Characteristics of Intramural Scar in Patients With Nonischemic Cardiomyopathy and Relation to Intramural Ventricular Arrhythmias

Benoit Desjardins, MD, PhD; Miki Yokokawa, MD; Eric Good, DO; Thomas Crawford, MD; Rakesh Latchamsetty, MD; Krit Jongnarangsin, MD; Hamid Ghanbari, MD; Hakan Oral, MD; Frank Pelosi Jr, MD; Aman Chugh, MD; Fred Morady, MD; Frank Bogun, MD

Background—Ventricular arrhythmias have been described to originate from intramural locations. Intramural scar can be assessed by delayed-enhanced MRI, but MRIs cannot be performed on every patient. The objective of this study was to assess the value of voltage mapping to detect MRI-defined intramural scar and to correlate the scar with ventricular arrhythmias.

Methods and Results—In 15 consecutive patients (3 women; age 55±16 years; ejection fraction, 49±13%) with structural heart disease, intramural scar was detected by delayed-enhanced MRI. All patients underwent endocardial unipolar and bipolar voltage mapping guided by the registered intramural scar. Scar volume by MRI was 11.7±8 cm^3 with a scar thickness of 4.6±0.7 mm and a preserved endocardial/epicardial rim of 3.3±1.6 and 4.8±2.6 mm, respectively. Endocardial bipolar voltage was 1.6±1.73 mV at the scar, 2.12±2.15 mV in a 1 cm perimeter around the scar, and 2.83±3.39 mV in remote myocardium without scar. The corresponding unipolar voltage was 4.94±3.25, 6.59±3.81, and 8.32±3.39 mV, respectively (P<0.0001). Using receiver–operator characteristic curves, a unipolar cut-off value of 6.78 mV (area under the curve, 0.78) and a bipolar cut-off value of 1.55 mV (area under the curve, 0.69) best separated endocardial measurements overlying scar as compared with areas not overlying a scar. At least 1 intramural ventricular arrhythmia was eliminated in all but 2 patients in this series.

Conclusions—Intramural scar can be detected by unipolar and bipolar voltage, unipolar voltage being more useful. Mapping and ablation of intramural arrhythmias originating from an intramural focus can be accomplished. **(*Circ Arrhythm Electrophysiol*. 2013;6:891-897.)**

Key Words: ablation ■ mapping ■ magnetic resonance imaging ■ ventricular arrhythmia

Ventricular arrhythmias in patients with ischemic and nonischemic cardiomyopathy are often associated with the presence of scar tissue. The location of scar in postinfarction patients is commonly in the subendocardium.[1] Scar in patients with nonischemic cardiomyopathy is often found in the midmyocardium[1] or the epicardium.[2] The location and extent of the scar can be precisely defined by delayed-enhanced MRI (DE-MRI), which has been found to help target arrhythmias originating from scar tissue.[3] Whereas voltage mapping has been used to define the extent of subendocardial and epicardial scar, intramural scar is difficult to detect.

Clinical Perspective on p 897

The purpose of this study was to assess whether intramural scar can be detected by endocardial voltage mapping, and to identify voltage cut-off values that indicate the presence of intramural scar. Furthermore, mapping data for ventricular arrhythmias were correlated with the intramural scar.

Methods

Patient Characteristics (Tables 1 and 2)

The subjects of this study were 15 consecutive patients (3 women; age 55±16 years; ejection fraction, 49±13%) with nonischemic cardiomyopathy referred for radiofrequency catheter ablation of symptomatic ventricular arrhythmias (ventricular tachycardia [VT], n=7; premature ventricular complexes [PVCs], n=6; both, n=2) in whom a predominant intramural scar was detected on DE-MRI. Four patients had cardiac sarcoidosis and 11 patients had idiopathic dilated cardiomyopathy. The patients were from among a pool of 28 consecutive patients with nonischemic cardiomyopathy referred for ablation of ventricular arrhythmias and who underwent MRI and had DE on MRI. Only patients with scar that did not reach the endocardium were selected for this analysis. The patients failed 1±1 antiarrhythmic medications. None of the patients had an implantable cardioverter defibrillator (ICD) at the time of the MRI. All but 2 patients with VT subsequently had an ICD implanted. One patient refused ICD implantation, and in the other patient, VT was hemodynamically tolerated and became noninducible postablation. Eight patients had ventricular tachycardia and 7 patients had

Received August 9, 2012; accepted July 26, 2013.

From the Division of Cardiology, University of Michigan Medical Center, Ann Arbor, MI (M.Y., E.G., T.C., R.L., K.J., H.G., H.O., F.P., A.C., F.M.); and the Department of Radiology, University of Pennsylvania Medical Center, Philadelphia, PA (B.D.).

The online-only Data Supplement is available at http://circep.ahajournals.org/lookup/suppl/doi:10.1161/CIRCEP.113.000073/-/DC1.

Correspondence to Frank Bogun, MD, Division of Cardiology, University of Michigan Health Systems, 1500 East Medical Center Drive SPC 5853, Ann Arbor, MI 48109-5853. E-mail fbogun@med.umich.edu

Table 1. Clinical Characteristics

Variables	
Number of patients	15
Age, y	55±16
Men/women, n	12/3
Left ventricular ejection fraction, %	49±13
Underlying cardiac disease, n	
DCM	11
Sarcoidosis	4
Arrhythmia, n	
PVC	6
VT	7
Both VT and PVCs	2
Scar location, n	
Septal scar	8
Free wall scar	8
Therapy, n	
β-Blockers	12 (80)
Antiarrhythmic drug including, amiodarone	6 (40)

DCM indicates dilated cardiomyopathy; PVC, premature ventricular complexes; and VT, ventricular tachycardia.

frequent PVCs with a PVC burden of 21±12%. When distinguishing different VT or PVC morphologies, the following aspects of the QRS complex were assessed: bundle branch block morphology, axis, amplitude, and QRS notching.

