Chagas' Cardiomyopathy: Prognosis in Clinical and Hemodynamic Profile C

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Abstract

Background: Patients with heart failure (HF) who are admitted showing poor perfusion and congestion (clinical-hemodynamic profile C) are the group that evolves with the worst prognosis in decompensated heart failure. However, there is little information in literature on the etiology of cardiopathy influences the outcome of patients in advanced stage.

Objective: To assess the outcome of patients admitted with clinical and hemodynamic profile C and verify the role of the etiology in this phase.

Methods: A cohort study was performed including patients with left ventricle ejection fraction (LVEF) < 45.0%, functional class IV and hospitalization presenting clinical-hemodynamic profile C. The group was divided into patients with chagasic (Ch) and non chagasic (NCh) cardiomyopathy. Statistical analysis used Student t test, Fisher exact test, chi-square and SPSS tests. The significance of p < 0.05 was considered.

Results: One hundred patients, with mean age 57.6 ± 15.1 years and mean LVEF of 23.8 ± 8.5%, were included. Among the patients studied, 33.0% were chagasic and, in comparison with NCh, had lower systolic blood pressure (Ch 89.3 ± 17.1 mmHg *versus* NCh 98.8 ± 21.7 mmHg, p = 0.03) and lowest average age - Ch 52.9 ± 14.5 years *versus* NCh 59.8 ± 14.9 years, p = 0.03). During follow-up of 25 months, mortality was 66.7% for Ch and 37.3% in NCh (p = 0.019). The Chagas disease etiology was an independent marker of poor prognosis in multivariate analysis with risk ratio of 2.75 (HF 95.0%, from 1.35 to 5.63).

Conclusion: In patients with advanced HF, Chagas disease is an important predictor of the worst prognosis. (Arq Bras Cardiol 2010; 95(4): 518-523)

Key words: Heart failure/complications; reperfusion; prognostic; Chagas cardiomyopathy.

Introduction

The advance of medicine has been improving the knowledge about heart failure (HF), enabling the development of new diagnostic methods, the determination of prognostic factors and the establishment of more effective treatments that enhance their development. However, HF is still a prevalent disease with a poor prognosis, especially in advanced stages of disease.

In this context, it is important to identify the clinical and laboratory characteristics of patients with decompensated HF, to determine those with a tendency to the worst prognosis. This makes possible to adopt specific measures and appropriate treatment for this group to improve the quality of life and increase survival.

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Over time, some criteria were identified and related to poor prognosis, among them functional class IV (NYHA), hyponatremia, hypotension, renal failure, exacerbated activation of the neurohormonal system, high BNP and clinical hemodynamic C profile[1-9].

In clinical and hemodynamic profile proposed by Stevenson[10], it is used two clinical parameters to stratify patients: congestion and perfusion. The congestion is diagnosed when the patient presents the following signs on physical examination: jugular stasis, pulmonary rales, sacral edema, lower limbs edema and hepatomegaly. The diagnosis of poor perfusion is done when the following signs are present: symptomatic systolic blood pressure lower than 90 mmHg, poor perfusion of the extremities, altered level of consciousness and pre-renal failure. When the patient shows signs of congestion, it is said that he/she is in "congested pattern" and it is not present, in "dry pattern". With respect to perfusion, it is hot, if well perfused and, it is cold, if poorly perfused. Following these criteria, we can find four clinical and hemodynamic profiles: profile A (hot and dry), profile B (hot and congested), profile L (dry and cold) and profile C (cold and congested).

The use of clinical-hemodynamic classification helps orient the drug therapy based on the profile of each patient and also allows the prognosis of outcome. In a study published in 2003, Stevenson et al demonstrated that patients with profile C were those who had the poorest performance among patients admitted with decompensated HF[11-13].

Brazilian studies have identified the Chagas cardiomyopathy, a disease very prevalent in our country, as associated with the worst prognosis when compared to other etiologies[14-15]. In a previous study by our group, we found that chagasic patients have the worst outcomes compared to other etiologies, however, this study included patients with preserved ventricular function and no selection for the clinical-hemodynamic profile[16]. We must also consider that the studies made by Stevenson et al[11], with evaluation of the clinical profile, were not included patients with Chagas cardiomyopathy.

In this study, we tried to fill this knowledge gap, checking if there is any relationship between the etiology and prognosis in patients with the most severe clinical-hemodynamic profile (type C).

In this study, we included patients admitted with heart failure with decompensated systolic dysfunction, functional class IV (NYHA) and clinical and hemodynamic profile C, and we assessed whether the evolution of Chagas disease patients would be different from patients with HF of other etiologies.

