, endocardial ablation had an impact on Epi-LAVA in 15 (83%) ICM, 2 (13%) NICM, and 11 (73%) ARVC patients, contributing to a potential reduction in epicardial RF applications.

Table 3 shows the characteristics of patients with complete, partial, and no elimination of Epi-LAVA by endocardial ablation. Patients with no impact of endocardial ablation on Epi-LAVA had the smallest low-voltage area in both endo- and epicardium. The presence of Endo-LAVA was associated with a greater impact of endocardial ablation on Epi-LAVA. In all patients with complete elimination of Epi-LAVA endocardially (6 of 6 [100%]) and most patients with partial elimination (15 of 22 [68%]), all Epi-LAVA corresponded with low endocardial unipolar voltage, compared with 3 of 18 (17%) patients with no elimination.

In 8 (7 ICM and 1 NICM) of 21 patients undergoing MDCT, all identified Epi-LAVA were located within the LV wall thinning segmentation. In all of these, endocardial ablation had an impact on Epi-LAVA (complete elimination in 2, and partial elimination in 6). The remaining 13 patients had presence of Epi-LAVA that were located outside the wall thinning (Fig. 3). None of these attained complete elimination of Epi-LAVA endocardially; 4 had partial impact of endocardial ablation on Epi-LAVA, and 9 had no impact.

Procedural and follow-up results. Mean procedure and RF time were 310 ± 65 min and 34 ± 14 min, respectively.

Table 1 Characteristics of the Study Population

| Age, yrs | 52 ± 16 |
| Male/female | 42/4 |
| Underlying structural heart disease |  |
| ICM | 18 |
| NICM | 13 |
| ARVC | 15 |
| Hypertension | 18 (39%) |
| LV ejection fraction | 38 ± 14 |
| ICD | 41 (89%) |
| NYHA III | 5 (11%) |
| Medications |  |
| Amiodarone | 36 (78%) |
| Beta-blocker | 43 (93%) |
| Prior failed ablation procedure | 4 (9%) |
| VT morphology, n | 2.0 (1.0, 3.0) |

Values are mean ± SD, median (quartiles), or n (%), unless otherwise indicated. ARVC = arrhythmogenic right ventricular cardiomyopathy; ICD = implantable cardioverter-defibrillator; ICM = ischemic cardiomyopathy; LV = left ventricular; NICM = nonischemic dilated cardiomyopathy; NYHA = New York Heart Association; VT = ventricular tachycardia.
Ventricular tachycardia (VT) that was hemodynamically tolerated was mapped in both endo- and epicardium in an arrhythmogenic right ventricular cardiomyopathy (ARVC) patient. The isochronal map during VT showed the critical isthmus of the VT reentrant circuit at the Epi basal postero-lateral region. The local electrograms at the critical isthmus displayed fractionated signals covering almost the entire cycle length of the VT. However, the critical isthmus was close to the right coronary artery rendering RF ablation at the region unwarranted.

The multielectrode catheter (PentaRayNav) was placed at the Epi slow conducting region. The ablation catheter was put at the Endo region facing the Epi PentaRayNav. The Epi PentaRayNav displayed fractionated pre-systolic potentials, whereas the Endo ablation catheter showed fewer fractionated potentials activating later, compared with the fractionated signals at the facing Epi site. Radiofrequency energy application on the Endo region terminated the VT after prolongation of VT cycle length. After termination of VT, LAVA were identified at the Epi critical isthmus of the VT re-entrant circuit (*). Endo ablation at the facing site was continued in sinus rhythm and eliminated the Epi LAVA completely. Abbreviations as in Figure 1.
Mean RF time on the epicardium was 12.5 ± 11.7 min. All identified LAVA were completely eliminated in 32 (70%) patients (13 of 18 [72%] ICM, 7 of 13 [54%] NICM, 12 of 15 [80%] ARVC). As shown in Figure 4, complete elimination of all Endo- and Epi-LAVA was more likely to be achieved in patients with impact of endocardial ablation on Epi-LAVA than those without (23 of 28 [72%] vs. 9 of 18 [50%], p = 0.021). In 14 patients, complete elimination of LAVA could not be achieved. Of these, 6 (1 ICM, 4 NICM, 1 ARVC) patients had epicardial LAVA that were located close to the coronary arteries or phrenic nerve. In the remaining 8 patients, LAVA could not be abolished, despite extensive ablation. Pericardial bleeding occurred in 4 patients. Three of them were managed conservatively, but 1 patient required surgical intervention. Pericardial bleeding only occurred in patients who received epicardial RF delivery. There was no phrenic nerve palsy, injury of coronary vessels, hepatic injury, or intra-abdominal bleeding.