Table 2. Relationship of Ventricular Arrhythmias to Ablation Outcome

Patient No.	No. of VAs, PVC/VT	No. of Eliminated Intramural VAs, PVC/VT	No. of E liminated Nonintramural VAs, PVC/VT	Approach	Outcome
1	6/0	2/0*	1/0	Endo RF LV	Effective
2	1/0	1/0*	0/0	Endo RF LV/RV	Effective
3	0/8	0/0	0/0	Endo RF LV	Ineffective
4	11/0	2/0	1/0	Endo RF	Partially effective
5	0/3	0/3	0/0	Endo/Epi RF LV	Effective
6	9/0	1/0*	1/0	Endo RF	Effective
7	6/0	1/0*	1/0	Endo RF	Effective
8	0/1	0/0	0/1*	Endo RF	Effective
9	0/1	0/0	0/0	Endo RF	Effective
10	0/13	0/4	0/0	Endo RF	Partially effective
11	6/0	1/0*	3/0	Endo/Epi RF	Partially effective
12	0/22	0/1	0/10*	Endo RF	Partially effective
13	0/6	0/1	0/1	Endo RF	Partially effective
14	0/1	0/1*	0/0	Endo/Cusp RF	Effective
15	12/0	1/0*	1/0	Endo RF LV/RV	Partially effective

Endo indicates endocardial; Epi, epicardial; LV, left ventricular; RF, radiofrequency ablation; RV, right ventricular; and VA, ventricular arrhythmias.

*Predominant clinical VA.

Cardiac MRI

The DE-MRI studies were performed on a 1.5-Tesla MRI scanner (Signa Excite CV/i; General Electric, Milwaukee, WI) with a 4- or 8-element phased array coil placed over the chest of patients in the supine position. Images were acquired with ECG gating during breath-holds. Dynamic short- and long-axis images of the heart were acquired using a segmented, k-space, steady-state, free precession pulse sequence (repetition time, 4.2 ms; echo time, 1.8 ms; in-plane spatial resolution, 1.4×1.4 mm; slice thickness, 8 mm). Fifteen minutes after administration of 0.20 mmol/kg of intravenous gadolinium DTPA (Magnevist; Berlex Pharmaceuticals, Wayne, NJ), 2-dimensional DE imaging was performed using an inversion recovery sequence[4] (repetition time, 6.7 ms; echo time, 3.2 ms; in-plane spatial resolution, 1.4×2.2 mm; slice thickness, 8 mm) in the short axis and long axis of the left ventricle at matching cine image slice locations. The inversion time (250–350 ms) was optimized to null the normal myocardium. The DE-MRIs were reviewed for the presence or absence of delayed enhancement by 2 observers blinded to the results of mapping and ablation. Discrepancies were resolved by consensus.

Image Integration and Data Analysis (Table 3)

After scar tissue was identified on the DE-MRI (Figure 1) using the full width at half maximum approach, the delayed-enhanced distribution on the DE-MRI was exported out of the short-axis DE-MRI images and was integrated along with the endocardial contours into the electroanatomic voltage map (Figure 2) using the CARTO MERGE software (Biosense Webster, Diamond Bar, CA). Three-dimensional registration was accomplished using 3 fixed reference points (aorta, left ventricular apex, and mitral annulus) of both MRI data and electroanatomic mapping data combined with surface registration. For mitral annular points, sites were selected on the electroanatomic map where both atrial and ventricular signals were present. This was performed in a similar manner as described in postinfarction patients,[5] and the mapping procedure then focused on the area where the scar projected on. Accuracy of the registration process was <5 mm as assessed by surface registration statistics.

Post hoc, the scar was displayed as a polar map with the projected unipolar and bipolar endocardial mapping points from the electroanatomic maps (Figure 3).

A receiver–operator characteristics curve was then constructed to assess voltage cut-off values for bipolar and unipolar voltage maps to detect intramural scar (Figure 4). Scar volume (cm^3) and intramural scar area (cm^2) as projecting onto the ventricular endocardium were determined.

Electrophysiological Study and Mapping

The study protocol was approved by the Human Research Committee. After informed consent was obtained, a 6-Fr quadripolar electrode catheter was introduced into the right femoral vein and positioned at the right ventricular apex. Programmed right ventricular stimulation was performed in all patients with 1 to 4 extrastimuli to induce VT. In 7 of the patients, a total of 50 VTs were induced (VT cycle length, 363±96 ms).

Electroanatomical mapping (CARTO; Biosense Webster) was performed with either a 4-mm-tip ablation catheter (Navistar) or a 3.5-mm-tip open irrigation ablation catheter (Thermocool). Electrograms were

Table 3. Comparison of Uni- and Bipolar Voltage Overlying Scar

Variables	Unipolar	Bipolar
Voltage over scar, mV	4.49±3.25*	1.62±1.73†
Voltage ≤1 cm^2 around scar, mV	6.59±3.81*	2.12±2.15†
Voltage at remote sites, mV	8.32±3.39*	2.83±2.34†

*Comparison of voltage over scar vs 1 cm surrounding scar vs remote areas was all $P<0.01$.

