The Treatment of Chronic Heart Failure Secondary to Chagas Cardiomyopathy in the Contemporary Era

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Abstract

Chronic Heart Failure affects about half patients with Chagas cardiomyopathy. Poor outcomes of CHF secondary to Chagas cardiomyopathy are relentless with an annual mortality approaching 20%, which is higher than that observed in non-Chagas disease heart failure. The pathophysiology of Chagas disease is similar to that found in non-Chagas disease heart failure with a marked activation of the neurohormonal system. No randomized trial has been conducted in patients with Chagas cardiomyopathy with CHF to assess the effect of a drug on mortality of such patients. Therefore, the treatment of CHF secondary to Chagas cardiomyopathy relies on drugs prescribed to patients with non-Chagas disease heart failure. Patients with Chagas disease heart failure have been classified into stages A to D according to the American College of Cardiology/American Heart Association. Little can be done to patients in the stage A of CHF; except for treatment of comorbidities. In patients in the stage B of CHF; aldosterone receptor antagonist, angiotensin converting enzyme inhibitors (ACEI), and Betablockers (BB) are indicated. In patients in the stage C of CHF, the same drugs are of value. In addition, diuretics, digoxin, angiotensin receptor blockers to patients intolerant to ACEI have also been used. Cardiac Resynchronization Therapy and Implantable Cardioverter Defibrillator may have indications similar to that of non-Chagas disease patients. In stage D of CHF, heart transplantation is a valid option for patients with this condition.

Key words: Chagas disease; heart failure; sudden cardiac death; Betablockers; Trypanosoma cruzi; angiotensin converting enzyme inhibitor.

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Introduction

Following an acute infection, all patients with Chagas disease will enter the chronic stage of the disease because spontaneous cure is very rare. Nevertheless, the majority of patients with chronic Chagas disease (about 60%) will remain with no evidence of disease in any organ, only a positive serology being evidence of previous infection (the so-called indeterminate form of the illness). However, about 20% of patients with chronic Chagas disease develop chronic cardiomyopathy many years later.1 Clinically, Chagas cardiomyopathy manifests by sudden cardiac death (SCD),2 thromboembolism3, precordial chest pain,4 arrhythmias and conduction defects4, and chronic heart failure (CHF).6 Chagas disease is the most important cause of CHF in areas where the disease is endemic, mainly in patients with the advanced forms of the disease.

CHF affects about 14% of an ambulatory patients’ cohort from an area where the disease is endemic5, and up to 76% of a hospital cohort from a tertiary referral center.7 Outcome of patients with chronic heart failure associated with Chagas cardiomyopathy is relentless even in the current area of heart failure therapy, with an annual mortality of 20%.9

In the contemporary era of CHF treatment, predictors of all-cause mortality for patients with CHF secondary to Chagas cardiomyopathy are left ventricular ejection fraction, hyponatremia, New York Heart Association Functional (NYHA) Class IV, digoxin use, and lack of Betablocker therapy.8

The prognosis of patients with Chagas cardiomyopathy with CHF is poorer than that observed not only in patients with mild to moderate CHF,9 but also in those with advanced CHF.10 Moreover, outcome of patients with Chagas cardiomyopathy with CHF are worse than that of patients with CHF secondary to Idiopathic Dilated Cardiomyopathy,11,12 ischemic cardiomyopathy,13 and hypertensive cardiomyopathy.14

There is no evidence-based guideline to guide the treatment of Chagas cardiomyopathy patients with CHF largely because this
disease is neglected. Therefore, we should rely on data obtained in the treatment of patients with non-Chagas disease heart failure. However, this is not an easy task in view of some peculiarities related to this illness. Therefore, this review summarizes our experience of everyday practice in the treatment of Chagas cardiomyopathy patients with CHF.

Clinical characteristics of CHF secondary to Chagas cardiomyopathy

Although left ventricular diastolic dysfunction can precede the appearance of overt CHF, a clinical picture of CHF with preserved left ventricular ejection fraction according to current recommendations for the diagnosis of such a syndrome has not yet been detected in patients with chronic Chagas heart disease. Therefore, in patients with Chagas cardiomyopathy with CHF, the syndrome is the consequence of reduced left ventricular ejection fraction.

