Electrophysiologic characterization of local abnormal ventricular activities in postinfarction ventricular tachycardia with respect to their anatomic location

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BACKGROUND Local abnormal ventricular activities (LAVA) in patients with scar-related ventricular tachycardia (VT) may appear at any time during or after the far-field electrogram. Although they may be separated from the far-field signal by an isoelectric line and extend beyond the end of surface QRS, they may also appear fused or buried within the QRS.

OBJECTIVE The purpose of this study was to characterize LAVA in postinfarction VT patients with respect to their anatomic locations.

METHODS Thirty-one patients with postinfarction VT underwent mapping/ablation during sinus rhythm with a three-dimensional electroanatomic mapping system. From a total of 18,270 electrograms reviewed in all study subjects, 1104 LAVA (endocardium 839, epicardium 265) were identified and analyzed.

RESULTS The interval from onset of QRS complex to ventricular electrogram (EGM onset) on the endocardium was significantly shorter than the epicardium ($P < .001$). EGM onset was shortest in the septal endocardium and longest in the inferior and lateral epicardium. There was a significant positive correlation between EGM onset and LAVA lateness as estimated by the interval from surface QRS onset to LAVA ($r = 0.52$, $P < .001$). LAVA were more frequently detected after the QRS complex in the epicardium (241/265 [91%]) than in the endocardium (551/839 [66%], $P < .001$). Only 43% of endocardial septal LAVA were detected after the QRS complex.

CONCLUSION Lateness of LAVA is affected to a large extent by their locations. The chance of detecting late LAVA increases when electrogram onset is later. Substrate-based approach targeting delayed signals relative to the QRS complex may miss critical the arrhythmogenic substrate, particularly in the septum and other early-to-activate regions.

KEYWORDS Catheter ablation; Ventricular tachycardia; Mapping; Three-dimensional mapping; Postmyocardial infarction; Local abnormal ventricular activities

ABBREVIATIONS **3D-EAM** = three-dimensional electroanatomic mapping; **ICD** = implantable cardioverter-defibrillator; **LAVA** = local abnormal ventricular activities; **LV** = left ventricle; **RV** = right ventricle; **VT** = ventricular tachycardia

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Introduction

Catheter ablation of scar-related ventricular tachycardia (VT) has been widely adopted for the management of patients requiring frequent therapy from their implantable cardioverter-defibrillator (ICD).[1,2] A substrate-based approach is attractive because poor hemodynamic tolerance during VT, multiple VT morphologies, or noninducibility can render the VT unmappable.[3,4] We reported that complete elimination of local abnormal ventricular activities (LAVA) is associated with superior survival free from recurrent VT during long-term follow-up.[5] LAVA are generated by poorly coupled viable fibers within the scar.[5–7] LAVA may appear at any time during or after the far-field ventricular electrogram in sinus rhythm. That is, LAVA may be separated from the far-field signal by an isoelectric line and extend beyond the end of the surface QRS, but LAVA may also appear fused or buried within the QRS. The lateness of local activation is thought to be due to local conduction delay in abnormal myocardial tissue where conduction is slowed by fibrosis.[6,7]

In theory, the left ventricular (LV) areas first excited in sinus rhythm are the endocardial septum below the attachment of the mitral valve.[8] The wave of excitation spreads from endocardium to epicardium. Epicardial posterobasal is the last region to

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be activated.[8] We hypothesized that LAVA characteristics would be affected not only by local conduction delay but also by their anatomic locations because the wavefront reaches the scar margin at different times according to their locations. This study was undertaken to test this hypothesis by assessing the detailed characteristics of LAVA with respect to their anatomic locations in patients with postinfarction VT.

Methods

Study population

This study enrolled 31 postinfarction patients (Table 1) undergoing VT ablation using a three-dimensional electroanatomic mapping (3D-EAM) system from November 2009 to January 2013. All patients had episodes of repetitive, sustained VT resistant to antiarrhythmic drug therapy requiring external cardioversion or ICD therapy. Three patients had undergone a prior unsuccessful ablation procedure. The mean age of infarction, which was defined as the time from first infarction to the ablation procedure, was 180 ± 95 months. Two patients had a left bundle branch block, and three had a right bundle branch block. Twelve patients had a nonspecific LV conduction disturbance, which are defined as QRS duration >110 ms but not meeting the criteria of left or right bundle branch block.[9] Written informed consent was obtained in all patients.