†Comparison of voltage over scar vs 1 cm surrounding scar vs remote areas was all $P<0.01$.

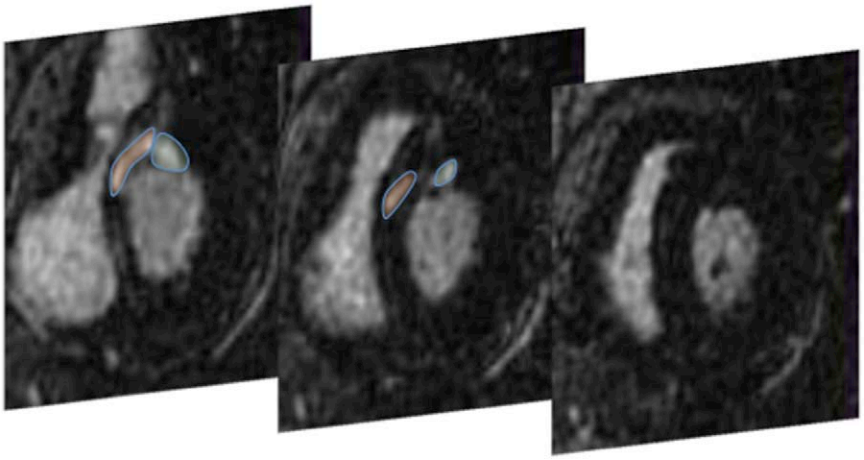

Figure 1. Stack of 3 short-axis views from a delayed-enhanced MRI image (basal, **left**; apical, **right**). In light orange, area of intramural delayed enhancement; in light blue, endocardial delayed enhancement secondary to 2 prior failed ablation procedures.

filtered at 50 to 500 Hz. The intracardiac electrograms and leads V1, I, II, and III were displayed on an oscilloscope and recorded at a speed of 100 mm/second. The recordings were stored on optical disc (EP Med, West Berlin, NJ). Endocardial mapping was performed in the left ventricle in all patients, and 246±99 points were recorded per patient. A bipolar and unipolar voltage map was generated during sinus rhythm. For PVCs, the site with the earliest local activation time resulting in elimination of the PVC by radiofrequency ablation was defined as critical. For hemodynamically tolerated VTs, sites with concealed entrainment were sought. A site was defined as critical if VT terminated during radiofrequency ablation in the presence of concealed entrainment, or if VT terminated at the earliest endocardial mapping site during radiofrequency energy delivery. For nontolerated VTs, an isthmus was defined as a site where a match of the QRS morphology between the pacemap and the VT was identified and the VT was no longer inducible after radiofrequency ablation. A site was considered to originate from an intramural scar if the endocardial breakthrough site of a PVC or VT was located at the endocardial area on to which the intramural scar projected (Figure 3). The mapping data were correlated with the MRI data to assess whether the mapped arrhythmias originated from the intramural scar.

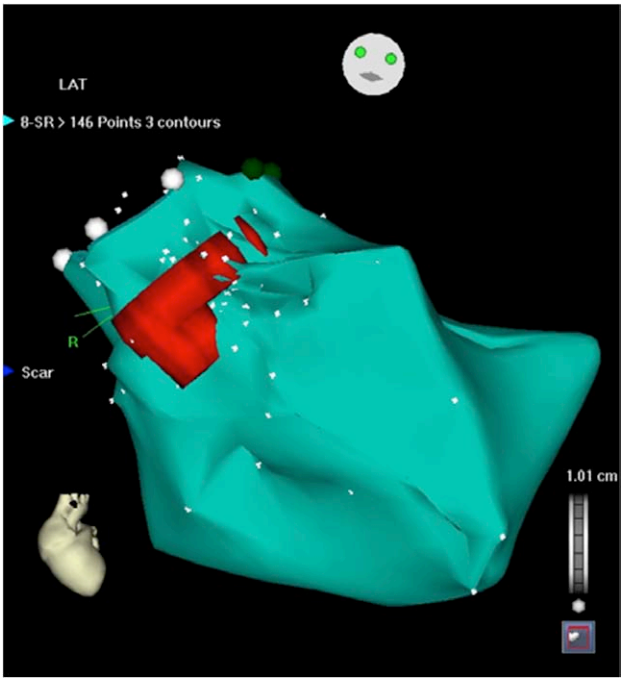

Figure 2. The registered intramural scar (red) is displayed on the anatomic shell of the electroanatomical map.

Low voltage was defined as a bipolar voltage amplitude ≤1.5 mV.[6] If PVCs were infrequent or if a targeted VT was not hemodynamically tolerated, pacemapping was used to identify the site of origin. Pacemapping was performed at areas with low bipolar voltage, the endocardium where the intramural scar projected on (Figure 2) as well as its surrounding vicinity. Once the mapping catheter was advanced into the arterial system, a bolus of 5000 U of heparin was used initially and heparin was then administered to obtain an activated clotting time of 300 seconds.

