Clinical and Therapeutics Aspects of Heart Failure Due to Chagas Disease

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OBJECTIVE

Describe the clinical and therapeutic characteristics of patients with heart failure (HF) secondary to chronic chagasic cardiomyopathy and evaluate if these characteristics are different from those found in other etiologies.

METHODS

A prospective analysis of the patients treated between August 2003 and June 2004 at a HF referral outpatient clinic was conducted.

RESULTS

Three hundred and fifty six patients diagnosed with HF were included in the study. Chagasic cardiomyopathy was the most common etiology (48% of the cases). Other etiologies included hypertensive cardiomyopathy in 19% of the patients, idiopathic dilated in 11% and ischemic in 9%. Patients with HF secondary to chagasic cardiomyopathy were more frequently from non-white ethnic groups (88 vs. 75%; p = 0.002), had a family history of Chagas disease (57 vs. 21%; p = 0.001), had the disease for a longer length of time (71 vs. 56 months; p = 0.034), had lower levels of education (4.4 ± 4.1 vs. 5.7 ± 4.2 years of study; p = 0.004), had a lower heart rate (69 ± 12 vs. 73 ± 13; p = 0.03) and a lower systolic blood pressure (121 ± 25 vs. 129 ± 28 mmHg; p = 0.006). There was also a higher incidence of the use of amiodarone (22 vs. 13%; p = 0.036) and artificial pacemakers (15 vs. 1%; p = 0.001). There was a lower usage of beta-blockers (39 vs. 59%; p = 0.001).

CONCLUSION

In this sample of HF outpatients, in a state with a high prevalence of Chagas disease, chagasic cardiomyopathy was the most common etiology and they presented some unique clinical and therapeutic characteristics in comparison to other heart failure patients.

KEY WORDS

Chagasic cardiomyopathy, heart failure, epidemiology.

According to data of the World Health Organization (WHO) Chagas disease is one of the most serious infectious diseases in Latin America. Considering the continent as a whole, current estimates place ninety million people at risk to contract the disease, thirteen million are infected and approximately 3 to 3.3 million have symptomatic forms of the disease[1,2]. Nevertheless, these estimates are not precise and do not reflect the realities of the different countries in the region.

In 1980, the prevalence of Chagas disease in Brazil was estimated at 4.2% corresponding to 6.5 million people[3]. Since that time, there has been a significant reduction in vectorial and blood transfusion transmission leading to a drastic decline in the onset of new cases. More recent estimates were adjusted for roughly 1.9 million infected people[4]. Although WHO has declared Brazil free of vectorial transmission, some small endemic colonies are still found, mainly in the state of Bahia[5,6]. Roughly 10% to 40% of the people who have Chagas disease develop some type of heart disease.[1] The most common complications include pulmonary or systemic thromboembolisms, conduction system disorders, bradyarrhythmias, severe ventricular arrhythmias, sudden death and congestive heart failure.

During the past few years substantial progress has been made in the areas of physiopathological understanding, diagnosis and treatment of heart failure. Nevertheless the majority of heart failure studies have been conducted in population samples with a low prevalence of Chagas disease. Since the conclusions of these studies do not directly apply to people with heart failure due to chronic chagasic cardiomyopathy, current treatment approaches for these patients could be different from those applied to patients with other etiologies.

The objective of this study is to describe the prevalence of chronic chagasic cardiomyopathy among the patients treated at a heart failure referral outpatient clinic in the state of Bahia and compare the epidemiological, clinical and therapeutic aspects of these patients with the characteristics of patients with other etiologies.

METHODS

This is a cross-sectional study with a sample of patients demanding medical attention. All patients were seen consecutively at an outpatient heart failure referral clinic and had their data prospectively recorded on a standard care form containing epidemiological and clinical data and treatment methods. This clinic provides care, without exceptions, to adults and children who generally speaking are from the middle to low social classes referred from other services in various cities throughout the state.

Only patients diagnosed with heart failure were included in the analysis. The diagnosis of the main heart failure etiology was established based on clinical criteria that included a detailed medical history, epidemiological data and a physical examination as well as complementary tests including an electrocardiogram at rest, echocardiogram and serological tests for Chagas disease. Evaluations were made in relation to a low sodium diet[7], angiotensin-converting enzyme inhibitors or angiotensin receptor blockers[8], beta-blockers[9,10] and spironolactone[11] as part of the standard treatment for heart failure[7,12].

