

QUARTERLY FOCUS ISSUE: HEART RHYTHM DISORDERS

# Electroanatomic Substrate and Ablation Outcome for Suspected Epicardial Ventricular Tachycardia in Left Ventricular Nonischemic Cardiomyopathy

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<b>Objectives</b>	The aim of the study was to define the epicardial substrate and ablation outcome in patients with left ventricular nonischemic cardiomyopathy (NICM) and suspected epicardial ventricular tachycardia (VT).
<b>Background</b>	Ventricular tachycardia in NICM often originates from the epicardium.
<b>Methods</b>	Twenty-two patients with NICM underwent detailed endocardial and epicardial bipolar voltage maps and VT ablation for suspected epicardial VT. Eight patients with normal hearts and idiopathic VT served to define normal epicardial electrograms. Low-voltage regions were also assessed for wide (>80 ms), split, or late electrograms.
<b>Results</b>	Normal epicardial bipolar voltage was identified as >1.0 mV on the basis of the reference population. Confluent low-voltage areas were present in 18 epicardial (82%) and 12 endocardial (54%) maps and were typically over basal lateral LV. In the 18 patients with epicardial VT on the basis of activation/pacemapping, the mean epicardial area was greater than the endocardial low-voltage area ( $55.3 \pm 33.5 \text{ cm}^2$ vs. $22.9 \pm 32.4 \text{ cm}^2$ , $p < 0.01$ ). Epicardial low-voltage areas showed 49.7% wide (>80 ms), split, and/or late electrograms rarely seen in the reference patients (2.3%). During follow-up of $18 \pm 7$ months, ablation resulted in VT elimination in 15 of 21 patients (71%) including 14 of 18 patients (78%) with epicardial VT.
<b>Conclusions</b>	In patients with NICM and VT of epicardial origin, the substrate is characterized by areas of basal LV epicardial > endocardial bipolar low voltage. The electrograms in these areas are not only small (<1.0 mV) but wide (>80 ms), split, and/or late, and help identify the substrate targeted for successful ablation. (J Am Coll Cardiol 2009;54:799–808) © 2009 by the American College of Cardiology Foundation

Endocardial ventricular tachycardia (VT) ablation in patients with left ventricular (LV) nonischemic dilated cardiomyopathy (NICM) is associated with lower success rates when compared with VT ablation in patients with ischemic cardiomyopathy (1–4). This difference in efficacy might be due to the presence of epicardial substrate and VT circuits in NICM that cannot be successfully ablated from the endocardium (1–4).

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The relevance and characteristics of the epicardial substrate have been suggested in small series of patients but have not been clearly defined (3,4). The objective of this study was to describe and compare the endocardial and epicardial

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substrate and to evaluate the outcome with VT ablation in a consecutive series of patients with NICM and VT suspected of being of epicardial origin.

## Methods

**Study population.** Detailed electroanatomic data were obtained from 22 consecutive patients with an NICM diagnosis who underwent epicardial sinus rhythm mapping and VT ablation in our institution over a 5-year period from

**Abbreviations  
and Acronyms**

<b>AV</b> = atrioventricular
<b>ECG</b> = electrocardiogram
<b>ICD</b> = implantable cardioverter-defibrillator
<b>LP</b> = late potential
<b>LV</b> = left ventricle/ ventricular
<b>NICM</b> = nonischemic cardiomyopathy
<b>RF</b> = radiofrequency
<b>VT</b> = ventricular tachycardia

June 2002 to November 2007. This dataset was selected to permit long-term follow-up outcome data for at least 1 year in all surviving patients. The decision for an epicardial approach was made on the basis of the characteristics of the VT in the surface 12-lead electrocardiogram (ECG) suggesting an epicardial origin (n = 2 patients) and/or failure of prior endocardial ablation (n = 20 patients) (5,6). In all 22 patients (19 men, age  $56 \pm 13$  years, LV ejection fraction:  $30 \pm 13\%$ ) the diagnosis of NICM

was established by the absence of significant (>75% stenosis) coronary artery disease, prior myocardial infarction, or primary valvular abnormalities. Other causes of dilated cardiomyopathy were also excluded, including right ventricular dysplasia/cardiomyopathy, cardiac sarcoidosis, and alcoholic cardiomyopathy. All study patients had a previous history of spontaneous sustained monomorphic VT documented either by surface ECG or stored intracardiac electrograms from an implantable cardioverter-defibrillator (ICD). An additional group of 8 patients with no evidence of structural heart disease and idiopathic VT were also studied to establish normal reference values for epicardial electrograms. All procedures were performed following the institutional guidelines of the University of Pennsylvania Health System, and all patients provided written informed consent.

**Sinus rhythm electroanatomical mapping.** Electroanatomical mapping of the endocardium and the epicardium during the baseline rhythm was performed at the same procedure with the CARTO system (Biosense Webster Inc., Diamond Bar, California) as previously described (2–4,7). A 4-mm solid distal-tip electrode and 2-mm ring electrode ablation catheter (NaviStar) or a 3.5-mm distal tip irrigated catheter (Navistar Thermocool, Biosense Webster Inc.) was used as the mapping catheter. Bipolar signals were filtered at 30 to 400 Hz and displayed at 200 mm/s. A detailed assessment of individual electrogram characteristics was also made offline. A retrograde transaortic approach was used to access the endocardial LV in all cases except 1 in which a transseptal puncture was necessary for LV endocardial access via the mitral orifice. Access to the pericardial space and epicardium was obtained with the technique described by Sosa et al. (8). Briefly, under general anesthesia, a Tuohy needle was introduced via a subxiphoid approach to gain access for sheath and mapping/ablation catheter placement.

