The Substrate and Ablation of Ventricular Tachycardia in Patients With Nonischemic Cardiomyopathy

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The term “nonischemic cardiomyopathy” (NICM) designates a myocardial disease characterized by mechanical and/or electrical dysfunction in the absence of significant coronary artery disease, valvular heart disease, hypertension, or congenital heart disease. Patients with NICM can present with different types of ventricular arrhythmias ranging from ventricular premature depolarizations (VPDs) to sustained monomorphic ventricular tachycardia (VT) and ventricular fibrillation. VT occurs in less than 5% of patients, but is associated with an increased risk of death. Although implantable cardioverter-defibrillators (ICD) remain the first-line therapy in these patients, frequent VPDs result in morphological and functional abnormalities of the ventricular myocardium, with progressive worsening of the left ventricular function. Importantly, in such instances, arrhythmia suppression by catheter ablation reverses the cardiomyopathic process and results in a significant improvement of the left ventricular systolic function and a decrease in the size of the left ventricle (LV). Clues to a VPD-induced cardiomyopathy are a high arrhythmia burden (>10,000 VPDs/day) and the presence of 1 dominant VPD-QRS morphology (>150 ms) may identify an increase in risk for the development of a cardiomyopathy. Ultimately, improvement in left ventricular function after successful ablation will confirm the diagnosis.

Anatomic Substrate

Necropsy studies in IDCM patients demonstrate grossly visible scars in 14% of patients and histological examination reveals multiple patchy areas of replacement fibrosis in 35% and 57% of sections of the right and left ventricles, respectively. Hypertrophied and atrophic myocytes, myofiber disarray, nuclear changes, and cytoskeletal disorganization are also observed. These findings are nonspecific and the result of the cardiac remodeling process that takes place in response to different biologic insults to the heart. Similar changes have been reported in patients with coronary artery disease and valvular heart disease. However, unlike other forms of structural heart disease, in which the proliferation of fibrotic tissue eventually...

Key Words: Cardiomyopathy; Catheter ablation; Mapping; Ventricular tachycardia
Link Between Fibrosis and Arrhythmogenesis

Increased fibrosis in the heart predisposes to both atrial and ventricular arrhythmias. In senescent mice, inducibility of VT increases with increasing fibrosis. In patients with IDC, the amount of fibrosis by histologic analysis correlates with the severity of abnormal propagation of electrical impulses. Consistent with these observations, the presence of fibrosis as quantified by late gadolinium enhancement in MRI studies is associated with a higher risk of ventricular arrhythmias and adverse cardiac outcomes in patients with IDC. The occurrence of ventricular arrhythmias appears to be related to the size and heterogeneity of the scar. Thus, patients with larger scars and larger border zones have a higher risk of ventricular arrhythmias. In addition to the size of the scar, the architecture and texture of the fibrosis also play an important role in arrhythmogenesis. Fibrosis may be distributed in a compact, patchy or diffuse manner. Patchy fibrosis, which is frequently reported in patients with IDC, consists of long collagen strands intermingled with myocardial bundles and predisposes to arrhythmias to a greater extent than compact or diffuse fibrosis. This is because patchy fibrosis is associated with important conduction delays secondary to zigzag propagation of electrical impulses between myocardial bundles.

In addition to fibrosis, several other factors, such as increased dispersion of refractoriness, altered expression and distribution of connexin proteins, and increased sympathetic activity (all of which have been reported in patients with IDC) further enhance the susceptibility to arrhythmias.

Electrophysiologic Substrate

The anatomic substrate of scar-related VT consists of islands of surviving myocardial fibers embedded in fibrotic tissue. The ensuing tissue discontinuities and the disruption of normal intercellular electrical coupling creates tortuous conduction pathways around electrically inert areas of fibrosis and source-sink mismatches that collectively result in slow conduction. Low-amplitude, fractionated electrograms are recorded in these regions. Based on this paradigm, attempts have been made by several electrophysiology laboratories to indirectly characterize the arrhythmogenic substrate by assessing the extent and distribution of abnormal electrograms. Early, conventional sinus rhythm endocardial mapping studies from our laboratory demonstrated that patients with IDC generally have fewer abnormal (ie, low-voltage, long-duration, or fractionated) electrograms than patients with coronary artery disease (Table 1). When patients with IDC were categorized based on arrhythmia presentation, the greatest percentage of abnormal electrograms existed in patients with sustained monomorphic VT (Table 2). Similar findings have been reported in patients undergoing intraoperative mapping during epicardial defibrillator patch electrode placement. Again, patients with inducible monomorphic VT had a greater incidence of abnormal endocardial and epicardial electrograms.
than patients in whom no VT or only ventricular fibrillation was induced (Figure 2). Notably, abnormal epicardial signals predominated in some patients whereas abnormal endocardial electrograms predominated in others. These findings are consistent with the concept that a fixed anatomic substrate because of increased fibrosis exists in IDCM patients with VT. The data also suggest a greater substrate burden in patients with VT. The endocardium and epicardium appear to be variably involved in the disease process, indicating that in some patients the VT circuit is located in the endocardium whereas in others it is located in the epicardium.