Electrophysiologic study

All antiarrhythmic drugs except amiodarone were discontinued for at least five half-lives before ablation, provided the stability of arrhythmia allowed it. ICD therapies were turned off, and the device programmed to a surveillance-only mode. A 6Fr steerable quadripolar or decapolar catheter (Xtrem, Sorin, Montrouge, France; Dynamic, Bard Electrophysiology, Lowell, MA) was inserted from the right femoral vein and placed at the right ventricular (RV) apex or into the coronary sinus. The LV endocardium was accessed by transseptal or retrograde transaortic approach. Pericardial access was obtained if a previous endocardial ablation had failed, if an epicardial substrate was suspected (based on VT morphology on surface ECG), or minimal or no endocardial scar. Pericardial access was obtained by a subxiphoid puncture. Electroanatomic mapping was performed during sinus rhythm using CARTO (Biosense Webster, Diamond Bar, CA) or NavX (St. Jude Medical, St. Paul, MN). Mapping was performed with an ablation catheter (Thermocool, Biosense Webster) and/or a multipolar high-density mapping catheter (PentaRay, Biosense Webster). PentaRay is an irrigated catheter with five splines, each with four poles of 1-mm electrode size and 4-4-4 mm interelectrode spacing. Bipolar signals were filtered from 30 to 250 Hz. We used the following voltage criteria: peak-to-peak bipolar amplitude <1.5 mV defined the low-voltage zone, amplitude of 0.5–1.5 mV the scar border zone, and amplitude <0.5 mV dense scar.[4]

Table 1 Patient characteristics (n = 31)

Age (years)	60 ± 10
Male	30 (97%)
Hypertension	20 (65%)
Diabetes mellitus	5 (16%)
LVEF (%)	30.4 ± 9.9
LVEF ≤30%	17 (55%)
QRS width in sinus rhythm (ms)	129 ± 36
Conduction disturbance	
Left bundle branch block	2 (6%)
Right bundle branch block	3 (10%)
Nonspecific left ventricular conduction disturbance	12 (39%)
QRS ≤110 ms	14 (45%)
Previous ablation	3 (10%)
Implantable cardioverter-defibrillator	26 (84%)
Medications	
Amiodarone	27 (87%)
Beta-blocker	29 (94%)
Statin	26 (84%)
Angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker	26 (84%)

Data are given as mean ± SD or n (%).
LVEF = left ventricular ejection fraction.

Definition of LAVA

As we previously reported,[5] LAVA during sinus rhythm were defined as electrograms with the following features: (1) sharp, high-frequency ventricular potentials distinct from the far-field ventricular electrogram, (2) occurring any time during or (most 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. LAVA have no quantitative definition because LAVA sometimes appear to be short duration and high amplitude (>1.5 mV). The key feature to confirm the presence of LAVA and to distinguish them from far-field potential is to demonstrate their poorly coupled nature to the rest of the myocardium. When LAVA appear fused with the far-field ventricular potential, ventricular pacing maneuvers were performed to distinguish them from far-field ventricular electrogram. RV pacing sometimes unmasked LAVA that were not obvious during sinus rhythm (Figure 1). Importantly, programmed stimulation could increase the delay of LAVA from far-field ventricular potential (Figure 1), based on the conduction properties of LAVA, that is, they are usually poorly coupled to the rest of the myocardium.

Radiofrequency ablation

To test inducibility, programmed ventricular stimulation was performed from the RV apex at basic drive cycle length 600 and 400 ms with up to triple extrastimuli decrementally to 200 ms or ventricular refractoriness, whichever occurred first. When VT was inducible and hemodynamically tolerated, ablation was guided by conventional activation and entrainment mapping.[10] After restoration of sinus rhythm, further ablation targeting LAVA was performed. In patients with noninducible or poorly tolerated VT, ablation of LAVA during sinus rhythm was performed. All areas displaying