Materials and methods

This is a cohort study, which included the consecutive patients admitted with decompensated congestive heart failure, from the emergency room of the *Instituto do Coração* - HCFMUSP and from *Hospital Auxiliar de Cotoxó*. Patients aged over 18 years, with an ejection fraction of left ventricle smaller than 45.0% and in profile C (cold and congested) were selected.

At admission, patients underwent anamnesis, physical examination and blood collection for serum sodium dosage, potassium, urea, creatinine, BNP, complete blood count and serology for Chagas disease.

All patients were classified according to clinical and hemodynamic profile of Stevenson and only those who showed signs of low output and congestion were selected. Criteria used for characterization of low output were the presence of at least two of the following signs or symptoms: symptomatic SBP (systolic blood pressure) less than 90 mmHg, poor perfusion in extremities (slowed capillary refill), altered level of consciousness or pre-renal failure. In characterizing the presence of congestion, and also requires the presence of at least two of them, use the following criteria: jugular stasis, pulmonary rales, edema in the sacral region, lower limbs edema or hepatomegaly. This evaluation was conducted simultaneously by two specialists in heart failure responsible for the study.

To identify the etiology of heart failure, we used the following criteria:

1) *Ischemic* - Inactive area on electrocardiogram, history of myocardial revascularization or coronary obstruction demonstrated by cineangiocoronariography;

2) *Chagasic* - Serology was requested by ELISA method and indirect immunofluorescence;

3) *Hypertension* - History of hypertension excluding other causes of cardiomyopathy;

4) *Valvopathy* - Changing primary valvar before cardiomyopathy and excluding other causes;

5) *Alcohol* - Patients who reported drinking alcohol in large quantities for more than 10 years and excluding other causes;

6) *Idiopathic* - When any other cause for cardiomyopathy was excluded.

The statistical analysis used Student t test, Fisher exact test, chi-square test and SPSS software. The significant $p < 0.05$ was considered. The survival curves were made with the model of Kaplan-Meier[17] model and compared by the log rank method. The risk ratio (HF 95.0%) was calculated by Cox regression

Results

In Jul/2006-Oct/2007 period, at Hospital Auxiliar de Cotoxo, 153 patients were admitted with decompensated HF and systolic dysfunction, with 100 patients (65.0%) showed profile C (congestion and poor perfusion present) 34 patients (22.0%) with clinical profile B (this congestion and good perfusion) and 19 patients (12.4%) with profile L (absence of congestion and poor perfusion present), as shown in Figure 1. Only patients with profile C were included in the study and followed up for up to 25 months.

Table 1 shows the main characteristics of hospitalized patients with profile C, group where 68.0% were male and 33.0% had positive serological tests for Chagas disease. Most patients needed a prescription for inotropic compensation (89.0% of patients).

Table 2 shows the main characteristics of the Chagasic (Ch) and non chagasic (NCh) population. It was found that patients with Chagas' were younger (52.9 ± 14.5 years old *versus* 59.8 ± 14.9, $p = 0.03$) had a lower mean left ventricle ejection fraction (LVEF) (20.8 ± 7.9% *versus* 25.2% ± 8.4%, $p = 0.01$), average systolic blood pressure lower 89.3 ± 17.1 mmHg *versus* 98.8 ± 21.7 mmHg, $p = 0.03$). The hospitalization time was similar in both groups: Ch 31.6 ± 21.3 days and NCh 27.1 ± 18.5 days; $p = 0,3$.

Data on mortality

During the follow-up of the studied population, the mortality rate was 11.0% and mortality during follow-up was around 47.0%. When comparing the group of chagasic patients with the non chagasic one, we found that mortality was higher in the chagasic one (Ch 66.7% versus NCh 37.3%, $p = 0.019$) (Figure 2).

Table 3 presents the main characteristics of patients who died and those who remained alive during the study. Patients who died were older, had a lower ejection fraction, renal function more deteriorated in the admission and higher plasma BNP levels.