Radiofrequency Ablation

Radiofrequency energy was delivered at sites of earliest endocardial activation during PVCs, at sites with concealed entrainment during VT, or at sites of origin as determined by pacemapping. The initial power setting was 30 W; applications of radiofrequency energy were titrated to achieve an impedance drop of 10 Ω. Ablation was performed during ventricular ectopy or VT whenever possible, and energy applications were continued for ≥30 seconds if adequate heating at the electrode–tissue interface was achieved. If the PVCs or VT ceased <30 seconds, the energy application was continued for 60 seconds and was followed by a second 60-second application. If the PVCs or VT did not cease in ≤30 seconds, the radiofrequency energy application was discontinued and additional mapping was performed. After ablation, programmed right ventricular stimulation was repeated. Successful catheter ablation was defined as cessation of the targeted PVCs or the noninducibility of VT. A partially effective procedure was defined as elimination of the clinical ventricular arrhythmia but not all of the nonclinical arrhythmias.

Follow-Up

All patients were seen in follow-up 3 to 6 months after the ablation procedure and thereafter every 12 to 48 months. Patients with ICDs were seen every 6 months in a device clinic. The mean duration of follow-up was 45±27 months. Postablation antiarrhythmic medication was continued or added in 6 patients in whom ablation was only partially effective or ineffective. In the remaining patients, antiarrhythmic medications were not continued.

Statistical Analysis

Variables are expressed as mean±1 SD. Variables were compared by Student *t* test, Fisher exact test, or by χ^2 analysis, as appropriate. If a cell size was <5, the Fischer exact test was used. Pearson correlation coefficient (*R*) was calculated to assess linear relationship between 2 continuous variables. A *P* value of <0.05 was considered statistically significant. Receiver–operator characterisics curves were determined to assess cut-off values for bipolar and unipolar voltage underlying intramural scar tissue (Figure 4). The statistical package of Matlab (Mathworks, Natick, MA) was used to perform the statistical analysis.

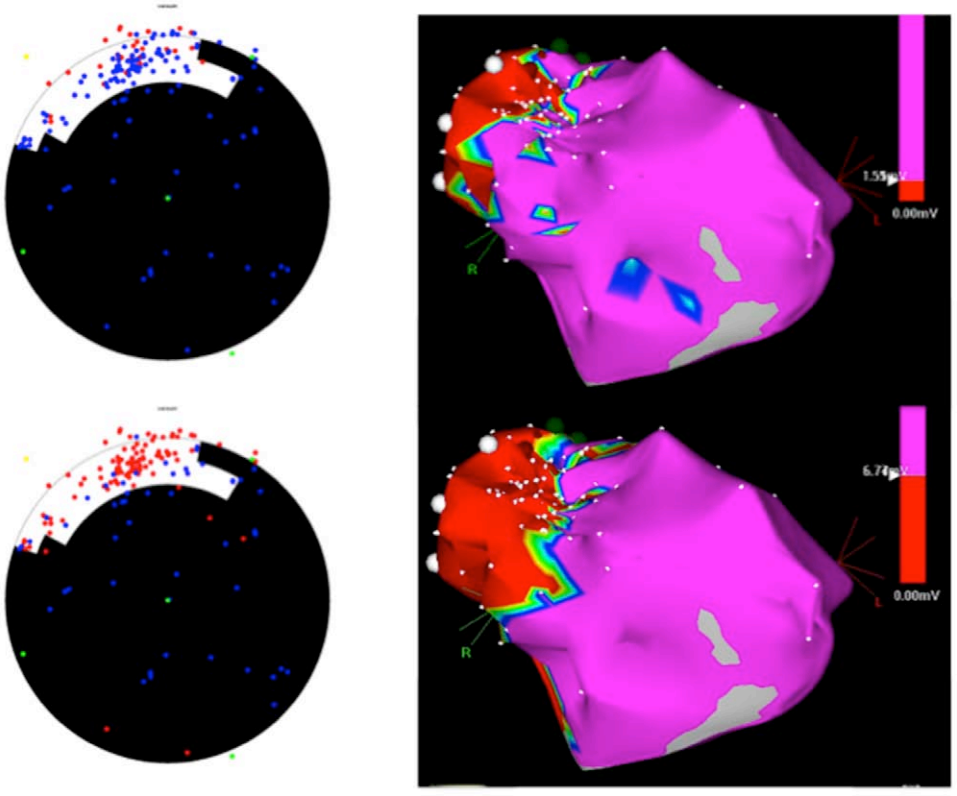

Figure 3. Left, Polar view of the delayed-enhanced MRI image of the same patient shown in Figure 1. Bipolar electroanatomical map (**top**; blue points, voltage ≥1.5 mV; red points, voltage <1.5 mV as it projects on the polar map). Unipolar endocardial electroanatomical mapping points projecting on the polar map (**bottom**; blue points, voltage ≥6.8 mV; red points, voltage <6.8 mV). **Right**, Corresponding bipolar (**top**) map with a cut-off voltage of 1.55 mV and the corresponding unipolar (**bottom**) map with a cut-off voltage of 6.8 mV.

Results

Scar Characteristics

Intramural scar had a volume of 11.7±8 cm^3 and an area projecting on the endocardium of 19.3±13.4 cm^2. The distance of the intramural scar from the endocardial surface was 3.3±1.6 mm. The scar was located in the septum in 8 out of 15 patients and in the free wall in 8 patients. The scar had a basal left ventricular location in 8 patients and was multifocal in 3 patients.