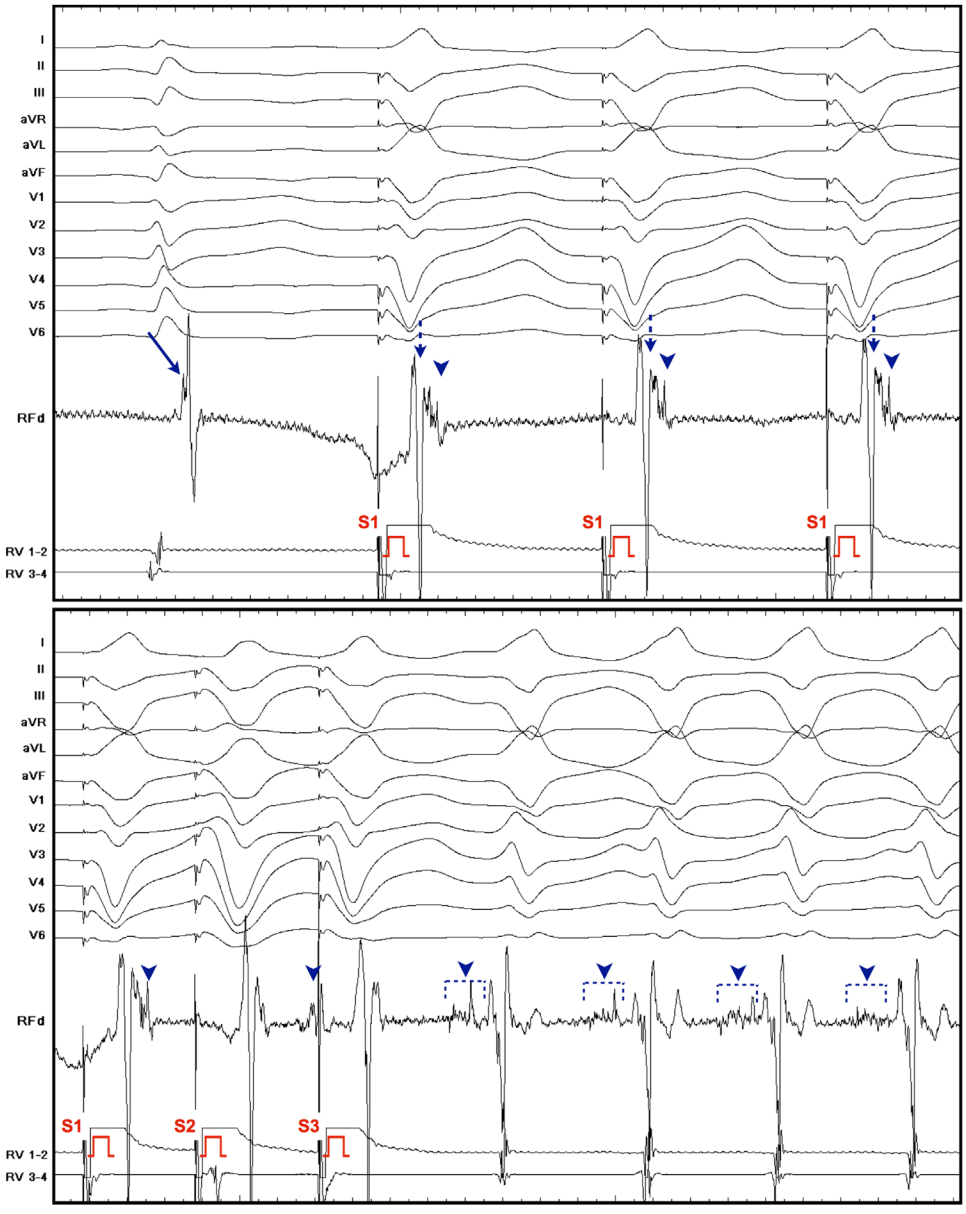

Figure 1 Local abnormal ventricular activities (LAVA) unmasked by ventricular pacing maneuvers. The local ventricular electrogram in sinus rhythm with far-field ventricular potential fused with abnormal sharp signal (*arrow*). Pacing from the right ventricle (RV(decoupled the LAVA (*arrowhead*) from the far-field potential (*dotted arrow*). Programmed RV stimulation increased the delay from the far-field potential. Ventricular tachycardia (VT) was induced after the stimulation (S3). LAVA became a presystolic fragmented potential during VT, which was associated with the slow conducting channel of this VT reentrant circuit.

LAVA were delineated and labeled on the 3D-EAM. Ablation was performed with a 3.5-mm open-irrigation catheter (Thermocool, Biosense Webster) with a power of 25–50 W endocardially and 25–35 W epicardially. Radiofrequency energy was delivered until elimination of LAVA was achieved.

Where LAVA appeared to follow a distinct activation sequence, the earliest signals were targeted first,[5] based on the hypothesis that the conducting channels of the VT reentrant circuit have interconnecting pathways, with orthodromic activation from the edge to the inside of the scar.[11] This ablation approach was performed for the purpose of a potential reduction of radiofrequency delivery by "disconnecting" the entire slow conducting channel from the rest of the ventricle instead of starting ablation at the latest signal and having to ablate the entire channel. If both endocardial and epicardial LAVA were detected, ablation was first performed endocardially, aiming to abolish the potentials transmurally, followed by epicardial ablation if required. Following ablation, areas previously displaying LAVA were remapped. In the presence of residual LAVA, radiofrequency ablation was continued. VT inducibility was reassessed by programmed stimulation using the same protocol, unless the original VT was hemodynamically unstable. The goal and ideal end-point of ablation was complete elimination of all identified LAVA.

Analysis of LAVA characteristics

The location of LAVA was documented on the 3D-EAM and segmented into seven regions: endocardial (septum, anterior, apex, inferior/lateral), and epicardial (anterior, apex, and inferior/lateral). As shown in Figure 2, the analysis of LAVA characteristics included (1) the amplitude of the signal (in mV), which were automatically obtained in 3D-EAM as peak-to-peak bipolar amplitude; (2) the interval from the

onset of the QRS complex on surface ECG to the onset of ventricular electrogram ([EGM onset] in ms); (3) the duration from onset of ventricular electrogram to end of LAVA ([EGM duration] in ms); (4) the interval from onset of QRS complex to end of LAVA ([LAVA lateness] in ms); (5) whether LAVA was clearly separated by an isoelectric interval; and (6) whether LAVA was detected after the end of the QRS complex. All measurements were obtained from the LAVA in sinus rhythm.

Statistical analysis

Categorical variables are expressed as number and percentage, and were compared using Pearson's χ^2 test or Fisher exact test, as appropriate. Continuous data for normally distributed variables are expressed as mean ± SD and compared by Student *t* test. Variables of LAVA characteristics were expressed as median [25, 75th percentiles] and compared using Mann-Whitney *U* test or Kruskal-Wallis test because these were non-normally distributed variables. Spearman rank correlation coefficients were calculated between LAVA lateness and EGM onset. All tests were two tailed, and $P < .05$ was considered significant.

