Chagas disease, caused by the parasite *Trypanosoma cruzi*, is a serious health problem in Latin America and is an emerging disease in non-endemic countries. In recent decades, the epidemiological profile of the disease has changed due to new patterns of immigration and successful control in its transmission, leading to the urbanization and globalization of the disease. Dilated cardiomyopathy is the most important and severe manifestation of human chronic Chagas disease and is characterized by heart failure, ventricular arrhythmias, heart blocks, thromboembolic phenomena, and sudden death. This article will present an overview of the clinical and epidemiological aspects of Chagas disease. It will focus on several clinical aspects of the disease, such as chronic Chagas disease without detectable cardiac pathology, as well as dysautonomia, some specific features, and the principles of treatment of chronic cardiomyopathy. (J Am Coll Cardiol 2013;62:767–76) © 2013 by the American College of Cardiology Foundation

Chagas disease (ChD) (American trypanosomiasis) is caused by the protozoan *Trypanosoma cruzi*. The disease was described in 1909 by the Brazilian physician Carlos Chagas, who named the parasite in honor of his mentor, Oswaldo Cruz (1). Dilated cardiomyopathy is the most important and severe manifestation of human chronic ChD and is characterized by heart failure, ventricular arrhythmias, heart blocks, thromboembolic phenomena, and sudden death (2). Several epidemiological and clinical aspects of ChD need to be reviewed, such as chronic ChD without detectable cardiac pathology, dysautonomia, and some specific features of chronic cardiomyopathy.

**Epidemiology**

Chagas disease is a zoonosis transmitted primarily through parasite-laden secretions from hematophagous triatomine insects. These insects, which serve as vectors, are present in South and Central America, Mexico, and the southern United States. The disease can also be transmitted through blood transfusions, organ donations, and from mother to child at birth, which are matters of concern in non-endemic regions (3). Oral transmission has recently been recognized as the cause of sporadic, small human outbreaks, mostly in the Amazon region (4). Accidental cases of laboratorial transmission have also been reported (5).

The World Health Organization estimates that 8 to 10 million people are infected worldwide, mostly in Latin America where the disease is endemic (6,7). In recent decades, the epidemiological profile has changed due to migratory movements, which have led to both the urbanization and globalization of the disease (7). Chagas disease was classically associated with poverty in rural areas, because Triatominae species grow in areas of poor housing. The urban migration from rural areas that occurred in Latin America in the 1970s and 1980s has changed the traditional epidemiological pattern of ChD into an urban infection (7). The disease is now observed in cities in the Americas and Europe where immigrants of endemic countries now live (3,8). Although the vector is found in the southern half of the United States, very few cases of insect-transmitted disease have been documented (3). The Centers for Disease Control and Prevention estimates that there are more than 300,000 people infected with *Trypanosoma cruzi* in the United States, and a calculated total of 30,000 to 45,000 individuals likely have undiagnosed Chagas cardiomyopathy (9), considering a conservative proportion of 10% to 15% with clinical disease. Many physicians consider Chagas to be a disease that is restricted to Mexico and Latin America, and this assumption causes general practitioners in the United...
Chagas disease frequently misdiagnosed as idiopathic cardiomyopathy. Similarly, patients with ChD are not aware of their infection and can potentially transmit the parasite through blood or organ donation (3).

**Economic burden of the disease.**

Beyond being a prevalent disease in both Latin America and developed countries, with clinical and epidemiological relevance, ChD is also important due to its economic burden (10,11). The early mortality and substantial disability caused by this disease, which often occurs in the most productive population, young adults, results in a significant economic loss (10). Cardiac and digestive complications frequently lead to the need for long-term treatment and surgical procedures, including pacemaker and implantable cardiac defibrillator insertion and heart transplantation, further increasing the costs related to the disease (12,13).

In Latin American countries, ChD is one of the most costly of the so-called “neglected tropical diseases” (i.e., diseases associated with poverty and neglected by media and policy makers with a major adverse impact on health, well-being, and socioeconomic development in low-income and developing countries) (14). Several studies have demonstrated the economic advantages of the prevention of the disease by vector control programs (13,15), a strategy proven to be effective in collaborative international initiatives in Latin America (16).