DE-MRI Voltage Mapping Correlation (Tables 2 and 3; Online-Only Data Supplement Tables I–III)

The mean bipolar voltage overlying the intramural scar was 1.62±1.73 mV, and the unipolar endocardial voltage overlying the intramural scar was 4.49±3.25 mV. An area of 1 cm^2 surrounding the intramural scar showed a mean bipolar voltage of 2.12±2.15 mV, and unipolar voltage in the scar-free area was 6.59±3.81 mV. Both bi- and unipolar voltage overlying the scar was significantly lower than the bi- and unipolar voltage at a distance of 1 cm from the scar (P<0.0001 mV, respectively). More remote areas had significantly higher bi- and unipolar voltage (2.83±2.34 and 8.32±3.39 mV, respectively; both P<0.0001 for comparisons of area underlying the scar and at a distance of 1 cm from the scar). By receiver–operator characteristic curves, the bipolar cut-off voltage that best separated endocardial sites overlying intramural scar as compared with sites without intramural scar was 1.55 mV (area under the curve, 0.69; sensitivity,

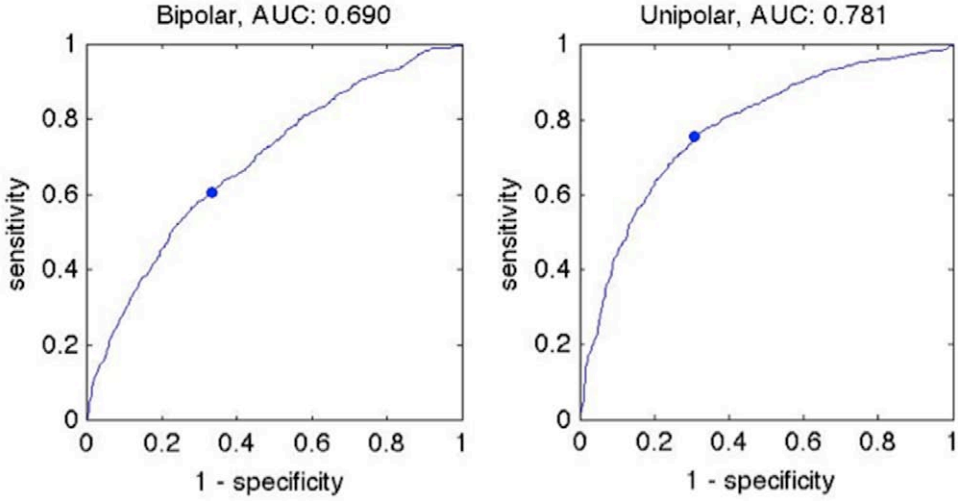

Figure 4. Receiver–operator characteristics curves of the bipolar (**left**) and unipolar (**right**) electroanatomical maps indicating intramural scar tissue. AUC indicates area under the curve.

61%; specificity, 66%). The unipolar cut-off voltage separating sites underlying an intramural scar from other sites without scar was 6.78 mV (area under the curve, 0.78; sensitivity, 76%; specificity, 69%). The bootstrapped 95% confidence intervals for the bipolar voltage cut-off was (1.33, 1.71) and for unipolar voltage cut-off was (6.28, 7.26).

Relationship Between DE-MRI and Catheter Ablation

Arrhythmias related to intramural scar were identified in 13 out of 15 patients. In 1 patient in whom epicardial mapping was performed using a subxyphoid access, 3 VTs were ablated from the epicardium. Critical sites were within the epicardium and not intramural. This patient was included in the analysis because the scar on MRI spared the left ventricular endocardium and extended to the epicardium without a rim of epicardial preserved voltage. The arrhythmias were eliminated in 7 out of 15 patients. In 6 out of 15 patients, the procedure was partially effective. In 2 out of 15 patients, the procedure was ineffective. In 1 patient, 2 ablation procedures failed before the patient referral. A cardiac MRI (Figures 1–3) showed an intramural scar that was not reached by the ablation lesions that caused focal endocardial delayed enhancement. Another mapping and ablation procedure with knowledge of the location of the intramural scar helped to identify the VT breakout site and ablate the VT. In 9 out of 15 patients, the predominant clinical ventricular arrhythmias originated intramurally. In the remaining patients, the predominant ventricular arrhythmias were either not intramural (n=1) or not precisely localized (n=5).

Intramural Scar and Scar-Related Arrhythmias (Table 2)

Direct recordings of the intramural scar were obtained in only 1 out of 15 patients who had a septal scar into which a multipolar flexible catheter could be advanced (Figure 5 and online-only Data Supplement Figure I). Low voltage and fractionated electrograms were present. Because the ablation catheter could not be advanced into the septal perforator branch, ablation was effectively carried out from both sides of the septum. In 2 more patients, septal arrhythmias were targeted from both sites of the septum effectively. In 1 patient, the arrhythmias were targeted from the endocardium and from the epicardium after a transcutaneous epicardial access was obtained. In the remaining 11 patients, only endocardial ablation was performed. Ablation was effective in 7 out of 15 patients, partially effective in 6 out of 15 patients, and ineffective in 2 out of 15 patients.