Results

Mapping data

Detailed LV endocardial mapping was performed in 30 patients and epicardial mapping in 14 patients. One patient did not undergo endocardial mapping because of intracardiac thrombus. The endocardium and epicardium were mapped with 410 ± 233 and 426 ± 245 points/map, respectively. Endocardial and epicardial low-voltage areas (bipolar voltage <1.5 mV) were identified in all patients. Eighteen patients had anterior infarction and 13 had inferior infarction. Fourteen of the anterior infarction patients and three of the inferior infarction patients had septal low-voltage area with the presence of septal LAVA. Three patients had the low-voltage area located at the anteroseptum and the inferior wall.

From a total of 18,270 electrograms mapped and reviewed in all study subjects, 1104 LAVA (endocardium 839, epicardium 265) were identified. Mapping data of 14 patients with septal scar and 17 patients without septal scar are summarized in Table 2. Endocardial and epicardial low voltage were not significantly different between patients with and without septal scar (endocardium: 106 ± 61 cm^2 vs. 88 ± 45 cm^2, $P = .37$; epicardium: 78 ± 24 cm^2 vs. 92 ± 45 cm^2, $P = .57$). There was no significant difference in LAVA density between patients with and those without septal scar (endocardium: 0.32 ± 0.15points/ cm^2 vs. 0.35 ± 0.23points/ cm^2, $P = .73$; epicardium: 0.18 ± 0.07points/ cm^2 vs. 0.25 ± 0.14points/ cm^2, $P = .23$).

Characteristics of endocardial and epicardial LAVA

The characteristics of 1104 LAVA (839 endocardial, 265 epicardial) were analyzed. There were clear differences in LAVA characteristics between the endocardium and epicardium. EGM onset on the endocardium was significantly earlier than on the epicardium (7.0 ms [–3.0 ms, 19.0 ms] vs. 29.0 ms [19.0 ms, 38.0 ms], $P < .001$). LAVA lateness on the endocardium was much shorter than on the epicardium (146 ms [123 ms, 185 ms] vs. 168 ms [149 ms, 218 ms], $P < .001$). Endocardial LAVA amplitude was significantly lower compared to the epicardial LAVA (0.34 mV [0.18 mV, 0.67 mV] vs. 0.40 mV [0.23 mV, 0.65 mV], $P = .024$).

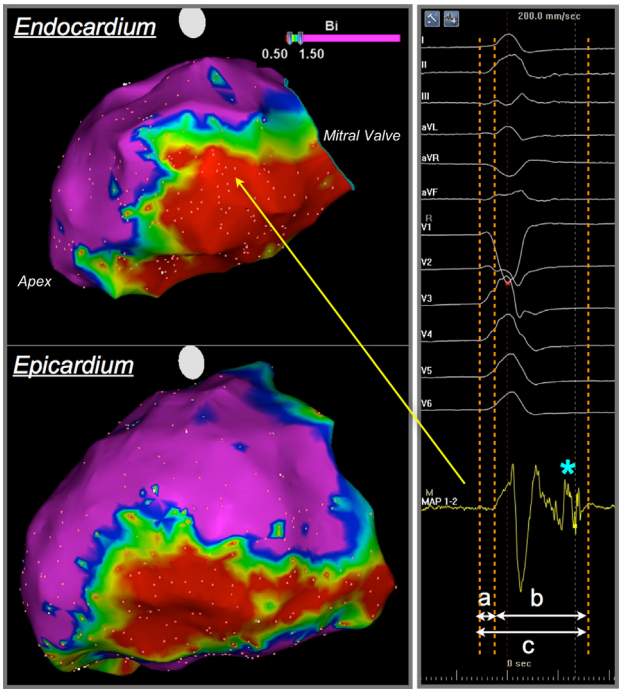

Figure 2 Assessment of local abnormal ventricular activities (LAVA) characteristics. Electroanatomic mapping was performed during sinus rhythm. A peak-to-peak bipolar amplitude <1.5 mV was defined as low-voltage zone, an amplitude 0.5–1.5 mV as border zone, and amplitude <0.5 mV as dense scar. Detailed assessment of LAVA characteristics was undertaken on the following points: interval from onset of surface QRS to onset of electrogram (EGM onset: *a*); electrogram duration (EGM duration: *b*); and interval from onset of surface QRS to end of LAVA (LAVA lateness: *c*). We also assessed signal amplitude (peak-to-peak bipolar amplitude), whether or not fractionated components (*asterisk*) were separated by an isoelectric line from the far-field signal, and whether or not fractionated components (*asterisk*) lasted beyond the QRS complex.

We found a continuum of lateness of LAVA with substantial number of LAVA occurring before the end of QRS complex. LAVA may occur any time during or after the QRS complex in sinus rhythm. Figure 3 shows number of LAVA plotted against an interval from the end of QRS complex to the end of LAVA, demonstrating the wide range over which they were detected (endocardial LAVA: 17 ms [–11 ms, 49 ms], epicardial LAVA: 60 ms [41 ms, 100 ms]). An interval >0 ms means that LAVA were detected after QRS end, which traditionally has been defined as "late potential." Epicardial LAVA (241/265 [91%]) were more frequently detected after the QRS complex than endocardial LAVA (551/839 [66%]).

