

Advanced management of ventricular arrhythmias in chronic Chagas cardiomyopathy



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Chagas cardiomyopathy is a parasitic infection caused by *Trypanosoma cruzi*. Structural and functional abnormalities are the result of direct myocardial damage by the parasite, immunological reactions, dysautonomia, and microvascular alterations. Chronic Chagas cardiomyopathy (CCC) is the most serious and important manifestation of the disease, affecting up to 30% of patients in the chronic phase. It results in heart failure, arrhythmias, thromboembolism, and sudden cardiac death. As in other cardiomyopathies, scar-related reentry frequently results in ventricular tachycardia (VT). The scars typically are located in the inferior and lateral aspects of the left ventricle close to the mitral annulus extending from endocardium to epicardium. The scars may be more prominent in the epicardium than in the endocardium, so epicardial mapping and ablation frequently are required. Identification of late potentials during sinus rhythm and mid-diastolic potentials during hemodynamically tolerated VT are the main targets for ablation.

High-density mapping during sinus rhythm can identify late isochronal regions that are then targeted for ablation. Preablation cardiac magnetic resonance imaging with late enhancement can identify potential areas of arrhythmogenesis. Therapeutic alternatives for VT management include antiarrhythmic drugs and modulation of the cardiac autonomic nervous system.

KEY WORDS Antiarrhythmic treatment; Cardiomyopathy; Catheter ablation; Chagas disease; Endo-epicardial approach; Implantable cardioverter-defibrillator; Neuraxial modulation; Ventricular tachycardia

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Introduction and epidemiology

Chagas disease is a zoonosis caused by the parasite *Trypanosoma cruzi*, which is transmitted to humans mainly by triatomine insects. Other less common routes of infection include oral transmission, transfusion of contaminated blood products, organ transplantation, and during delivery. The disease is endemic in South and Central America. Its prevalence is approximately 6–7 million individuals, resulting in 21,000 deaths each year.^{1,2} It is currently an emerging health problem in countries such as the United States, Europe, Japan, and Australia, mainly due to global migration. In addition, autochthonous vector transmissions of *T. cruzi* in the southern states of the United States has been documented in several cases.^{3–5} Chronic Chagas cardiomyopathy (CCC) develops in up to 30% of patients in the chronic phase and can lead

to heart failure (HF), arrhythmias, thromboembolism, and sudden cardiac death (SCD).^{6–11} Globally, CCC is the most common cause of dilated cardiomyopathy not related to coronary or valvular disease. The purpose of this article is to review CCC-related ventricular arrhythmias.

Pathogenesis of Chagas cardiomyopathy

The pathogenic mechanisms involved in CCC include direct myocardial damage by the parasite, immunological alterations, dysautonomia, and microvascular lesions.^{12,13} The current consensus is that persistence of *T. cruzi* is directly related to cell death and the induced immune response. For this reason, CCC is considered an acquired inflammatory cardiomyopathy in which the parasite load is directly related to the intensity of the inflammation and the severity of the disease.^{5,14} A mechanism of molecular mimicry between parasite epitopes and host antigens favors a crossover autoimmune response. Chronic *T. cruzi* infection causes direct autonomic nerve damage, leading to neuronal loss

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KEY FINDINGS

- A high index of clinical suspicion is required to detect chronic Chagas cardiomyopathy in patients with ventricular tachycardia (VT) of uncertain etiology in endemic and nonendemic regions.
- Patients with drug-refractory VT and/or electrical storm can benefit from catheter ablation.
- A combined endo-epicardial approach in these patients reduces the recurrence of VT.
- Neuraxial modulation and cardiac surgical denervation can be of potential benefit in patients with VT recurrence after ablation.

with parasympathetic denervation and myocardial remodeling.^{5,8,15–18} Perivascular inflammation in patients with CCC can cause structural and functional changes in the microvasculature, resulting in vasospasm, focal ischemia, increased platelet aggregation, thrombus formation, and increased expression of endothelin-1 and thromboxane A₂. Microvascular alterations and lack of arteriolar contraction due to inflammation-induced vasodilator substances lead to impaired myocardial perfusion in distal areas of the coronary branches, resulting in tissue death, the presence of segmental disorders of contractility, scar formation, and repolarization abnormalities in the electrocardiogram (ECG).^{19–26}

Pathophysiology of arrhythmias in Chagas cardiomyopathy

It is well established that the mechanism of sustained ventricular tachycardia (VT) in CCC is scar-related reentry.^{27–29} The main arrhythmogenic substrates in CCC are necrotic and fibrotic lesions secondary to chronic myocarditis.^{5,14} The inflammatory process results in dense scars within which some surviving myocytes are arranged. These changes cause alterations in the electrical coupling that result in slow conduction, unidirectional block, and development of reentrant circuits.^{30–32} Coexistence of denervated with hypernervated areas in the injured myocardium could result in ventricular arrhythmias and SCD during sympathetic activation.^{33,34} In some patients, the presence of surviving myocardium between the mitral valve and scar area can behave as a conducting isthmus, allowing the development of a macroreentrant circuit.³⁵

The left ventricle (LV) is the site of origin of sustained VT in more than 90% of cases. The main arrhythmic substrate of the LV is located in the basal inferolateral region in approximately 70%–82% of patients and in the apical region. This may be the result of ischemia caused by low coronary distal perfusion pressure.^{36–38}

An interesting feature of CCC is that myocardial scars tend to be larger in the epicardium compared to the endocardium, and many patients have a high prevalence of

epicardial circuits. In 1 study, electroanatomical mapping showed larger low-voltage areas on the epicardial surface compared to the endocardium ($112 \pm 74 \text{ cm}^2$ vs $61 \pm 22 \text{ cm}^2$; $P = .01$), with 82% of patients having larger epicardial scars.^{27–29}

Diagnostic evaluation of ventricular arrhythmias in Chagas cardiomyopathy

CCC may be associated with certain characteristics useful in the differential diagnosis with other cardiomyopathies that could help improve detection in patients with VT of uncertain etiology. Table 1 summarizes the clinical characteristics that increase the index of suspicion for CCC in patients with ventricular arrhythmias.^{5,39–41}

ECG

The ECG is a useful tool for screening patients for CCC due to its high sensitivity (83%) and negative predictive value (96%).⁴² The test is inexpensive, is available worldwide, and together with the clinical evaluation represents the first step to the evaluation of these patients.