In multivariate analysis, only two independent markers of poor prognosis were identified: chagasic etiology - risk ratio of 2.75 (HF 95%, 1.35 - 5.63) and Age - risk ratio was 1.045

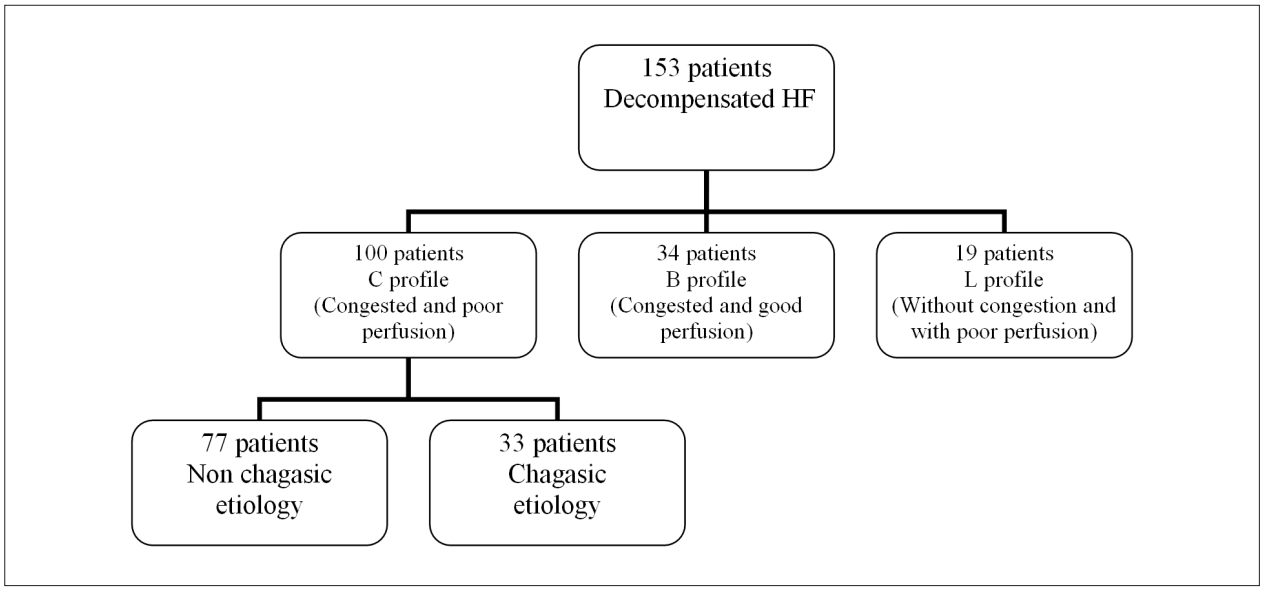

Figure 1 - Patients selection.

Table 1 - Clinical and laboratory characteristics of the studied population

Characteristic	Average and standard deviation
Age (years)	57.6 ± 15.1
LVEF %	23.8 ± 8.5
Urea at admission (mg/dl)	74.4 ± 42.7
Creatinine at admission (mg/dl)	1.7 ± 0.9
Sodium at admission (mEq/l)	137.3 ± 3.9
BNP at admission (pg/ml)	1,885 ±1,662
SBP (mmHg)	95.5 ± 20.7
Characteristics	**%**
Male	68
Vessel-active drug use	89
Etiology:	
Chagasic	33
Ischemic	29
Hypertensive	17
Valvopathy	8
Alcoholic	7
Idiopatic	13
Hospital mortality	11
General mortality (25 months)	47%

Table 2 - Clinical and laboratory characteristics of patients with chagasic and non chagasic etiology

	Chagasic (Ch)	Non chagasic (NCh)	
N	33	67	
Characteristic	**n (%)**	**n (%)**	
Male	18 (54.5%)	50 (74.6%)	0.04
VAD drugs	30 (91%)	59 (88%)	0.66
Characteristics	**Average and standard deviation**	**Average and standard deviation**	
Age (years)	52.9 ±14.5	59.8 ±14.9	0.03
SBP (mmHg)	89.3 ± 17.1	98.8 ± 21.7	0.03
LVEF	20.8 ± 7.9	25.2 ± 8.4	0.01
Sodium (mEq/l)	136.2 ± 4.0	137.8 ± 3.8	0.06
Initial urea (mg/dl)	60.5 ± 28.4	81.3 ± 46.9	0.007
Initial creatinine (mg/dl)	1.5 ± 0.7	1.8 ± 1.0	0.149
Hemoglobin (g/dl)	13.3 ± 2.2	13.1 ± 2.1	0.716
Hematocrit %	40.9 ± 5.9	39.5 ± 5.4	0.238
BNP (pg/ml)	2,176 ± 1,904	1,721 ± 1,502	0.259
% Hospital mortality	11.94	9.09	0.67
% General mortality (25 months)	66.7%	37.3%	0.019

(HF 95%, 1.02 - 1.07). The ejection fraction was not a marker of the worst prognosis in multivariate analysis.