Hsia et al used electroanatomic mapping to further characterize the myocardial substrate in 19 patients with IDCM and sustained VT. Previous studies in patients without structural heart disease who underwent electroanatomic mapping had defined abnormal bipolar electrograms as those having a voltage <1.5 mV (the minimum voltage for 95% of the studied bipolar electrograms). In view of those findings and to account for the presence of patchy scarring in some patients, Hsia et al defined abnormal endocardium as contiguous bipolar electrograms having a voltage <1.8 mV. All patients undergoing endocardial mapping had defined abnormal endocardium as contiguous bipolar electrograms having a voltage <1.8 mV. All patients undergoing endocardial mapping had abnormal endocardial and epicardial electrograms. (Endo) and epicardial (Epi) electrograms according to VT inducibility in patients with idiopathic dilated cardiomyopathy. Patients with inducible VTs have a greater proportion of abnormal endocardial and epicardial electrograms than patients with noninducible VTs. Notably, a similar percentage of abnormal endocardial and epicardial electrograms exists in both patients with inducible and noninducible VTs. (Adapted with permission from reference 30.) VT, ventricular tachycardia.

The concept of intramural and epicardial scarring without endocardial involvement was clearly illustrated by Haqqani et al. In a series of 266 consecutive patients with IDCM and VT, the authors identified 31 patients with unipolar electrograms suggestive of scarring confined to the basal interventricular septum. Of them, 9 patients had normal endocardial bipolar voltage. Intracardiac echocardiography and periprocedural cardiac MRI demonstrated isolated midmyocardial septal abnormal echogenicity and hyperenhancement suggestive of scarring in 7 patients. The VT origin was mapped to the septal substrate. It appears, therefore, that in some patients with IDCM the arrhythmogenic substrate is located entirely intramurally and within the septum. The scar may remain undetected during bipolar voltage mapping and its delineation would rely on cardiac MRI and unipolar voltage mapping. Another indicator of an isolated intraseptal substrate is the demonstration of delayed or apically displaced transmural breakthrough together with the recording of abnormal endocardial electrograms during pacing from the right basal interventricular septum while

Table 1. Influence of Underlying Heart Disease on Endocardial Electrogram Characteristics

<table>
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<tr>
<th>Patients (n)</th>
<th>CAD</th>
<th>Cardiomyopathy</th>
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<tbody>
<tr>
<td>Normal sites (%)</td>
<td>50±24</td>
<td>84±16*</td>
</tr>
<tr>
<td>Abnormal sites (%)</td>
<td>43±21</td>
<td>15±18*</td>
</tr>
<tr>
<td>Fractionated sites (%)</td>
<td>7±11</td>
<td>1±3*</td>
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<tr>
<td>Late sites (%)</td>
<td>12±14</td>
<td>2±5*</td>
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*P<0.001; *P<0.005. CAD, coronary artery disease. Reproduced with permission from reference 30.

*P<0.05 VT vs. No VT, NSVT and CA. CA, cardiac arrest; NSVT, nonsustained ventricular tachycardia. Reproduced with permission from reference 30.

Figure 2. Extent of abnormal endocardial (Endo) and epicardial (Epi) electrograms according to VT inducibility in patients with idiopathic dilated cardiomyopathy. Patients with inducible VTs have a greater proportion of abnormal endocardial and epicardial electrograms than patients with noninducible VTs. Notably, a similar percentage of abnormal endocardial and epicardial electrograms exists in both patients with inducible and noninducible VTs. (Adapted with permission from reference 30.) VT, ventricular tachycardia.
The presence of epicardial scars can be inferred without accessing the epicardium from the 12-lead ECG, unipolar endocardial electrograms, and imaging studies, including intracardiac echocardiography and MRI. The presence of a Q wave in lead I during VT can predict an epicardial origin in the basal superior or lateral aspect of the LV with 88% sensitivity and specificity.