Evaluations were also made on the use of digoxin, furosemide, amiodarone, hydralazine and nitrates that are safe agents and recommended to reduce morbidity associated with heart failure. Dosages of the agents used for the heart failure treatment were converted to ordinal variables: 1 = none; 2 = low dosage; 3 = moderate dosage; 4 = high dosage. High dosages were considered as dosages higher or equal to the maximum dosage recommended in the guidelines for heart failure treatment and low dosages similar to the initial dosages described[7,13]. Regular use of medication indicates that the patient had taken more than 90% of the dosages of the prescribed medication. Since the study was exclusively observational there were no ethical conflicts.

Student's t-test was used to compare averages and the chi-square and Fisher exact test were used for proportions. The Mann-Whitney test was used to determine the associations between ordinal and etiological variables. Multiple linear regression models were used to evaluate the adjusted association between more than one independent variable and a continuous dependent variable, specifically heart rate and systolic blood pressure. The significance level adopted was 5% for two-tailed hypotheses. The statistical tests were processed using the software program SPSS version 9.0 for Windows.

RESULTS

Between August 2003 and June 2004, 356 patients diagnosed with heart failure were consecutively seen. The average age of the sample studied was 54 ± 13 years and 53% were male. In reference to ethnic groups, the majority were mulattos (42%), followed by blacks (39%) and whites (19%). The most common etiology was chagasic cardiomyopathy corresponding to 48.3% of the cases, followed by hypertensive cardiomyopathy (19%), idiopathic dilated cardiomyopathy (11%), ischemic cardiomyopathy (9.1%), valvulopathies (3.1%) and other etiologies (9.6%) that encompass the etiologies alcoholic, viral, postpartum, hypertrophic and restrictive among others. Table 1 describes the characteristics of the patients according to the main etiology.

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Comparison of the clinical characteristics for patients with and without chagasic cardiomyopathy etiology did not reveal any differences between average age, prevalence of males, previous history of dyspnea or edema, consumption of alcoholic beverages or diastolic blood pressure. There was a previous history of strokes for 19% of the patients with chagasic cardiomyopathy and 15% of the other patients (p = 0.31). There were fewer patients with chagasic cardiomyopathy in the white ethnic group (12 vs. 26%; p = 0.002) and they had lower levels of education, systolic blood pressure and heart rates (table 2). Patients with chagasic cardiomyopathy presented a higher incidence for a family history of Chagas disease (57 vs. 21%; p = 0.001).

Table 1 – Clinical characteristics of the patients according to the main heart failure etiology.

Etiology	Chagasic Cardiomyopathy	Hypertensive Cardiomyopathy	Idiopathic Cardiomyopathy	Ischemic Cardiomyopathy
Number of patients (%)	170 (48)	69 (19)	40 (11)	32 (9)
Age in years (± SD)	54.4 ± 12	58 ± 13	51 ± 13	58 ± 12
Males (%)	49	50	62	59
Ethnic group: White (%)	12	16	27	45
Mulatto (%)	45	42	43	32
Black (%)	42	42	30	23
Origin: Salvador (%)	67	72	60	75
Education (in years)	4.4 ± 4.1	5.1 ± 3.9	6.0 ± 3.8	4.9 ± 4.0
Alcohol consumption (shots/wk)*	0.7 ± 2.9	1.4 ± 4.9	1.0 ± 3.0	0.3 ± 1.6
History of dyspnea (%)	88	93	90	97
History of edema (%)	60	65	54	72
FC NYHA III or IV (%)	16	16	10	19
FC NYHA II (%)	59	63	58	59
Disease duration (months)	71 ± 67	65 ± 89	61 ± 46	49 ± 39
History of strokes (%)	19	16	20	6.3
Family history of Chagas (%)	57	20	21	23
Systolic BP (mmHg ±SD)	121 ± 22	142 ± 24	122 ± 21	130 ± 24
Diastolic BP (mmHg ±SD)	79 ± 13	88 ± 15	79 ± 13	79 ± 16
Heart rate (bpm ±SD)	69 ± 12	74 ± 12	73 ± 12	72 ± 12

FC = Functional Class; NYHA = New York Heart Association; BP = Blood Pressure.
*Shot of alcohol = any volume of beverage containing 20 g (0.7 oz.) of ethylic alcohol.