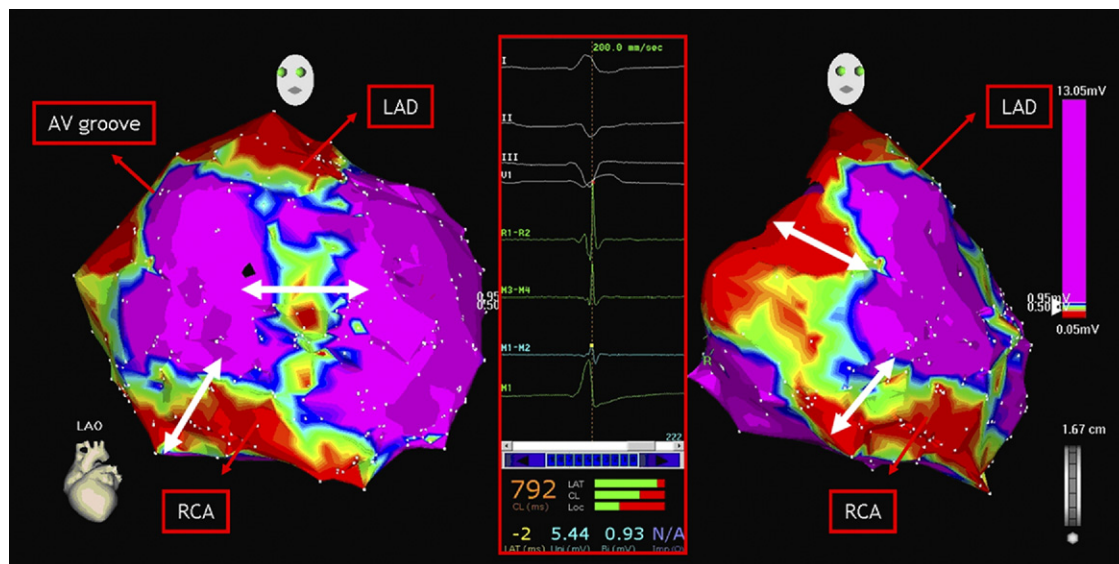
**Reference values for defining voltage abnormality with electroanatomical mapping.** The reference value for defining abnormal electrogram voltage in the LV endocardium was previously established at 1.5 mV with the CARTO

system (7). To define normal epicardial signal amplitude and characteristics, we studied 8 additional patients (3 men, mean age  $47 \pm 16$  years) with structurally normal hearts and idiopathic VT or frequent ventricular premature depolarizations who underwent epicardial mapping for suspected epicardial VT (Table 1). Detailed electroanatomical mapping of the epicardium was performed during sinus rhythm in all 8 patients with a 4-mm solid distal-tip electrode and 2-mm ring electrode ablation catheter (NaviStar). A mean of  $212 \pm 102$  epicardial points was recorded/patient. Low-voltage areas have been previously described around the atrioventricular (AV) groove as well as surrounding the large coronary vessels as a result of the normal distribution of fat tissue on the epicardium (9,10). To attempt to delineate the influence of fat and coronary anatomy and further define normal epicardial electrogram characteristics, we reassessed electrogram characteristics both before and after excluding the region within 1.5 cm of large epicardial coronary vessels defined by coronary angiography and those areas outside that margin (Fig. 1). In 3 of the 8 reference patients with idiopathic VT focal VT/ventricular premature depolarization origin was identified at the epicardial LV base in 2 patients and at the epicardial LV apex in 1 patient. No electrogram abnormalities were recorded in sinus rhythm from the sites of origin. In the 5 remaining patients an epicardial origin for VT was not identified despite the detailed mapping, and VTs were mapped and ablated from the aortic sinus of Valsalva (n = 3), the coronary sinus (n = 1), or the proximal anterior interventricular vein (n = 1), consistent with their idiopathic VT syndrome.

**Abnormal electrogram morphology: definitions.** To further characterize low-amplitude signals on the epicardium, all low-amplitude signals were also analyzed offline to determine whether they: 1) were wide: electrograms >80-ms duration; 2) were split: electrograms with 2 or more distinct components with >20-ms isoelectric segment between peaks of individual components; or 3) demonstrated late potentials (LPs): electrograms with a distinct onset after the QRS. These electrogram characteristics were not considered mutually exclusive.

<b>Table 1</b> Baseline Characteristics of Reference Patients Without Structural Heart Disease Undergoing Epicardial Mapping					
Patient #	Age (yrs)	Sex	LVEF (%)	AAD at Time of Procedure	Clinical Arrhythmia
1	54	F	65	None	NSVT
2	44	F	60	None	PVC
3	50	M	60	Propafenone	SMVT
4	22	F	65	None	SMVT
5	37	M	55	None	SMVT
6	43	F	55	Sotalolol	PVC
7	51	F	70	None	NSVT
8	78	M	60	Sotalolol	PVC

AAD = antiarrhythmic drugs; LVEF = left ventricular ejection fraction; NSVT = nonsustained ventricular tachycardia; PVC = premature ventricular complex; SMVT = sustained monomorphic ventricular tachycardia.