As the disease expands beyond Latin America, there is a growing concern with regard to its global economic burden. A recent study estimates global costs of $7.19 billion/year, exceeding many prominent diseases globally, such as cervical cancer and rotaviruses (11). More than 10% of these costs emanate from the United States and Canada, where ChD is not endemic and the disease is not recognized as a significant health problem (11).

**Clinical Aspects**

Chagas disease classically presents in an acute or initial phase, which is followed by a chronic phase that can be categorized into indeterminate, cardiac, or digestive forms with different clinical manifestations (17). Severe acute disease occurs in <1% of patients, and the clinical manifestations include acute myocarditis, pericardial effusion, and/or meningoencephalitis (17,18). The incidence of acute infection has substantially decreased since the near interruption of transmission by vectors and via blood transfusions in most Latin American countries. Acute ChD can also occur due to acute Trypanosoma cruzi transmission to an organ recipient or reactivation of chronic infection related to immunosuppressive states (19).

Once the acute phase subsides, patients enter an indeterminate phase of the disease that is defined by the presence of infection and is confirmed by either serological or parasitological tests; a normal electrocardiogram (ECG); normal radiological examinations of the chest, esophagus, and colon; and the absence of the clinical signs and symptoms of the disease (20,21). In another classification system, patients in this stage have been reported to have chronic ChD with no detectable pathology (22). Most infected people in endemic areas are in this stage of the disease, and approximately 40% of these patients might persist for years in this clinical situation (23). However, most of these patients evolve from an indeterminate to a chronic form, and new ECG abnormalities or evidence of definite cardiopathy developed in 1.8% to 5% of patients each year (20,23,24). Most elderly ChD patients developed ECG abnormalities during the indeterminate form of the disease, which generally predominates in young ChD patients but is rare in elderly persons (25).

Patients with the indeterminate form of the disease have an excellent prognosis, and their life expectancy is similar to individuals without ChD (20,21,23). Nevertheless, some of these patients have abnormal responses when tested by noninvasive cardiac exams (20,21,26–29). However, the prognostic values of these subclinical cardiac abnormalities remain uncertain.

In general, one-third of these patients will develop chronic symptomatic ChD 2 decades after the initial infection (17,30). Clinical presentations of this phase is related to the pathological involvement of specific organs—particularly the heart, esophagus, or colon—which are grouped into 3 major forms of the disease: cardiac; digestive; or cardio-digestive (30,31). Heart disease is the most important clinical aspect of ChD, due to its frequency and severity. The chronic phase lasts throughout life and results in a shortened survival rate (2,32–34).

The myocardium damage in Chagas heart disease is generally a progressive process that can be classified into stages (A, B, C, and D), according to the international recommendations adapted to ChD (35) (Table 1). Those with a normal ECG are considered to have the indeterminate phase of the disease (stage A). The appearance of ECG abnormalities implies disease progression (stage B) and precedes the appearance of symptoms of heart failure (stages C and D). Sudden death can interrupt this course at any time, even before the development of symptoms (in Stage A or B), and death can occur due to progressive heart failure or stroke.

The earliest manifestations of Chagas heart disease are usually conduction system abnormalities, most frequently right-bundle branch block or left anterior fascicular block (36,37), segmental left ventricular (LV) wall motion abnormalities (38) (Figs. 1A and 1B), and diastolic dysfunction (39,40). Dilated cardiomyopathy is the most serious form of the chronic phase of ChD, with high mortality (32–34). It can be manifested by ventricular
dysfunction with heart failure, arrhythmias, heart blocks, sudden death, and thromboembolic events (2,30,41). The clinical presentation of ChD varies according to the degree of myocardial damage. The mild cardiac form of heart disease can also occur without LV dysfunction and is frequently characterized only by the presence of asymptomatic abnormalities on the ECG (17). Dilated cardiomyopathy can also occur without LV dysfunction and is associated with ventricular arrhythmias (69) and seems to have prognostic value (33,38).