The absence of Q waves in inferior leads also suggests an epicardial VT with a sensitivity of 94% and a specificity of 63%. A 4-step algorithm combining morphology and interval criteria, which characterize delayed conduction in the initial portion of the QRS, has been proposed.

Unipolar electrograms, because of their “wider” field of view, are attenuated by the accumulation of electrically inert collagen fibers replacing excitable cardiac tissue. This is particularly useful when the scarring occurs in regions remote from the endocardium that are not detected by bipolar electrograms. Studies from our laboratory demonstrate that endocardial unipolar signals of less than 8.3 mV in the LV and less than 5.5 mV in the right ventricle (RV) are predictive of epicardial and/or midmyocardial scars (Figures 4, 5). Intra-cardiac echocardiography can also identify the presence of nonendocardial substrates as increased echogenic regions.


diagram

**Figure 3.** Epicardial sinus rhythm bipolar voltage map from a patient with Idiopathic dilated cardiomyopathy (modified postero-anterior view). A patchy area of abnormal bipolar voltage situated at the basal-mid-lateral region of the left ventricle can be seen. Black dots indicate electrograms with late potentials and pink dots represent fractionated electrograms. Examples of abnormal electrograms are presented. ECG tracings are lead V6 and electrograms from the ablation catheter (RF1-2, RF3-4).
Figure 4. Modified left lateral (LL) and inferior (INF) views of the left ventricle from a patient with idiopathic dilated cardiomyopathy. (A, B) Endocardial sinus rhythm bipolar and unipolar voltage maps respectively. (C) Epicardial bipolar voltage map. Purple indicates areas of preserved bipolar voltage (>1.5 mV in A and >1 mV in C) and unipolar voltage (>8.3 mV in B). Red represents dense electroanatomic scars (<0.5 mV). Rainbow colors indicate the border zone. (A) A small endocardial low bipolar voltage located at the basal segment of the left ventricle is observed. (B) A much greater unipolar low-voltage area extending from the mitral valve to the apex and inferiorly suggests an intramural/epicardial scar. (C) Epicardial bipolar voltage map confirms the existence of a large area of abnormal voltage located at the basal and mid-lateral wall.

Figure 5. Right anterior oblique (RAO) and anteroposterior (AP) projections of electroanatomic sinus rhythm voltage maps of the right ventricle from a patient with arrhythmogenic right ventricular cardiomyopathy. Purple represents areas of preserved bipolar voltage (>1.5 mV in A and >1 mV in C) and unipolar voltage (>5.5 mV in B). Red represents dense electroanatomic scars (<0.5 mV in A and C; <3.5 mV in B). Rainbow colors represents the border zone. (A) Basal area of abnormal endocardium. (B) Endocardial unipolar voltage map suggests a much greater area of abnormal epicardium extending up to the pulmonary valve and anteriorly to the apical region. This is subsequently confirmed during epicardial-voltage mapping (C).
s. A review of all 12-lead ECGs, including ICD-stored electrograms, documenting all “clinical” VTs will help regionalize the site of origin of the tachycardia.

At our institution, detailed electroanatomic mapping during sinus rhythm is initially performed to assess the extent of endocardial electrographic abnormality. As discussed earlier, electroanatomic scars are generally defined as confluent regions of bipolar voltage having an amplitude less than 1.5 mV. It should be stressed, however, that this cutoff value was derived from studies in patients without structural heart disease and represents a statistical cutoff for the voltage amplitude value. Of note, this cutoff has not been validated in patients with IDCMI and other NICMs by comparison with pathologic analysis or MRI imaging. Therefore, in addition to electrogram voltage, we pay close attention to electrogram fractionation and late potentials indicative of abnormal slow conduction both within and outside the low-voltage areas. These sites are tagged for later reference (Figure 3).

The analysis of endocardial unipolar voltage maps provides information about the existence of intramural or epicardial scars when confluent regions with unipolar electrograms <8.3 mV in the LV and <5.5 mV in the RV are observed (Figures 4.5).

