Letter to the Editor

Is Chagas cardiomyopathy an independent risk factor for patients with heart failure?

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Abstract

Some studies showed increased mortality in chagasic patients but most of these studies did not perform statistical adjustments to socioeconomic variables. The main objective of this study was to investigate if there is an independent association between Chagas etiology and mortality in patients with heart failure and moderate to severe left ventricle systolic dysfunction. Stratified analysis by the variables associated to chagasic etiology and multivariate analysis through logistic regression were performed to evaluate the relationship between Chagas cardiomyopathy and one-year mortality. Among 417 patients initially evaluated, 191 had the inclusion criteria. The mortality was higher in patients with Chagas cardiomyopathy than in the patients with other etiologies (log rank test; $p = 0.036$). At one-year follow-up, the mortality in chagasic patients was 21.6% versus 10.6% in the remaining (relative risk $= 2.03$; 95% CI $= 0.98$–4.2; $p = 0.05$). At logistic regression, educational level was identified as a confounder variable of the association between Chagas cardiomyopathy and one-year mortality. This association was no more statistically significant after adjustment for educational level (odds ratio $= 1.67$; 95% CI $= 0.63$–4.41). In this study, Chagas cardiomyopathy was a marker of worse prognosis, but was not independently associated to increased one-year mortality in outpatients with heart failure and moderate to severe systolic dysfunction.
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Keywords: Chagas cardiomyopathy; Mortality; Educational status; Heart failure; Congestive

1. Introduction

In several countries of Central and South America, Chagas disease is one of the main causes of heart failure [1]. However, even in these countries, few studies on heart failure patients included a significant proportion of Chagas cardiomyopathy, probably due to selection bias. Some studies described a worse prognosis in chagasic patients when compared to other etiologies [2–5], but most of them where performed in non-endemic zones where the prognosis may be better [6]. The main objective of this study is to investigate if there is an independent association between Chagas etiology and mortality in a series of patients with heart failure selected from an endemic zone of Chagas disease.

2. Methods

Patients were prospectively evaluated at an academic hospital. Consecutive patients with the following characteristics were included: diagnosis of heart failure and left ventricle ejection fraction $\leq 45\%$ by echocardiography [10]. Study protocol was approved by the institution's human research committee.

The follow-up was made at one year of admission.

2.1. Statistical analysis

Patients were divided in two groups, according to the etiology: chagasic and non-chagasic. Bivariate analyses were performed between basic characteristics and the groups with and without Chagas disease, and the patients alive or not at one-year follow-up. Crude relative risk of the

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association between etiology of heart failure and mortality was calculated. Stratified analysis by the variables associated to the etiology with $p < 10\%$ was done to obtain stratum-specific relative risk, as well as for initial evaluation of confounding and interaction. The Breslow–Day homogeneity test was also used in the identification of covariates that potentially modify the effect, being considered significant at a p value $< 20\%$. Multivariate analysis were made through models of non-conditional logistics regression, using the backward strategy, where the dependent variable was mortality and the main independent variable was etiology (chagasic or not). The significant level for all the remaining associations was 5% bicaudal. The software Statistical Package for Social Sciences (SPSS), version 9.0 for Windows (SPSS, Chicago, IL), was used.

3. Results

Between August 2003 and June 2004, 417 new patients were admitted in the clinic. Among them, 52 (13%) did not have the confirmation of the diagnosis of heart failure on subsequent visits and 214 (51%) did not present the criteria of systolic dysfunction. Among the 214 patients that do not have inclusion criteria by echocardiography, 80 (37%) presented normal systolic function and 134 (63%) mild systolic dysfunction. The 191 patients with diagnosis of heart failure and moderate to severe left ventricle systolic dysfunction, were included in the analysis. One-year follow-up was obtained in 168 (88%). In 20 (11%) of them, follow-up was obtained before one year, totalizing 188 (99%) patients with some data about their evolution. The patients with Chagas cardiomyopathy had several clinical, laboratory and therapeutic characteristics different from the patients with the other etiologies (Table 1).

When evaluated through the log rank test, Chagas disease was associated with higher mortality ($p = 0.036$). At one-year follow-up there were 16 deaths (21.6%) among the patients with Chagas disease and 10 (10.6%) among the remaining patients (relative risk $= 2.03$; 95% confidence interval $= 0.98$–4.2; $p = 0.05$).

By logistics regression, we identified education level as a confounding variable of the association between chagasic etiology and death within one year. After adjustment for education level, the association between Chagas cardiomyopathy and one-year mortality was no more statistically significant (OR $= 1.67$; 95% CI $= 0.63$–4.41).

4. Discussion

In some studies with heart failure patients, the Chagas cardiomyopathy had higher mortality in comparison with the other etiologies [2–5]. In our study, these patients had a relative risk of death twice larger than the other etiologies. But they also had a larger prevalence of worse prognostic

Table 1
Patients' characteristics according to the etiology on admission

Etiology	Chagasic $n = 89$ (46.6%)	Non-chagasic $n = 102$ (53.4%)	p
Male (%)	53.8	59.4	0.39
Age (years)	54.0 ± 12.6	52.7 ± 13.4	0.73
Caucasian race (%)	11.4	24.0	0.03
Years of formal education ≤4 years (%)	75.3	54.0	0.004
Hypertension (%)	32.2	61.4	0.001
Stroke (%)	22.2	14.0	0.14
Artificial pacemaker (%)	17.8	1.0	0.001
Systolic blood pressure (mm Hg)	117.8 ± 21.9	127.1 ± 25.5	0.01
Diastolic blood pressure (mm Hg)	77.6 ± 12.4	81.11 ± 15.8	0.11
Cardiac rate (beats/min)	70.2 ± 12.9	73.9 ± 13.5	0.08
LV ejection fraction on echocardiography (%)	36.6 ± 10.8	35.5 ± 9.4	0.54

SD = standard deviation/ NYHA = New York Heart Association/ LV = left ventricle.

factors as, for example, lower education level [7], lower blood pressure [8], lower frequency of Caucasian race [9], and less frequent use of beta-blockers [10]. After we performed an adjusted analysis for these variables, the association between Chagas disease and mortality is reduced and loses statistical significance. Most of previous studies did not perform the adjustment for variables that reflect the socioeconomic or education level. The only one that made these adjustments found that care delivered through the Public Health System was associated to higher mortality in patients with heart failure [5] and that adjusting for this marker of socioeconomic status, on a hierarchical model, Chagas' heart disease had a predictive value on mortality. The difference between the result of this study and ours may be related to our smaller sample size or to some differences between the samples. In our study, albeit the patients had a similar left ventricle ejection fraction, they were outpatients, and none of them had insurance.

Chagas cardiomyopathy was the main etiology of heart failure in the present study and was associated to one-year mortality. However, this association was not independent of the educational status, suggesting that Chagas disease is not a risk factor, but a risk marker among the patients with heart failure.

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