Original article

Functional Classification versus Ejection Fraction in Patients with Heart Failure and Chagas Disease

Comparação entre Classificação Funcional e Fração de Ejeção em Pacientes com Insuficiência Cardíaca na Doença de Chagas

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Abstract

Introduction: Chagas disease, an infection caused by the protozoan Trypanosoma cruzi, is an important health problem worldwide that causes cardiac dilation, arrhythmias, and death. Heart failure is a complex syndrome with high morbidity and mortality rates that progresses with similar complications. The New York Heart Association functional classification is used to categorize heart failure severity and stratify heart disease risks and therapies. A reduced left ventricular ejection fraction measured by echocardiography is directly related to a poor prognosis.

Objective: To compare the relationship between New York Heart Association functional classification and left ventricular ejection fraction in Chagas versus no Chagas disease outpatients.

Methods: Cross-sectional study in a cohort of patients followed at a heart failure clinic. Medical records, clinical interviews, functional classification, and left ventricular ejection fraction by echocardiography were analyzed. The data were filed in a database and analyzed using SPSS software.

Results: A total of 127 patients with heart failure were selected from August 2018 to July 2019. Of them, 34 (26.8%) had Chagas disease and 93 (73.3%) had no Chagas disease. There was a predominance of men (53.5%) and patients aged > 60 years (61.4%). There was also a predominance of functional class II. Of the Chagas and no Chagas disease patients, 71% versus 93% had a reduced ejection fraction, 21% versus 6% had a mid-range ejection fraction, and 8% versus 1% had a preserved ejection fraction, respectively.

Conclusion: There was an association between advanced functional class and reduced left ventricular ejection fraction, especially in Chagas patients, information that can be used for outpatient follow-up.

Keywords: Chagas disease; Heart failure; Stroke volume

Resumo

Introdução: A doença de Chagas é uma infecção causada pelo protozoário *Trypanosoma cruzi*. É considerada um importante problema de saúde do mundo, tendo como manifestações a dilatação cardíaca, arritmias e morte. A insuficiência cardíaca é uma síndrome complexa e de elevada morbimortalidade, que evolui com complicações semelhantes. Para categorizar a gravidade da insuficiência cardíaca, utilizamos a classificação funcional da *New York Heart Association*, para estratificar risco e terapias para cardiopatias. Além disso, a reduzida fração de ejeção do ventrículo esquerdo, medida pelo ecocardiograma, tem relação direta com mau prognóstico.

Objetivo: Comparar a relação entre a classificação funcional pela *New York Heart Association* e a medida da fração de ejeção do ventrículo esquerdo em pacientes ambulatoriais chagásicos e não chagásicos.

Metódos: Estudo de corte transversal na coorte, composto de pacientes acompanhados em ambulatório de insuficiência cardíaca. Foram realizadas avaliação de prontuários, entrevista clínica e verificação da classificação funcional e da fração de ejeção do ventrículo esquerdo pelo ecocardiograma. Os dados foram arquivados em banco de dados e analisados pelo *Statistical Package for the Social Sciences*.

Resultados: No período de agosto de 2018 a julho de 2019, foram selecionados 127 indivíduos com insuficiência cardíaca. Destes, 34 (26,8%) eram portadores da doença de Chagas e 93 (73,3%) eram não Chagas. Observou-se predominância do sexo masculino (53,5%) e de idade >60 anos (61,4%). Houve predomínio da classe funcional II nos grupos. Em relação à fração de ejeção dos pacientes chagásicos e não chagas, observou-se que, respectivamente, 71% contra 93% dos pacientes tinham fração de ejeção reduzida, 21% *versus* 6% tinham fração de ejeção intermediária e 8% *versus* 1% fração de ejeção preservada.

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Conclusão: Houve associação entre classe funcional avançada e reduzida fração de ejeção do ventrículo esquerdo principalmente em chagásicos, podendo ser usada para acompanhamento evolutivo ambulatorial.

Palavras-chave: Doença de Chagas; Insuficiência cardíaca; Volume sistólico.