**Diastolic dysfunction** is an important hallmark of chronic ChD and usually precedes systolic dysfunction (39,40). Chronic myocarditis damage might impair ventricular relaxation and diastolic filling. As the disease progresses and cardiac damage develops into LV dysfunction, reduced myocardial compliance leads to an increase in left atrial pressure. In general, systolic dysfunction and impairment of LV filling coexist in Chagas cardiomyopathy (64,70). Echocardiographic parameters to estimate LV filling pressures are predictors of functional capacity (71) and mortality in patients with Chagas cardiomyopathy (32,64,72). Interestingly, the early transmitral flow velocity to the early diastolic velocity of the mitral annulus (E/e’ ratio) (a marker of LV filling pressure) has an effect on mortality in Chagas cardiomyopathy, which is different from other dilated cardiomyopathies (Figs. 1E and 1F). A previous study showed that, in patients with mild or moderate systolic dysfunction, an E/e’ ratio of more than 15 was a powerful predictor of mortality. However, in patients with severe systolic dysfunction, an increased E/e’ ratio was inversely associated with mortality (72).

Right ventricular impairment is also reported as a typical feature of ChD. Previous studies demonstrated right ventricular dysfunction in asymptomatic patients with ChD and with a normal ECG and chest x-ray (73–75). In general, the LV is frequently affected, whereas right ventricular involvement is usually evident only in association with LV dysfunction (76). Occasionally, apical aneurysm of the right ventricle might be the only detectable abnormality in Chagas cardiomyopathy (77) (Fig. 1B). Right ventricular function is also an important determinant of exercise capacity (78) and prognosis (79).

### Ventricular dysfunction

Segmental LV wall motion abnormalities are frequent findings in ChD and can represent an early manifestation of the disease (28,42). The segments frequently involved are the inferolateral wall and the LV apex with preserved anteroseptal contraction (28). The prevalence of apical aneurysm varies widely and depends on the stage of the disease and the accuracy of the test used for the diagnosis. Left-ventricular apical aneurysms are found in 8.5% of asymptomatic patients with mild cardiac damage (28) (Fig. 1A) and in 45% of patients with LV systolic dysfunction and heart failure (64). Aneurysms are predictors of mural thrombus and stroke (65,66); however, their association with the risk of death is controversial (64,67). Recently, a study using cardiac magnetic resonance imaging confirmed that the presence of wall motion abnormalities and delayed enhancement by cardiac magnetic resonance imaging was more frequent in the inferolateral and apical segments (68). Patients frequently experience chest pain associated with segmental contractile abnormalities, which raises the suspicion of coronary artery disease. The presence of normal coronary angiograms in such patients suggests ChD. Regional contractility abnormality is associated with ventricular arrhythmias (69) and seems to have prognostic value (33,38).

### Diastolic dysfunction

Chagas cardiomyopathy is characterized by a chronic myocarditis that involves all cardiac chambers and damage to the conduction system (2,43). The pathogenesis involves parasite persistence in cardiac tissue (44), continuous low-grade parasitemia, and immune-mediated myocardial injury (45–47), with the contribution of autonomic damage (48–51) and microvascular disturbances (52,53).

Despite having a similar clinical presentation, Chagas cardiomyopathy has some peculiar characteristics, compared with idiopathic dilated cardiomyopathy (54) (Table 2). Previous studies demonstrated that patients with Chagas cardiomyopathy have worse long-term outcomes than patients with non-Chagas cardiomyopathy (55–58). This worse prognosis has been related to the persistence of myocardial activity due to the direct participation of the parasite (44) or to immunological mechanisms (45–47), thus leading to interstitial myocardial fibrosis throughout the myocardium (29). However, a biopsy study showed no difference in the quantity of interstitial myocardial collagen between patients with Chagas and idiopathic dilated cardiomyopathy (59). The poor prognosis of ChD might also be attributed to the severity of ventricular arrhythmias (60), to dysautonomia (43,61), and to myocardial perfusion abnormalities (62,63). Once LV remodeling and failure are established, neurohumoral activation per se can lead to a vicious cycle of progression of the disease similar to what happens with other cardiomyopathies. Nonetheless, the pathogenesis of ChD is complex, and the reason why ChD has a worse prognosis remains to be established.