One patient with ICM died of severe heart failure with recurrence of VT storm 48 h after the ablation procedure. One patient with ICM died of a noncardiac cause 5 months after the intervention. After a median follow-up period of 11 months, 31 (67%) patients were free from both death and VT recurrence. Patients who achieved complete elimination of Endo- and Epi-LAVA were more frequently free from VT recurrence and death (25 of 32 [78%] vs. 6 of 14 [43%], p = 0.024). Of 6 patients in whom endocardial ablation abolished all Epi-LAVA, 5 patients were free from VT recurrence and death, and 1 patient experienced VT recurrence. Three patients underwent redo procedures, 2

### Table 2

<table>
<thead>
<tr>
<th>Predictor of Successful Epi-LAVA Elimination From Ablation at Facing Endo Site</th>
<th>Success (n = 48)</th>
<th>Failure (n = 125)</th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>RF parameters</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RF time, s</td>
<td>68 (56, 88)</td>
<td>65 (55, 87)</td>
<td>0.60</td>
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<tr>
<td>Average temperature, °C</td>
<td>38 (36, 40)</td>
<td>39 (37, 40)</td>
<td>0.36</td>
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<tr>
<td>Average impedance, Ω</td>
<td>140 (130, 155)</td>
<td>143 (130, 165)</td>
<td>0.25</td>
</tr>
<tr>
<td>Power, W</td>
<td>35 (30, 36)</td>
<td>35 (30, 38)</td>
<td>0.37</td>
</tr>
<tr>
<td>Electrophysiological parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of opposite Endo-LAVA</td>
<td>32 (67%)</td>
<td>62 (50%)</td>
<td>0.044</td>
</tr>
<tr>
<td>Electrogram-duration of the target Epi-LAVA, ms</td>
<td>143 (116, 186)</td>
<td>110 (86, 140)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Electrogram-duration of opposite Endo-LAVA, ms</td>
<td>110 (96, 131)</td>
<td>114 (95, 138)</td>
<td>0.66</td>
</tr>
<tr>
<td>Bipolar amplitude of the target Epi-LAVA, mV</td>
<td>0.26 (0.21, 0.34)</td>
<td>0.71 (0.34, 1.24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bipolar amplitude of opposite endocardium, mV</td>
<td>0.35 (0.21, 0.61)</td>
<td>0.54 (0.22, 1.03)</td>
<td>0.041</td>
</tr>
<tr>
<td>Unipolar amplitude of opposite endocardium, mV</td>
<td>2.52 (2.02, 2.96)</td>
<td>4.51 (3.38, 5.51)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are median (quartiles) or n (%).

Endo = endocardial; Epi = epicardial; LAVA = local abnormal ventricular activities; RF = radiofrequency.