Segmental wall motion abnormalities (SWMA) as detected by either echocardiography or heart catheterization are a precursor of asymptomatic left ventricular systolic dysfunction (NYHA Class I), with its annual incidence varying from 7% to 15%. Asymptomatic left ventricular systolic dysfunction/left ventricular dilatation has been observed in 3% to 20% of chronic Chagas disease patients as detected by echocardiography, and in 39% of patients underwent left ventricular catheterization. Asymptomatic left ventricular systolic dysfunction is a powerful independent predictor of subsequent overt CHF in patients with Chagas cardiomyopathy. In most cases, CHF secondary to Chagas cardiomyopathy manifests with left-sided heart failure, dyspnea (NYHA Class II to IV) and fatigue being the cardinal symptoms. However, many patients may show right-sided cardiac failure as well. Isolated-right-sided heart failure is rare. The predominance of right-sided heart failure, as described by Dias et al. in 1945, has not been routinely observed in the contemporary era.

SCD is the mode of death in about 41 to 45% of patients with CHF secondary to Chagas cardiomyopathy and in the vast majority of cases, it is caused by malignant ventricular arrhythmia. Stroke-related mortality in patients with this condition is 17%. Autopsy studies have revealed that pulmonary embolism may be found in up to 37% of patients who died of CHF secondary to Chagas cardiomyopathy. Intractable pump failure appears to be the most important cause of death in patients with Chagas disease heart failure, mainly in those with advanced forms of the disease, affecting up to 43% of patients with this condition.

Stages of CHF secondary to Chagas cardiomyopathy

CHF due to Chagas disease can be classified into stages A, B, C, and D, similarly to what has been done for patients with non-Chagas disease heart failure. Stage A refers to all patients in the indeterminate form of the disease, who are potentially at risk for developing CHF. The stage B refers to patients with evidence of chronic Chagas heart disease without left ventricular dysfunction, and are characterized by the presence of ventricular arrhythmias, intraventricular conduction disturbances or segmental wall motion abnormalities without left ventricular systolic dysfunction (B1). Patients with asymptomatic left ventricular systolic dysfunction form the stage B2. Patients with past or previous clinical picture of CHF are assigned to group C, whereas those with refractory symptoms are classified in the group D. Figure 1 illustrates the treatment of Chagas disease heart failure according to the stages of CHF secondary to Chagas cardiomyopathy.

Treatment of CHF in patients with Chagas cardiomyopathy

Non-pharmacological treatment

A low-sodium diet has usually been recommended to patients with non-Chagas disease heart failure. However, there is little scientific evidence that a low-sodium diet is of benefit to patients with this condition. Indeed, no salt restriction (a diet with 6 g salt daily) seems to be better than salt restriction in patients with CHF. The situation may be particularly difficult in the setting of Chagas disease heart failure because hyponatremia or even serum sodium levels < 140 mEq/L are independent predictors of mortality for such patients. A low-sodium diet could potentially contribute to the appearance of abnormal sodium serum levels because such patients have increased urinary sodium losses. Furthermore, because systemic arterial pressure is usually lower than that observed in Chagas disease patients, patients with CHF secondary to Chagas cardiomyopathy cannot tolerate target doses of angiotensin converting enzyme inhibitors (ACEI) because of systemic arterial hypotension. Therefore, it seems to be prudent not to recommend sodium restriction in the dietetic regimen of all patients with Chagas disease heart failure. Rather, salt restriction must be considered on an individual basis.

Another point regarding diet that deserves further consideration is the daily magnesium content ingestion. Because patients with CHF secondary to Chagas cardiomyopathy have a low income, proper ingestion of magnesium might not be achieved, and this could explain the prevalence of hypomagnesemia of 33%, and low levels of magnesium in muscle of 66%, in patients with Chagas cardiomyopathy with CHF. The consequence of hypomagnesemia is the increase propensity to digitalis intoxication as well as the appearance of malignant ventricular arrhythmias. Thus, a diet rich in magnesium content appears to be of benefit for patients with CHF secondary to Chagas cardiomyopathy.