Ablation Targets and Strategy
After defining the electroanatomical substrate during sinus rhythm, VTs are induced by programmed stimulation. Most tachycardias occurring in patients with NICM are caused by scar-related reentry. Therefore, the same mapping principles that are used for postinfarction tachycardias can be used in NICM VT. If the VT is hemodynamically tolerated, activation mapping is performed in order to identify sites of presystolic activity preceding the QRS onset by at least 40–50 ms. Entrainment with concealed fusion and return cycle length ≤30 ms from the tachycardia cycle length will define the site of origin of the VT. For unstable VT, pacing from low-voltage regions that are used for postinfarction tachycardias can be used in NICM VT. If only a minimal endocardial electrogram abnormality exists and no critical components of the circuits are identified, unipolar voltages maps should be assessed. When confluent regions of low unipolar electrograms suggest the presence of epicardial substrates, epicardial mapping inside the coronary venous system or percutaneous epicardial mapping is performed. As previously discussed, to avoid misinterpretation of low-voltage areas attributable to fat, abnormal electrograms are defined by both voltage information (ie, <1.0 mV) and the presence of electrograms demonstrating fractionation, prolonged duration and/or late potentials.

Prior to ablation, caution should be exercised to avoid phrenic nerve and coronary artery injuries. We perform high output pacing from the intended site of ablation to identify the phrenic nerve, and coronary angiography to identify major coronary arteries located within 10 mm of the selected ablation site. When necessary, the phrenic nerve can be displaced away from the epicardium by inflating a balloon in the pericardial space or by introducing air or saline until phrenic nerve capture is lost or until the blood pressure drops significantly.

At present there is no consensus as to the optimal ablation strategy and lesion set for patients with NICM.43 Our endpoint is noninducibility of all VT with aggressive programmed stimulation. However, this goal is difficult to achieve in all patients with NICM. The overall long-term success rate for VT control varies between 50% and 70%.43,44

**Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)**

ARVC is an inherited myocardial disease characterized by replacement of the myocardium by fibrous and fatty tissue that predisposes to ventricular arrhythmias and sudden cardiac death. Familial aggregation occurs in up to 50% of cases. The disease is most often transmitted either as an autosomal dominant trait with incomplete penetrance (most common) or as an autosomal recessive trait (rare).45,46 VT, occurring in up to 64% of patients,47 usually originates in the RV and exhibits left bundle branch block morphology. Reentry is the predominant mechanism, as suggested by the fact that tachycardias can be initiated by programmed stimulation and that they can be entrained.48

**Anatomic Substrate**
Macroscopically, ARVC is characterized by global RV dilatation, wall thinning, and the presence of ventricular aneurysms. The aneurysms are typically located on the anterior wall of the pulmonary infundibulum, the right ventricular apex, and the inferolateral wall close to the tricuspid valve (the so-called “triangle of dysplasia”).45,47,48 Histologic examination reveals myocyte loss with replacement by fibrofatty tissue. The disease process usually begins in the epicardium or intramural layers and then progresses to the endocardium.49 The LV is affected in up to 76% of cases, with pathologic changes mainly confined to the basolateral and posteroseptal segments.45-47

**Electrophysiologic Substrate**
It has been hypothesized that ARVC is caused by mutations in genes encoding desmosomal proteins.49 Desmosomes are protein complexes located in the intercalated discs and are involved in intercellular mechanical adhesion and electrical conductivity.46 Impaired desmosomal function results in poor mechanical coupling between myocytes, with myocyte detachment and death and secondary fibrofatty infiltration and inflammation.49 In addition, mutations in desmosomal proteins are associated with altered connexin-43 expression and distribution. These structural changes may provide the substrate for the development of ventricular arrhythmias in patients with ARVC.51,52

Remodeling of gap junctions occurs in the initial phases of the disease process, before other significant structural changes, including accumulation of fibrotic and adipose tissue, have developed.53,54 This may explain why in some patients sudden cardiac death is the first manifestation of the disease.55 In later stages, replacement of myocardium by fibrous tissue and development of scars predispose to stable macro-reentrant VT.