**Figure 1** Epicardial Voltage Map of a Patient With a Structurally Normal Heart and Idiopathic Ventricular Tachycardia

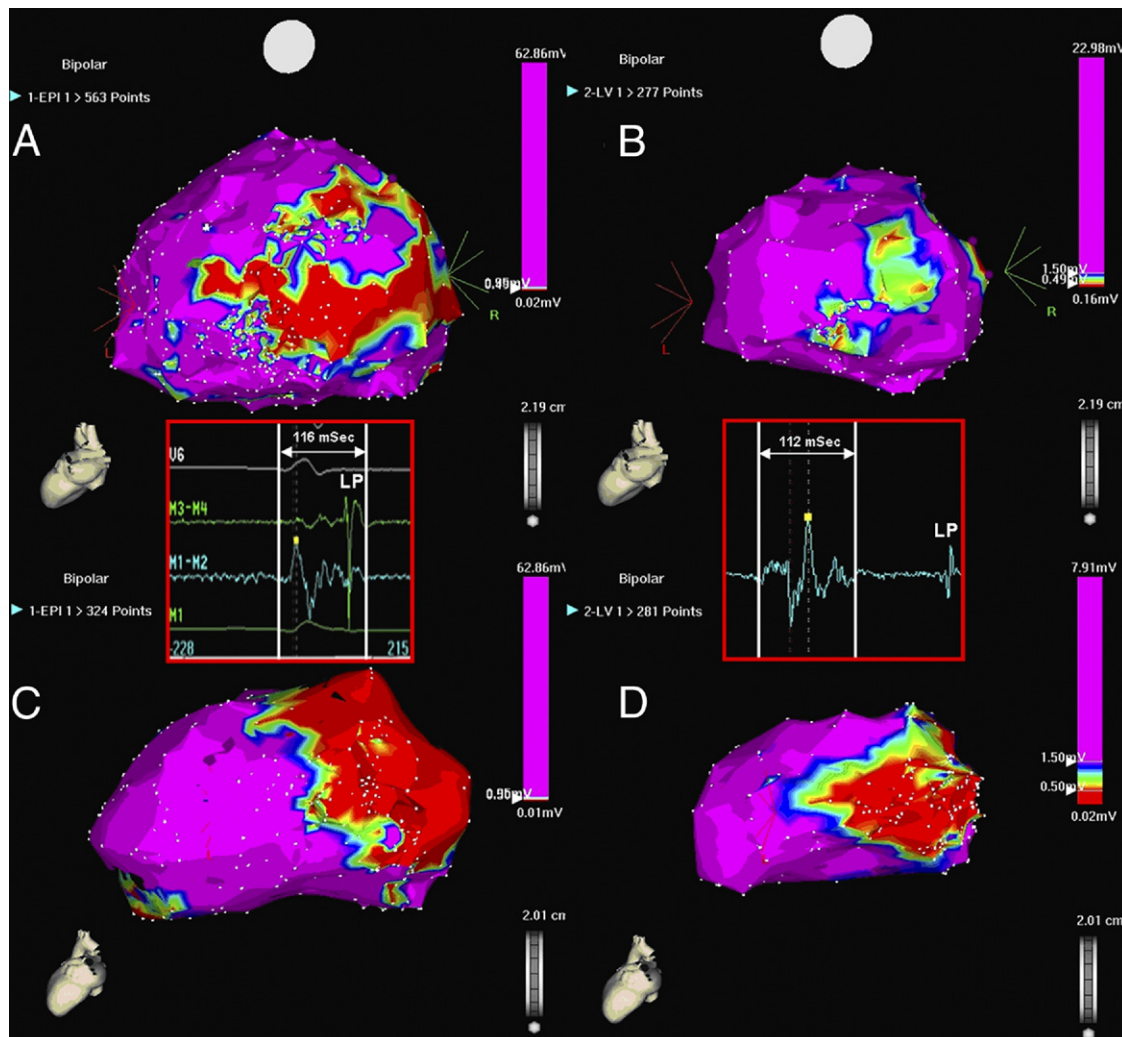
Left anterior oblique (left) and right anterior oblique (right) views showing low-voltage areas (<1.0 mV) corresponding to normal distribution of epicardial fat around the left anterior descending coronary artery (LAD), right coronary artery (RCA), and atrioventricular (AV) groove. These areas were excluded to calculate the normal reference values of epicardial bipolar signals by using an imaginary 1.5-cm width line (white arrow line) along the course of the coronary vessels and the AV groove defined by cine-angiography. An electrogram recorded from the AV groove low-voltage area is displayed in the middle of the figure. Note that low voltages in the AV groove are not associated with abnormal electrogram morphologic characteristics.

**Defining confluent area of low voltage.** The confluent area of low voltage on the endocardium and epicardium was measured with the area measurement software available on the CARTO mapping system (Fig. 2). On the epicardium the areas within 1.5 cm of the large epicardial coronary vessels and AV groove were excluded in the analysis of confluent epicardial low voltage. The coronary anatomy was defined by coronary angiography. Importantly, the percentage of abnormal electrograms that were late, wide, or split was also determined in all confluent epicardial low-voltage zones (including the AV groove and region of large epicardial vessels). We hypothesized that the area of confluent low amplitude in the course of coronary vessels and AV groove due to normal distribution of epicardial fat would tend to display otherwise normal signal morphologic characteristics. In contradistinction, the region of low voltage away from the epicardial vessels and AV groove would tend to show not only low-amplitude signals but also wide, late, and split electrograms consistent with an abnormal arrhythmogenic substrate. The confluent area of markedly low voltage (<0.5 mV) defined as “dense scar” was also assessed on the endocardium and epicardium after excluding the immediate perivascular region as described.

**Epicardial to endocardial distance.** To more completely define the electroanatomic substrate, the overall epicardial to endocardial distance was estimated at the region of VT site of origin and region of the planned ablation sites with the electroanatomic mapping system. At least 2 opposite points in each map were measured, and the mean distance obtained was

designated as the epicardial to endocardial distance (Fig. 3). To ensure an accurate estimation of the real distance, catheter contact was corroborated by the presence of stable intracardiac signals as well as with evidence of pacing capture from each point used for the distance measurements.

**Electrophysiological study and identification/ablation of epicardial VT.** All patients underwent programmed stimulation at right ventricular and LV endocardial sites. The stimulation protocol included the delivery of up to triple extrastimuli from  $\geq 2$  ventricular sites at  $\geq 2$  drive cycle lengths. Standard mapping techniques were then used. When the VT was stable and well-tolerated, endocardial and/or epicardial activation mapping and entrainment mapping were employed (11). If the VT was not well-tolerated or not reproducibly initiated, detailed characterization of the arrhythmia substrate was performed, and all sites demonstrating distinct LPs were identified. If the VT was not well-tolerated, pacemapping was used in and around the abnormal substrate to define the approximate exit site of the VT circuit within the substrate or a site with a long stimulus to QRS interval with a QRS match suggesting a more critical component of the VT circuit. The combination of LPs during sinus rhythm, a long stimulus–QRS interval during pacemapping, and a good pacemap QRS match suggested the likelihood of proximity to VT origin/circuit when a substrate-based ablation strategy was used (7,11–13). Substrate-based ablation from the site of the best pacemap targeted the region of defined abnormal substrate and was typically extended to incorporate surrounding LPs (<3-cm



**Figure 2** Epicardial and Endocardial LV Voltage Maps From 2 Patients With NICM and Epicardial VT

Epicardial (A, C) and endocardial left ventricular (LV) (B, D) voltage maps from 2 patients with nonischemic cardiomyopathy (NICM) and epicardial ventricular tachycardia (VT). Color range represents voltage amplitude. **Purple-colored** areas represent normal epicardium ( $>1.0$  mV) and endocardium ( $>1.5$  mV), and dense scar is depicted in **red** ( $<0.5$  mV). (A) Posteroanterior modified view of the epicardial voltage map showing a low-voltage zone in the basal and mid-lateral LV. (B) Endocardial LV voltage map of the same patient showing a smaller low-voltage area in the lateral wall with no dense scar ( $<0.5$  mV). Left lateral modified view of the epicardial (C) and endocardial LV map (D) of another patient showing scar distributed in proximity to the mitral annulus over the basal lateral LV. In both cases abnormal electrograms were recorded in the low-voltage zones ( $>80$  ms, split, and late potentials [LP]).