Fluid restriction is another component of the non-pharmacological treatment of CHF. In patients with non-Chagas disease heart failure, fluid restriction has been recommended only to patients in the stage D, who are more prone to develop hyponatremia. This electrolyte abnormality appears because of marked activation of the Renin-Aldosterone-Vasopressin system, culminating in dilutional hyponatremia. Since a similar mechanism may occur in patients with Chagas cardiomyopathy with CHF, it is reasonable...
to suggest fluid restriction to patients with more advanced forms (stages C and D) of CHF secondary to Chagas cardiomyopathy.

Vaccination against pneumococcus and influenza has routinely been advised to patients with non-Chagas disease heart failure.24 Because infection is an important cause of heart failure decompensation in patients’ cohort comprised of Chagas and non-Chagas patients,31 one can suggest vaccination against pneumococcus and influenza to patients with compensate CHF secondary to Chagas cardiomyopathy.

Exercise training is a major point in the non-pharmacological treatment of patients with Chagas cardiomyopathy with CHF. Exercise training decreases morbidity, but not mortality, in patients with non-Chagas disease heart failure.23-25 In the setting of Chagas disease heart failure, a randomized trial has shown that Chagas disease patients with CHF were found to have an increase in physical capacity as well as in a quality of life score following a 12 week-supervised walking program.32 Therefore, exercise training, under supervision, can be suggested as part of the non-pharmacological treatment of patients with Chagas cardiomyopathy with CHF.

**Pharmacological treatment**

Patients with CHF secondary to Chagas cardiomyopathy have been classified in several stages of heart failure according to the method used by the American Heart Association/American College of Cardiology adapted to Chagas disease.22

**Stage A**

Etiologic treatment could have a place in the treatment of adult patients in the indeterminate form (stage A). However, there is no evidence from randomized clinical trials to support its use in adult patients with this condition. The treatment of comorbidities, mainly systemic arterial hypertension (SAH), is imperative in Chagas disease patients at risk of developing CHF, as seen in non-Chagas disease patients.23 In this sense, it is important to emphasize that the association of Chagas disease and SAH is one of the most important cause of CHF in referral centers for CHF treatment.23 Therefore, treatment of SAH is crucial for Chagas disease patients in the stage A of CHF.

**Stage B**

A recent randomized trial with benznidazole has demonstrated that this drug has no benefit in terms of disease progression to patients with this condition.24 Therefore, etiologic treatment cannot be recommended to Chagas disease heart failure patients in this stage of CHF. Another important point is related to the presence of asymptomatic left ventricular systolic dysfunction. In patients with non-Chagas disease heart failure, Betablockers, ACEI, and Mineralocorticoid/Aldosterone receptor blockers,23-25 have formally been indicated to halt disease progression and the consequent appearance of overt CHF. However, no study has addressed this question in Chagas disease patients, and guidelines do not recommend such drugs to patients with this condition. Nonetheless, inasmuch as the activation of the Renin-Angiotensin-Aldosterone System appears to be similar in Chagas and non-Chagas disease patients with CHF,25-27 it would be reasonable to suggest such drugs for the treatment of asymptomatic left ventricular dysfunction in patients with CHF secondary to Chagas cardiomyopathy in the stage B.

**Stage C**

Patients with overt CHF have a pathophysiological mechanism similar to that seen in non-Chagas disease patients. This means that a marked neurohormonal activation occurs in such patients, as shown by increased plasma renin activity and serum noradrenaline levels.25,27 In addition, increased muscle sympathetic nerve activity suggestive of sympathetic overactivity has been detected in such patients, but not in those at stage A.28 Furthermore, increased adrenaline levels in the coronary sinus of patients with Chagas cardiomyopathy with CHF have been observed, thus suggesting a facilitation process of myocardial noradrenaline uptake, culminating in myocardial toxicity, independent of peripheral circulating catecholamine levels, as seen in animals with isoproterenol-induced cardiomyopathy.29 Therefore, neurohormonal activation does occur in patients with overt CHF due to Chagas cardiomyopathy, and can be more intense than that observed in non-Chagas patients. Thus, treatment with ACEI, Betablockers and mineralocorticoids antagonists are potentially useful in the treatment of patients with this condition.