### Table 1

<table>
<thead>
<tr>
<th>Stages *</th>
<th>Findings</th>
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<tbody>
<tr>
<td>A</td>
<td>Patients present no symptoms of heart failure and no structural heart disease (normal ECG and chest x-ray)</td>
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<tr>
<td>B1</td>
<td>Asymptomatic patients with ECG changes (arrhythmias or conduction disorders); mild echocardiographic contractile abnormalities with normal global ventricular function can also be present</td>
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<tr>
<td>B2</td>
<td>Patients with decreased left ventricular ejection fraction who have never had any signs or symptoms of heart failure</td>
</tr>
<tr>
<td>C</td>
<td>Patients with left ventricular dysfunction and prior or current symptoms of heart failure</td>
</tr>
<tr>
<td>D</td>
<td>Patients with symptoms of heart failure at rest, refractory to maximized medical therapy (NYHA functional class IV) that require specialized and intensive interventions</td>
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*See Andrade et al. (35). ECG = electrocardiogram; NYHA = New York Heart Association.

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Thromboembolism. Thromboembolic events are relatively frequent in ChD and constitute the third cause of death (80). Brain embolism is the most common clinically recognized event, followed by limb and pulmonary embolisms. Stroke can be the first manifestation of the disease in asymptomatic patients (41,65,81–84). Therefore, ChD has been considered an often unrecognized cause of stroke and should be regularly included in its differential diagnosis in Latin American patients. Left ventricular systolic dysfunction, left atrial volume enlargement, apical aneurysm, mural thrombus, and cardiac arrhythmias seem to be important risk factors in the genesis of ischemic stroke related to Chagas cardiomyopathy (41,66,81).

Arrhythmias. Chagas heart disease is considered an arrhythmogenic cardiomyopathy characterized by a wide variety of...
abnormalities of the conduction system, such as bradyarrhythmias and tachyarrhythmias. Frequent, monomorphic, or polymorphic ventricular premature beats, including couplets and runs of nonsustained ventricular tachycardia (VT), are a common finding in Holter monitoring or exercise testing (85). The severity of ventricular arrhythmias tends to correlate with the degree of LV dysfunction but can also occur in patients with normal ventricular function (86). Episodes of nonsustained VT, being more frequent than in other cardiomyopathies, are observed in approximately 40% of patients with mild wall motion abnormalities and in almost all patients with heart failure (60). Nonsustained VT on 24-h Holter monitoring or exercise testing is an independent predictor of mortality (33,87).

Sustained VT is another hallmark of the disease and is the main triggering factor of sudden death in chronic Chagas heart disease (80). This life-threatening arrhythmia might arise from various regions in both ventricles, but LV inferolateral scarring is the main source of sustained VT reentry circuits (88). In addition, there is a good topographic correlation between myocardial perfusion, wall motion abnormalities, and areas that originate VT (88). Atrial fibrillation typically occurs in patients with advanced heart failure and is characterized by a relatively low ventricular rate, which is related to the coexistence of ventricular conduction disturbances (2). Chagas disease is usually a primary cause of atrioventricular block in Latin American countries and is specifically caused by widespread and distal fibrosis of the conduction system. Sinus node dysfunction is also a concern, and those patients are frequently candidates for the implantation of pacemakers (2). In comparison with pacemaker patients without ChD, Chagas pacemaker patients are significantly younger and have a lower LV ejection fraction and more frequent ventricular arrhythmias during Holter monitoring (89).

Dysautonomia. Since the original description by Chagas and Villela (90), several studies have documented the occurrence of vagal dysfunction in patients with ChD (26,91).

Chagas disease patients have reduced vagal modulation over the sinus node, which causes a reduced heart rate response to physiological and pharmacological stimuli (26). These abnormalities occur early in the course of the disease and before the development of LV dysfunction (26,91). The pathogenesis of vagal dysfunction is not completely understood but involves both denervation related to the destruction of vagal neuron ganglia cells and nerve fibers, likely due to the inflammatory process (92), and circulating autoantibodies with in vivo muscarinic cholinergic antagonistic activity, which might provoke desensitization and/or down-regulation of the muscarinic receptors (93).