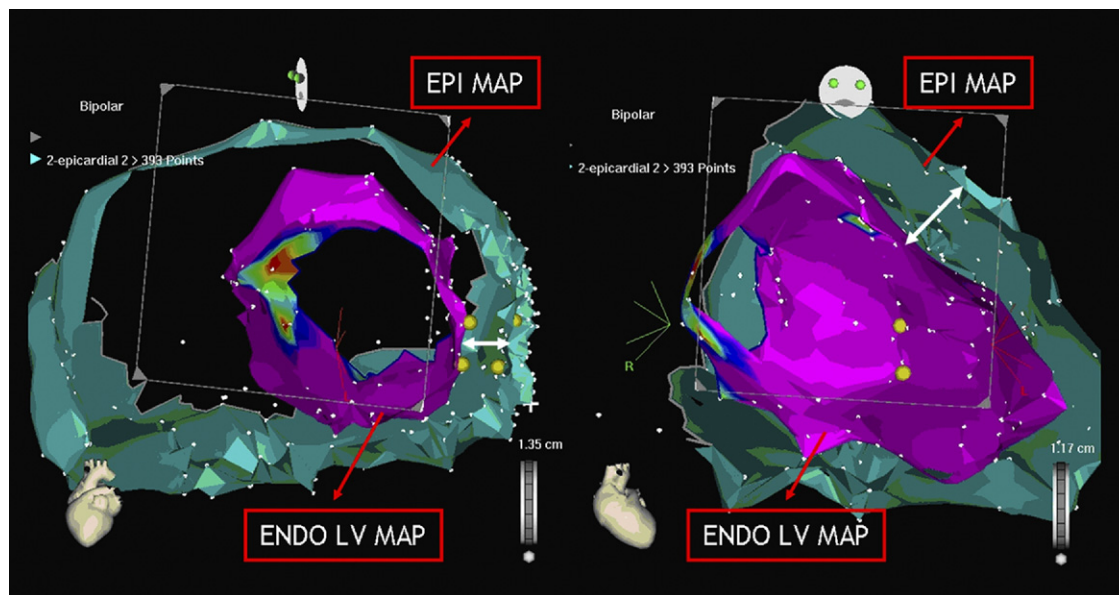
distance) within the lesion set and to transect the substrate or extend as a line to an anatomic boundary but no closer than 1 cm to a coronary vessel or site demonstrating phrenic nerve capture with 10- to 20-mA pacing output. Successful elimination of targeted VT was used as proof of the suspected sites' participation in that VT. Typical parameters for effective lesion creation were not to exceed  $45^{\circ}\text{C}$  for an irrigated tip and  $55^{\circ}\text{C}$  for nonirrigated tip ablation, targeting an impedance drop of 12 to 15 ohms. The acute success of ablation was defined when sustained monomorphic VT could not be induced at the end of the procedure.

**Follow-up assessment.** Ventricular tachycardia recurrence after hospital discharge was assessed by interrogation of the

ICD (present in 21 of 22 patients), patient interview, and ECG recording obtained with the onset of any arrhythmia symptoms. The ICD was routinely programmed to include a monitor zone that identified rates  $>120$  beats/min to facilitate identification of any asymptomatic recurrences of VT.

**Statistics.** All electroanatomic measurements (number of points, total scar area, dense scar area, area with late and/or split potentials) were normally distributed with the 1-sample Kolmogorov-Smirnov test against a normal distribution. Continuous data are expressed as mean  $\pm$  SD or range, as appropriate. For comparing continuous variables, the Student paired  $t$  test was used when comparing endo-





**Figure 3** Epicardial to Endocardial Distance Measurements

Clipped planes in the left anterior oblique (left) and right anterior oblique views (right). White arrows show the endocardial (ENDO) to epicardial (EPI) distance in the lateral and the anterior wall, respectively, assessed with electroanatomic mapping. LV = left ventricular.

cardial and epicardial characteristics among the same patients, and the Student unpaired *t* test was used when comparing the characteristics of VT patients with control subjects with normal voltage. For comparison of noncontinuous variables, the McNemar test was used. A *p* value  $\leq 0.05$  was considered statistically significant.

## Results

Baseline characteristics of the 22 patients in the study are listed in Table 2. All patients had been previously treated with at least 1 antiarrhythmic drug. The mean LV ejection fraction was  $30 \pm 13\%$ , and the mean number of prior ablation attempts/patient was 1.8 (range 0 to 6 attempts/patient).

A total of 73 VTs were induced in the 22 patients (mean 3.3, range 1 to 7) with a mean cycle length of  $392 \pm 109$  ms. One or more epicardial VT circuits/origins could be identified in 18 patients. In the remaining 4 patients the VT circuit/origin was confined to the endocardium (*n* = 3) or was presumed to be mid-myocardial (*n* = 1) and did not involve the epicardium with the same detailed mapping/ablation techniques.

**Reference values for epicardial electrograms.** A mean of  $212 \pm 102$  epicardial points was recorded/patient from the 8 reference patients without structural heart disease. The mean bipolar epicardial electrogram amplitude was  $3.2 \pm 2.5$  mV, and 95% of all bipolar signal voltages were above 0.61 mV. The mean bipolar electrogram amplitude—once excluding the regions of large coronary vessels and AV groove—was  $3.6 \pm 2.6$  mV, and 95% of all bipolar signals were above 0.94 mV. On the basis of this analysis, we used

a signal amplitude  $>1.0$  mV to define a normal amplitude on the epicardium.