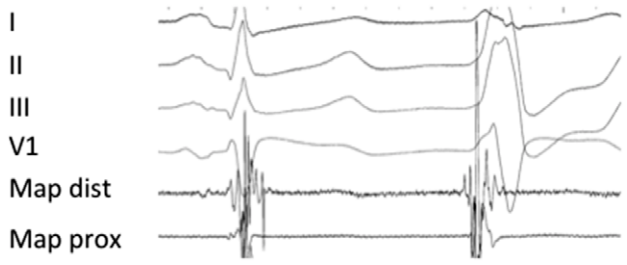

Figure 5. Recordings from an intramural focus resulting in premature ventricular complexes (PVCs) via a multipolar catheter positioned within a perforator vein. The recordings show a low-voltage fragmented electrogram with a late potential during sinus rhythm. During PVC, the sharp component of the electrogram precedes the PVC by 35 ms.

Follow-Up

During follow-up, the PVC burden in patients with frequent PVCs was reduced from 28±13% to 0.9±0.3% in patients with effective procedures ($P<0.01$). Three patients with VT and 2 patients with PVCs had recurrences of their arrhythmias. One out of 3 VTs was intramural, and 1 out of 2 patients with PVCs had an intramural site of origin.

Discussion

Main Findings

This report shows that intramural scar harbors ventricular arrhythmias. Intramural scar can be precisely located by DE-MRI. Endocardial mapping with the use of bipolar and unipolar voltage can be used to identify intramural scar.

Intramural Scar and Nonischemic Cardiomyopathy

Intramural scar can be a major challenge when targeting arrhythmias in patients with nonischemic cardiomyopathy. In patients with nonischemic cardiomyopathy, the arrhythmogenic substrate of VT is most often confined to scar tissue.[3] In this series of patients with nonischemic cardiomyopathy, we focused on consecutive patients with intramural scar. Patients had either idiopathic dilated cardiomyopathy or cardiac sarcoidosis. Intramural scar has been described in both forms of cardiomyopathy.[7,8] The lower efficacy of radiofrequency ablation in patients with nonischemic cardiomyopathy even when a combined endo- and epicardial approach is used[9,10] may be because of intramural foci that are difficult to reach from the endocardium or the epicardium. In this series, the identification of an intramural focus helped to focus the mapping procedure on a particular area of the heart that was investigated by pacemapping and activation mapping. Haqqani et al[11] described a series of patients with nonischemic cardiomyopathy in whom a septal scar was present. In their series, there were some patients with an intramural scar, and the authors reported unipolar voltage abnormalities that might help to characterize the intramural scar. No registration with the MRI-defined scar, however, was used to identify bi- and unipolar cut-off values exactly. Hutchinson et al[12] described endocardial unipolar voltage characteristics in patients with epicardial scar. However, registration of MRI-based scar data was not used to correlate scar with voltage data.

Placing the recording electrodes directly within the myocardium by way of the coronary venous system helped to identify the arrhythmogenic substrate. It is not surprising that low amplitude and fragmented electrograms were recorded from intramural scars. Unfortunately, in the only patient in whom direct recordings of the intramural scar was accomplished through a perforator vein, the ablation catheter could not be advanced within the vein, and ablation from both aspects of the septum was performed and eliminated this patient's ventricular arrhythmia. We demonstrated that it is possible to advance an ablation catheter within a perforator branch and

ablate an arrhythomgenic focus effectively within the septum in patients without structural heart disease.[13] Because direct recording of an intramural scar by the coronary venous system was not accomplished in the majority of patients, projection of the intramural scar on the corresponding endocardium helped to identify a region of interest. Because MRI data may not be present in all patients, the use of bi- and unipolar electrograms may help to identify the extension of the intramural scar when mapping is performed at the adjacent endocardium.

Mapping and Ablation

The intramural arrhythmias were eliminated when radiofrequency energy was delivered from both endocardial sites of a septal scar. The location of the intramural scar was helpful in the mapping part of the procedure to allow optimal placement of the ablation catheter in order to target endocardial breakthrough sites. The highest success rate was when the intramural scar was confined to the interventricular septum. The higher success rate may be due to the ability to achieve deep lesions when delivering radiofrequency energy with the ablation catheter being in a perpendicular position to the endocardial tissue.

An extendable needle catheter having a 5- to 7-mm needle with the ability to record, pace, and ablate has been previously described.[14] Knowledge of the exact location of the scar in conjunction with voltage mapping and intraprocedural scar registration[5] can enable the electrophysiologist in precisely placing the needle within the scar. Recordings of abnormal electrograms, as shown from our intramyocardial scar recordings, and identification of matching pacemaps at these locations may improve exact localization of the arrhythmogenic substrate. Such an approach can increase the success rate when dealing with the challenges of an intramurally located arrhythmogenic substrate.

Prior Publications

Spears et al[15] investigated the relationship between biolar and unipolar voltage in patients with nonischemic cardiomyopathy. In contradistinction to this article, that study was not focused on patients with predominantly intramural scar and no correlation between arrhythmias and scar tissue was established. The present study extends the findings of Spears et al by demonstrating the association of ventricular arrhythmias with intramural scar.

Limitations

The study is limited by its small sample size. Only patients with idiopathic dilated cardiomyopathy and cardiac sarcoidosis were included, and the findings may not apply to all patients with nonischemic cardiomyopathy. A distinction between intramural and epicardial scar was not attempted in this patient population. The scar was predominantly intramural by MRI in all patients. The intramural scar extended to the epicardium in 1 patient, and the VTs were ablated from the epicardium in this patient. Critical sites for ventricular arrhythmias were not identified in all patients, and, therefore, it is unclear whether failure of ablation was because of an intramural location of the arrhythmia or because of another site of origin. It is possible that longer applications of radiofrequency energy than used in this study might have resulted in improved outcomes of ablation of intramural ventricular arrhythmias. Systematic mapping of both aspects of the ventricular septum containing the intramural scar was not performed in this study.

