

## Major Article

# Epidemiological features, echocardiographic findings, and parasite load in patients with Chagas disease

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### Abstract

**Introduction:** Chagas disease is a major public health problem that is endemic in Brazil and Latin America. This study aimed to determine the socioeconomic, demographic, and clinical characteristics of 171 patients (mean age, 45 years; female, 65%) with Chagas disease at Hospital Universitário de Brasília, Federal District, Brazil. **Methods:** We implemented this cross-sectional study using a clinical epidemiological questionnaire, electrocardiography, echocardiography, and quantitative detection of *Trypanosoma cruzi* DNA in blood using qRT-PCR. **Results:** Among the patients, 26.3% had a full elementary education, and 13.2% were illiterate. Most (63.6%) were economically classified as class C, and 51.5% were born in Bahia state. A total of 62.0% participants reported previous contact with the triatomine bug. The clinical forms of the disease were indeterminate (69.51%), cardiac (15.24%), digestive (10.37%), and mixed (4.88%). The most common electrocardiographic abnormality was complete right bundle branch block in association with a divisional anterosuperior block. Only 14.6% of the patients complied with benznidazole medication for at least 60 days, and 164 of them were assessed by echocardiography. The parasite load was positive in 56% of the patients. **Conclusions:** Chagas disease affected mostly women, with the indeterminate chronic form of the disease.

**Keywords:** Epidemiological profile. University hospital. Chagas disease.

### INTRODUCTION

Chagas disease (CD) remains a major public health issue in Brazil and Latin America<sup>1-3</sup>. About 2 - 3 million individuals in Brazil are infected and ~6,000 deaths are recorded annually<sup>1</sup>, whereas 8 - 10 million are infected in Latin America<sup>4</sup>.

Although CD has been considered a rural disease, its geographical distribution has recently widened, possibly due to the success of programs to control vector transmission in endemic areas as well as regional and international migration<sup>5</sup>. The disease has also spread to the USA and some European countries<sup>5,6</sup>. Although this might be associated with the distribution of the chronic form of CD, other serious conditions associated with undetermined and cardiac and digestive forms,

might impose a cost burden on health systems. In addition, transmission through other routes such as maternal and oral, and reactivation in immunosuppressed individuals could be involved. Few systematic, population-based studies have hindered an estimated evaluation of the magnitude of CD in Brazil. Until the 1960s<sup>1</sup>, CD typically affected younger manual laborers in rural areas who were not well-educated, and possibly infected via vector transmission. The estimated prevalence of CD at that time was 4.2% of the total population of 6.5 million, and mostly involved rural areas<sup>1</sup>. However, CD has now spread to urban areas of Brazil as a result of migration and intensified along with urban-industrial development since the 1970s. In fact, an estimated 65% of the population with CD in Brazil is thought to currently reside in urban areas<sup>7</sup>.

The migration and urbanization phenomena have improved the survival rates of patients affected by the disease. Development has improved housing conditions, decreased rural populations, and granted more access to health care systems where patients can access cardiopathy-specific medications, permanent

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pacemaker implants, cardiac transplantation, and stricter blood donor screens<sup>8</sup>. The urbanization of Brazil and the increased survival of individuals infected with *Trypanosoma cruzi* have led to the emergence of associations and interactions with other chronic diseases such as hypertension, diabetes mellitus and immunosuppressed states such as HIV and transplantation that promote CD reactivation<sup>4</sup>.

The social costs are very high because CD affects patients of reproductive age, and therapeutic options as well as research investment are limited. Therefore, a study of the characteristics of patients with CD and attention from public health agencies are justified. Appropriate patient follow-up and the creation of a health care network adapted to this new reality have become essential, especially when considering that CD can cause severe cardiopathy.

Therefore, we aimed to determine the socioeconomic, demographic and clinical characteristics, echocardiographic findings and parasite loads of patients with CD treated at Brasilia University Hospital (HUB). The patients were derived from a cohort selected for an evaluation of factors that could predict progression to cardiac CD.