Mineralocorticoid/aldosterone receptor antagonists have been suggested for the treatment of all patients with left ventricular dysfunction not associated with Chagas cardiomyopathy because they improves survival.23-25 Experimentally, spironolactone not only increases survival, but also attenuates myocardial inflammation and the remodeling process in a hamster model of this disease.25 In patients with Chagas cardiomyopathy and CHF, spironolactone is safe.43 Therefore, taking into account the beneficial effects of mineralocorticoid/aldosterone receptor antagonists on survival of non-Chagas disease patients with CHF, and the potential benefits of such drugs in Chagas disease patients as well, mineralocorticoid/aldosterone receptor antagonists have been indicated for patients with Chagas cardiomyopathy with CHF.24

ACEI inhibitors are the cornerstone of treatment of patients with CHF not related to Chagas disease to improve morbidity and mortality.23-25 In the context of CHF associated with Chagas cardiomyopathy, a few studies have shown a salutary effect as well. A small randomized, cross-over, placebo-control trial performed in 15 patients with Chagas cardiomyopathy with CHF during 12 weeks showed that captopril induced a decrease in heart rate, a reduction in urinary catecholamine levels, an increase in the plasma renin levels, and a reduction in the number of premature ventricular contractions on Holter monitoring in comparison to placebo.42

In an open-label study enrolling 20 patients with CHF due to Chagas cardiomyopathy, Szajnbak et al. found a beneficial effect of enalapril on left ventricular diastolic dysfunction following a 2-month treatment.43 A beneficial effect of enalapril (40 mg/daily) in Framingham score, quality of life, in the cardiothoracic index, brain natriuretic peptide (BNP), and chemokine levels was found in another open-label study carried out on 42 patients with this condition.44 Collectively, such findings showed a decrease in the neurohormonal activation in patients with CHF secondary to Chagas cardiomyopathy. For this reason, ACEI have been recommended for all patients with CHF due to Chagas cardiomyopathy.24

Beta-blocker therapy is another key point in the treatment of CHF secondary to Chagas cardiomyopathy. Beta-blockers have been indicated to all patients with CHF because they improve all-cause mortality of patients with non-Chagas disease heart failure.23-25 In addition, in contrast to ACEI, Betablockers decrease the incidence of SCD in patients with this condition.25 In Chagas disease heart failure, Betablockers have a salutary effect as well. In an uncontrolled study performed in 9 patients with severe CHF (8 in ambulatory Class IV, 1 in Class III; left ventricular ejection fraction 20 ± 6%), the administration of metoprolol (25-50 mg/daily) markedly decreased heart rate, increased systemic arterial pressure, increased left ventricular ejection fraction, and reversed...
left ventricular remodeling after 10 weeks of treatment.46
A prospective sub-analysis of the REMADHE study, a non-
randomized, placebo-controlled trial, compared the use of
Betablockers in 24 patients on and in 44 patients not on these
drugs, half of them with severe CHF, in a 1326±39 days follow
up. There was a marked decrease in mortality in patients
receiving Beta-Blocker therapy in comparison with patients not
receiving these drugs.47 A retrospective longitudinal cohort study
performed on 231 patients with CHF due to Chagas disease,
followed for 19 (7-46) months with an overall mortality of 52%,
showed a marked decrease in all-cause mortality. Importantly,
even a small dose of carvedilol positively influenced survival of
patients with this ailment, and no detrimental effect associated
with Beta-Blocker therapy was observed.48