LAVA characteristics with regard to anatomic location

All LAVA were further assessed according to their anatomic locations. Endocardial LAVA were located septally in 207,

Table 2 Mapping data of patients with and without septal scar

	All patients (n = 31)	Patients with septal scar (n = 14)	Patients without septal scar (n = 17)	*P* value
Earliest activation before QRS onset (ms)	−4.8 ± 8.0	−3.4 ± 6.8	−5.9 ± 8.8	.40
Mapping points per map (points/map)				
Endocardium	410 ± 233	425 ± 227	397 ± 246	.75
Epicardium	426 ± 245	559 ± 403	373 ± 146	.43
Low-voltage area (<1.5 mV) (cm²)				
Endocardium	97 ± 53	106 ± 61	88 ± 45	.37
Epicardium	88 ± 40	78 ± 24	92 ± 45	.57
Dense scar area (<0.5 mV) (cm²)				
Endocardium	55 ± 44	60 ± 49	50 ± 41	.57
Epicardium	49 ± 32	42 ± 28	52 ± 34	.59
LAVA density in low voltage (<1.5 mV) (points/cm²)				
Endocardium	0.34 ± 0.19	0.32 ± 0.15	0.35 ± 0.23	.73
Epicardium	0.23 ± 0.13	0.18 ± 0.07	0.25 ± 0.14	.23

Data are given as mean ± SD.
LAVA = Local abnormal ventricular activities.

anteriorly in 103, apically in 254, and inferior/laterally in 275. Epicardial LAVA were located anteriorly in 59, apically in 101, and inferior/laterally in 105. Figure 4 shows the 3D-EAM of patients who displayed both septal and inferolateral substrates. The activation timing of local electrograms was different according to their locations. There was a significant difference in EGM onset between regions ($P < .001$ for both endocardial and epicardial regions; Figure 5A). Endocardial septal LAVA had the earliest EGM onset among all endocardial and epicardial regions (–2 ms [–10 ms, 5 ms]). The epicardial inferior/lateral LAVA had the latest EGM onset (35 ms [28 ms, 44 ms]). EGM duration was significantly different among endocardial regions ($P < .001$) but not among epicardial regions ($P = .82$; Figure 5B). The median of EGM duration in the endocardial septal LAVA was shortest among all endocardial and epicardial regions (124 ms [98 ms, 144 ms]). A significant difference in LAVA lateness was found between regions ($P < .001$ for endocardial regions, $P = .022$ for epicardial regions; Figure 5C). Only 3% of endocardial septal LAVA were clearly separated by an isoelectric line from far-field ventricular potential (Figure 5D), whereas LAVA in other regions had a higher incidence. The vast majority of epicardial LAVA were detected after the end of surface QRS (anterior 80%, apex 91%, inferior/lateral 97%). On the endocardium, 64% of anterior LAVA, 69% of apex LAVA, 81% of inferior/lateral LAVA, and only 43% septal LAVA were detected after the QRS (Figure 5E).

Figure 6 shows a scatter plot of LAVA lateness vs. EGM onset of all LAVA. There was a significant positive correlation between EGM onset and LAVA lateness in both the endocardium ($r = 0.47$, $P < .001$) and epicardium ($r = 0.58$, $P < .001$). This correlation held true regardless of whether patients had conduction disturbance ($r = 0.56$, $P < .001$) or QRS width ≤110 ms ($r = 0.52$, $P < .001$).

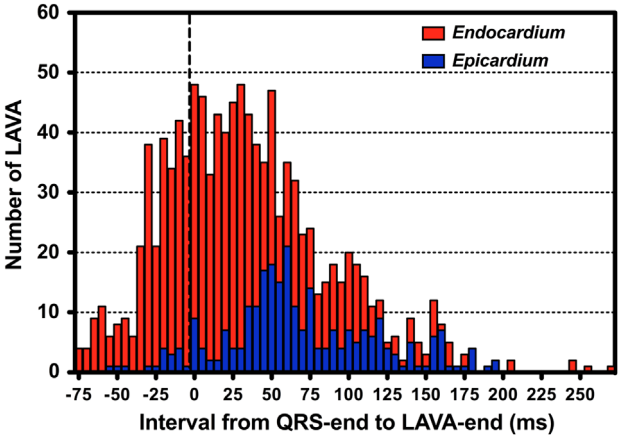

Figure 3 Endocardial and epicardial local abnormal ventricular activities (LAVA) histogram. Number of LAVA plotted against interval from end of QRS complex (QRS end) to end of LAVA (LAVA end). Bin size was 5 ms.