Introduction

Chagas disease, an infection caused by the protozoan *Trypanosoma cruzi* and transmitted by hematophagous triatomine insects, is considered a worldwide health problem. An estimated 15 million people are infected worldwide, with over 100 million people at risk of infection, mainly in Latin American and developing countries.[1]

Chagas disease is among the 13 most neglected tropical diseases in the world, with Chagas cardiomyopathy being its most severe clinical presentation.[2] It is often complicated by decompensated heart failure (HF), resulting in important consequences to the heart's function and performance and a determinant of disease progression.[3]

HF is a cardiac dysfunction that progresses with an inadequate oxygen supply to meet the metabolic demands of the tissues. It is a serious disease, with high morbidity and mortality rates, that also represents a serious public health problem.[4] The New York Heart Association (NYHA) Functional Classification (FC), described in 1928 and reviewed in 1994, is an instrument that stratifies HF by severity by assessing the prognosis or effect of myocardial disease regarding signs and symptoms and the degree of physical limitations to usual activities imposed by heart disease.[5]

HF patients can be classified into four categories. Class I corresponds to the absence of symptoms during the performance of usual activities, with effort limitations similar to those of healthy people; class II corresponds to the presence of mild symptoms when performing usual activities; class III refers to the presence of moderate symptoms with marked limitations when performing usual activities; and class IV corresponds to the presence of symptoms at rest (physical disability). Despite being widely used worldwide and having high prognostic value, the NYHA FC is subjective and, therefore, can be subject to interpretation bias.[5,6]

According to Mady et al.,[3] mortality increases in Chagas disease or other forms of HF due to complications and myocardial deterioration. Accordingly, a low left ventricular ejection fraction (LVEF) has shown a relationship with poor prognosis for Chagas disease patients. The LVEF, that is, the ratio between the ejected stroke volume and end-diastolic volume, can be assessed through echocardiography.[2]

This study aimed to compare NYHA FC frequency and LVEF measurement between Chagas disease and no Chagas disease patients treated at an HF outpatient clinic.

Methods

This cross-sectional study included an existing cohort, specifically patients diagnosed with HF and followed up at the Heart Failure and Cardiomyopathy Outpatient Clinic of a reference center. HF syndrome was defined as standardized, and LVEF was measured using the Teicholz and/or Simpson method.[7,8] Chagas etiology was defined by two positive serological tests using different laboratory methods. The inclusion criteria were age older than 18 years, with echocardiogram results and, consequently, recent LVEF (at the latest in the last year of follow-up), and with Chagas disease and no Chagas disease heart disease with NYHA FC recorded in medical charts. Patients for whom data for minimal variables were incomplete were excluded.

Clinical interviews were conducted to define cardiovascular symptoms, evaluate medical records, and establish the NYHA FC and LVEF of patients in routine consultations at the outpatient clinic.

Demographic variables such as sex (male versus female), skin color (Black, Pardo, and White), and age (18–59 years versus ≥ 60 years) were evaluated in addition to NYHA FC (I, II, III, and IV) and LVEF measured by echocardiography in the previous six (reduced, <40%; mid-range, 40–49%; and preserved, ≥50%).

SPSS and Stata software were used for performing descriptive statistics, calculating means/proportions to compare variables between the two groups, and determining the prevalence ratio to analyze the prevalence of the factors studied.

The results are presented in a table and in graphs built using Excel 2016 software. The protocol was approved by the Research Ethics Committee of the Prof. Edgard Santos University Hospital (CAAE: 951089185.0000.0049), and all patients signed an informed consent form.

Results

A total of 127 HF patients were selected between August 2018 and July 2019 to be followed up. Of them, 34 (26.8%) had Chagas disease and 93 (73.3%) had no Chagas disease. There was a predominance of men (53.5%) aged 60 years or older (61.4%) (Table 1). In this population, 2.3% had a preserved LVEF (≥50%), 10.2% had a mid-range LVEF (40–49%), and 86.5% had a reduced LVEF.

Of the total number of patients with a preserved LVEF in this study, 75% had Chagas disease. There were no differences in frequency between the sexes or age groups or between Black and Pardo patients. Among patients with a mid-range LVEF, there was a predominance of Chagas disease (53.8%), men (53.8%), patients aged ≥ 60 years (76.1%), and Pardo individuals (53.8%).