Finally, a retrospective cohort study has compared outcome of
632 patients with CHF, CHF secondary to Chagas cardiomyopathy
was the third most common cause of CHF, before and after
2000, 1 year following hospitalization. It was discovered that
there was a marked decrease in all-cause mortality after 2000,
when Betablocker therapy increased from 34 to 72% of patients.
Moreover, Betablocker therapy was an independent predictor of
survival.49 Collectively, the scientific data available at this time
suggest that Beta-blocker therapy is not detrimental, and may
have a positive impact on patients with Chagas cardiomyopathy
with CHF. For this reason, Betablockers have been recommended
for the treatment of patients with such a condition.50

A central question in the treatment of Chagas disease heart
failure is the association of Betablockers with ACEI because the
appearance of symptomatic systemic arterial hypertension,
which can affect up to 39% of outpatient patients with this
illness. In patients with mild to moderate CHF, we suggested
to start the treatment with Betablockers until the targeted
doses, and then start ACEI, for several reasons.6 First, the
effect on survival is the same if the therapeutic regimen starts
with ACEI or Beta-blocker therapy in non-Chagas disease
heart failure.49 Second, Betablockers, but not ACEI, avert SCD
in such patients.49 Third, SCD affects mainly Chagas disease
patients with mild to moderate CHF.21 Fourth, activation of the
sympathetic nervous system appears to occur first before that of
the Renin-Aldosterone system.49 Fifth, the probability that a
Betablocker reaches the target dose following a targeted dose
of ACEI is low.50

Based on the facts outlined earlier, we continue to recommend
this therapeutic approach to Chagas cardiomyopathy patients
with CHF at this time. In patients with severe heart failure, we
suggest to start the treatment with diuretics, ACEI, and perhaps
digoxin, until patients reach the compensation state. After this, we
suggest to start Betablockers. In the case Beta-blockers are not
tolerated, the ACEI daily dose should be reduced, as low doses of
ACEI are not related to increased mortality in patients with non-
Chagas disease heart failure.51,52 and then Betablockers should be
given to reach targeted dose or the maximal tolerated dose.6

Digoxin has been used in patients with CHF not associated
with Chagas cardiomyopathy to decrease morbidity, mainly
hospitalization.22-25 In patients with CHF secondary to Chagas
cardiomyopathy, digital appears to be safe.53 However, a study
performed in a contemporary era of heart failure treatment
showed that digoxin use is an independent predictor of all-
cause mortality in patients with Chagas disease heart failure.5
Furthermore, it has been demonstrated that a substantial number
of patients with CHF secondary to Chagas cardiomyopathy are
found to have increased digoxin serum levels, even at the toxic
level.54 Therefore, digoxin levels should be monitored in patients
with Chagas cardiomyopathy with CHF, and serum levels
adjusted to non-toxic levels (<1 ng/ml). No study has addressed
the use of ivabradine in patients with Chagas cardiomyopathy
with CHF thus far.

Angiotensin receptor blockers are recommended to patients with
non-Chagas disease heart failure, mainly to those intolerant to such
drugs because of side effects.23-25 In a cohort of 231 prospectively
followed patients with CHF secondary to Chagas cardiomyopathy,
losartan (45.1 ± 13.5 mg/daily) has been given to 22% of patients
with no major side-effects.41 Therefore, it seems reasonable to
recommend angiotensin receptor blockers to patients with
this condition intolerant to ACEI therapy.26 The association of
hydralazine with nitrates has been used in afro-descendants
patients with chronic heart failure not associated with Chagas
disease.23-25 No study has been assessed the usefulness of such
drugs in the context of Chagas disease heart failure. Despite this,
this drug association has been suggested for patients with Chagas
cardiomyopathy with CHF in afro-descendant patients, and in
those with a contraindication for ACEI or angiotensin receptors
blockers in Brazilian guidelines for heart failure treatment.57