The most frequent abnormalities are right bundle branch block, left anterior fascicular block, polymorphic premature ventricular complexes, and abnormal ventricular repolarization. In addition, sinus nodal dysfunction, atrioventricular block, and atrial fibrillation are frequently observed. As expected, the prevalence of ECG abnormalities varies according to the population studied.^{43,44} Abnormalities in the intraventricular conduction system are a marker of myocardial damage in Chagas disease. Nevertheless, it is important to clarify that no single ECG finding is pathognomonic for CCC. The right bundle is more sensitive to damage because of its length and therefore is the most frequently affected, followed by the anterior division of the left bundle (Figure 1). Hence, right bundle branch block is the most prevalent and specific ECG abnormality when found in individuals with Chagas disease, with a positive predictive value of 80.77% (95% confidence interval [CI] 78.17–83.13).^{43,45,46}

A normal ECG, of course, does not exclude myocardial damage. Intravenous administration of ajmaline can unmask latent conduction disturbances in one-third of patients with Chagas disease without evidence of cardiac involvement.⁴⁷ However, observational studies have shown that people with normal ECG and positive Chagas disease serology have a good prognosis after 5 to 10 years of follow-up.^{48,49} Finding *de novo* abnormalities on the ECG helps to identify patients with reduced LV ejection fraction. The duration of the QRS complex is also directly related to ventricular size and is inversely proportional to LV ejection fraction. The greater the number of ECG alterations found in the same patient, the greater the myocardial involvement and the worse the prognosis.^{5,50,51} The increase in the duration of the QRS complex or the development of new ECG changes are sufficient reasons to re-evaluate ventricular function.⁵²

Holter ECG monitoring

Documentation of premature ventricular contractions is a common finding (10%–55%) in patients with CCC. Its presence is attributed to myocardial damage and is correlated with the recording of late potentials in the signal-averaged ECG. In patients with CCC having abnormal resting ECG and HF, premature ventricular contractions are observed in up to 99%, which can be polymorphic (87%) and manifest with repetitive phenomena such as duplets or in episodes of nonsustained ventricular tachycardia (NSVT).^{50,53}

Magnetic nuclear resonance

Cardiac magnetic resonance imaging (MRI) provides excellent spatial resolution useful for recognizing structural cardiac changes not identified by other imaging techniques. Furthermore, the use of late gadolinium enhancement can identify the presence of areas of fibrosis and edema, even in indeterminate cases (Figure 2). The extent of myocardial fibrosis is directly correlated with the severity of the disease and inversely with LV ejection fraction.^{54–56} MRI makes it possible to precisely delineate the dense scar and visualize the corridors of viable tissue that may support VT.⁵⁷ Patients with ≥ 2 contiguous segments of transmural fibrosis are more likely to have VT (relative risk [RR] 4.1; $P = .04$).^{56,58} For their identification, special image processing software has been implemented, which includes MRI and computed tomography (Figure 3). Finally, the presence and area of the scar are strong predictors of VT and mortality.⁵⁹

Electrophysiological study

An electrophysiological study is indicated in symptomatic patients, in those with conduction abnormalities or VT, or in patients with reduced LV function. Patients with conduction disturbances in the ECG, compromised ventricular function, or ventricular aneurysms are more likely to have inducible VT during the study.⁶⁰

CCC and risk of SCD

The severity of ventricular arrhythmias in CCC usually are related to the degree of ventricular dysfunction; however, they also can be found in patients with preserved ventricular function, constituting an “isolated arrhythmogenic form” of the disease.⁶¹ This feature distinguishes CCC from other forms of heart diseases and explains why these patients are more susceptible to early SCD.^{5,12}

MRIs with late enhancement have shown that the severity of ventricular arrhythmias correlate with the presence of scars and fibrosis.^{54,56} In addition, regional sympathetic denervation as observed with ¹²³I-metaiodobenzylguanidine identifies an arrhythmogenic substrate.^{62,63}

SCD is considered the main cause of mortality in patients with CCC and can account for 55%–65% of cases.^{5,12,64} More recently, observational studies suggest a reduction in mortality with the use of beta-blockers.^{65,66}

Table 1 Clinical features that increase the index of suspicion for chronic Chagas heart disease in patients with ventricular arrhythmias

Demographic
Predominantly male
Age at diagnosis: 30–50 y
Epidemiological background
Origin or childhood residence in Latin America
Children of mothers from endemic zones
Travelers who spend time in endemic areas
Blood transfusion (recipient of organ transplant)
Concomitant clinical manifestations
Palpitations, syncope, thoracic pain
Thromboembolic events
Biventricular or predominantly right ventricular dysfunction
Compromise of other systems
Megacolon
Megaesophagus
Common ECG abnormalities
RBBB \pm LAFB
Frequent polymorphic premature ventricular contractions
NSVT
ST-T changes (mimicking ischemic heart disease)
Abnormal Q waves
Atrioventricular block
Sinus nodal dysfunction
Atrial fibrillation
Common echocardiographic findings
Left ventricular aneurysm in the apex or inferolateral wall
Dilated cardiomyopathy
Segmental abnormalities of myocardial contraction.
Right ventricular enlargement with reduced contractility
Mural thrombus
Cardiac magnetic resonance imaging
Late apical and inferolateral enhancement
Dilated cardiomyopathy \pm ventricular perfusion defects/ segmental abnormalities of myocardial contraction
Findings in perfusion scintigraphy
Perfusion defects without significant coronary artery obstruction

ECG = electrocardiography; LAFB = left anterior fascicular block; NSVT = nonsustained ventricular tachycardia; RBBB = right bundle branch block.