However, the role of cardiac sympathetic dysautonomia has been less frequently studied. Cardiac sympathetic denervation has been detected in some ChD patients by iodine-123 meta-iodobenzylguanidine scintigraphic studies.

### Table 2: Features of Chagas Cardiomyopathy Compared With Idiopathic Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th></th>
<th>Chagas Cardiomyopathy</th>
<th>Idiopathic Cardiomyopathy</th>
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<tbody>
<tr>
<td>Serology for T cruzi</td>
<td>Predominance of male sex, age at diagnosis of 30 to 50 years of age; in some endemic regions where the transmission was halted. Chagas cardiomyopathy is now a problem of elderly persons.</td>
<td>Blacks and male subjects have a 2.5-fold increase in risk; most patients are first observed between the ages of 20 and 50 years.</td>
</tr>
<tr>
<td>Demographic data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidemiology</td>
<td>Childhood resident of a rural endemic area in Latin America.</td>
<td>Familial disease; alcohol consumption; recent viral illness.</td>
</tr>
<tr>
<td>Clinical manifestation</td>
<td>Symptoms of palpitations, syncope, chest pain, thromboembolic events, biventricular heart failure, usually with predominant right-sided failure in advanced stages.</td>
<td>Symptoms of left-sided heart failure predominate with diminished exercise capacity and progressive exertional dyspnea. Papillomata and peripheral edema are less common. Systemic and pulmonary emboli are usually observed in patients who have more advanced heart failure.</td>
</tr>
<tr>
<td>ECG</td>
<td>Right bundle-branch block often associated with left anterior hemiblock, premature ventricular beats, ST-T changes, abnormal Q waves, various degrees of AV block, sick sinus syndrome, and low QRS voltage.</td>
<td>Initially only nonspecific repolarization abnormalities are detected. Conduction abnormalities occur in over 80% of cases and include first-degree AV block, left bundle-branch block, and nonspecific interventricular conduction delays. Right bundle-branch block is uncommon.</td>
</tr>
<tr>
<td>Holter-24 h/ exercise testing</td>
<td>Complex and frequent ventricular arrhythmias, usually asymptomatic; spontaneously or exercise-induced ventricular tachycardia; occurrence of bradyarrhythmias, as advanced AV block and sinus sick syndrome.</td>
<td>Ventricular arrhythmias are common, but syncope and sudden death are rarely the initial manifestations of the disease; bradyarrhythmias with indication of pacemaker are less frequent than Chagas disease</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>Apical left ventricular aneurysm; mural thrombus, especially in the apex of the left ventricle; segmental left ventricular wall motion abnormalities with akinesia or hypokinesia of infero-lateral wall with preserved anteroseptal contraction; diastolic dysfunction in early stages, and associated involvement of the right ventricle.</td>
<td>Left ventricular dilation with global hypokinesia; considerable variability in the extent of segmental wall-motion abnormalities because of altered regional-wall stress; mural thrombi are frequently present in the left ventricle and not infrequently in the atria.</td>
</tr>
<tr>
<td>Myocardial scintigraphy</td>
<td>Perfusion defects without obstructive coronary artery disease.</td>
<td>Evidence of reversible and fixed perfusion abnormalities.</td>
</tr>
<tr>
<td>Involvement of digestive system</td>
<td>Megaesophagus and/or megacolon.</td>
<td>Absent.</td>
</tr>
<tr>
<td>Outcome</td>
<td>High frequency of sudden unexpected death and poor prognosis compared with non-Chagas cardiomyopathy.</td>
<td>Outcome has been improved with the current treatment of heart failure.</td>
</tr>
</tbody>
</table>

AV – atrioventricular; ECG – electrocardiogram.
in the early stages of the disease (21,23,26). In advanced heart failure patients, there are reduced levels of catecholamines in Chagas cardiomyopathy compared with patients with heart failure of other etiologies (94,95). The pathogenesis of the sympathetic abnormalities is likely the same as the vagal lesions and involves both denervation, related mainly to the inflammatory process (96), and autoantibodies against beta-adrenoceptors (97).