The mean bipolar voltage registered in the distribution of the major coronary vessels and the AV groove was  $1.4 \pm 1.8$  mV with 95% of the signals above 0.19 mV (Fig. 1). These areas revealed a paucity of abnormal electrograms, with only 2.2% of signals being wide and 0.9% split, and none of the electrograms demonstrated any LP (Table 3).

**Low-voltage and dense scar areas.** The mean number of points recorded/patient with LV cardiomyopathy was  $227 \pm 127$  and  $363 \pm 147$  in the LV endocardial and epicardial maps, respectively (Tables 4 and 5). Low-voltage areas ( $>2$  cm<sup>2</sup>) were present in 12 of 22 LV endocardial maps (54%) and in 18 of 22 epicardial maps (82%) (*p* = NS). For the 22 study patients the mean low-voltage area on the endocardium was  $30.2 \pm 43.7$  cm<sup>2</sup> versus  $46.4 \pm 37.3$  cm<sup>2</sup> on the epicardium (*p* = 0.2). “Dense scar” areas ( $<0.5$  mV) were present in 10 of 22 (45%) and 16 of 22 (73%) of the LV endocardial and epicardial maps, respectively (*p* = NS). Mean “dense scar” area tended to be greater on the epicardium ( $12.2 \pm 20.8$  cm<sup>2</sup> vs.  $27.2 \pm 32.1$  cm<sup>2</sup>, *p* = 0.07). A total of 10 patients showed an abnormal epicardial map with a normal endocardial map, whereas only 3 patients showed abnormal endocardial with normal epicardial map. Finally, in 1 patient both endocardial and epicardial maps showed no confluent area of low voltage. Seven patients had a considerably greater abnormal epicardial substrate (more than 10-cm<sup>2</sup> difference) compared with endocardial substrate, whereas in only 1 patient was this relationship reversed. Thus, 17 (77.2%) patients in the

**Table 2** Baseline Characteristics of Patients With Nonischemic Cardiomyopathy and VT

Patient #	Age (yrs)	Sex	LVEF (%)	ICD	AAD at Time of Procedure	No. of Prior Procedures	Epicardial VT and Substrate
1	52	M	30	Yes	Sotalol	1	Yes
2	70	M	30	Yes	IV lidocaine + sotalol	0	Yes
3	63	M	13	Yes	Amiodarone + mexiletine	1	No
4	39	M	50	Yes	IV procainamide	2	Yes
5	51	M	45	Yes	Metoprolol	1	Yes
6	35	M	10	Yes	Sotalol + amiodarone	1	No
7	65	M	40	Yes	Amiodarone	1	Yes
8	64	M	5	Yes	Amiodarone + mexiletine	1	Yes
9	50	M	45	Yes	Amiodarone	2	No
10	44	M	25	No	Metoprolol	2	Yes
11	75	F	40	Yes	Amiodarone	1	Yes
12	48	M	45	Yes	Propafenone	3	Yes
13	32	F	41	Yes	Metoprolol	1	Yes
14	71	M	16	Yes	Amiodarone + mexiletine	2	No
15	48	M	15	Yes	Amiodarone + IV lidocaine	2	Yes
16	59	M	20	Yes	Amiodarone	2	Yes
17	53	M	30	Yes	Amiodarone + mexiletine	5	Yes
18	65	M	35	Yes	Amiodarone + mexiletine	3	Yes
19	51	M	45	Yes	IV lidocaine	1	Yes
20	69	M	20	Yes	Amiodarone + IV lidocaine	1	Yes
21	78	M	25	Yes	Amiodarone + IV lidocaine	6	Yes
22	51	F	30	Yes	IV lidocaine	1	Yes

ICD = implantable cardioverter-defibrillator; IV = intravenous; VT = ventricular tachycardia; other abbreviations as in Table 1.

overall group had low-voltage areas predominantly over the epicardium, whereas only 4 (18.2%) patients had low-voltage areas predominantly over the endocardium.

All 18 patients with an epicardial VT circuit/origin demonstrated during the electrophysiological study based on entrainment and/or pacemapping had abnormal low-voltage areas consistent with scar on the epicardial map. The mean epicardial low-voltage area ( $<1.0$  mV with abnormal electrograms) in this subgroup of patients was significantly larger than the endocardial low-voltage area ( $55.3 \pm 33.5$  cm<sup>2</sup> vs.  $22.9 \pm 32.4$  cm<sup>2</sup>,  $p = 0.004$ ). Dense scar ( $<0.5$  mV) was also more predominant in the epicardial maps of this group ( $33.3 \pm 32.5$  cm<sup>2</sup> vs.  $10.5 \pm 19.6$  cm<sup>2</sup>,  $p = 0.01$ ).

**Table 3** Distribution of Abnormal Epicardial Electrograms in Epicardial Low-Voltage Areas

	Epicardial Normal Heart* (n = 8)	Epicardial NICM† (n = 18)	p Value
>80 ms	2.2%	27.5%	<0.001
Split	0.9%	33%	<0.001
LP	—	25.8%	<0.001
>80 ms + split	0.8%	25.7%	<0.001
>80 ms + LP	—	10.9%	<0.001
>80 ms + split + LP	—	10.6%	<0.001
>80 ms/split or LP	2.3%	49.7%	<0.001

Low voltage areas  $<1.0$  mV. Results reported as percent of total electrograms sampled. \*In normal heart group, low-voltage area included signals along an imaginary 1.5-cm width line through the theoretical course of the left anterior descending artery, right coronary artery, and the atrioventricular groove—no abnormal signals were recorded away from these areas. †In the 18 nonischemic cardiomyopathy (NICM) patients, abnormal electrograms were assessed in the confluent abnormal low-voltage areas away from vascular structures.  
LP = late potential.

Only 1 patient (6%) in this subgroup of patients had a larger endocardial versus epicardial low-voltage area (Fig. 4). In contrast (Table 6), patients in whom an epicardial VT circuit/origin could not be demonstrated and subsequently had an ablation attempt only from the endocardium ( $n = 4$ ) showed abnormal low-voltage areas only over the endocardium (mean area  $<1.5$  mV,  $62.5 \pm 75.5$  cm<sup>2</sup>, mean endocardial dense scar area  $15.7 \pm 25.3$  cm<sup>2</sup>). All 4 patients had small areas of low voltage recorded from the epicardium either along the course of the coronary arteries or the AV groove with rare abnormal electrograms ( $>80$ -ms width in 3.1%, split in 5.5%, none with LP) consistent with the observations also noted in the reference population.