## METHODS

This descriptive study included 171 patients aged > 18 years. All were diagnosed with CD according to the criteria of the 2015 Brazilian Consensus on CD, had positive serological chemiluminescence and indirect hemagglutination findings at the cardiology and infectious disease units at HUB, and were followed up between April 2016 and December 2017<sup>9</sup>. The patients were invited to enroll in the study during routine clinical appointments and were included after completing structured a clinical epidemiological questionnaire and undergoing a thorough clinical evaluation, routine hematological and biochemical laboratory tests, electrocardiography and conventional echocardiography. Blood samples were collected to identify *T. cruzi* DNA using quantitative real-time polymerase chain reaction (qRT-PCR)<sup>10</sup>. The evaluated variables included sociodemographic data (age, sex, education level, marital status, household income, employment status, economic classification<sup>11</sup>, location of residence, probable location of infection), clinical history (current complaints), lifestyle habits (smoking, alcohol consumption, sedentary lifestyle), comorbidities, medications, previous benzimidazole treatment and the findings of a physical examination.

The clinical forms of CD were classified according to the criteria published by the 2015 Brazilian Consensus on CD<sup>9</sup>. Echocardiography proceeded using a TUS-A 400 ultrasound System (Toshiba Medical Systems Corp., Otawara, Japan). The biplane method of disks (modified Simpson rule) is the currently recommended 2D method of left ventricular ejection fraction (LVEF) assessment recommended by the American Society of Echocardiography and the European Association of Cardiovascular Imaging<sup>12</sup>. Diastolic function was evaluated from mitral inflow E/A profiles and annular tissue Doppler curves ( $e^{\prime}/a^{\prime}$ ) as recommended by the American Society of Echocardiography and the European Association of Cardiovascular Imaging<sup>13</sup>.

The Ethics Committee of the School of Medicine at Brasilia University approved the study (date, 04/29/2016; protocol number, 1.521.680), which proceeded in accordance with the Helsinki Declaration of 1964, as revised in 1975, 1983, 1989, 1996, and 2000. All included patients provided written, informed consent to participate in all procedures associated with the study.

## Statistical Analysis

Statistical analyses included descriptions of the data according to the variables of interest. Categorical data are represented as absolute and relative frequencies and quantitative data are shown as measures of central tendencies and dispersion. The normality of distributions at a 5% level of statistical significance was analyzed using Kolmogorov-Smirnov tests. The database was created and analyzed using the Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL, USA).

## RESULTS

Among 164 (95.91%) of the 171 patients who were evaluated by conventional echocardiography, 158 (96%) of them volunteered to participate in qRT-PCR tests for *T. cruzi* DNA. **Table 1** shows that most of the patients were female, (n = 112, 65%) and the median age of the entire cohort was 45 (range 24 - 74) years. Overall, 88 (51.5%) patients were originally from Bahia state in northeast Brazil, whereas 108 (63.2%) resided in the Federal District. Most patients had some education, but 23 (13.2%) were illiterate. Most patients were married or were in a stable relationship (n = 116, 67.8%). Regarding self-reported ethnicity, 60% (n = 103) were mixed/Pardo (Moreno), 19.9% (n = 34) were Caucasian and 13.5% (n = 23) were Afro-Brazilian. Based on economic classification, most patients were class C (n = 77, 63.7%), and a minority (n = 6, 63.5%) were class E. At the time of the interview, 94 (55%) patients stated that they were employed, mostly in domestic jobs or assisting in general services. Among lifestyle habits, 133 (77.8%) patients did not consume alcoholic beverages, 12 (7%) smoked and 88 (51%) had sedentary lifestyles. Of those who were employed, work required a considerable amount of walking (6%), and heavy physical activities (49%).