Table 2 – Clinical characteristics of chagasic and non-chagasic patients

	Chagasic Cardiomyopathy	Non-chagasic Cardiomyopathy	p
Number of patients (%)	170 (48)	187 (52)	-
Age in years (± SD)	54 ± 12	54 ±14	0.78
Males (%)	49	55	0.29
Whites (%)	12	25	0.002
Origin: Salvador (%)	67	71	0.34
Education (in years)	4.4 ± 4.1	5.7 ± 4.2	0.005
Alcohol consumption (shots/wk)*	0.7 ± 2.9	1.2 ± 5.1	0.32
History of dyspnea (%)	88	94	0.07
History of edema (%)	60	62	0.68
FC NYHA III or IV (%)	15	16	0.85
FC NYHA II (%)	59	59	0.93
Disease duration (months)	71 ± 67	55 ± 63	0.03
Family history of Chagas (%)	57	21	< 0.001
History of strokes (%)	19	15	0.29
History of hypertension	37	62	< 0.001
Systolic BP (mmHg ±SD)	121± 22	130 ± 26	0.001
Diastolic BP (mmHg ±SD)	79 ± 13	82 ± 16	0.20
Heart rate (bpm ±SD)	69 ± 12	73 ± 13	0.004

FC = Functional Class; NYHA = New York Heart Association; BP = blood pressure. *Shot of alcohol = any volume of beverage containing 20 g (0.7 oz.) of ethylic alcohol.

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Table 3 describes the treatments used. When evaluated as ordinal variables the dosages of some medications used for heart failure treatment were similar between the patients with chronic chagasic cardiomyopathy and the others: angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (p = 0.32), digoxin (p = 0.34), furosemide (p = 0.84), spironolactone (p = 0.35), amlodipine (p = 0.31). Nevertheless, the beta-blocker dosage was lower (p = 0.001) and moderate to high dosages were even more uncommon for patients with the chagasic etiology (20 vs. 49%; p < 0.001). The use of artificial permanent pacemakers was higher for chagasic patients (15 vs. 1%; p < 0.001), as well as the use of amiodarone (22 vs. 13%; p = 0.036). Average systolic blood pressure levels for patients with chagasic cardiomyopathy was consistently lower than the non-chagasic patients after adjustment for the use of beta-blockers (p = 0.001) and for a history of hypertension (p = 0.001). Similarly heart rate averages were consistently lower than non-chagasic patients even after adjustment for the use of amiodarone (p = 0.004), beta-blockers (p = 0.011) or artificial pacemakers (p = 0.006).

DISCUSSION

Even though there are estimates for the reduction of the prevalence in Latin America, Chagas disease is one of the main problems of public health and a leading cause of heart failure in endemic areas[1,2,5,14]. In spite of this fact, there is a shortage of medical literature dealing with the topics of epidemiology and relevance of new therapies for heart failure secondary to Chagas disease.

In this study, conducted at a state referral center, there was a higher incidence of chagasic cardiomyopathy as the etiology of heart failure despite the fact that the majority of the patients were from Salvador, the state capital, a region that is prominently industrialized. During the past few decades there has been an intensive migration process from the rural areas to urban centers and these patients that are on average 54 years old were probably infected in rural areas before the vectorial transmission control programs have been effectively implemented during the past twenty years[15]. The majority of the patients were black or mulattos. Although this finding could compromise the generalization of the results for other populations, it corresponds to the demographic profile of the region where the study was conducted as well as some other Brazilian regions.