As for patients with a reduced LVEF (<40%), there was a predominance of no Chagas disease (78.2%), men (53.6%), patients aged ≥ 60 years (60%), and Pardo individuals (50%). There was a significant statistical difference between having Chagas disease and HF severity due to a reduced LVEF.

As for the frequency of NYHA FC, there was a predominance of FC II in both groups. In Chagas disease patients, equivalent frequencies (12%) were found between FC III and IV, while FC I had a frequency of only 9%. In the group of no Chagas disease patients, the frequency was 30% for FC III, followed by 12% for FC IV, and only 1% for FC I (Figure 1).

The evaluation of the relationship between LVEF in Chagas disease patients showed that 71% of patients had a reduced LVEF, 21% had a mid-range LVEF, and 8% had a preserved LVEF. In no Chagas disease patients, the pattern was similar, with a predominance of patients having a reduced LVEF (93%), followed by mid-range (6%), and preserved (1%) (Figure 2), demonstrating a similar distribution in the two studied populations.

Patients with a reduced LVEF showed a predominance of NYHA FC II (61%), followed by FC III (25%), and FC IV (14%). Patients with a mid-range LVEF showed a predominance of FC II (61%), followed by FC III (31%), and FC I (8%). On the other hand, patients with preserved LVEF showed a predominance of FC I (75%), followed by FC II (25%) (Figure 3).

Table 1 – Distribution of 127 patients by demographic variables and ejection fraction on echocardiogram.

Variable	n (%)	Ejection fraction						P value
		Preserved		Mid-range		Reduced		
		n	%	n	%	n	%	
Chagas disease								
Yes	34 (26.8)	3	75.0	7	53.8	24	21.8	
No	93 (73.3)	1	25.0	6	46.2	86	78.2	0.004
Sex								
Male	68 (53.5)	2	50.0	7	53.8	59	53.6	
Female	59 (46.5)	2	50.0	6	46.2	51	46.4	0.990
Age, years								
34-59	49 (38.6)	2	50.0	3	23.1	44	40.0	
≥60	78 (61.4)	2	50.0	10	76.1	66	60.0	0.440
Skin color								
Black	46 (36.2)	2	50.0	5	38.5	39	35.4	
Pardo	64 (50.4)	2	50.0	7	53.8	55	50.0	
White	17 (13.4)	-	-	1	7.7	16	14.5	0.871
Total		4	2.3	13	10.2	110	86.5	

Mean age; ejection fraction in % on echocardiography.

Discussion

This cross-sectional analysis of a cohort of HF patients considered the relationships between LVEF, NYHA FC, and HF etiology between Chagas disease and no Chagas disease patients. We found a significant association between advanced FC and worse LVEF, especially in patients with Chagas disease.

Disagreements between the clinical presentation defined by NYHA FC and complementary diagnostic methods sometimes cannot be used as comparative models in medical evaluation, even when using other severity indicators such as LVEF by echocardiography, scintigraphy, serum brain natriuretic peptide dosage, magnetic resonance, or heart tomography, possible divergences may reflect the stability of different instruments, pathophysiological understanding, therapeutics, and HF syndrome compensation.[7,8]

Most patients studied in this population had a reduced LVEF (86.5%), and the no Chagas disease etiology predominated, regardless of the fact that the study was conducted in an endemic region for Chagas disease and at the reference clinic in the state.[9] A study by Coles et al.,[10] which also made no distinctions between HF etiologies, reported a different frequency, with most patients presenting with a preserved LVEF (52%), followed by a reduced (35%) and mid-range (13%) LVEF. A discordant result was also reported by Koh et al.,[11] for whom most of the population studied had a preserved LVEF (56%), followed by a reduced (23%) and mid-range (21%) LVEF. These divergent proportions can be explained by different locations and studies, outpatient populations, and study objectives. A greater number of patients with a preserved LVEF may prevail in population-based perspective studies.[9,10,12]

In this study, a reduced LVEF predominated in male patients (53.6%), whereas there was no sex-based difference for patients with a preserved EF. Borlaug et al.[13] showed similar results by identifying a bimodal distribution of LVEF, with a preponderance of men with a reduced and preserved LVEF also reported by several studies. Such information is strong