Treatment and prognosis

Benznidazole and nifurtimox are the only antitrypanosomal drugs with proven efficacy. In accordance with the 2018 American Heart Association Scientific Statement on Chagas Cardiomyopathy, benznidazole is the first-line treatment because it has better tolerance, is more widely available, and is the best studied drug. Treatment is indicated in all patients with acute Chagas disease as soon as parasitological or serological confirmation is obtained, with parasite elimination and cure achieved in 60% to 90%. Success is high in cases of congenital transmission, achieved in >90% of infants treated during the first year of life.^{5,67–69} The role and efficacy of these medications in CCC are less certain. Trypanocidal treatment in patients with established Chagas cardiomyopathy was assessed in the landmark BENEFIT (BENZnidazole Evaluation For Interrupting Trypanosomiasis) trial. The study randomized 2854 patients from 5 endemic countries in Central and South America to benznidazole or placebo. After mean follow-up of 5.4 years, a clear reduction in parasite detected by

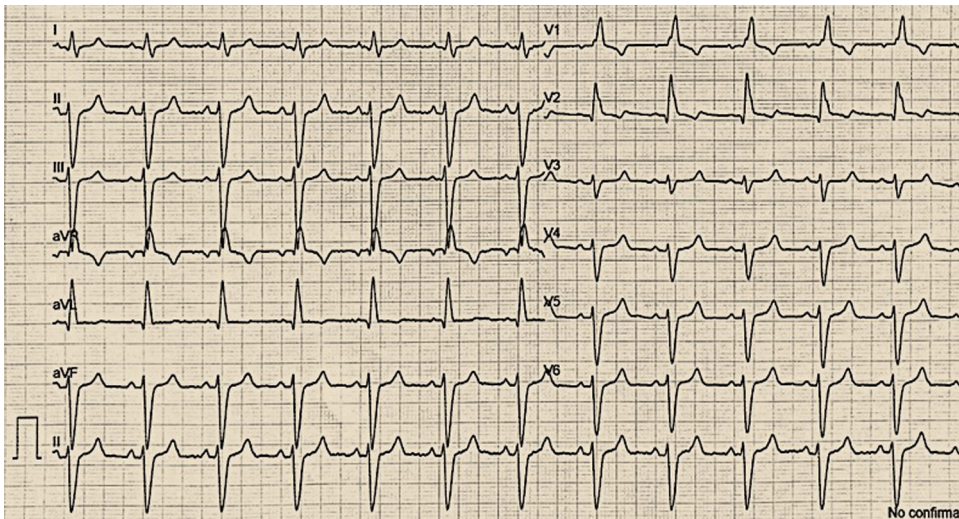


Figure 1 Electrocardiogram of a patient with chronic Chagas cardiomyopathy showing a right bundle branch block and a left anterior fascicular block.

polymerase chain reaction was documented; however, there was no difference in the primary composite outcome, which included death, HF, and other clinically relevant cardiovascular events.⁷⁰ Comparative data from observational studies suggest that the prognosis of patients with HF due to CCC is less favorable and the mortality rate higher than in patients with other etiologies of HF.^{71,72} In CCC, all-cause mortality at 1, 5, and 10 years of follow-up is estimated at 12%, 35%, and 60%, respectively. As mentioned in the section on [CCC and risk of SCD](#), in up to 65% of patients the final event is

related to SCD, 25%–30% to progressive HF, and 10%–15% to stroke. The main risk factors associated with mortality are VT, HF, LV dilation, and/or systolic dysfunction.⁷³ Different variables related to the risk of death have been evaluated in patients with CCC. In a study conducted in 424 patients with CCC using a separate validation cohort of 153 patients, 6 predictors were identified and are now part of the Rassi score: New York Heart Association (NYHA) functional class III or IV (5 points); cardiomegaly (5 points); segmental or global LV systolic dysfunction on