**Table 1** shows the distribution of the epidemiological characteristics associated with clinical forms. At the time of the interview, 137 (80%) patients lived in urban areas, 160 (93.6%) lived in rural areas and 129 (75.0%) lived in “wattle and daub” dwellings. A total of 106 (62.0%) had previous contact with the triatomine bug, and 28 (49.1%) had relatives aged < 40 years with cardiac problems. Comorbidities in the 171 patients comprised arterial hypertension in 37 (21.6%), dyslipidemia in 35 (20.5%), depression/anxiety in 27 (15.8%), and diabetes in 9 (7.8%). Medications prescribed to the patients included antidiabetics, lipid-lowering drugs, antidepressants and others. The most frequent medications reported by 33 (19%) patients were angiotensin-converting enzyme inhibitors and renin-angiotensin system blockers. (**Table 2**). With respect to benzimidazole (BNZ), 59 (34.5%) patients were treated and

**TABLE 1:** Distribution of social and demographic characteristics of 171 participants according to clinical forms of Chagas disease at HUB, Brasília.

		Indeterminate	Cardiac	Mixed	Digestive	P*
Sex	M	31 (26.7%)	14 (48.3%)	5 (62.5%)	9 (50.0%)	0.014
	F	85 (73.3%)	15 (51.5%)	3 (37.5%)	9 (50.0%)	
Median age (IQR)		45.00 (12.00)	45.00 (16.00)	50.00 (14.00)	45.50(14.00)	0.647
Illiterate		16 (13.8%)	2 (6.9%)	2 (25.0%)	3 (16.7%)	0.108
Elementary 1		21 (18.1%)	(13.8%)	0.0	1 (5.6%)	
Elementary 2		23 (19.8%)	11 (37.9%)	5 (62.5%)	6 (33.3%)	
Incomplete high school		20 (17.2%)	4 (13.8%)	0.0	3 (16.7%)	
Completed high school		22 (19.0%)	6 (20.7%)	1 (12.5%)	4 (22.5%)	
Completed university		14 (12.5%)	2 (6.9%)	0.0	1 (5.6%)	
Caucasian		25 (21.6%)	2 (6.9%)	3 (37.5%)	4 (22.5%)	
Afro-Brazilian		15 (12.9%)	7(24.1%)	0.0	1 (5.6%)	0.503
Asian		2 (1.7%)	3 (10.3%)	0.0	1 (5.6%)	
African		69 (59.5%)	17 (58.6%)	5 (62.5%)	12 (66.7)	
Indigenous		1 (0.9%)	0.0	0.0	0.0	
Unknown		3 (2.6%)	0.0	0.0	0.0	
Declined to inform		1 (0.9%)	0.0	0.0	0.0	
Economic level	A	1 (0.9%)	0.0	0.0	0.0	0.858
	B	18 (15.5%)	3 (10.3%)	0.0	2 (11.1%)	
	C	73 (62.9%)	20 (69.0%)	5 (62.5%)	11 (61.1%)	
	D	19 (16.4%)	6 (20.7%)	3 (37.5%)	4 (22.2%)	
	E	5 (4.3%)	0.0	0.0	1 (5.6%)	
Employed		66 (56.9%)	12 (41.4%)	4 (50.0%)	12 (66.7%)	0.348
Domestic worker		20 (17.5%)	0	1 (12.5%)	3 (15.8%)	0.546
General services		15 (14.3%)	2 (6.9%)	2 (25.0%)	4 (22.2%)	
Trades services		17 (14.7%)	6 (20.7%)	0.0	2 (11.1%)	
Missionary		0.0	1 (3.4%)	0.0	1 (5.3%)	
Health care		2 (1.7%)	0.0	0.0	0.0	
Teacher		4 (3.4%)	0.0	0.0	1 (5.6%)	
Pensioner/retired		3 (2.6%)	0.0	0.0	1 (5.6%)	
Government employee		2 (1.7%)	0.0	0.0	1 (5.6%)	
Rural worker		5 (4.3%)	4 (13.8%)	1 (12.5%)	1 (5.6%)	
Homemaker		5 (4.3%)	2 (6.9%)	0.0	1 (5.6%)	
Rural residence		20 (17.2%)	7 (24.1%)	4 (50.0%)	3 (16.7%)	0.129
Urban residence		96 (82.8%)	22 (75.9%)	4 (50.0%)	15 (83.3%)	
Previously bitten by triatomine		69 (59.5%)	21 (74.2%)	6 (75.0%)	10 (55.6%)	0.760
Family history of Chagas disease		84 (72.4%)	22 (75.9%)	4 (50.0%)	13 (72.2%)	0.465
Lived in rural area		107 (92.2%)	28 (96.6%)	8 (100.0%)	17 (94.4%)	0.805
Median time outside endemic area (years)		20.00 (31.00)	20.00 (30.00)	10.00 (35.00)	26.00 (18.00)	0.262