A major limitation of the unipolar voltage data is that there is a substantial overlap of unipolar low voltage between scar zones and regions of no scar. This makes it difficult to define the border of the intramural scar precisely. A cardiac MRI with delayed enhancement remains the gold standard for exact demarcation of scars and, therefore, is preferable over voltage mapping for defining intramural scar.

Clinical Implications

Intramural scar can be detected by unipolar and bipolar mapping data. However, voltage mapping cannot precisely define the borders of intramural scar. A cardiac MRI is more accurate than a voltage map for characterization of intramural scar. Registration of intramural scar helps to identify a region of interest where the mapping procedure can focus on. The incremental value of scar registration for ablating intramural ventricular arrhythmias remains to be determined.

Sources of Funding

Drs Bogun and Oral have received a grant from the Leducq Foundation. Dr Desjardins was supported by National Institutes of Health grant 7K23EB006481.

Disclosures

None.

References

1. McCrohon JA, Moon JC, Prasad SK, McKenna WJ, Lorenz CH, Coats AJ, Pennell DJ. Differentiation of heart failure related to dilated cardiomyopathy and coronary artery disease using gadolinium-enhanced cardiovascular magnetic resonance. *Circulation*. 2003;108:54–59.
2. De Cobelli F, Pieroni M, Esposito A, Chimenti C, Belloni E, Mellone R, Canu T, Perseghin G, Gaudio C, Maseri A, Frustaci A, Del Maschio A. Delayed gadolinium-enhanced cardiac magnetic resonance in patients with chronic myocarditis presenting with heart failure or recurrent arrhythmias. *J Am Coll Cardiol*. 2006;47:1649–1654.
3. Bogun FM, Desjardins B, Good E, Gupta S, Crawford T, Oral H, Ebinger M, Pelosi F, Chugh A, Jongnarangsin K, Morady F. Delayed-enhanced magnetic resonance imaging in nonischemic cardiomyopathy: utility for identifying the ventricular arrhythmia substrate. *J Am Coll Cardiol*. 2009;53:1138–1145.
4. Simonetti OP, Kim RJ, Fieno DS, Hillenbrand HB, Wu E, Bundy JM, Finn JP, Judd RM. An improved MR imaging technique for the visualization of myocardial infarction. *Radiology*. 2001;218:215–223.
5. Gupta S, Desjardins B, Baman T, Ilg K, Good E, Crawford T, Oral H, Pelosi F, Chugh A, Morady F, Bogun F. Delayed-enhanced MR scar imaging and intraprocedural registration into an electroanatomical mapping system in post-infarction patients. *J Am Coll Cardiol Cardiovasc Imaging*. 2012;5:207–210.
6. Marchlinski FE, Callans DJ, Gottlieb CD, Zado E. Linear ablation lesions for control of unmappable ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. *Circulation*. 2000;101:1288–1296.
7. Roberts WC, McAllister HA Jr, Ferrans VJ. Sarcoidosis of the heart. A clinicopathologic study of 35 necropsy patients (group 1) and review of 78 previously described necropsy patients (group 11). *Am J Med*. 1977;63:86–108.
8. Assomull RG, Prasad SK, Lyne J, Smith G, Burman ED, Khan M, Sheppard MN, Poole-Wilson PA, Pennell DJ. Cardiovascular magnetic resonance, fibrosis, and prognosis in dilated cardiomyopathy. *J Am Coll Cardiol*. 2006;48:1977–1985.
9. Hsia HH, Callans DJ, Marchlinski FE. Characterization of endocardial electrophysiological substrate in patients with nonischemic

cardiomyopathy and monomorphic ventricular tachycardia. *Circulation*. 2003;108:704–710.
10. Soejima K, Stevenson WG, Sapp JL, Selwyn AP, Couper G, Epstein LM. Endocardial and epicardial radiofrequency ablation of ventricular tachycardia associated with dilated cardiomyopathy: the importance of low-voltage scars. *J Am Coll Cardiol*. 2004;43:1834–1842.
11. Haqqani HM, Tschabrunn CM, Tzou WS, Dixit S, Cooper JM, Riley MP, Lin D, Hutchinson MD, Garcia FC, Bala R, Verdino RJ, Callans DJ, Gerstenfeld EP, Zado ES, Marchlinski FE. Isolated septal substrate for ventricular tachycardia in nonischemic dilated cardiomyopathy: incidence, characterization, and implications. *Heart Rhythm*. 2011;8:1169–1176.
12. Hutchinson MD, Gerstenfeld EP, Desjardins B, Bala R, Riley MP, Garcia FC, Dixit S, Lin D, Tzou WS, Cooper JM, Verdino RJ, Callans DJ, Marchlinski FE. Endocardial unipolar voltage mapping to detect epicardial ventricular tachycardia substrate in patients with nonischemic left ventricular cardiomyopathy. *Circ Arrhythm Electrophysiol*. 2011;4:49–55.
13. Yokokawa M, Good E, Chugh A, Pelosi F Jr, Crawford T, Jongnarangsin K, Latchamsetty R, Oral H, Morady F, Bogun F. Intramural idiopathic ventricular arrhythmias originating in the intraventricular septum: mapping and ablation. *Circ Arrhythm Electrophysiol*. 2012;5:258–263.
14. Sapp JL, Cooper JM, Zei P, Stevenson WG. Large radiofrequency ablation lesions can be created with a retractable infusion-needle catheter. *J Cardiovasc Electrophysiol*. 2006;17:657–661.
15. Spears DA, Suszko AM, Dalvi R, Crean AM, Ivanov J, Nanthakumar K, Downar E, Chauhan VS. Relationship of bipolar and unipolar electrogram voltage to scar transmurality and composition derived by magnetic resonance imaging in patients with nonischemic cardiomyopathy undergoing VT ablation. *Heart Rhythm*. 2012;9:1837–1846.