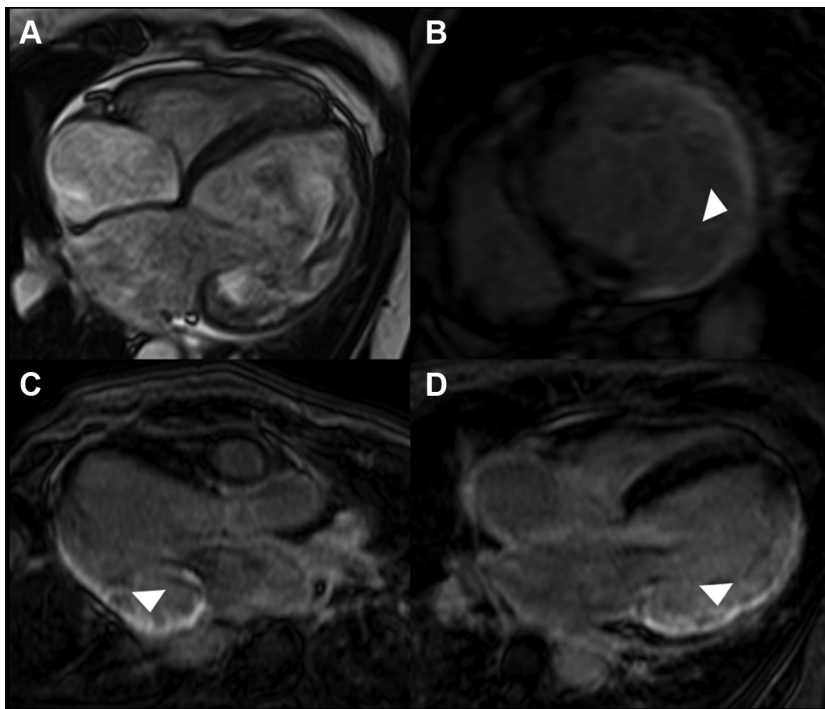


Figure 2 Cardiac magnetic resonance imaging (MRI) in a patient with chronic Chagas cardiomyopathy. **A:** An enlarged left ventricle can be seen in cine MRI sequence. After administration of gadolinium, the presence of late enhancement with transmural extension is observed in the short (**B**), long parasternal (**C**), and four-chamber (**D**) axes, indicating the presence of fibrosis at the level of the anterior wall, in the middle and basal segments of the inferolateral and anterolateral walls, and in the basal segment of the inferior wall (arrows).

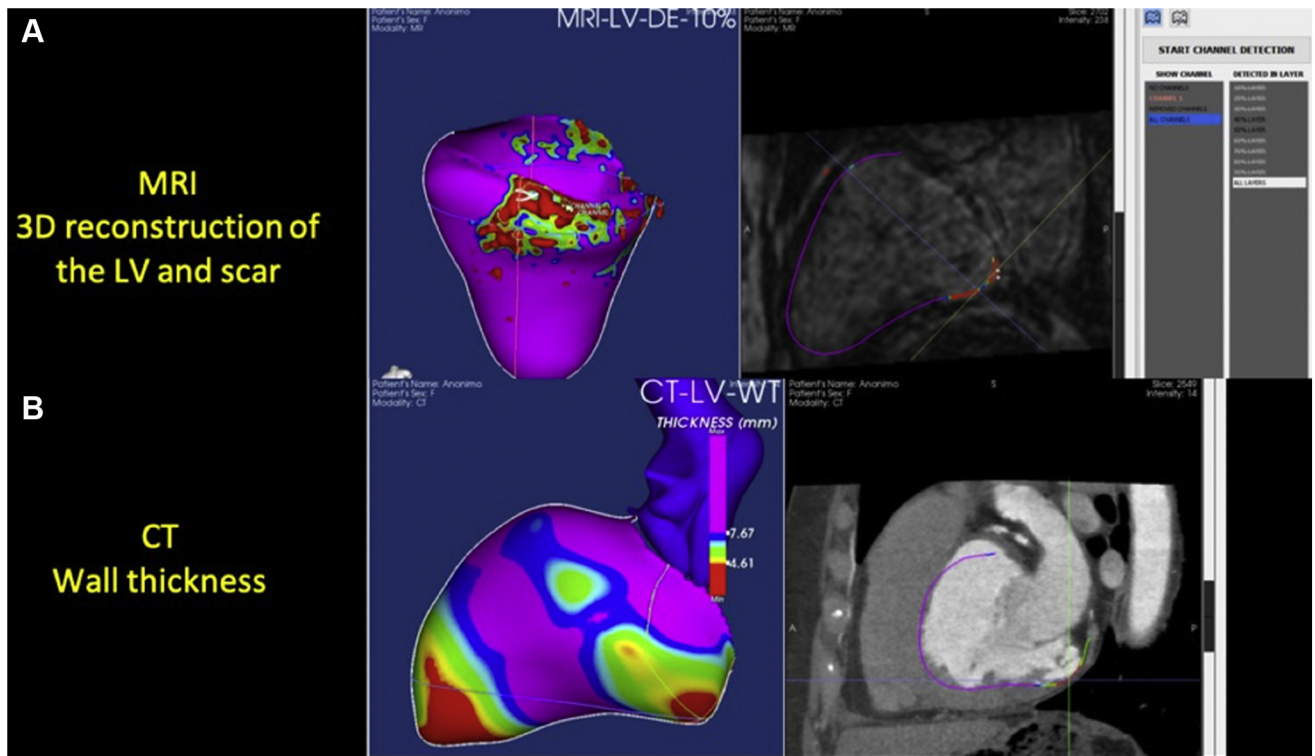


Figure 3 Three-dimensional (3D) reconstruction of the left ventricle (LV) by magnetic resonance imaging (MRI) and cardiac computed tomography (CT) in a 59-year-old patient with chronic Chagas cardiomyopathy. **A:** Signal intensity map obtained by cardiac MRI. Contrast at the subendocardial level is observed, identifying the cicatricial and transition regions at the posterobasal level. Coding of signal intensity: normal myocardium is purple; nucleus of the scar area is red; and border area is blue-green-yellow. **B:** Automatic 5-layer creation of LV wall thickness as seen by CT. The thinner areas (red) are located in the posterobasal and apical region of the left ventricle. The thickest regions are shown in purple.

echocardiogram (3 points); NSVT on 24-hour Holter or stress test (3 points); low QRS voltage on 12-lead ECG (voltage in each limb lead ≤ 0.5 mV) (2 points); and male gender (2 points). With the resulting score, patients are classified into 3 groups: low risk (0–6 points); intermediate risk (7–11 points); and high risk (12–20 points). Five-year mortality in these groups is 2%, 18%, and 63%, respectively.⁷⁴ Subsequently, Ribeiro et al⁵³ developed a predictive score made up of 3 risk factors: reduced ejection fraction, VT, and prolonged filtered QRS complex. The score showed optimal discrimination to identify patients at low, moderate, and high risk of death, comparable to the score by Rassi et al.⁷³ Subsequently, de Souza et al⁷⁵ developed a risk score for SCD, based on 4 risk factors encompassing premature ventricular complexes, severe LV dysfunction, syncope, and QT dispersion by ECG. The score demonstrated good performance in predicting the risk of SCD, which is the most common cause of death overall in patients with Chagas disease.⁷⁵ A simple scale recently published for predicting 2-year mortality risk in Chagas cardiomyopathy is the SaMI-TROP (São Paulo-Minas Gerais Tropical Medicine Research Center) score, which was developed and validated to be used in remote areas with limited technological resources. The score includes abnormal N-terminal pro-B-type natriuretic peptide (NT-proBNP) (55 points); QRS duration ≥ 150 ms (15 points); NYHA functional class higher than I (15 points); age (per 10 years); and heart rate ≥ 80 bpm (20 points). Abnormal NT-proBNP adjusted by age was the strongest

predictor of death. A low-risk score was set as a predicted probability of dying in 2 years $< 2\%$ (< 50 points); intermediate risk was $\geq 2\%$ to 10% (50–100 points), and the high-risk category had predicted risk of $> 10\%$ (> 100 points).⁷⁶