**Abbreviations:** Domestic employment, housekeeper, child caregiver, house cleaner, gardener; **F:** female; median (interquartile interval); **Freq:** frequency; General services, cook, kitchen assistant, firefighter, maid, kitchen maid, street cleaner, concierge, security; Health care, assistant, nursing assistant, lab technician; **HUB:** Brasília University Hospital; **M:** male; Trades services, attendant, treasurer, clerk, hairdresser, merchant, deliverer, waiter, manicurist, assembler, repository, cab driver. \*Pearson chi-square tests with Monte Carlo correction for qualitative variables and Kruskal-Wallis tests for quantitative variables.

112 (65.5%) were not. Among those treated with BNZ, 24 (14%) completed the treatment course and 15 (8.8%) did not. All 171 patients were assessed by electrocardiography. The most prevalent electrocardiographic abnormality associated with cardiac and mixed forms, was complete right bundle branch block (RBBB) associated with a divisional anterosuperior block (ASDB) in 11 (6%) patients, complete right bundle branch

block (RBBB) in 7 (4%), and first-degree atrioventricular block in 3 (2%). The clinical forms of CD were indeterminate, cardiac, digestive and mixed in 114 (69.51%), 25 (15.24%), 17 (10.37%) and 8 (4.88%) patients, respectively. The distribution of the cardiac forms was A (n = 10), B1 (n = 9), B2 (n = 4), and C (n = 12). Echocardiographic abnormalities were associated with indeterminate CD in 22 (19.64%)