Ventricular arrhythmias are frequently found in patients with
CHF, and amiodarone has been recommended to treat such
abnormalities mainly in patients with symptomatic ventricular
arrhythmias.27 In the setting of Chagas cardiomyopathy
patients with CHF, in whom ventricular arrhythmias can be
found in the resting ECG of about half of patients,41 and non-
sustained ventricular tachycardia in up to 73% of patients,42
amiodarone could have a place in the treatment of ventricular
arrhythmias. However, amiodarone is not devoid of potential
harmful complications. In fact, it has been associated with
increased mortality in patients with Chagas cardiomyopathy
with CHF in the more advanced forms of the syndrome,27 and
with inducible ventricular arrhythmias at Electrophysiologic Study.65
Thus, amiodarone should be used with caution in patients with
symptomatic ventricular arrhythmias in the stage C of CHF
secondary to Chagas cardiomyopathy.

Atrial fibrillation can be found in up to 30% of patients with
CHF secondary to Chagas cardiomyopathy.44 In such patients,
anticoagulation indication is similar to the recommendation
for non-Chagas disease patients with CHF.24 However, there
are two points that deserve further consideration. One is the
presence of apical left ventricular aneurysm, which affects about
21% of patients with this condition,26 and is an independent
predictor of cardioembolic stroke in such patients.26 Accordingly,
patients with CHF secondary to Chagas cardiomyopathy with
this morphological abnormality have been suggested to be
anticoagulated,23 and we endorse such an opinion. Another point
is the risk score for thromboembolism worked out by Souza
et al.57 Such authors performed a longitudinal cohort study in
chronic Chagas disease patients, not necessarily with CHF,
observing that left ventricular systolic dysfunction, left ventricular
apical aneurysm, primary T changes in the 12-lead ECG, and age
> 48 years, were independent predictors of stroke. By performing
a risk score, they suggested anticoagulation to patients with a
score > 4. Nevertheless, it should be noted that patients with
left ventricular dysfunction, primary T changes in the resting
ECG, and age > 48 years should be anticoagulated. This does
not is in agreement with current guidelines for HF treatment.23-25
Therefore, we recommend anticoagulation therapy for patients
with CHF secondary to Chagas cardiomyopathy on the basis of
the presence of atrial fibrillation and left ventricular apical
aneurysm, as mentioned earlier.

Diuretics have largely been used in the treatment of congestive
symptoms in non-Chagas disease patients with CHF.\textsuperscript{23-25} In patients with Chagas disease heart failure, diuretics have also been used to achieve this goal.\textsuperscript{41} Furthermore, diuretics, particularly furosemide, have been shown to have no negative impact on mortality in patients with this condition. In addition, the association of hydrochlorothiazide with furosemide in patients in whom 160 mg of furosemide alone has not relieved either dyspnea or edema, has also been shown to be not detrimental to patients with CHF secondary to Chagas cardiomyopathy in our experience.\textsuperscript{41} Therefore, diuretics can be offered to patients with Chagas cardiomyopathy with CHF failure to relieve systemic or pulmonary congestion at the lowest dose possible. A close monitoring of renal function, volume status, and systemic arterial pressure is necessary.

Cardiac Resynchronization Therapy (CRT) is an important tool in the treatment of non-Chagas disease heart failure patients because it improves morbidity and mortality in patients with a left ventricular ejection fraction < 35\%.\textsuperscript{23-25} CRT has been indicated mainly to patients with CHF and left bundle branch block (LBBB) with QRS duration of 150 milliseconds or greater and NYHA class II to IV on maximal medical therapy (class of recommendation: I).\textsuperscript{23} Patients with a QRS duration greater than 120 milliseconds and but less than 150 milliseconds with LBBB and NYHA Class II to IV on maximal medical therapy can be considered to CRT as well (class of recommendation: IIa).\textsuperscript{23} A less established indication for CRT is that of patients with a non-LBBB pattern. Patients with this ECG pattern and QRS duration greater than 150 milliseconds and NYHA Class II have been recommended to undergo CRT (class of recommendation: IIb). Finally, patients with a non-LBBB pattern and a QRS greater than 120 milliseconds and less than 150 milliseconds and NYHA Class III or ambulatory class IV can be considered for CRT as well (Class of recommendation: IIb).\textsuperscript{25}