LAVA delay and low voltage

The distribution of LAVA in dense scar, border zone, normal voltage was 64%, 33%, and 3% on the endocardium, and 59%, 37%, and 4% on the epicardium, respectively. LAVA with normal voltage were usually located near the border of low-voltage area (not farther than 20 mm). There was no significant difference in EGM onset between dense scar and border zone on both endocardium and epicardium (endocardium: 7.0 ms [–2.0 ms, 17.0 ms] vs. 6.0 ms [–4.5 ms, 21.0 ms], $P = .49$; epicardium: 30.0 ms [18.5 ms, 37.0 ms] vs. 26.0 ms [19.0 ms, 39.0 ms], $P = .62$). However, LAVA lateness in the dense scar was much later than the border zone on both endocardium and epicardium (endocardium: 154 ms [130 ms, 193 ms] vs. 135 ms [117 ms, 161 ms], $P < .001$; epicardium: 182 ms [151 ms, 232 ms] vs. 160 ms [146 ms, 193 ms]; $P = .002$). EGM duration in the dense scar was also significantly longer than the border zone on both endocardium and epicardium (endocardium: 148 ms [124 ms, 180 ms] vs. 128 ms [107 ms, 154 ms], $P < .001$; epicardium: 152 ms [130 ms, 192 ms] vs. 136 ms [121 ms, 160 ms], $P = .001$). The very delayed LAVA (LAVA lateness >200 ms) were almost exclusively located within low-voltage area (23% in border zone, 76% in dense scar).

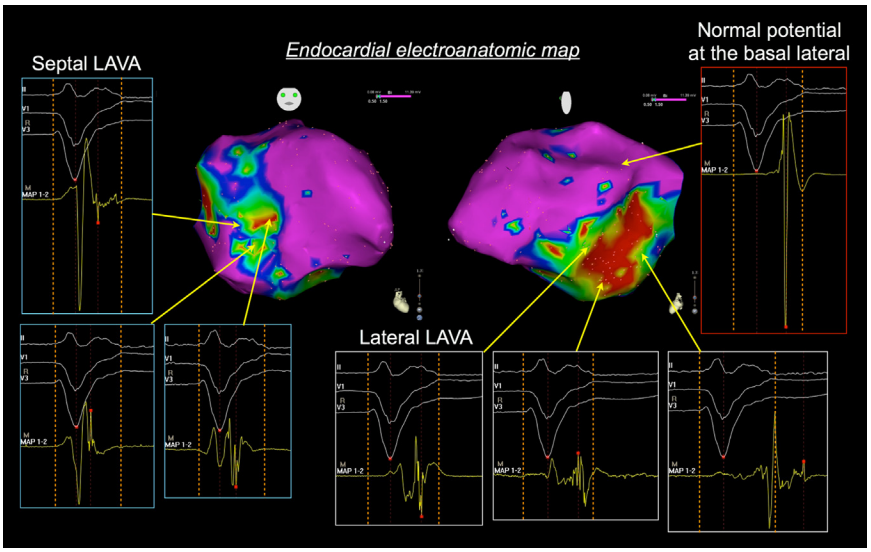

Figure 4 Different timing of local electrograms according to their locations. This patient with ischemic cardiomyopathy had both septal and lateral scar. The timing of the far-field signal of septal local abnormal ventricular activities (LAVA) was earlier than that of lateral LAVA. The simple, high-amplitude electrogram was found at the basal lateral region, with activation timing later than the septal LAVA.

Relation between clinical characteristics and LAVA characteristics

The maximal EGM duration did not significantly correlate with LV ejection fraction (r = –0.29, $P = .11$) or baseline QRS width (r = 0.27, $P = .15$). The maximal EGM duration was similar between patients taking and those not taking amiodarone (193 ms [155 ms, 261 ms] vs. 180 ms [124 ms, 245 ms], $P = .41$). There was a significant correlation between maximal EGM duration and infarct age (r = 0.50, $P = .008$), whereas infarct age did not correlate with EGM onset (r = 0.14, $P = .50$).

Ablation results

Radiofrequency ablation targeting LAVA was performed in all patients. Mean procedure and radiofrequency times were 275 ± 76 minutes and 39 ± 22 minutes, respectively. In 13 patients (42%), complete elimination of all identified LAVA could not be achieved. Two patients had epicardial LAVA that were located close to the coronary arteries and/or phrenic nerve. Cardiac tamponade occurred during one procedure, preventing complete LAVA elimination. In 10 patients, LAVA could not be abolished despite extensive ablation. Of these, eight had scar involving septum. Two patients with septal scar underwent