**TABLE 2:** Distribution of clinical characteristics according to the clinical form of Chagas disease at HUB, Brasília.

	Indeterminate	Cardiac	Mixed	Digestive	P*
Hypertension	26 (22.4%)	5 (17.2%)	2 (25.0%)	4 (22.2%)	0.941
Dyslipidemia	30 (25.9%)	2 (6.9%)	2 (25.0%)	1 (5.6%)	0.240
Depression	12 (10.3%)	2 (6.9%)	0.0	1 (5.6%)	0.904
Anxiety	8 (6.9%)	2 (6.9%)	1 (12.5%)	1 (5.6%)	0.957
Diabetes	9 (7.8%)	0.0	0.0	0.0	0.932
Hyperthyroidism	3 (2.6%)	1 (3.4%)	0.0	0.0	0.817
Gastritis	2 (1.7%)	0.0	0.0	0.0	0.893
Acquired immunodeficiency syndrome	0.0	1 (3.4%)	0.0	0.0	0.349
Asthma	1 (0.9 %)	0.0	0.0	1 (5.6%)	0.479
Hypothyroidism	3 (2.6%)	0.0	0.0	0.0	0.817
Celiac disease	1 (0.9%)	0.0	0.0	0.0	0.853
Antiphospholipid syndrome	0.0	1 (3.4%)	0.0	0.0	0.349
ACEI/ABR	25 (21.6%)	4 (13.8%)	2 (25%)	2 (11.1%)	0.566
Lipid-lowering agent	11 (9.5%)	1 (3.4%)	0.0	0.0	0.579
Antidepressant	8 (6.9%)	2 (6.9%)	0.0	1 (5.6%)	0.901
Beta-blocker	3 (2.6%)	7 (24.1%)	0.0	0.0	0.002
Omeprazole	5 (4.3%)	1 (3.4%)	1 (12.5%)	2 (11.1%)	0.352
Aspirin	4 (3.4%)	1 (3.4%)	0.0	0.0	0.882
Spirolactone	0.0	1 (3.4%)	0.0	0.0	0.320
Diuretic	12 (10.3%)	2 (6.9%)	0.0	0.0	0.700
Amiodarone	1 (0.9%)	0.0	0.0	0.0	0.746
Warfarin	0.0	1 (3.4%)	0.0	0.0	0.320
Antidiabetic agents	4 (3.4%)	1 (3.4%)	0.0	0.0	0.900
Other drugs	12 (10.3%)	3 (10.3%)	0.0	0.0	0.740
Consumption of alcoholic drinks	22 (19.0%)	9 (31.0%)	2 (25.0%)	5 (27.8%)	0.515
Smoking	8 (6.9%)	1 (3.4%)	0.0	2 (11.1%)	0.751
Physical activity	53 (45.7%)	15 (51.7%)	6 (75.0%)	10 (55.6%)	0.334
Benznidazole	38 (22,2%)	10(5,8%)	5 (2,9%)	6 (3,5%)	0,960
Positive PCR	63 (56.7%)	16 (55.2%)	6 (75.0%)	7 (43.8%)	0.578
Parasite load <sup>†</sup>	0.01 (0.09)	0.02 (0.12)	0.05 (8.63)	0.00 (0.01)	0.038

\*Pearson chi-square tests with Monte Carlo correction for qualitative variables and Kruskal-Wallis test for quantitative variables. **ACEI/ABR:** angiotensin-converting enzyme inhibitors; **HUB:** Brasília University Hospital; **PCR:** polymerase chain reaction. †Quantitative evaluation of parasite load equivalent to number of parasites/100 ng DNA.

patients, but this was benign or associated with aging, in 8 (38.09%) with cardiac CD, 4 (23.53%) with digestive CD, and 4 (50%) with mixed CD. Cardiac variables determined by conventional echocardiography did not significantly differ (**Table 3**). Apical thrombus with apical aneurysms was found in only 2 (1.8%) of 164 patients in association with cardiac CD. Table 2 shows the findings of 158 (96%) of 164 patients who underwent qRT-PCR tests for *T. cruzi* DNA. The parasite load was positive in 63 (56.7%), 16 (55.2%), 7 (43.8%) and 6 (75%) patients with indeterminate, cardiac, digestive and mixed forms of CD, respectively. The amount of parasites significantly differed among CD classifications (**Table 2**), being the parasitic load was greater for the mixed, than for the cardiac, indeterminate and digestive forms.

## DISCUSSION

The mean age of our study cohort was 45 years and women were predominant. Most participants had completed at least an elementary education, were employed in domestic or general services jobs, and resided in the Federal District. About 62% of them reported contact with the triatomine bug. As this cohort was derived mostly from an outpatient clinic, the predominance of females might be related to a greater demand for medical services by women, as determined by Bozelli et al.<sup>14</sup>, Vizzoni et al.<sup>15</sup>, and Martins-Melo et al. in a recent meta-analysis<sup>1</sup>. The age of our participants was similar to those reported by Bozelli et al.<sup>14</sup> and Araújo et al.<sup>16</sup>, but differed from those described by Vizzoni et al.<sup>15</sup>, Alves et al.<sup>17</sup> and Pereira et al.<sup>18</sup>, who reported