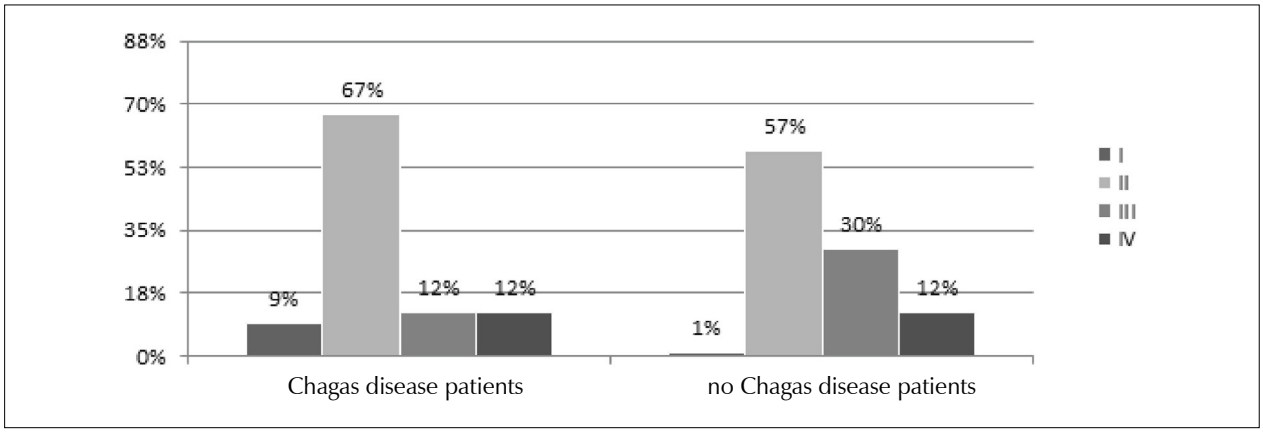

Figure 1 – *Frequency of Chagas disease versus no Chagas disease patients by New York Heart Association functional class.*

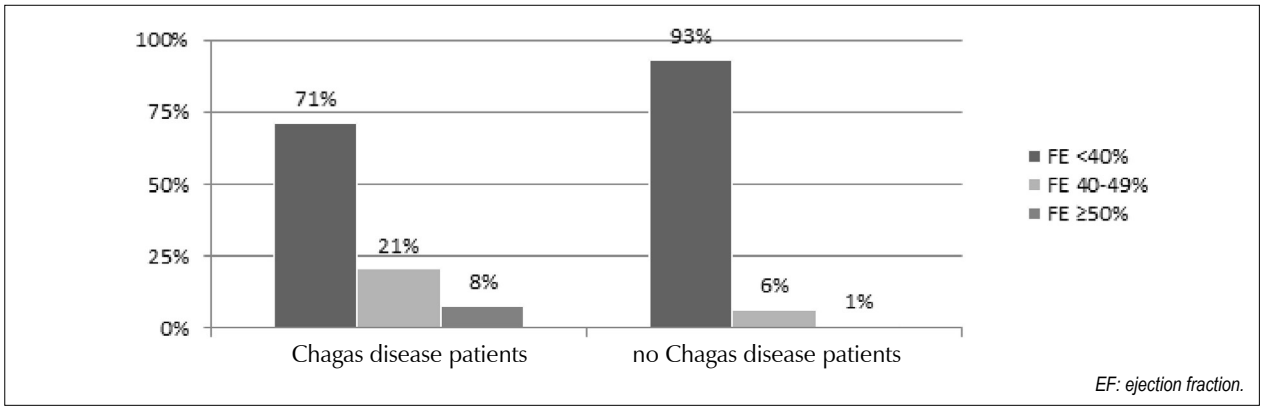

Figure 2 – *Frequency of Chagas disease and no Chagas disease patients by left ventricle ejection fraction.*