Despite the fact that interventricular conduction delay affects about 57\% of patients with CHF secondary to Chagas cardiomyopathy (41\% with RBBB, 16\% with LBBB),\textsuperscript{41} CRT has rarely been used in the treatment of patients with this condition. A non-randomized longitudinal study performed on 72 patients with CHF secondary to Chagas cardiomyopathy has shown an increase in the left ventricular ejection fraction and reversed remodeling in such patients on a 47 month mean follow up.\textsuperscript{41} Therefore, CRT has the potential to benefit many Chagas disease patients with CHF. Therefore, it is reasonable to indicate CRT to patients with Chagas cardiomyopathy with CHF with a clinical profile similar to that of non-Chagas disease patients in whom CRT is an accepted treatment modality.\textsuperscript{49}

Implantable Cardioverter-Defibrillator (ICD) is a major option for prevention of SCD in patients with CHF not associated with Chagas cardiomyopathy with a left ventricular ejection fraction < 35\%,\textsuperscript{23-25} Nonetheless, primary prevention of SCD in the context of Chagas cardiomyopathy has rarely been carried out. Cardinalli-Neto et al compared the clinical course of 19 Chagas disease patients with CHF with that of 13 patients with CHF secondary to non-Chagas disease dilated cardiomyopathy (mean left ventricular ejection fraction=17.1 \pm 5.9\%). The number of patients shocked was similar in both groups. However, the frequency of ventricular fibrillation was higher in Chagas than in non-Chagas disease patients.\textsuperscript{50} Now, there is no reason to not advise ICD implantation for primary prevention of SCD in patients with CHF secondary to Chagas cardiomyopathy unless for economic constraints.

**Stage D**

At this stage, non-Chagas disease patients are found to have persistent Class III/IV symptoms, fluid retention, marked physical incapacity, frequent hospitalizations for treatment of CHF, left ventricular ejection fraction < 30\%, despite maximal medical therapy.\textsuperscript{25} Patients with CHF secondary to Chagas cardiomyopathy may not tolerate Betablocker therapy if ACEI is optimized, usually use digoxin, have NYHA Class IV symptoms, low serum sodium levels, and a marked decrease in the left ventricular ejection. In this situation, 1-year mortality approaches 100\% with medical treatment.\textsuperscript{8} Cell therapy is not of benefit for patients with Chagas cardiomyopathy with CHF.\textsuperscript{61} Such patients, therefore, could be potentially considered for heart transplantation. Exceptionally, mechanical circulatory support can be offered to patients with this condition.

**Conclusions**

Non-pharmacological and pharmacological treatment of patients with CHF secondary to Chagas cardiomyopathy are similar to those recommended for patients with non-Chagas disease heart failure. Physicians dealing with this disease should be on the alert to this fact. Furthermore, it should be emphasized that Betablockers are not detrimental for patients with this condition, and because such drugs avert SCD in patients with CHF, they must be introduced early in the treatment of the syndrome. When possible, they can be given before ACEI to achieve target doses. ICD and CRT are of value in the treatment of patients with this condition. With no support of evidence-based medicine, this is the best we can do to treat CHF associated with the second most important neglected disease in the world.

**Declarations of Interest:**

The authors declare no conflicts of interest.

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The authors state that they abide by the “Requirements for Ethical Publishing in Biomedical Journals.”\textsuperscript{62}

**References**


52. Packer M, Poole-Wilson PA, Armstrong PW, Cleland JG, Horowitz JD, Massie BM, Rydén L, Thygesen K, Uretsky BF. Comparative effects of low and high doses of the angiotensin converting enzyme inhibitor, Lisinopril, on morbidity or mortality in chronic heart failure. Atlas study group. Circulation 1999 Dec; 100 (23): 2312-8. doi: 10.1161/01.CIR.100.23.2312


62. Shewan LG, Coats AJS, Henein M. Requirements for ethical publishing in biomedical journals. International Cardiovascular Forum Journal 2015;2:2 DOI: 10.17987/icfj.v2i1.4

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