**TABLE 3:** Conventional echocardiographic variables at HUB, Brasília.

	Indeterminate (n =114)		Cardiac (n = 25)		Mixed (n = 8)		Digestive (n = 17)		P*
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
LVEDV (mL/m <sup>2</sup> )	27.81	3.08	27.37	4.48	26.97	2.53	26.72	5.46	0.168
LA (mm/m <sup>2</sup> )	18.02	3.80	16.79	4.15	15.87	5.72	17.85	3.51	0.484
RV (mm/m <sup>2</sup> )	14.55	4.12	14.31	5.17	14.19	5.17	14.17	5.61	0.836
TAPSE (cm)	2.51	0.65	2.27	0.43	2.72	0.79	2.56	0.48	0.070
Color Doppler S Wave (cm/s)	13.40	2.72	13.60	2.45	13.40	2.85	13.45	2.90	0.776
RA VOL (mL/m <sup>2</sup> )	17.20	8.15	14.80	11.10	14.80	9.33	16.60	5.23	0.663
TEI / RV	0.39	0.33	0.41	0.35	0.43	0.39	0.40	0.38	0.750
FAC RV %	0.44	0.18	0.41	0.11	0.34	0.31	0.46	0.21	0.495
LA Vol (mL/m <sup>2</sup> )	18.75	9.23	17.63	6.78	23.90	11.68	20.73	8.85	0.578
LVEF %	70.16	10.52	69.90	12.61	70.28	8.80	67.53	13.07	0.839
LV MASS (g/m <sup>2</sup> )	71.30	25.95	65.70	29.80	60.45	20.75	64.15	22.23	0.230
Mitral flow E velocity (cm/s)	77.90	28.70	82.30	25.70	90.80	26.85	79.90	24.80	0.335
Mitral flow A velocity (cm/s)	58.70	22.37	63.20	23.10	51.35	53.38	60.00	34.50	0.762
S Vel (cm/s)	7.90	1.90	7.90	1.10	8.80	1.50	7.90	1.60	0.373
A' Vel (cm/s)	8.90	2.80	9.30	2.15	8.55	1.10	8.90	2.20	0.630
E' Vel septal	10.00	3.40	9.70	2.80	11.00	3.18	9.40	3.65	0.537
E/A RATIO	1.33	0.68	1.30	0.63	1.42	0.94	1.57	0.77	0.439
Average e'' (cm/s)	11.15	3.57	11.05	4.50	11.72	4.86	9.97	2.72	0.544
Mitral DT (ms)	0.19	0.07	0.20	0.08	0.18	0.07	0.20	0.059	0.297
E/e' (average e')	7.08	2.80	7.35	3.33	7.98	4.60	8.10	2.98	0.610

\*Kruskal-Wallis tests. Abbreviations: **DT**: deceleration time; **EF**: ejection fraction; **FAC**: fractional area change; **HUB**: Brasília University Hospital; **LA**: left atrium; **LV**: left ventricle; **RA**: right atrium; **RV**: right ventricle; **TAPSE**: tricuspid annular plane systolic excursion; **TE/RV**: myocardial performance index of right ventricle; **VEL**: velocity; Vol, volume.

a more advanced group. We consider that this difference was due to the types of patients who use the HUB service. Most are referred from hemocenter screening; others are diagnosed during prenatal care and some are referred from primary care.

Our patients had an average education duration of four years, and were thus better educated than those in previous studies (**Table 1**)<sup>19,20</sup>.

Most patients recalled having been bitten by the triatomine bug, reinforcing the hypothesis of infection via vector transmission. These findings were similar to those published by others<sup>20</sup>.