Dysplastic regions in the setting of ARVC are manifested as contiguous low-voltage, long-duration electrograms.56 Notably, good correlation has been reported between low-voltage areas delineated by electroanatomic mapping and histopathologic findings of myocyte loss and fibrofatty replacement.56 In fact, electroanatomic mapping is able to detect scars in otherwise concealed forms of ARVC and may improve the accuracy of differential diagnosis between ARVC and other structural heart diseases such as inflammatory cardiomyopathy and idiopathic right ventricular outflow tract tachycardia.56

The endocardial low-voltage abnormalities are adjacent to the tricuspid and/or pulmonic valve and extend for a variable distance toward the apex, involving both the right ventricular wall and to a lesser extent the interventricular septum.57 The apex is typically spared. Scars adjacent to the mitral valve can be observed in patients with left ventricular involvement. Notably, exit sites for VT circuits are situated within regions
of abnormal electrogram voltage, thereby confirming the involvement of these areas in the arrhythmogenic mechanism.

Consistent with pathologic findings suggesting predominantly epicardial/midmyocardial involvement in the disease process, we have noted that the epicardial scar burden is greater than the endocardial scar burden (Figure 5). 58,59 In a series of 18 ARVC patients, Polin et al 59 found that the epicardial low-voltage area was on average 3-fold larger than the corresponding endocardial low-voltage area. The epicardial scar had a predominantly perivalvular distribution that matched the endocardial scar.

This disproportionate epicardial and endocardial involvement is associated with delayed and abnormal impulse propagation and is arrhythmogenic. Haqani et al 60 reported on 18 patients with ARVC; 6 reference patients with no structural heart disease who underwent detailed endocardial and epicardial sinus rhythm electroanatomic mapping were also studied. In the reference patients, epicardial and endocardial activation preceded in a similar fashion, with a small relative time difference suggestive of rapid endocardial to epicardial depolarization. In the ARVC patients, epicardial activation was significantly slower than endocardial activation and occurred in a pattern that appeared to be independent of the pattern of endocardial activation. This suggests delayed epicardial electrical activation and electrical uncoupling between the endocardium and epicardium, conceivably secondary to a significant amount of midmyocardial fibrosis. This finding may explain the propensity of ARVC patients to develop ventricular arrhythmias confined to the epicardium and the need for epicardial mapping and ablation to achieve long-term control of arrhythmia.

Mapping and Ablation

Tachycardias in the setting of ARVC are inducible with programmed stimulation and can be entrained. Reentry involving the regions of abnormal electrograms is the most likely mechanism. Therefore, the same mapping principles discussed for IDCMI can be applied to patients with ARVC.

Most VT sites of origin cluster within the low-voltage pericricuspid and/or peripulmonic region, usually within 2–3 cm of the valve's orifice. 46 In patients with larger scars, the VT can exit toward the apical extent of the scar, but still within the region of abnormal electrogram voltage. Therefore these regions are initially targeted by activation, entrainment and pace mapping.

Activation and entrainment mapping can be used in hemodynamically stable VT. Presystolic activity at the earliest activated site usually precedes the QRS by at least 30–50 ms. 46,55 Its participation in the reentry circuit should be confirmed by entrainment. In patients with noninducible or untolerated VTs, substrate mapping and pace mapping can be used to delineate the region of low-voltage electrogram and then to identify putative components of the reentry circuits.

The acute success rate of ablation ranges in different studies between 50% and 90%. 55 The variable outcome reported in different reports can be attributed to differences in mapping techniques, endpoints and operator experience. Overall, substrate-based approaches are associated with better acute and long-term success rates, a finding that has been attributed to the patchy distribution of the scar harboring multiple regions of slow conduction. 55

As discussed before, because of the more extensive epicardial than endocardial substrate, a more aggressive ablation approach targeting both the epicardium and endocardium is oftentimes required. In a series of 13 consecutive ARVC patients who had previously undergone unsuccessful endocardial ablation, repeat ablation targeting epicardial circuits was associated with a long-term success rate of 77%. 58 Of note, the areas targeted by ablation in that study were situated opposite normal endocardium in 77% of patients, sometimes separated by more than 1 cm from the opposite endocardial surface. This thickening, together with the presence of midmyocardial scarring, may explain why endocardial-only ablation was not effective during the index ablation procedure. This concept is further supported by the results of a study reported by Bai et al 59 in which 49 patients with ARVC were assigned to either endocardial-only or combined endocardial and epicardial ablation approach. After a follow of 3 years, 52% and 85% of patients, respectively, were free of VT recurrence and did not receive ICD therapy. Of note, 22% and 69% patients, respectively, ceased antiarrhythmic drug therapy. Collectively, these data clearly indicate that combined endocardial and epicardial ablation is associated with better long-term results in terms of freedom from arrhythmia recurrence.