Antiarrhythmic treatment

Recommendations for antiarrhythmic management in patients with CCC are based on observational data and are extrapolated from the results of studies in the management of cardiac diseases of other etiologies. Because ventricular arrhythmias in CCC usually are related to the presence of HF, optimal pharmacologic management of this clinical condition is essential.⁷⁷ Amiodarone has been the most widely used drug for its multiple antiarrhythmic effects and its best safety profile in ventricular dysfunction. Furthermore, it has been attributed an apparent trypanocidal effect that may increase its efficacy.^{78–80} However, its potential toxicity must be taken into account, which includes liver injury, hypothyroidism or hyperthyroidism, and pulmonary toxicity.⁸¹ This drug is considered a therapeutic adjunct in patients with CCC who have an implantable cardioverter-defibrillator (ICD) with a history of recurrent VT.^{5,82,83}

ICDs and Chagas cardiomyopathy

Patients with Chagas heart disease experience a higher rate of malignant ventricular arrhythmia and resultant SCD than other populations with dilated cardiomyopathy matched by

ventricular dysfunction.^{50,84} However, data supporting the use of ICDs for the treatment of patients with CCC are limited. Regarding the use of the ICD as a primary prevention strategy in patients with Chagas cardiomyopathy, there is no solid evidence based on randomized studies supporting its indication. Even when NSVT has been identified as an independent predictor of all-cause mortality and SCD in patients with CCC having LVEF between 30% to 50%, there is no clear guideline on the best strategy to follow. In this context, the prognostic role of programmed ventricular stimulation has been studied, and a significant association between inducible sustained VT and SCD has been found. Nevertheless, it is worth noting that in this study, all patients with induced sustained VT were treated with amiodarone.⁸⁵ Although the use of ICDs has been recommended in patients with CCC and LVEF <40%,⁸⁶ a significant number of SCD occurs in patients with LVEF > 40%, and in these subjects there is no adequate way to establish their risk. Programmed ventricular stimulation may be an option, but new and larger studies are needed. The CHAGASICS trial (CHronic use of Amiodarone aGAINSt Implantable cardioverter-defibrillator therapy for primary prevention of death in patients with Chagas cardiomyopathy Study) currently is underway to compare the use of amiodarone vs ICD implantation as a primary prevention strategy in patients with CCC.⁸⁷

The indication for ICD as a secondary prevention strategy does not differ from that established for other pathologies. According to the 2018 American Heart Association Scientific Statement on Chagas Cardiomyopathy, specific scenarios in which there is consensus on the benefit of ICD insertion for secondary prevention include patients with aborted SCD, spontaneous sustained VT, syncope secondary to VT, and LVEF <35%, as well as a history of syncope and sustained inducible VT during an electrophysiological study.^{5,88}

Patients with CCC tend to present frequent effective ICD shocks due to their increased arrhythmic activity. The number of shocks received can be deleterious, contributing to mortality by inducing myocardial necrosis and promoting or worsening ventricular dysfunction.⁸⁹ Combined administration of amiodarone and beta-blockers has contributed to reducing the number of therapies in other cardiomyopathies and should be considered in patients with CCC who receive frequent ICD shocks.⁸² Antitachycardia pacing strategies represent a safe, effective, and painless therapy for ventricular tachyarrhythmias, with a large body of clinical evidence supporting their routine use in primary and secondary ICD recipients, and could be considered in patients with CCC.⁹⁰ Another recommendation is to perform ablation if possible before implanting an ICD. Other predictors of poor prognosis include LV ejection fraction <30%, age >65 years, and low educational level.¹²

Mapping strategies and catheter ablation of VT

Catheter ablation of VT is indicated in patients with drug-refractory monomorphic VT, those with an electrical storm (ES), and in patients suspected of having a discrete source

of the arrhythmia.^{5,91,92} In a recent study of 38 patients with an ES who underwent catheter ablation, of whom 42.1% had CCC, the procedure was associated with acute ventricular arrhythmia suppression in all patients. Freedom rates from ES and VT were 92.1% and 60.5%, respectively. Older patients and those with lower LVEF had increased mortality. Epicardial access was three times more frequent in patients with CCC (25% vs 7.7%). Patients with CCC were younger (60 vs 67 years; $P = .033$), significantly more were women (50% vs 9.1%; $P = .005$), and had higher LVEF (0.40 vs 0.28; $P < .001$) than the other patients. Long-term outcome of CCC patients was similar to that of the overall population in terms of freedom from VT/ventricular fibrillation (62.5% vs 59.1%; $P = .832$); freedom from ES (93.8% vs 90.9%; $P = .748$); and overall mortality (25% vs 31.8%; $P = .729$).⁹³