Hypertension was the most frequent (21.6%) comorbidity which agrees with previous studies that found a 20%-25% prevalence of arterial hypertension in Brazil<sup>21-25</sup>. The second most common comorbidity was dyslipidemia, at 20.5%. The prevalence of dyslipidemia widely varies depending on the cultural and lifestyle habits of the population studied; for example, the estimated prevalence of dyslipidemia in the adult Brazilian population is 20%-30%<sup>26</sup>. Chronic diseases can lead to depression, and in CD, this association is attributed to psychological factors. However, Villar-Pereira et al. have associated immunological and neurochemical disorders with depressive manifestations in animal models<sup>27</sup>. Little is known about rates of depression among patients with CD. Osaki et al. identified symptoms of depression in 40.9% of 110 patients, particularly in those with heart disease<sup>28</sup>. Only 8% of our patients reported depression. This might be underestimated owing to the limitations of "self-referred" information derived from patients.

Overall, 24 (14.6%) of our patients were treated with benznidazole, which was lower than that previously reported<sup>29-32</sup>. This could be explained by low acceptance of or compliance with recommended treatment or because the present study involved outpatients who were in routinely followed up as part of the HUB service.

The distribution of the clinical CD forms among patients at HUB has not been previously reported. Most of our patients were diagnosed with the indeterminate form of the disease (64.3%), which is in contrast to recently published findings<sup>14</sup>. This might have been because our cohort was derived from outpatient clinics and HUB is a referral center for CD in the Federal District that accepts patients referred after screening by Hemocentro, which is the blood bank in Brasília.

An accurate way to evaluate amounts of protozoan DNA in the serum of individuals infected by *T. cruzi* is qRT-PCR. We found a statistically significant difference in parasitic load among different forms of CD using qRT-PCR. The parasitic load was significantly higher for the mixed, than the cardiac, indeterminate and digestive forms. This finding differs from previously published findings suggesting that the parasite load decreases with higher chronicity<sup>33</sup>. This finding should be carefully analyzed owing to the small sample size of the groups studied. One explanation for this could be the influence of treatment on parasite load. However, 34.5% of our study population was treated with BNZ and a significant difference among clinical forms was not found.

Echocardiography is a valuable tool for evaluating patients with CD, as it can assess cardiac function and structure, which complements information obtained by electrocardiography. Because ventricular segmental contractility in patients with CD is associated with disease progression, echocardiography has been routinely applied in survival studies<sup>34-38</sup>. Left ventricular apical aneurysms are found in about 2% of patients with CD, and in 24% of patients with electrocardiographic abnormalities<sup>34</sup>. Two (1.8%) of our patients had apical aneurysms and 33 (19.3%) had electrocardiographic abnormalities. However, these depend on the type of study and the predominant clinical forms. Other studies have generated different results; Pereira et al.<sup>18</sup> and Andrade et al.<sup>35</sup> respectively detected electrocardiographic abnormalities and changes in 48% and 10.8% of patients.

Aneurysms are associated with left ventricular thrombi and embolic stroke within two years of their detection. Apical aneurysms and intracavitary thrombi are the main factors associated with cerebrovascular ischemic events in patients with CD. Subclinical atherosclerosis assessed by carotid IMT does not appear to play a major role in the genesis of ischemic events in CD<sup>39,40</sup>. Therefore, these patients need rigorous follow-up using methods that can detect early changes, considering that the clinical behavior of indeterminate CD is heterogeneous, and factors associated with progression to more severe forms remain unknown.

The present study characterized outpatients with CD treated at a referral university hospital, and highlighted female predominance, younger age, and a higher average level of education.

The present study is a preliminary investigation to determine the composition of a clinical cohort in which to evaluate the progression of CD to the cardiac form. We determined the characteristics of a population treated at a tertiary teaching hospital, which should contribute to the composition of samples in subsequent studies. All possible prognostic variables, such as treatment with specific medications, will be evaluated in such a clinical cohort. We highlighted the importance of the descriptive data presented in this study because the sample consisted predominantly of women diagnosed with the undetermined form of CD. A study of prognostic factors in specific groups is important to understand the progression of CD and to contribute to technological improvements in the detection of CD progression and treatment.

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### Conflicts of interest

The authors have no conflicts of interest to declare.

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