Cardiac Sarcoidosis

Sarcoidosis is a multisystem inflammatory disease of unknown etiology characterized by the formation of noncaseating granulomas. 44 The heart is the third most commonly affected organ, after the lungs and the thoracic lymph nodes. 45 Clinically overt cardiac sarcoidosis occurs in 5% of patients with systemic sarcoidosis. 44,62 Based on autopsy data, however, cardiac involvement ranges from 27% to 58% of patients. 52–54 The clinical presentation depends on the location, extent and activity of the disease process and includes conduction abnormalities, arrhythmias, and congestive heart failure. 46 Patients with cardiac sarcoidosis are at increased risk of sudden cardiac death, which occurs secondary to bradyarrhythmias and ventricular tachyarrhythmias. 66

Anatomic Substrate

The inflammatory process is initiated in the myocardium with the formation of epithelioid cell granulomas and later extends towards the epicardium and endocardium. 44,67 The lesions are distributed in a patchy fashion and involve predominantly the basal left ventricular free wall and the basal interventricular septum. 58,69 The papillary muscles, the RV, and the atria may also be involved. 70,71 Three histological stages have been described: edema, granulomatous infiltration and fibrosis with scarring. 62 Consistent with the pathologic findings, MRI studies report regions of hyperenhancement predominantly distributed toward the base of the heart, either transmurally or epicardially. 68,72

Electrophysiologic Substrate

VT can be the first event before other clinical manifestations are apparent. 72 The tachycardias have a reentrant mechanism, as suggested by the fact that they can be initiated with programmed stimulation and can be entrained. 72 Multiple tachycardias are commonly observed in the same patient. Confluent endocardial and/or epicardial regions of low-amplitude electrograms have been reported in both the left and the right ventricles in all patients with monomorphic VT. 72,73 In addition, isolated potentials can be recorded during sinus rhythm at effective ablation sites. 37,73 Most VT circuits in the RV are located in proximity to the tricuspid and/or pulmonic annuli, consistent with the predominantly basal ventricular involvement observed in both pathologic and imaging studies. 73 The involvement of the interventricular septum appears more common than in patients with ARVC. Frequently, however, there is significant
overlap and many patients with sarcoid will fulfill task force criteria for ARVC.

Mapping and Ablation
Arrhythmias in patients with cardiac sarcoidosis are often difficult to control by pharmacologic therapy only. In a study by Jefic et al.\(^{23}\) of 42 patients with cardiac sarcoidosis, 21 (50%) developed ventricular arrhythmias, 9 of whom (43%) did not respond to immunosuppressive or antiarrhythmic drugs. Therefore, many patients will require adjunctive catheter ablation in addition to ICD implantation. Most tachycardias are caused by scar-dependent reentry and, therefore, mapping relies on substrate mapping, activation mapping, entrainment and pace mapping as described for arrhythmias in patients with dilated cardiomyopathy. In the studies by Koplan et al.\(^{22}\) and Jefic et al.,\(^{23}\) the medium term success rate was 25% and 56%, respectively. Jefic et al also reported a significant reduction in the number of VT episodes in patients with arrhythmia recurrence after ablation.\(^{23}\)

Chagas Cardiomyopathy
Chagas disease is caused by infection with the protozoan parasite Trypanosoma cruzi. It is estimated that approximately 10 million people are infected with Chagas disease worldwide, primarily in Latin America, and that 25 million are at risk of contracting the disease.\(^{7,24,25}\) Most of the acute infections are subclinical with either no symptoms or a relatively mild and nonspecific febrile illness that resolves spontaneously in 4–8 weeks. Most patients remain asymptomatic for a variable period of time lasting from several months to their entire lifetime.\(^{26}\) In some patients, subclinical cardiac involvement can be demonstrated as regional LV wall abnormalities and areas of cardiac fibrosis on echocardiography and cardiac MRI.\(^{35,77}\) Between 10–40% of the patients will develop chronic symptoms from involvement of various organs, mainly the heart and digestive system.\(^{77}\) Chronic chagasic cardiomyopathy, the most severe manifestation of Chagas disease, is one of the most arrhythmogenic cardiomyopathies.\(^{77}\) Sudden cardiac death, usually because of VT and ventricular fibrillation, occurs in 51–65% of patients.\(^{44}\)