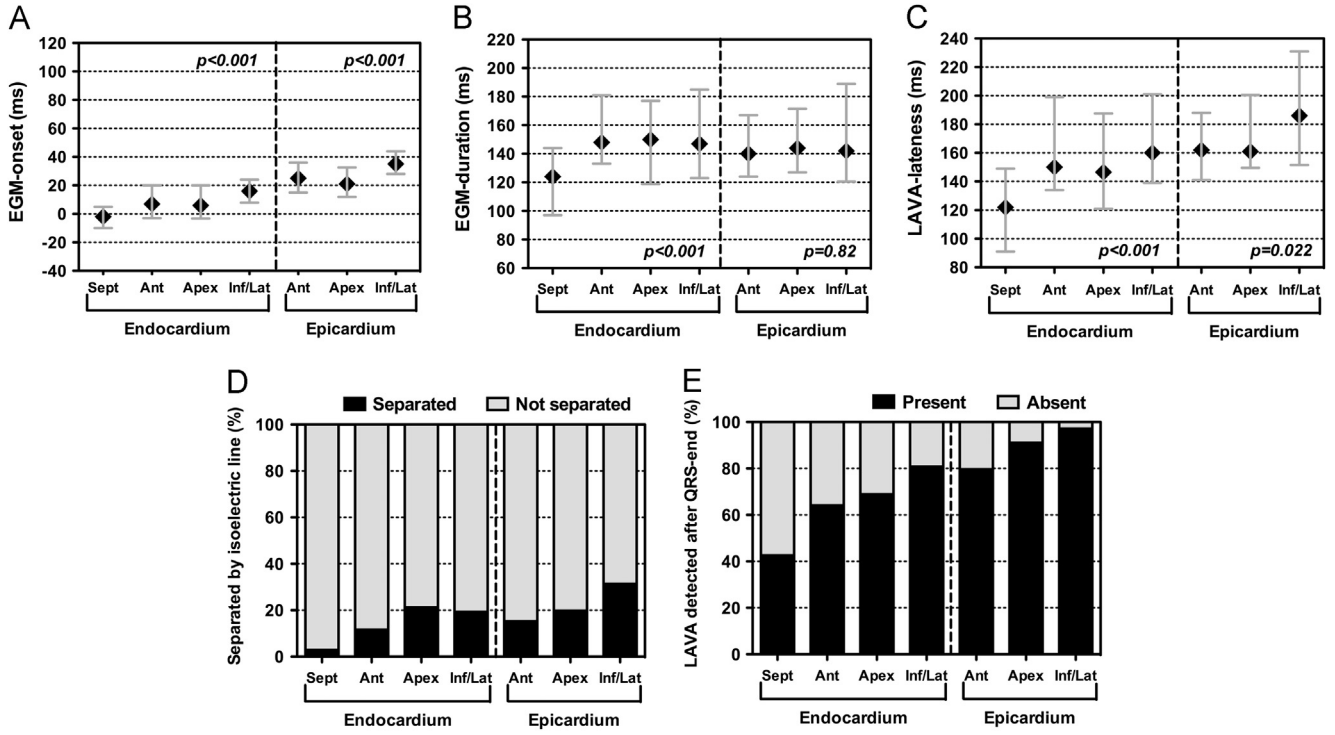

Figure 5 Comparison of local abnormal ventricular activities (LAVA) characteristics among seven segments. A significant difference was found in EGM onset (**A**), EGM duration among endocardial regions (**B**), and LAVA lateness among regions (**C**). Only 3% of septal LAVA were separated by an isoelectric line from the far-field ventricular potential (**D**). Only 43% of septal LAVA were detected after the QRS complex (**E**).

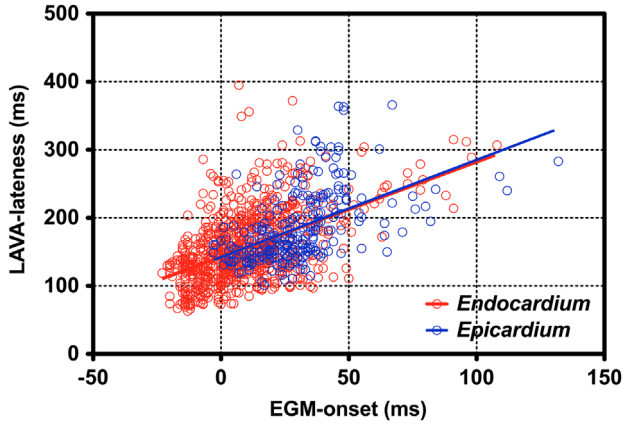

Figure 6 Correlation between electrogram (EGM) onset and local abnormal ventricular activities (LAVA) lateness. A scatter plot of all LAVA (endocardium 839, epicardium 265) is shown. There was a significant positive correlation between EGM onset and LAVA lateness in both endocardium and epicardium.

ablation from the RV septum, but their septal LAVA still persisted after the ablation. During median follow-up time 11 months, 22 patients (71%) were free from both death and ICD therapies (antitachycardia pacing, shock, or both).

Discussion

This is the first study demonstrating the different characteristics of LAVA with regard to their anatomic locations. The main findings are that LAVA delay is determined primarily by the following three parameters: (1) LAVA location in endocardium vs. epicardium; (2) anatomic location of the scar (i.e., septal vs. inferior and lateral); and (3) local conduction disturbances around and within the scar.