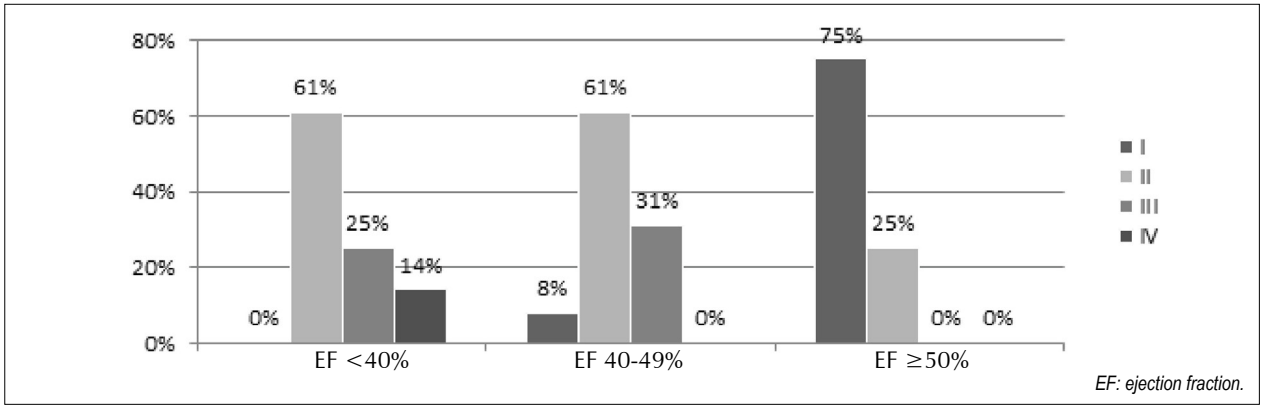

Figure 3 – *Distribution of patients by New York Heart Association functional class and left ventricular ejection fraction.*

evidence that LVEF (reduced and preserved) suggests distinct disease processes.

HF is a prevalent syndrome in the older population.[1,14] Borlaug et al.[13] reported that the mean age of the population with a preserved LVEF was 74 years versus 70 years for the population with a reduced LVEF. These data corroborate the results found in the present study, according to which patients with a reduced LVEF were older. Chioncel et al.[12] showed similar results with a mean population age of over 60 years for patients with a reduced or preserved LVEF (69 versus 64 years old, respectively). These data highlight the frequency of HF with a preserved LVEF in older patients, mainly dependent on diabetes, hypertension, and ischemic heart disease.[1,7,14] On the other hand, Martins et al.[15] reported a divergent result, with a predominance of patients with a preserved LVEF (63%) regardless of HF etiology.[16]

The present study showed a predominance of Chagas disease patients with a reduced LVEF compared with no Chagas disease patients (71% versus 93%), demonstrating greater FC severity in this outpatient population. Corroborating data presented by Mady et al.[3] indicated a positive association between NYHA FC regardless of class and LVEF in patients with the cardiac form of Chagas disease. The comparison of these data with the current results shows a similar marked tendency of Chagas disease patients to have a reduced LVEF.[3,15]

The analysis of the distribution between NYHA FC and LVEF in this study showed a predominance of NYHA FC II in the groups of patients with a reduced (61%) or mid-range (61%) EF. These results suggest that clinical, comorbidity, biological, and therapeutic determinants sustain that the higher the patient's EF, the lower the NYHA FC, indicating a better prognosis with a more favorable clinical condition.[7,8]

On the other hand, the lack of studies on the frequency and distribution of HF patients using NYHA FC and reduced LVEF and the low representation of Chagas disease in large published series was considered a difficulty for a greater approach and comparative understanding of the data. Finally, due to the recent advent of the mid-range EF classification (40–49%), insufficient studies including this data are available to enable frequency or association analyses.[1,7]

Conclusion

Although the group populations have different HF etiologies, Chagas disease versus no Chagas disease, the relationship between FC and LVEF was very similar in terms of outpatient clinical compensation symptoms, which are determinant in NYHA FC stratification, with FC II predominating without the

influence of a reduced cardiac function on echocardiography. This suggests a state of clinical HF compensation, and it should be a goal for patients to remain under optimized treatment. In addition, most patients presented with a reduced LVEF and NYHA FC II, an often asymptomatic stage of heart disease. Furthermore, LVEF is indirectly linked to NYHA FC severity, i.e., the higher the NYHA FC, the lower the LVEF and vice versa regardless of HF etiology.

Authors' contributions

Preparation: JS, LN, and RA; data collection: JS and RA; data analysis: MGA and RA; discussion: MGA and RA.

Conflict of interest

The authors have declared that they have no conflict of interest.

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