**Distribution of low-voltage areas.** The 12 patients with low-voltage areas on the endocardial map had the abnormal low-voltage area located over the basal LV in proximity to the mitral and aortic valve annuli. One patient had the low-voltage area extending from the base to the apex. In the same manner, 16 of the 18 patients with epicardial low-voltage area demonstrated the abnormality over the basal LV (Fig. 2), typically involving the corresponding lateral LV free wall (13 of 18 patients, 72%). Of the remaining 2 patients with epicardial low-voltage areas and epicardial VT, 1 had the abnormal low-voltage distribution over the LV mid-lateral wall and 1 over the basal area involving the right ventricular free wall and extending well beyond the boundaries of the left anterior descending coronary artery over the basal LV.

**Distribution of abnormal electrograms.** Abnormal electrograms were measured as a percentage of the total number

**Table 4** Mapping Findings in Patients With Nonischemic Cardiomyopathy and Ventricular Tachycardia

Patient #	Epicardial Involved	Map	No. of Points Mapped	Low-Voltage Area (cm <sup>2</sup> )	Percent of Surface	Percent of Dense Scar (≤0.5 mV)	Location	Endo–Epi Distance (mm)
1	Yes	Endo	538	52.6	17.6%	4.8%	Basal-mid septum	25
		Epi	548	109.3	28.3%	21.2%	Basal-mid anterolateral	
2	Yes	Endo	210	—	—	—	—	17
		Epi	424	25.5	7.2%	—	Basal inferior	
3	No	Endo	156	—	—	—	—	5
		Epi	238	—	—	—	—	
4	Yes	Endo	95	—	—	—	—	18
		Epi	284	82.9	34.6%	16.5%	Basal inferolateral	
5	Yes	Endo	348	21.9	10.8%	1.4%	Basal inferolateral	17
		Epi	753	31.9	11.8%	6.7%	Basal inferolateral	
6	No	Endo	544	172.5	44.2%	14.9%	Basal-mid septum	14
		Epi	483	—	—	—	—	
7	Yes	Endo	282	46.5	22.6%	12.0%	Basal lateral	22
		Epi	329	63.7	21.7%	16.6%	Basal lateral	
8	Yes	Endo	277	20.2	7.0%	—	Basal lateral	15
		Epi	586	100.9	28.8%	18.3%	Basal-mid lateral	
9	No	Endo	336	40.5	18.5%	9.4%	Basal anteroseptal	10
		Epi	331	—	—	—	—	
10	Yes	Endo	152	—	—	—	—	13
		Epi	243	31.0	16.3%	8.7%	Basal inferior	
11	Yes	Endo	205	—	—	—	—	18
		Epi	475	3.7	2.1%	—	RV/LV base	
12	Yes	Endo	160	—	—	—	—	9
		Epi	476	22.1	7.6%	1.9%	Basal lateral	
13	Yes	Endo	119	—	—	—	—	15
		Epi	339	50.9	20.5%	—	Basal inferolateral	
14	No	Endo	203	37.3	14.8%	—	Basal anterolateral	14
		Epi	254	—	—	—	—	
15	Yes	Endo	194	41.2	19.7%	13.1%	Basal anteroseptal	21
		Epi	160	100.0	84.5%	79.1%	Basal-apex anterolateral	
16	Yes	Endo	155	—	—	—	—	15
		Epi	301	97.8	54.0%	48.2%	Basal-mid inferolateral	
17	Yes	Endo	249	124.7	49.8%	31.8%	Basal-apex inferolateral	11
		Epi	197	30.5	19.6%	14.4%	Basal anterolateral	
18	Yes	Endo	118	26.4	13.9%	6.6%	Basal septum	17
		Epi	275	55.0	19.9%	5.8%	Basal-mid anterolateral	
19	Yes	Endo	181	—	—	—	—	15
		Epi	393	35.0	13.0%	7.1%	Basal-mid inferolateral	
20	Yes	Endo	109	24.9	13.8%	3.6%	Basal-mid anterolateral	22
		Epi	153	51.6	20.8%	4.0%	Basal-apex anterolateral	
21	Yes	Endo	89	55.4	29.5%	12.5%	Basal inferolateral	14
		Epi	363	88.4	39.2%	31.8%	Basal inferolateral	
22	Yes	Endo	217	—	—	—	—	20
		Epi	376	15.8	7.5%	0.8%	Mid-lateral	

Low-voltage areas are considered as <1.5 mV with the endocardial (Endo) maps and <1.0 mV with the epicardial (Epi) maps.  
LV = left ventricular; RV = right ventricular.

of electrograms recorded in each low-voltage region. In the 12 endocardial LV maps with confluent low-voltage areas, the mean percentage of electrograms from these regions included 33.9% that were >80-ms wide, 33.8% split, and 21.1% demonstrating LPs. In comparison and strikingly similar, in the confluent low-voltage areas in the 18 epicardial maps with associated epicardial VTs, 27.5% of electrograms were >80-ms wide, 33% split, and 25.8% showed

LPs (Table 3). Of note, an average of 49.7% of electrograms recorded from confluent epicardial areas of abnormal electrogram voltage demonstrated signals that were wide, split, or late. No patient with confluent areas of epicardial low voltage away from major coronary vasculature in the setting of NICM and epicardial VT had <20% of the recorded electrograms demonstrating the described abnormalities.

Table 5	Endocardial and Epicardial Electroanatomical Mapping Features	
	Endocardial LV (n = 22)	Epicardial Map (n = 22)
No. of points	228 ± 127	363 ± 147
Total area (cm <sup>2</sup> )	246 ± 62	366 ± 179
Low voltage*	12 (54)	18 (82)
Dense scar (<0.5 mV)	10 (45)	16 (73)

Values are mean ± SD or n (%). \*Low voltage considered as <1.5 mV for the endocardium and <1.0 mV for the epicardium for >2 cm<sup>2</sup> area.  
LV = left ventricle.