### Table 3

<table>
<thead>
<tr>
<th>Patients With Complete, Partial, and No Elimination of Epi-LAVA Endocardially</th>
<th>Complete Elimination of Epi-LAVA Endocardially (n = 6)</th>
<th>Partial Elimination of Epi-LAVA Endocardially (n = 22)</th>
<th>No Impact of Endo Ablation on Epi-LAVA (n = 18)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>56 ± 15</td>
<td>53 ± 16</td>
<td>50 ± 16</td>
<td>0.65</td>
</tr>
<tr>
<td>Male</td>
<td>6 (100%)</td>
<td>19 (86%)</td>
<td>17 (94%)</td>
<td>0.63</td>
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<tr>
<td>LV ejection fraction</td>
<td>36 ± 17</td>
<td>39 ± 16</td>
<td>38 ± 9</td>
<td>0.86</td>
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<td>Medications</td>
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<tr>
<td>Amiodarone</td>
<td>5 (83%)</td>
<td>17 (77%)</td>
<td>13 (72%)</td>
<td>0.38</td>
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<tr>
<td>Beta-blocker</td>
<td>6 (100%)</td>
<td>20 (91%)</td>
<td>17 (94%)</td>
<td>0.61</td>
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<td>Underlying structural heart disease</td>
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<tr>
<td>ICM</td>
<td>4 (67%)</td>
<td>11 (50%)</td>
<td>3 (17%)</td>
<td>0.002</td>
</tr>
<tr>
<td>NICM</td>
<td>0 (0%)</td>
<td>2 (9%)</td>
<td>11 (61%)</td>
<td></td>
</tr>
<tr>
<td>ARVC</td>
<td>2 (33%)</td>
<td>9 (41%)</td>
<td>4 (22%)</td>
<td></td>
</tr>
<tr>
<td>VT morphology, n</td>
<td>1.5 (0.8, 4.0)</td>
<td>1.5 (0, 3.0)</td>
<td>2.0 (1.0, 2.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Endo total low-voltage area, cm²</td>
<td>65.0 (47.5, 107.8)</td>
<td>59.1 (40.4, 86.7)</td>
<td>12.6 (5.1, 40.1)</td>
<td>0.010</td>
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<tr>
<td>Epi total low-voltage area, cm²</td>
<td>97.9 (43.3, 120.2)</td>
<td>101.0 (49.4, 117.8)</td>
<td>47.6 (39.8, 68.0)</td>
<td>0.030</td>
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<tr>
<td>Presence of Endo-LAVA</td>
<td>6 (100%)</td>
<td>18 (82%)</td>
<td>7 (39%)</td>
<td>0.003</td>
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<tr>
<td>Amplitude of Epi-LAVA, mV</td>
<td>0.37 (0.33, 0.45)</td>
<td>0.39 (0.24, 0.74)</td>
<td>0.67 (0.43, 1.31)</td>
<td>0.041</td>
</tr>
<tr>
<td>Duration of Epi-LAVA, ms</td>
<td>156 (121,195)</td>
<td>139 (116, 163)</td>
<td>108 (90, 149)</td>
<td>0.044</td>
</tr>
<tr>
<td>All Epi-LAVA within abnormal Endo unipolar voltage zone</td>
<td>6 (100%)</td>
<td>15 (68%)</td>
<td>3 (17%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD, median (quartiles), or n (%).

Abbreviations as in Tables 1 and 2.
of whom had LAVA successfully eliminated during the initial procedure, and the other had persistent LAVA. The repeat epicardial procedure with percutaneous subxiphoid access was successfully performed in all patients. Both patients who achieved complete LAVA elimination at the index procedure had LAVA recovery. Repeat ablation eliminated all LAVA.

**Discussion**

This study describes the feasibility and safety of a novel approach for modification of subepicardial VT substrate from endocardial ablation and demonstrates the following:

1. Endocardial RF was associated with Epi-LAVA elimination at the facing site in 28% of applications,
and complete or incomplete elimination was achieved in 61% of patients overall, thereby reducing the need for epicardial ablation.

2. The underlying structural heart disease was a major determinant of success, because only 8% of endocardial applications eliminated the facing Epi-LAVA in NICM, compared with 28% in ICM and 40% in ARVC.

3. The electrophysiological characteristics of the targeted region were also important; the most delayed and lowest bipolar amplitude Epi-LAVA were more prone to complete elimination. Similarly low unipolar amplitude in the facing endocardium was associated with greater success.

4. Endocardial ablation was more likely to eliminate epicardial substrate when delivered in a thin-walled region of the LV (<5 mm at MDCT).

These findings indicate that epicardial scar homogenization by complete elimination of poorly coupled bundles through endocardial ablation is more readily achieved within the most severe scars.

**Elimination of epicardial LAVA by endocardial transmural lesion.** Recurrent VT originating from the subepicardium is thought to be an important reason for failure of epicardial ablation (26–30). Elimination of epicardial arrhythmia substrate with endocardial ablation is conventionally thought to be impractical, because transmural ventricular lesions are probably rare with the current ablation technology. Endocardial substrate-based ablation targeting delayed and fragmented local potentials has been reported but never used while monitoring the epicardial facing site. In this study, the multielectrode mapping catheter placed epicardially was used, not only for high-density mapping, but also as a landmark of the target Epi-LAVA location, guiding the operator to the facing endocardial site exactly. It also enables online monitoring of the impact of endocardial ablation on Epi-LAVA.