Factors determining LAVA lateness

The targets of substrate-based ablation are surviving myocardial bundles within the fibrotic scar. Their signals are frequently assimilated to potentials occurring after the surface QRS, producing what have traditionally been called "late potentials." However, we observed a continuum of "lateness" and many LAVA occurring before the end of the surface QRS. The timing of near-field and far-field electrograms around and within the scar was influenced by their anatomic location. It is intuitive that given two scars of identical electrical properties, the one struck later by an activation front would hold a higher proportion of late signals. This is because the local near-field abnormal activation usually occurs after the far-field signal. Therefore, our hypothesis was that late LAVA would be more likely to occur in late-activating regions of the ventricle and vice versa. We assessed LAVA according to location and timing of the local far-field electrogram. A previous study had demonstrated underrepresentation of late potentials as assessed by signal-averaged electrogram in anterior infarction compared with inferior infarction, which might be explained by the different timing of the electrogram onset.[12]

We found that the timing of electrogram onset was significantly different between endocardial and epicardial regions. Our observation is in line with a prior study using the isolated human heart.[8] An excitation wavefront reaches a great part of the LV endocardium in 30 ms except at the posterobasal area and spreads toward the epicardium. The last LV region to be excited is the posterobasal epicardium. The present study found that the lateness of LAVA correlated well to the timing of the electrogram onset. In consequence, the chance of detecting late LAVA increases when electrogram onset is later. Therefore, it is not surprising that the majority of epicardial LAVA are detected after the QRS complex. In contrast, delayed LAVA are less likely to be found in the endocardial septum, which is activated earlier, at least 30 ms earlier than the basal inferolateral region.

Interestingly, only 3% of septal LAVA were separated from the far-field ventricular potential by an isoelectric line. Septal VT substrate may be located in the subendocardium or intramural myocardium, whereas full-thickness scar is less common.[13] This makes the vector of depolarization potentially more complex. This may explain the relative paucity of LAVA separated from the far-field signal by an isoelectric line as well as the lower incidence of delayed LAVA. Our findings suggest that patients with septal scar may frequently require ventricular pacing maneuvers to decouple the nondelayed LAVA from the far-field ventricular electrogram.

We should emphasize that the timing of LAVA is also affected by local conduction delay. LAVA occurring very late after the far-field potential as a result of reduced conduction velocity in surviving fibers were more likely to be found in the dense scar area. This finding is consistent with previous studies in which the regions responsible for generating delayed abnormal signals usually are those classified as being in the inner channel of reentrant circuits, which often disperse in the dense scar rather than in the scar border zone.[11,14,15] Most of the very delayed LAVA were identified in the dense scar even though the timing of far-field electrogram onset was comparable to that in the scar border zone. In addition, older infarct age, which allows postinfarct remodeling by collagenous fiber deposition in the scar,[6,16] was associated with greater duration of local abnormal signal. However, infarct age did not correlate with the timing of far-field electrogram onset. These observations suggest that the lateness of LAVA can be affected by poor local conduction depending on the severity of fibrosis and infarct architecture, which may contribute to delay in propagation after the activation wavefront reaches the scar margin.

Clinical implications

So-called "late potentials," which usually are defined as potentials recorded after the end of surface QRS, have been proposed as a target of substrate-based ablation.[11,14,15,17–19] In prior studies, late potentials could not be found in between 3% and 29% of postinfarction VT patients.[17–20] In 4 patients (13%) in this study, all LAVA were buried within the QRS complex and would not have been identified using the previous definitions. Furthermore, more than half of septal

LAVA did not extend beyond the end of the QRS complex and fell short of "late potential" criteria.

Although very delayed abnormal signals may have high specificity for prediction of critical isthmus of VT,[15] critical sites for generation and perpetuation of VT may not necessarily have late potentials. A prior study reported that late potentials during sinus rhythm were absent in 29% of central VT reentrant circuits and in 46% of VT termination sites.[20] Although application of an arbitrary cutoff such as the end of the surface QRS appears simple and is reasonably specific, it may miss a critical arrhythmia substrate.

LAVA within the same scar may show a distinct activation sequence, which increases the likelihood of a critical isthmus of a reentrant circuit. It may be possible to eliminate the circuit by targeting the earliest LAVA. However, we should keep in mind that different directions of wavefront propagation can change the characteristics of LAVA, that is, the presence or absence of local abnormal delayed potentials at critical sites of the reentrant circuit may depend on the direction of activation during mapping.[21]

Study limitations

Because substrate mapping during paced rhythm was not systematically performed, LAVA characteristics during pacing rhythm could not be assessed. We focused on the assessment of LAVA characteristics during sinus rhythm in these study subjects. However, it remains speculative whether or not pacing at sites with normal electrograms in sinus rhythm brings out LAVA. The characteristics of LAVA during both sinus rhythm and paced rhythm in the same procedure merit further evaluation.

The activation map during sinus rhythm may look subtly different from patient to patient depending on conduction disturbance. However, the overall pattern of LV depolarization was not be changed—from the septum to inferior and lateral, from endocardium to epicardium. Importantly, a positive correlation between electrogram onset and lateness of LAVA held true regardless of the presence of conduction disturbance.

Finally, it was difficult to measure the amplitude of both LAVA and far-field components separately when they were completely fused each other. The amplitude of LAVA electrograms in the scar border zone as well as normal voltage area might be overestimated because they were more likely to be early-coupled LAVA fused with far-field signal. Detailed mapping with pacing maneuvers may be warranted, especially at the border of the low-voltage area.

Conclusion

The lateness of LAVA is determined to a large extent by when the activation wavefront reaches the scar margin as well as poor conduction at the edge of and within the scar. Substrate-based ablation strategy that only targets signals that are late compared to the QRS complex may miss critical arrhythmogenic substrate, particularly in the septum and other early-to-activate regions.

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