**Epicardial to endocardial distance.** The endocardial to epicardial distance in the region of ablation was measured in all 22 patients (Fig. 3). The mean distance obtained in the overall group was 15.9 mm (range 8 to 25 mm). The group of patients with a demonstrated epicardial VT circuit/origin had a greater epicardial to endocardial distance when compared with patients without epicardial VT circuit/origin who were ablated only from the endocardium (16.9 mm, range 9 to 25 mm vs. 11.5 mm, range 8 to 14 mm, p = 0.02).  
**Ablation results.** In the overall group, a mean of 13.5 ± 15.9 and 13.8 ± 10.8 radiofrequency (RF) lesions were applied to the endocardium and epicardium, respectively. The 4 patients whose VT was ablated only from the endocardium received a mean of 22.5 ± 17 RF lesions.

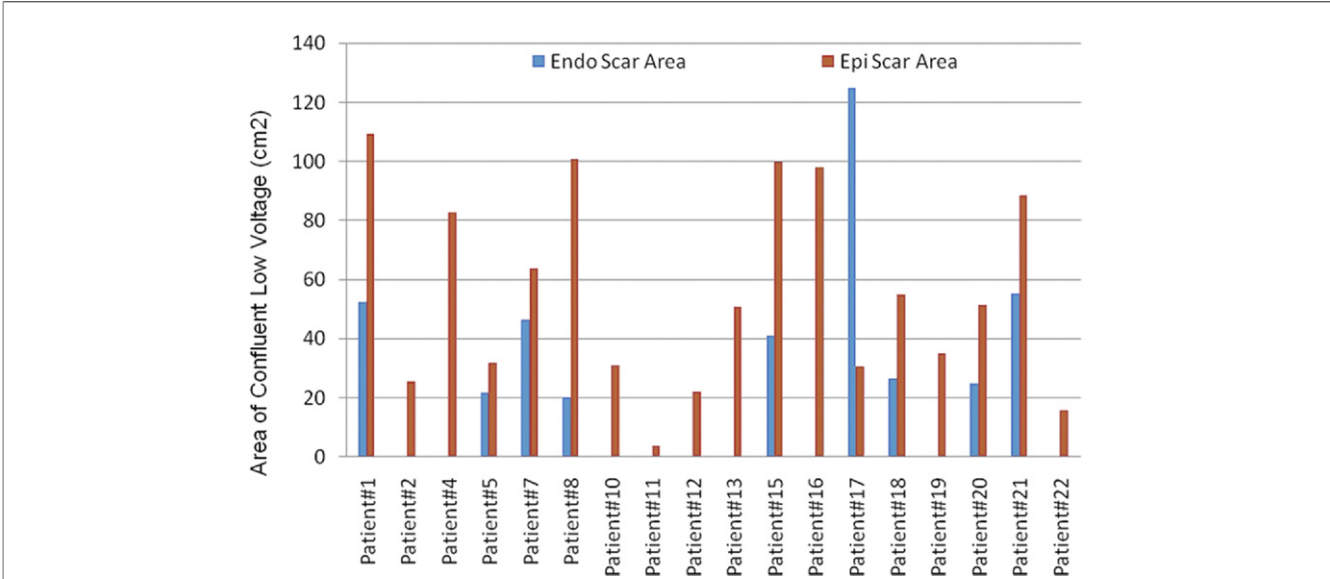
One patient had bleeding upon pericardial puncture presumably due to right ventricular puncture that required drainage. No endocardial ablation had been performed. In this patient, epicardial mapping was completed, but because of recurrent transient hypotension without further bleeding, the procedure was aborted before ablation could be per-

Table 6	Comparison of Demographic and Clinical Characteristics of Patients With Endocardial Ablation Only With Those Patients With Epicardial VT		
	NICM Endo Abl Only (n = 4)	NICM Epi Abl (n = 18)	Overall (n = 22)
Male sex	4 (100)	15 (83)	19 (86)
Age	55 (35–71)	56 (32–78)	56 (32–78)
EF (%)	21 ± 16	32 ± 12	30 ± 13
Clinical VT CL (ms)	445 ± 40	379 ± 90	396 ± 84
ICD	4 (100)	17 (94)	21 (95)
No. of prior procedures	1.5 (1–2)	1.8 (0–6)	1.8 (0–6)
No. of induced VTs	4.7 (3–7)	3 (1–6)	3.3 (1–7)

Values are n (%), mean (range), or mean ± SD.  
CL = cycle length; EF = ejection fraction; ICD = implantable cardioverter-defibrillator; NICM Endo Abl = patients with endocardial ventricular tachycardia circuit; NICM Epi Abl = patients with epicardial ventricular tachycardia circuit; VT = ventricular tachycardia.

formed, and no long-term sequelae were observed. Therefore, we have ablation results in 21 patients.

Radiofrequency energy delivery resulted in noninducibility of all VT in 14 of 21 patients (67%). Successful ablation in patients ablated only from the endocardium was achieved in 2 of the 4 patients. In 1 remaining patient with unsuccessful endocardial ablation, a rapid “non-clinical/non-targeted” VT was still inducible, and in the other patient, despite gradual slowing and termination of targeted VT, the arrhythmia remained inducible. Because no epicardial substrate was identified, we presumed this latter VT was from an intramural source. Patients with a demonstrated epicardial substrate and probable epicardial involvement for the VT circuit/origin underwent acutely successful VT ablation in 71% of cases (12



**Figure 4** Epicardial and Endocardial Area of Confluent Low Voltage in the 18 Patients With Epicardial VT

Epicardial (Epi) (red) and endocardial (Endo) (blue) area of confluent low voltage in the 18 patients with epicardial ventricular tachycardia (VT) identified on the basis of entrainment mapping, pacemapping, and successful elimination of VT with epicardial ablation.



of 17 patients). The remaining 5 patients who still had inducible VT at the end of the epicardial procedure had a coronary vessel or phrenic nerve capture within 1 cm of the desirable ablation location so that RF energy was not delivered at those sites. In the overall group, a nonirrigated catheter was used in the first 6 patients (27%), both nonirrigated and irrigated catheters in 6 patients and only an irrigated catheter in the last 10 patients studied. The transition to irrigated ablation occurred because of difficulties achieving adequate ( $>20$  W) epicardial power delivery in 2 of the first 6 patients that we believe might also have contributed to the lack of acute efficacy.