Both low bipolar amplitude of the target Epi-LAVA and low unipolar amplitude at the facing endocardial region were strongly associated with the successful elimination of Epi-LAVA transmurally. These findings might indicate that transmural Epi-LAVA elimination is more feasible in regions of wall thinning. Where Epi-LAVA are located outside the wall thinning area, it seems to be difficult to penetrate deep enough into the myocardium to disrupt the intramural or subepicardial circuits. We found that the negative predictive value for elimination of Epi-LAVA from the endocardium outside the LV wall thinning areas was 100%. These findings allow the operator to avoid ineffective RF energy applications on the endocardium. In patients with NICM, Epi-LAVA elimination from the facing endocardial site is more difficult. This might be explained by our finding of a lower proportion of Epi-LAVA within the wall thinning segmentation in NICM than in ICM. This ablation technique yields maximal

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**Figure 4** Patient Flow Chart and Procedure Outcome

Abbreviations as in Figure 1.
benefit in patients with ARVC. A prior study of in vivo lesion assessment has demonstrated that transmural lesions are more likely to be attained in the RV—not unexpected, because the ventricular wall here is thinner compared with the LV (13).

Impact of elimination of endocardial LAVA on epicardial substrate. Even if endocardial ablation cannot eliminate the Epi-LAVA at the facing site transmurally, a subset of epicardial scar had no LAVA anymore after complete elimination of Endo-LAVA. The presence of Endo-LAVA was significantly associated with the impact of endocardial ablation on Epi-LAVA, suggesting the presence of the interconnecting channels between endo- and epicardial LAVA regions. This phenomenon is less common in NICM compared with ICM. This is consistent with the known characteristics of scar in different types of structural heart disease; that is, arrhythmia substrates in NICM are located predominantly intramurally or subepicardially with the minimal subendocardial substrate (3), whereas the ischemic scar usually progresses from the subendocardium to the epicardium within the territory of the culprit coronary arteries.

Clinical implications. Epicardial mapping and ablation might conventionally be started directly before the endocardial attempt if the epicardial substrate is thought to be responsible for VT perpetuation. However, our findings show that some epicardial ablations can be avoided if endocardial ablation is performed first. Elimination of Epi-LAVA endocardially can diminish the need for epicardial RF energy delivery, increasing the safety of ablation. Furthermore, the present technique has the possibility to improve the efficacy of ablation, because it may eliminate subepicardial surviving fibers, which could have been impossible to eradicate from the epicardium because of the existence of epicardial fat and coronary vessels.

The present study provides a valuable clue suggesting the anatomic and electrophysiological characteristics that predict the impact of endocardial ablation on epicardial arrhythmia substrate modification. This approach is less useful if Epi-LAVA are located outside the LV wall thinning area as imaged by contrast-enhanced MDCT, if there is no substrate at the corresponding endocardial region, or if the unipolar voltage of corresponding endocardial region is normal. Also, it is less effective for substrate in NICM. Further development of alternative approaches is warranted to improve the efficacy of ablation in these less favorable situations.

Study limitations. Although this ablation technique was performed in consecutive patients prospectively, RF parameters such as ablation time and power were not systematically standardized in each RF energy application for the purpose of this study. Moreover, we did not deliver higher-power or longer RF selectively at healthier regions with normal voltage and nonthinned sites in an attempt to make a deeper lesion. Although our data provided no justification for high-power output or prolonged ablation delivery, we cannot rule out the possibility that this more aggressive strategy might be associated with a higher rate of Epi-LAVA elimination. However, extensive endocardial ablation to get rid of Epi-LAVA might increase the risk for complications such as volume overload, steam pop or cardiac perforation, and thromboembolic events.

Conclusions

Elimination of epicardial LAVA from endocardial ablation is feasible and has maximum benefit in patients with ARVC and ischemic cardiomyopathy where the epicardial substrate is located in a thin myocardial wall. This novel approach has the potential to reduce or obviate the need for epicardial RF energy delivery, and therefore could be performed before epicardial ablation for the modification of epicardial arrhythmia substrate.

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Key Words: ablation ● arrhythmia ● epicardium ● local abnormal ventricular activities ● ventricular tachycardia.

APPENDIX

For a supplemental Methods section, please see the online version of this article.