During the ablation procedure, a detailed electrophysiological study is required, in combination with high-density 3-dimensional maps (Figure 4). As mentioned in the section on Pathophysiology of arrhythmias in Chagas cardiomyopathy, the areas of fibrosis and scar tend to be located in the apical, inferolateral, and basal regions of the LV (Figure 5), with transmural or subepicardial substrates (Figure 6 and Supplemental Video 1). Occasionally, only an epicardial substrate can be identified. Cutoff values for bipolar voltage maps of both endo- and epicardial surfaces are identical to other forms of cardiomyopathy (bipolar amplitudes <0.5 mV: dense scar; 0.5–1.5 mV: areas of intermediate amplitudes defined as border zone; >1.5 mV: normal myocardium). Unipolar endocardial voltage may indicate an epicardial substrate in CCC patients with normal bipolar endocardial voltage or with a small endocardial scar. Cutoff values of 8.3 mV are used in patients with Chagas disease, similar to that for other cardiomyopathies.^{24,91} In relation to the duration of local electrograms, values >46 ms identify abnormal areas of slow conduction, with sensitivity and specificity of 83% and 86%, respectively.²⁷ Placement of a multipolar electrode catheter in the coronary sinus can facilitate the diagnosis of submitral reentry and epicardial late potentials. As in other cardiomyopathies, the strategy for VT ablation in Chagas disease varies with the number and morphology of induced VTs and their hemodynamic tolerance. When a hemodynamically tolerated VT is induced, the ablation target is mid-diastolic potentials that are part of the reentrant circuit as demonstrated with the entrainment technique. In patients in whom VT cannot be induced or is hemodynamically unstable, late potentials in the region of scar are identified and targeted for ablation and elimination of the reentrant circuits. Differential ventricular pacing can unmask late potentials that may not be obvious in sinus rhythm (Figure 5C). Once the electrograms with delayed components have been identified, a pacemapping strategy can be performed to better identify the critical isthmus and the exit of the circuit.^{24,94} In a recent study, a functional substrate map that examines propagation during sinus rhythm for wavefront discontinuities and conduction slowing was shown to identify regions that are critical for reentry. This novel voltage-independent,

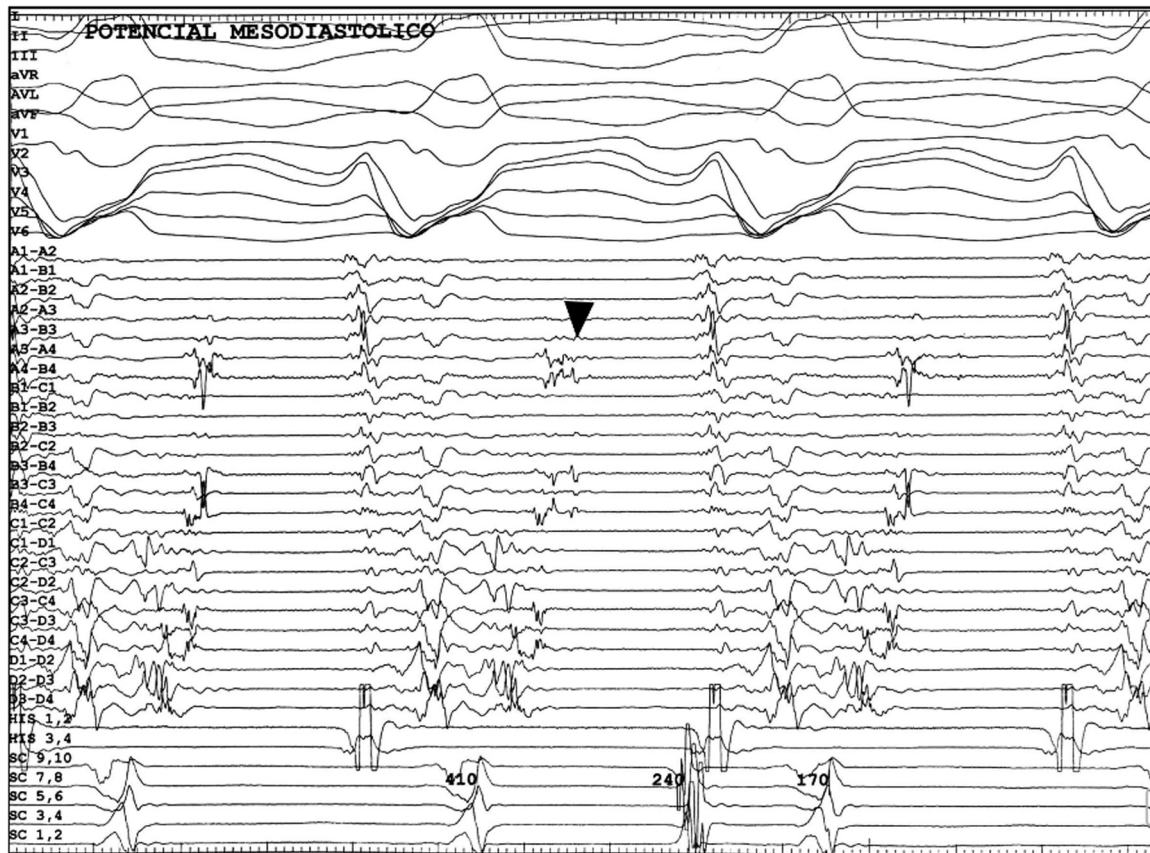


Figure 4 Mid-diastolic endocardial potentials (*arrow*) recorded during ventricular tachycardia with a high-density mapping multipolar electrode catheter. Surface electrocardiogram, coronary sinus (SC), His bundle (HIS), and high-density multipolar electrodes (A, B, C, D, 1–4) are simultaneously displayed.

high-density mapping display can demonstrate the functional substrate for VT during sinus rhythm and guide targeted ablation ([Supplemental Video 2](#)).⁹⁵