A low prevalence of ischemic cardiomyopathy as a heart failure etiology was found in this sample when compared to the prevalence in other countries[7], and even other Brazilian states[16]. This finding could be a result of the fact that the average age of the patients evaluated was low or since the study is cross-sectional, it is possible that there is a higher lethality rate for ischemic cardiomyopathy. It was observed that the average duration and acknowledgement of the heart failure condition was higher for the patients with chagasic cardiomyopathy which could be related to an earlier discovery of the disease through electrocardiograph alterations and serologic diagnoses of Chagas disease. Nevertheless this lower lethality cannot be attributed to this since no cohort studies have been conducted to address this question.

In this study no significant association was found between chronic chagasic cardiomyopathy and variables such as age, gender and origin. However, the findings of a higher incidence in non-white ethnic groups with a family history of Chagas and lower education levels can be justified by the close association between the forms of the disease transmission and the social, economic and cultural levels of the population[1].

Table 3 – Treatment methods according to the main heart failure etiology.

	Chagasic Cardiomyopathy	Non-chagasic Cardiomyopathy	p
Number of patients (%)	170 (48)	187 (52)	-
Regular use of medication (%)	81	76	0.33
Low sodium diet (%)	66	65	0.91
Use of ACE or ARB (%)	87	87	0.91
Moderate/high dosage of ACE or ARB (%)	80	80	0.94
Use of beta-blockers (%)	39	59	0.001
Moderate/high dosage of beta-blockers (%)	20	49	< 0.001
Use of furosemide (%)	71	74	0.50
Use of digoxin (%)	61	68	0.15
Use of spironolactone (%)	50	56	0.25
Use of amlodipine (%)	4.1	7.0	0.25
Use of amiodarone (%)	22	13	0.036
Use of hydralazine (%)	7	7	0.86
Use of nitrates (%)	9	11	0.54
Permanent artificial pacemaker	15	1	< 0.001

ACE = Angiotensin-converting enzyme inhibitors; ARB = Angiotensin receptor blockers

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Despite the use of similar dosages of cardiovascular medication for the heart failure patients it is particularly interesting that the patients with Chagas disease have significantly lower systolic blood pressure levels and heart rates. These findings could be explained by the lower incidence of hypertension in this sample and by the higher incidence of sinus node dysfunction among the Chagas patients[17]. These findings could justify the limited use of beta-blockers, mainly in moderate to high dosages in the patients with chagasic cardiomyopathy. However, the higher incidence of artificial permanent pacemakers did not have an association with the concomitant increase of beta-blocker use.

In reference to the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers the results revealed a similar incidence of moderate to high dosages between the chagasic and non-chagasic patients, according to current recommendations[13]. The use of amiodarone, although there are no documented benefits in clinical trials, is recommended by specialists for the treatment of complex arrhythmias for Chagas disease[18,19], justifying its higher use among the Chagas patients in this sample. The low usage rates for hydralazine and nitrates in a predominately black and mulatto population is justifiable since the data were collected before the publication of the A-HEFT study[20].

Even though they are not usually represented in clinical trials for heart failure, patients with chagasic cardiomyopathy with exception of the use of beta-blockers receive medicinal treatment that is similar to patients with other etiologies. Despite the fact that innovative treatment strategies for heart failure due to Chagas disease are currently being investigated in our midst, the effectiveness of simpler treatment methods in this population has not yet been documented. Even worse, there are no reliable data available in our medical literature in relation to the epidemiology of Chagas disease as a cause of heart failure.

A relevant datum found in our cases in relation to the impact on the patients' quality of life, and coinciding with autopsy findings, was the history of strokes (19%) in Chagas patients that can be justified by the high incidence of embolisms with this cardiopathy[22].

In conclusion, chagasic cardiomyopathy was the main cause of heart failure in our patients. Despite the effective measures of public health in the combat of vectorial and blood transfusion transmission, there is still a significant number of people in the South American continent with the chagasic cardiopathy and therefore it should remain as one of the leading causes of heart failure during the next few years. Considering the high prevalence rates for rheumatic cardiopathies and the increased incidence of ischemic cardiopathies in Latin America, we can predict a substantial increase in the incidence of terminal heart disease in the next few decades.

Population studies are required in order to confirm our prevalence findings, cohort studies are needed to establish prognoses in accordance with the heart failure etiology and randomized clinical trials are needed to evaluate if the therapeutic options generally used for heart failure apply to people with Chagas disease.

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

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