CLINICAL PERSPECTIVE

Ventricular arrhythmias that arise from intramural scar can be difficult to treat with catheter ablation. Myocardial scars can be defined as areas of delayed contrast enhancement on MRI. MRIs, however, cannot be performed in all patients. This study demonstrates that unipolar endocardial voltage maps can be used to identify intramural scar as defined by cardiac MRI. A cut-off value of ≤6.78 mV best differentiated areas with underlying intramural scar as compared with areas without intramural scar, but cannot precisely define the scar border region. Registration of MRI images in an electroanatomic mapping system can help focus the mapping procedure to the region of interest, but the incremental value of this approach for guiding ablation of intramural ventricular arrhythmias remains to be determined.

Circulation
Arrhythmia and Electrophysiology

Characteristics of Intramural Scar in Patients With Nonischemic Cardiomyopathy and Relation to Intramural Ventricular Arrhythmias

Benoit Desjardins, Miki Yokokawa, Eric Good, Thomas Crawford, Rakesh Latchamsetty, Krit Jongnarangsin, Hamid Ghanbari, Hakan Oral, Frank Pelosi, Jr, Aman Chugh, Fred Morady and Frank Bogun

Circ Arrhythm Electrophysiol. 2013;6:891-897; originally published online August 28, 2013;
doi: 10.1161/CIRCEP.113.000073
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-3149. Online ISSN: 1941-3084

Supplemental Material

Supplement Table 1: Sensitivity and Specificity using different Voltage Cut-off Values for detection of Intramural Scar

Voltage cut-off	Sensitivity	Specificity	PPV	NPV
Bipolar				
- 0.5 mV	29	90	75	55
- 1.0 mV	48	78	70	59
- 1.5 mV	60	68	66	62
Optimal bipolar				
- 1.55	61	66	65	62
Unipolar				
- 7.9 mV	84	54	65	76
- 6.5 mV	73	71	72	72
- 5.5 mV	64	80	77	68
Optimal Unipolar				
- 6.78 mV	76	69	72	74

Supplement Table 2: Distribution of Mapping Points Depending on Voltage and Location on Relative to Scar: Bipolar voltage

Scar location	Voltage <0.5 mV	Voltage 0.5-1.5 mV	Voltage >1.5 mV
Scar	192 (30%)	197 (31%)	252 (39%)
1 cm to scar	186 (23%)	242 (30%)	392 (48%)
Remote	84 (11%)	186 (23%)	525 (66%)

Number include mapping sites (%).

Supplement Table 3: Distribution of Mapping Points Depending on Voltage and Location Relative to Scar: Unipolar voltage

Scar location	Voltage <3 mV	Voltage 3-6.78 mV	Voltage >6.78 mV
Scar	197 (31%)	292 (46%)	152 (24%)
1 cm to scar	158 (19%)	342 (40%)	338 (41%)
Remote	51 (6%)	183 (23%)	561 (71%)

Number include mapping sites (%).

Supplement Figure 1

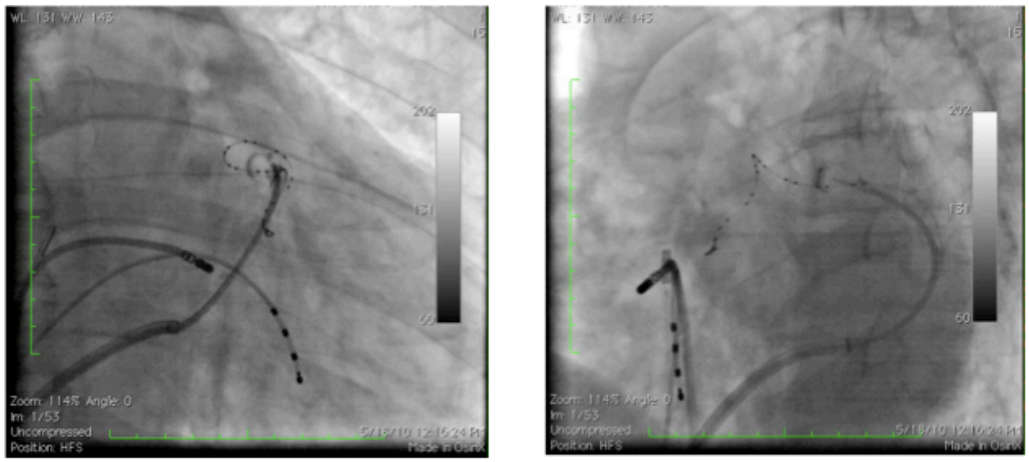

Figure legend :

Supplement Figure 1: Right ventricular oblique and left ventricular oblique view of a multipolar catheter within a perforator branch. The multipolar catheter is in contact with the intramural scar.