Discussion

Among patients who were hospitalized with decompensated HF and systolic dysfunction, those with profile C (cold and congested) represent a more severe group, which has marked hypotension more frequently, high BNP, impaired renal function, hyponatremia and the need for positive inotropic support for compensation. This group has a poor prognosis and usually requires a hospital stay longer for clinical compensation.

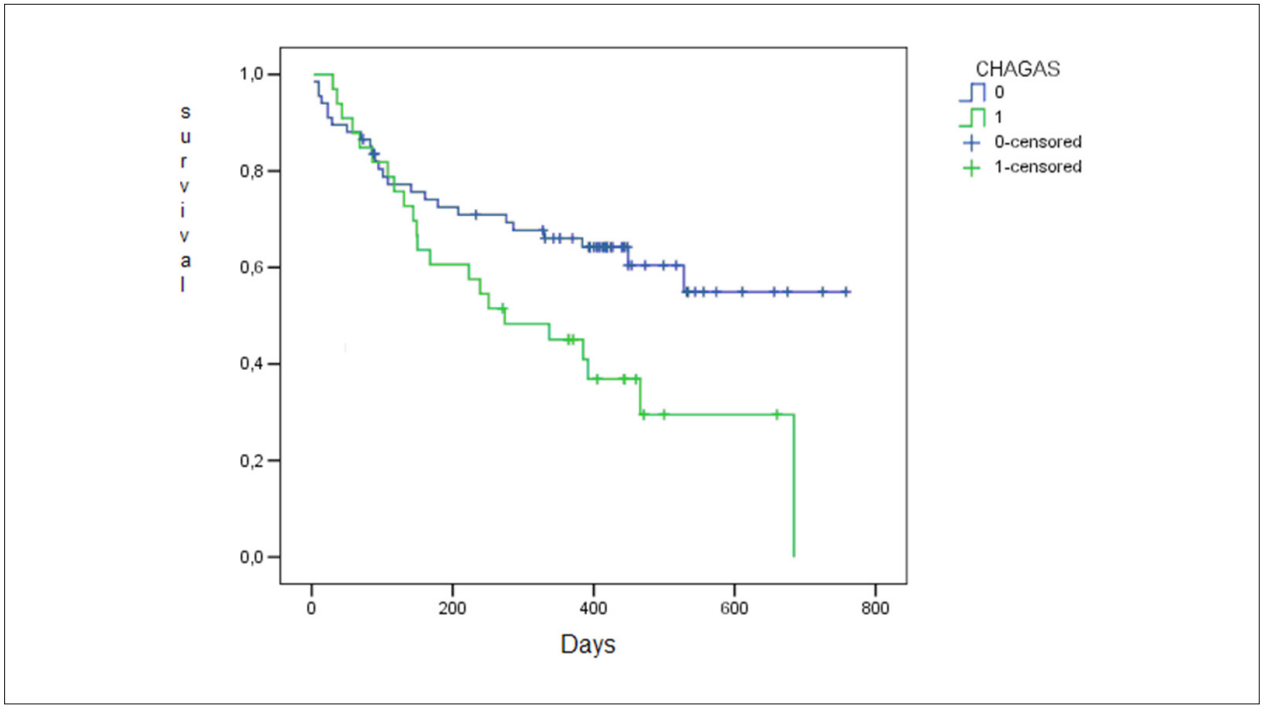

Fig. 2 - Mortality according the cardiomyopathy etiology - chagasic cardiomyopathy - green line and non chagasic cardiomyopathy - blue line. P = 0.019 (log rank)

Table 3 - Clinical and laboratory characteristics of the patients who died during the study and of those who remain alive

Variable	Death Yes Average and standard deviation	Death Non Average and standard deviation	*p*
Age (years)	62.4 ± 14.0	53.3 ± 14.8	0.002
LVEF %	21.3 ± 7.4	26.0 ± 8.9	0.005
Initial Hb (g/dl)	12.8 ± 2.1	13.5 ± 2.1	0.10
Initial Ht(%)	39.9 ± 5.6	40.0 ± 5.6	0.9
Initial urea (mg/dl)	84.4 ± 48.0	65.6 ± 35.5	0.03
Initial creatinine (mg/dl)	1.8 ± 0.9	1.5 ± 0.9	0.12
Initial Na (mEq/l)	136.9 ± 4.0	137.7 ± 3.9	0.33
BNP (pg/ml)	2,382 ± 2,017	1,411 ± 1,052	0.007
Initial SBP (mmHg)	93.8 ± 19.2	97.1 ± 22.0	0.45

The use of clinical-hemodynamic classification in decompensated patient has been very useful to guide treatment in this phase. The patient who presents congestion without signs of poor perfusion (profile B) may be treated with diuretics and vasodilators to control hypervolemia and peripheral vascular resistance. The patient who presents congestion associated with poor perfusion needs, beyond the hypervolemia treatment with diuretics, drugs that also control the low cardiac output, such as inotropes and vasodilators.