The clinical and prognostic values of autonomic nervous system disturbances in ChD patients remain a matter of debate. There is a well-established association between impaired autonomic cardiac modulation and sudden death in other clinical settings (98). Therefore, many investigators believe that the autonomic nervous system abnormalities can have a pathophysiological role in the genesis of ventricular arrhythmias and sudden death in patients with ChD. Some clinical evidence supports this hypothesis, because of the association of meta-iodobenzylguanidine defects and sustained VT (99) and the occurrence of abnormal heart rate dynamics before the spontaneous onset of ventricular tachyarrhythmias in Chagas heart disease (100). Moreover, augmented T-wave variability, which might also be related to autonomic control, has been reported as a potential marker of a high risk of sudden death in a small sample of patients (101). However, until now, there has been no robust evidence to support the routine use of noninvasive assessment of the integrity of sympathetic-vagal cardiac regulation for risk stratification of sudden death in patients with ChD.

**Treatment: General Aspects**

The treatment of ChD involves both parasite-specific therapy and adjunctive therapy for the management of the heart failure. Anti-parasitic therapy is indicated for patients with acute infection, in children and recently infected persons, in those with congenital form of the ChD, and reactivation due to immunosuppression (35). Previous studies have suggested that anti-trypansomal treatment can slow progression of chronic disease, but it is still a matter of debate (2,102–105). Currently available drugs (benznidazole and nifurtimox) require a prolonged course, carry a substantial risk of adverse effects, and need careful monitoring. An ongoing multicenter trial (BENEFIT [Benznidazole Evaluation for Interrupting Trypanosomiasis]) to assess the effects of etiological therapy on cardiac outcomes in patients with chronic Chagas cardiomyopathy will likely to solve this controversy (106).

The therapeutic approaches for the management of Chagas cardiomyopathy follow the standard recommendations for treatment of heart failure due to other conditions (2). However, treatments are based on data from large clinical trials that did not focus specifically on heart failure secondary to ChD. Moreover, there are some peculiarities in the pathophysiology of Chagas cardiomyopathy with potentially therapeutic implications. Angiotensin-converting enzyme inhibitors and beta-blockers are the cornerstone therapy for the management of patients with Chagas cardiomyopathy (107). Although beta-blockers have been avoided in ChD patients, because of bradyarrhythmias, some studies have demonstrated that beta-blocker therapy is safe and was associated with better survival (107,108). Its effects on the adrenergic system seem to be an attractive strategy to prevent sudden cardiac death (109,110).

Heart transplantation is the treatment of choice for well-selected patients with advanced heart failure, including those dependent on inotropic drugs and/or circulatory support (35,109). Survival among ChD patients seems to be better than that reported for patients transplanted, because of other types of cardiac disease (111). A major concern in the heart transplant recipient is the consequence of long-term immunosuppressive therapy after transplant that carries the risk of reactivation of *T. cruzi* infection (112). As a consequence of the persistent donor organ shortage, there has been growing interest for alternative strategies, in particular in mechanical circulatory support. Left ventricular assist devices have been used in some patients, usually as a bridge to transplantation (113,114).

**Prevention of sudden death.** A major therapeutic goal in the management of Chagas cardiomyopathy is primary and secondary prevention of sudden death, which is generally caused by ventricular fibrillation, preceded or not by VT (115). Implantable cardioverter-defibrillator (ICD) therapy is the standard treatment for secondary prevention of sudden death, as in those recovered from sudden death, with spontaneous sustained VT or with syncope with induced VT at the electrophysiological study (116,117). Secondary prevention with ICD can be even more useful in patients with ChD than other cardiopathies, due to the high arrhythmogenic profile of the former: ChD etiology was associated with poorer survival compared with idiopathic disease (55) and with a 2.2-higher chance of an ICD appropriate therapy delivery, in comparison with other ICD recipients (116).