Anatomic Substrate
Macroscopically, chagasic cardiomyopathy is characterized by segmental wall motion abnormalities in the inferolateral segment of the LV and aneurysms.\(^{44}\) The most characteristic lesion is ventricular apical aneurysm.\(^{78}\) Histologic examination reveals inflammatory infiltrates, variable degrees of cellular damage and marked reparative fibrosis.\(^{79,80}\) Fibrosis is distributed predominantly in the epicardium.\(^{84}\) Surviving myocardial fibers can be observed distributed in a random fashion within the areas of fibrosis.\(^{84}\) Myocardial damage and fibrosis most frequently occur at the apex, the basal inferolateral wall, in the posterior left ventricular wall, and in the conduction system.\(^{43,82}\) VTs are often reported to often originate in these regions, but similar to other NICMs, most arrhythmias appear to be associated with a perivalvular substrate.\(^{81,83}\)

Electrophysiologic Substrate
Similar to other NICMs, VTs in Chagas disease can be reproducibly induced with programmed stimulation and can be entrained,\(^{81}\) which suggests reentry as the underlying electrophysiologic mechanism. As previously mentioned, the tachycardias arise from regions of fibrosis, most frequently from the basal antero- and inferolateral segments of the LV. Electrograms recorded in this region often demonstrate fractionation and late components as well as early and/or continuous diastolic activity during tachycardia.\(^{81}\)

A high prevalence of epicardial VT exists in Chagas disease. Electroanatomic studies demonstrate low-voltage areas consistent with scars in all patients with VT, with >80% of patients presenting with larger epicardial than endocardial scars.\(^{84}\)

Mapping and Ablation
The tachycardias are caused by reentry and therefore the mapping technique described in patients with IDCM can be used in patients with Chagas disease. Limited data exist on ablation in patients with Chagas cardiomyopathy. The initial attempts at endocardial ablation were associated with disappointing results. D’Avila\(^{85}\) reported on a series of 24 consecutive patients who underwent endocardial ablation between 1991 and 1996. After an average of 26 months of follow-up, only 17% of patients remained VT-free. In 1996 Sosa et al pioneered the technique of percutaneous epicardial access and catheter ablation in patients with Chagas cardiomyopathy; 2 years later the same group described the results of a combined endocardial and epicardial mapping and ablation approach in 10 patients with Chagas disease and recurrent VT.\(^{86}\) In total, 18 different tachycardias could be induced, 14 of which were categorized as having an epicardial origin based on activation and entrainment mapping. With regard to treatment, 6 patients underwent epicardial ablation guided by epicardial mapping and 4 patients underwent endocardial ablation guided by epicardial mapping. The earliest activation site during VT was more frequently situated on the epicardium. In addition, epicardial mid-diastolic and continuous electrical activity were noted in all patients. Patients who underwent epicardial ablation had no recurrences during follow-up of 5–9 months. In contrast, 2 patients who underwent endocardial ablation had VT recurrences during follow-up. These limited data suggest that the arrhythmogenic substrate in patients with Chagas cardiomyopathy and VT is often located in the epicardium and that epicardial mapping and ablation should be considered as the initial ablation strategy.

Conclusions and Future Directions
The substrate of VT in the setting of NICM is uniquely distributed. Nonischemic VTs originate in regions of low-voltage fractionated electrograms. These electrographic abnormalities are consistent with scarring and are typically distributed in the basal perivascular segments of the left and right ventricles. The fibrotic areas predominantly involve the epicardium/midmyocardium in some patients and the endocardium in other patients. Approximately 30% of VTs involve the epicardium.\(^{46}\) Larger epicardial than endocardial scars have been observed in patients with epicardial VT. Although ablation has emerged as an important therapeutic option in patients with NICM, it is generally less successful than in patients with ischemic VTs because of the midmyocardial nature of the scars. New catheter technology allowing for the creation of deeper ablation lesions that could interrupt intramural reentry circuits, integration of real-time cardiac MRI reconstruction of scar architecture, and more efficient methods of monitoring the contact between the ablation catheter and the myocardium might improve the acute and long-term success rates of ablation in patients with NICM.\(^{86}\)

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Disclosures

None.

References