Studies that used the clinical and hemodynamic profile in a general hospital showed that the profile B (hot and congested) is the most common among patients who were hospitalized with decompensated HF, described in approximately 50.0% of patients hospitalized for compensation. Profile C (cold and congested) is second in frequency, being described in approximately 20.0% of patients, followed by profile L (cold and dry), 3.5%[11-13]. In our hospital, a referral center for the treatment of heart failure, the numbers are substantially different, being C the most frequently identified profile, in approximately 65.0% of hospitalized patients.

In this population, in which we studied the hospital mortality (11.0%) and the follow-up (47.0%) one, both conditions were high. In previous work from our group, we had already documented that the mortality of patients who are treated in our hospital is high and larger than the one described in the records and many cohorts[18]. This increased mortality due, probably, to the increased intensity of clinical manifestations and severity of cardiopathy of the patients who seek for and are admitted to a tertiary hospital. In the previous study[18], the mortality of patients hospitalized between the years 2005-2006 was 8.8%, a rate that is higher than that reported in the registry ADHERE[9] (4.0%). However, when we stratified the patients according to severity, we observed that in our hospital 75.6% were hospitalized with systolic BP below 115 mmHg compared to 18.5% in the ADHERE registry. Comparing the evolution of more severe patients in the ADHERE Registry, the mortality rate was 20.9% and our 16.9%, showing no significant difference when comparing patients of similar severity. The mortality rate of 11.0% of this current study, higher than the study of 2005/2006, may also be related to patient selection, since for the current study we selected only patients with more severe profile (profile C).

Cardiomyopathy by Chagas disease remains a very prevalent disease in Brazil, including São Paulo. The impairment of the cardiac muscle in this disease is complex, involving auto immune responses, myocardial impairment, autonomic nervous system impairment and an intense inflammatory process. When comparing the evolution of patients with Chagas cardiomyopathy with that of other etiologies, it appears that the prognosis of Chagas disease in symptomatic cases is worse.

Rassi Jr et al[19], in a predominantly outpatient population, identified some predictors of mortality in patients with Chagas cardiomyopathy: functional class III and IV (NYHA), evidence of cardiomegaly on chest radiography, left ventricular dysfunction by echocardiogram, evidence of non sustained ventricular tachycardia by Holter, low QRS voltage on electrocardiogram and male. In this study of Rassi Jr et al, only 10.4% of patients had functional class III and IV, data that characterizes that this population was consisted of patients with less severe cardiopathy than that included in our work. In another study, Freitas et al[14] also related to chagasic etiology with poor prognosis, but for this evaluation outpatients were used, which also have a less severe clinical profile.

In the study by Stevenson et al, which examined the mortality of different profiles, chagasic etiology described mortality of about 40.0% in the first year of follow up for patients with profile C. In our study, the mortality of non chagasic patients was similar to that found by Stevenson, but that of chagasic patients was higher, about 60.0% of patients dying within the first year of follow-up. Although chagasic patients have had a worse prognosis, they presented better levels of creatinine and urea than the non chagasic. A fact that might contribute to better renal function is the age of chagasic patients, who were significantly younger than the NCh ones.

In the last decade, we have been seeing an increase in the number of publications on decompensated HF, which improves the understanding in this most critical phase of the disease. In the Brazilian guideline on acute HF, published in 2009[20], the following clinical and hemodynamic markers are highlighted as having the worst prognosis: low cardiac output refractory congestion, renal failure, persistent third heart sound, and arterial hypotension. Regarding etiology, the guidance mentions HF as a probable factor of poor prognosis, but without more consistent evidences[20].

Reviewing the literature, we found that so far no study has specifically compared the evolution of chagasic and non chagasic patients with advanced HF, and that at the time of admission, they presented profile C. This study filled this gap and showed that chagasic etiology is also an independent factor of poor prognosis in advanced stage of heart failure with systolic dysfunction.

Our data indicate that all patients with advanced HF deserve aggressive treatment, since HF is a disease with malignant characteristics and that the modern treatment can modify this trend. However, we must remember that the group of chagasic patients has an even worse prognosis. Despite the advances in this area of medicine, the patient with Chagas cardiomyopathy remains a major challenge in clinical practice.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

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