The choice of the best primary prevention strategy for sudden death in Chagas cardiomyopathy is much more controversial. Although both amiodarone and ICD therapy have been used and indicated for high-risk subjects (35,115,118), data from ChD patients are scanty, and clinical evidence supporting these recommendations is mostly derived from results obtained in other cardiopathies. Moreover, how to identify those high-risk subjects is still uncertain, because most available prediction models were designed to recognize death from all causes (and not arrhythmic death) (33,87,119). The extension of current ICD guidelines for primary prevention of sudden death in Chagas cardiomyopathy patients (118) is supported, because the survival benefit of ICD therapy is not disease-specific (120,121) and because this benefit, observed in randomized clinical trials, was confirmed and extended in observational studies, including to populations different from original trials (121). However, the economic burden of the indication of ICD for a large number of Chagas
cardiomyopathy patients in Latin American countries, where ChD is endemic, was not fully appreciated, and the treatment might not be cost-effective in developing countries (122). The use of amiodarone for high-risk subjects, especially those with nonsustained VT and LV systolic dysfunction, is recommended by current guidelines (35). Nonetheless, the value of this drug in preventing sudden death has not been demonstrated in ChD, and studies conducted in patients with dilated cardiomyopathy showed no reduction in overall mortality with its use, in spite of a modest reduction in the incidence of sudden cardiovascular death, as well as significant pulmonary and thyroid toxicity (123). A clinical trial comparing amiodarone with ICD in primary prevention of sudden death in high-risk ChD patients was designed (CHAGASICS [Amiodarone Against ICD Therapy in Chagas Cardiomyopathy for Primary Prevention of Death], NCT01722942), although participant recruitment has not yet begun. Amiodarone might have a valuable role in decreasing the number of appropriate shocks in ICD recipients and might be used routinely just after ICD insertion (35).

Permanent pacemaker implantation is an effective treatment for symptomatic sinus sick syndrome and advanced atrioventricular blocks in ChD (124), and indications should follow current international guidelines (118).

Prognosis. The prognosis of ChD depends on the clinical form at diagnosis. Patients with the indeterminate form have an excellent prognosis. The patients who presented with dilated cardiomyopathy evolve with progressive deterioration of ventricular function, complex ventricular arrhythmias, and high mortality rates. Although the evolution of Chagas heart disease is poorly understood, longitudinal studies demonstrated that many factors can be associated with the progression of cardiac damage, including male sex, exposure to reinfection, parasite strain, genetic background, age, severity of acute infection, nutritional status, alcoholism, and other concomitant diseases (17,34,119). The host immune response is also an important determinant of outcome (125). A previous study with asymptomatic Chagas patients showed that the pattern of specific autoantibodies correlates with the development of clinical manifestation (97). Additionally, polymorphisms in tumor necrosis factor-alpha (126), CCR5 (127,128), and chemokines and chemokine receptors are associated with the development of chagasic cardiomyopathy (129).

Previous studies on prognosis have followed patients across the spectrum of ChD to determine the range of annual mortality rates across studies (varying from 0.2% to 19.2%). The most consistent independent predictors of death identified in most of the studies were LV dysfunction, New York Heart Association functional class, and nonsustained VT during 24-h Holter monitoring (34). Rassi et al. (33) developed a score to predict death that combined these variables, and each variable was assigned a number of points. Symptoms of heart failure are expressed as New York Heart Association functional class III or IV (5 points), evidence of cardiomegaly on a chest x-ray (5 points), segmental or global wall-motion abnormality on echocardiography (3 points), nonsustained VT on 24-h Holter monitoring or stress testing (3 points), low QRS voltage on ECG (2 points), and male sex (2 points). A risk score derived from the combination of points attributed to each of these features accurately classified patients into a low-, medium-, or high-risk group, with 10-year mortality rates of 10%, 44%, and 84%, respectively. This score was validated in 2 external cohorts (33,130).

Conclusions

In recent decades, remarkable progress has been made in the prevention and control of ChD. However, ChD still represents a major public challenge in Latin America and an emerging health problem in non-endemic countries. Heart disease, secondary to a progressive chronic myocarditis, is the most important clinical manifestation of the disease and presents with several typical features and a high mortality rate.

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Key Words: Chagas disease • dilated cardiomyopathy • heart failure.