A minimum of 1 year follow-up was obtained for all surviving patients who underwent ablation (range 12 to 33 months, mean  $18 \pm 7$  months). Fifteen of the 21 patients (71%) had no VT during follow-up. Fourteen of these 15 patients underwent epicardial ablation.

During the first year of follow-up 2 patients underwent cardiac transplant, and 4 patients died during follow-up. No patient died suddenly. Two patients died from progressive heart failure, and 2 patients died from noncardiac causes. One additional patient underwent transplant at 16 months. Of these 7 patients with transplant or death, 4 had VT before death or transplant.

Of the 14 patients who survived  $>1$  year without transplant, 12 (86%) had no VT during follow-up. One patient had 2 isolated VT recurrences, and 1 additional patient had recurrent VT requiring repeat ablation and antiarrhythmic drug changes. Antiarrhythmic medications were not routinely eliminated after ablation. Of the 14 surviving patients, 5 were taking amiodarone at a dose  $\leq 200$  mg/day, and 3 patients were taking sotalolol.

## Discussion

This is the first study to establish criteria for normal bipolar epicardial electrograms and then to use this reference data to characterize the epicardial electroanatomical substrate in a large series of patients with NICM. Our results show that patients with NICM and VT suspected to originate from the epicardium, either because the 12-lead ECG was suggestive or because previous unsuccessful endocardial ablation had been attempted, are likely to have a large epicardial substrate represented by confluent low-voltage areas with abnormal electrogram signals consistent with scar in up to 82% of patients. Moreover, in patients with confirmed epicardial VT on the basis of entrainment and/or pacemapping, the epicardial scar area was larger than the endocardial LV scar area. Finally, these epicardial low-voltage areas have a typical distribution similar to that previously described for endocardial LV maps, usually located in basal lateral areas of the LV (1,2).

Previous studies had reported the endocardial and/or epicardial features in patients with ischemic dilated cardiomyopathy and in a smaller number of patients with NICM (1–4,13–15). Soejima et al. (3) described the epicardial electroanatomical characteristics of 7 patients with NICM

not amenable to endocardial VT ablation. All of these patients had low-amplitude regions in the epicardium consistent with scar. The average epicardial scar area was  $37.5 \pm 10.4$  cm<sup>2</sup>, which was only modestly lower than the epicardial mean low-voltage area in the 18 patients included in our study who demonstrated an epicardial substrate and VT origin ( $55.3 \pm 33.5$  cm<sup>2</sup>).

Low-voltage areas have been described in the epicardium as a result of the normal distribution of fat tissue (9,10). The presence of epicardial fat might also represent an important obstacle to the effectiveness of VT ablation. To avoid a misclassification of low-voltage areas due to epicardial fat or major coronary vasculature as abnormal, we established a reference standard in 8 patients without structural heart disease and idiopathic VT. Our results show that normal epicardial electrograms demonstrate bipolar signal amplitude that is typically above 0.94 mV; whereas signal amplitude associated with fat and/or large vessel coronary anatomy might demonstrate significantly lower amplitude. Importantly, despite the lower amplitude, the presence of “abnormal” electrogram signal characteristics in these areas is indeed unusual (2.3%). In contrast, within “true low-voltage areas” in NICM and epicardial VT, nearly 50% of electrograms are typically markedly abnormal. In fact, the minimum percentage of abnormal electrograms in the low-voltage area associated with an epicardial VT was 20%. Thus, the decision about whether a low-voltage epicardial area is really “scar” and represents an appropriate substrate for VT should rely on location and extent of the confluent voltage abnormality as well as on the presence of abnormal electrogram signals ( $>80$  ms, split, or LP). The presence of LPs seems to be most specific for identifying the epicardial VT substrate in that they were never observed in the reference group (Table 3).

Another important finding of the study is the fact that patients with an epicardial VT circuit/origin are more likely to have a greater epicardial to endocardial distance determined by electroanatomic mapping than patients who can be successfully ablated from the endocardium. In the presence of a greater distance, ablation lesions delivered from the endocardial surface might not reach the deeper intramural or epicardial aspect of the circuit even with irrigated ablation.

Finally, long-term elimination of VT was achieved in the majority of patients with aggressive epicardial ablation. This supports data from other smaller series and emphasizes the importance of this approach in the management of VT in this setting (3). Despite the VT control, a significant number of patients ultimately required transplant, and overall mortality remained high in this patient population.

**Study limitations.** The study population with NICM was selected in that the patients had either failed previous endocardial ablation attempts or had 12-lead ECG suggesting an epicardial VT origin. Thus, these findings might not be extrapolated to the entire population of patients with NICM and VT. Importantly, the group of 4 patients in

which the detailed mapping and ablation outcome demonstrated that the epicardium was not part of the VT circuit is small; thus, the hypothesis that the location of the VT circuit could be surmised by the location (endocardial vs. epicardial) of the largest extent of the abnormal voltage and electrogram area is suggested but not proven by these data.

Although special attention was given to obtain accurate measurements of the epicardial to endocardial distance, the use of the CARTO system for this purpose has not been yet validated with established imaging techniques in this setting. Finally, anatomic-pathological correlation of the low-voltage areas with associated marked electrogram abnormalities is not available in our study. Nevertheless, the absence of such electrogram abnormalities in low-voltage regions bordering major coronary vessels is compelling. Our observations should serve as a useful guide for distinguishing fat/coronary vasculature from abnormal anatomic areas that serve as the substrate for VT. Ongoing studies in explanted hearts should confirm these observations.

## Conclusions

In patients with NICM and VT unamenable to endocardial ablation or with ECG criteria suggesting an epicardial origin, the presence of an epicardial substrate represented by sizable confluent abnormal low-voltage areas ( $<1.0$  mV) located predominantly over the basal lateral LV is common. At least 20% of signals in the low-voltage area should be wide ( $>80$  ms), split, and/or late to definitively identify an epicardial scar that might serve as a substrate for VT. An ablation strategy that targets these epicardial VT and the VT substrate can result in intermediate-term arrhythmia control in most patients.

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