Endocardial ablation has remained the initial approach since new developments in catheter ablation technology (ie, open irrigation and contact force sensing), and larger and deeper lesions can be created from the endocardial surface that can reach even an epicardial substrate. However, in some patients, the segmental lesion is intramural, and the circuit is predominantly kept by subepicardial fibers. Therefore, endocardial radiofrequency applications may not reach the intramyocardial and subepicardial fibers involved in the reentrant circuit. The transthoracic epicardial approach has been used since 1995 for mapping and ablation of sustained VT in patients with CCC and subsequently has also been applied in patients with other heart diseases.⁹⁶

Recent studies have shown that a VT ablation strategy with a combined endo-epicardial approach in patients with CCC significantly reduces the recurrence of ventricular arrhythmias, without an increase in perioperative complications when performed by experienced groups ([Figure 6](#)).^{24,27,97–100} In a recent randomized controlled study, the efficacy and safety of an endo-epicardial ablation approach (group 1) vs an endocardial approach (group 2) were evaluated in patients with CCC associated with VT. In group 1, nonreinducibility

of arrhythmia was achieved in 86% compared to 60% in group 2. At follow-up, 40% of patients in group 1 had VT recurrence compared to 80% in group 2. Some patients in group 2 with recurrence due to VT underwent an epicardial approach. There were no differences in the safety of the procedure between the 2 groups.¹⁰¹ During epicardial mapping, it is important to routinely identify areas where stimulation results in capture of the phrenic nerve to better define the substrate modification strategy and avoid phrenic nerve paralysis. Due to the frequent close distribution to the scar region to the circumflex coronary artery and its marginal branches, it is recommended to place the ablation catheter in the area related to the critical isthmus at the level of the epicardium and perform coronary angiography in the left and right anterior oblique projections before proceeding with the ablation. Catheter orientation aiming at the epicardium and not to the parietal pericardium is of critical importance to avoid damage to extracardiac structures.^{24,102,103}

Other therapies

Radiofrequency ablation is one of the strategies used in patients with VT refractory to antiarrhythmic management; however, the success rate and long-term results remain suboptimal. For this reason, it is convenient to have other

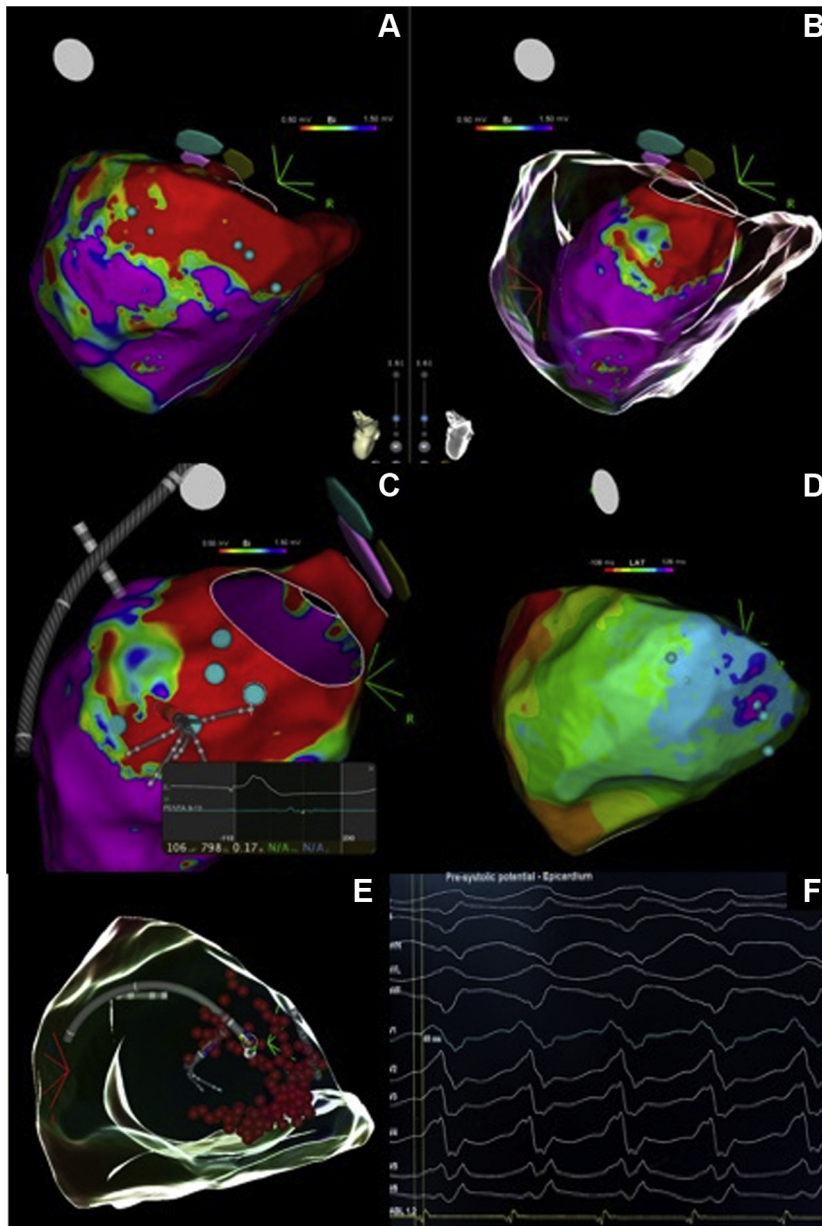


Figure 5 Endo-epicardial electroanatomic voltage map of the left ventricle (LV) in a patient with chronic Chagas cardiomyopathy showing a large basal inferolateral transmurular scar (*red*), larger in the epicardium (**A**) than in the endocardium (**B**). **C**: Endocardial activation mapping during apical right ventricular stimulation demonstrates late potentials (*inset*) located at the posterior and basal region of the LV. **D**: Epicardial isochronal activation map of the LV in the posteroanterior view demonstrating late activation (*purple*) with isochronal crowding in the posterior wall close to the mitral annulus. **E**, **F**: Epicardial mapping and ablation during ventricular tachycardia in the inferolateral region of the LV. Presynaptic potentials are recorded 49 ms before the beginning of the QRS complex during tachycardia.

therapeutic alternatives.^{104,105} One of these strategies is neuraxial modulation, in order to reduce sympathetic tone. One method is thoracic epidural anesthesia that results in block at the T1–T5 level, which is not selective and affects both the afferent and efferent signals. This option usually is utilized as a bridge to definitive measures and can be effective in up to 75%–80% of cases, with a quick onset of action and easy access.^{105,106}

Injection of local anesthetics into the stellate ganglion is available to temporarily block the lower third of the ganglion.

This strategy is acutely effective in up to 90% of cases by reducing sympathetic impulses in the heart and in the head, neck, and diaphragm.¹⁰⁷

Another option is cardiac surgical denervation, a procedure that involves removing the lower part of the stellate ganglion and the T2–T4 nodes.¹⁰⁸

Conclusion

Ventricular arrhythmias are life-threatening complications of CCC and result in increased morbidity and mortality. SCD

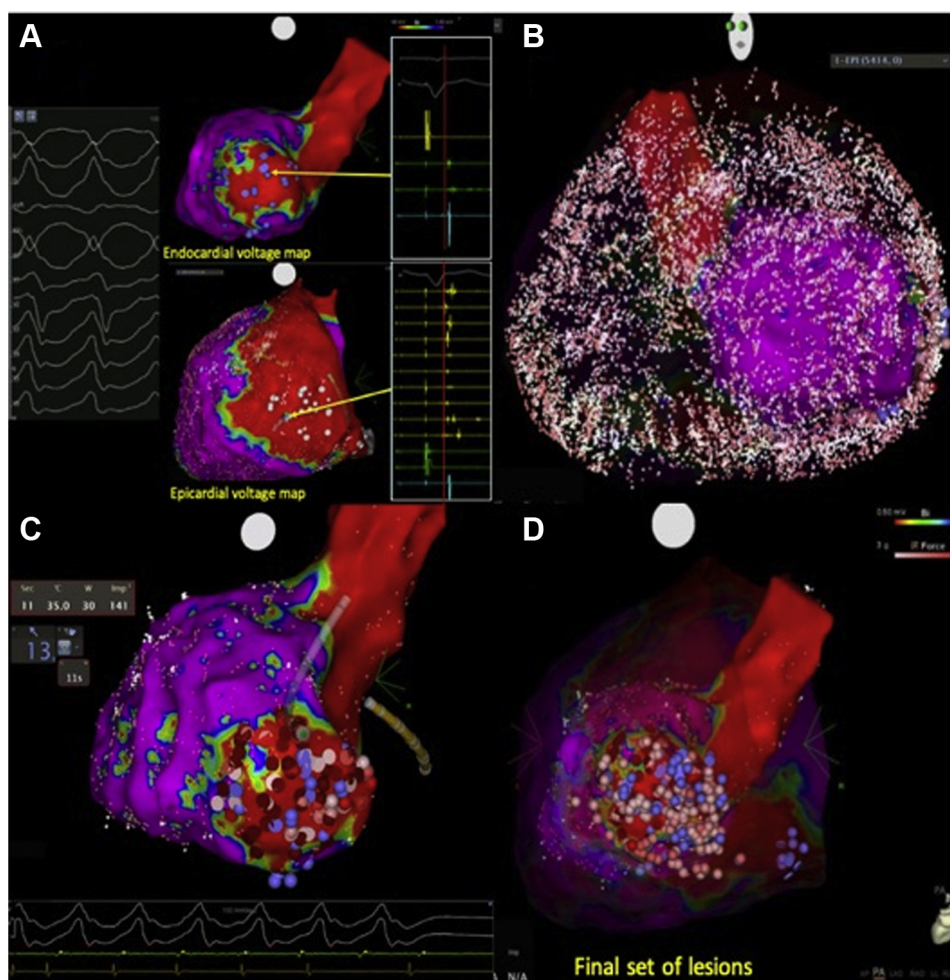


Figure 6 **A:** Endo-epicardial bipolar voltage map in a patient with chronic Chagas cardiomyopathy and ventricular tachycardia. An aneurysm with low voltage and scar (*red*) is observed at the posterobasal region of the left ventricle. Note the greater extension of the scar in its epicardial aspect. Within the scar, late potentials occurring after the end of the QRS complex (*insets*) are observed both in the endocardial aspect (mapping catheter) and in its epicardial aspect (high-density multielectrode catheter). **B:** High-density bipolar epicardial map (5414 points) made with a high-density multielectrode catheter. **C:** Termination of ventricular tachycardia during radiofrequency ablation. **D:** Final set of lesions from the epicardial aspect (*blue, pink, red dots*) delivered at sites with late potentials.

due to malignant ventricular arrhythmias remains a public health problem in Latin America. Due to global migration, CCC is an emerging health problem in other regions. Ventricular arrhythmias are more common with advanced forms of cardiomyopathy, but it also can occur as the first manifestation of cardiac involvement. Identifying high-risk patients who require specific therapies and invasive procedures (ICD implantation, ablative therapies, neuraxial modulation) remains an important challenge in clinical practice. The presence of areas of fibrosis, autonomic dysfunction, and chronic inflammation contribute to the development of VT. An interesting feature of CCC is that fibrosis and scar can be more prominent in the epicardium than in the endocardium. A combined endo-epicardial approach significantly reduces the recurrence of ventricular arrhythmias, without increasing the rates of perioperative complications when performed by experienced groups. Alternative therapies such as neuraxial modulation and cardiac surgical denervation have shown a potential benefit in patients with VT recurrence after ablation.

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Authorship

All authors attest they meet the current ICMJE criteria for authorship.

Appendix Supplementary data

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