Electrocardiogram and Chagas Disease

A Large Population Database of Primary Care Patients

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ABSTRACT

Background: Chagas disease (ChD) used to be a disease restricted to Latin America, but has become a worldwide problem due to migration of infected individuals to developed countries. Electrocardiography has been considered an essential exam to evaluate ChD patients.

Objective: This study sought to identify prevalent electrocardiographic abnormalities in a large sample of ChD patients evaluated in the primary care setting.

Methods: This retrospective observational study assessed all consecutive digital 12-lead electrocardiograms (ECG) performed by the Telehealth Network of Minas Gerais, Brazil, from January 1 to December 31, 2011. In that time, the service attended primary care patients in 660 cities in the Minas Gerais province. ChD was self-reported, and the individuals who did not report having ChD were considered noninfected. The prevalence of electrocardiographic abnormalities was assessed.

Results: Self-reported ChD patients comprised 7,590 (2.9%) of 264,324 patients who underwent ECG during the study period. The mean age for ChD patients was 57.0 ± 13.7 years, and 64.1% of patients were women. The most common comorbidities were hypertension (61.3%), diabetes (9.1%), and dyslipidemia (6.9%), and 10.7% were smokers. The most frequent electrocardiographic abnormalities were nonspecific repolarization abnormalities (34.6%), right bundle branch block (RBBB) (22.7%), left anterior hemiblock (LAH) (22.5%), ventricular premature beats (5.4%), and atrial fibrillation (5.4%). Only 31.5% of the patients had no electrocardiographic abnormality versus 61.2% in noninfected individuals ($p < 0.001$). The prevalence of normal ECG decreased with aging and was significantly lower than for noninfected individuals in all age groups. Pacemaker rhythm (odds ratio [OR]: 13.3, 95% confidence intervals [CI]: 11.5 to 15.4), RBBB (OR: 10.7, 95% CI: 10.1 to 11.4), especially in association with LAH (OR: 12.1, 95% CI: 11.2 to 13.0), second atrioventricular block (OR: 4.1, 95% CI: 2.5 to 6.6), and third atrioventricular block (OR: 13.3, 95% CI: 11.5 to 15.4) were strongly related to ChD.

Conclusions: In this large sample of primary care patients with ChD, there was a high prevalence of electrocardiographic abnormalities. Pacemaker rhythm, RBBB, especially in association with LAH, and second and third atrioventricular block were strongly related to ChD.

Chagas disease (ChD) is endemic in Latin American countries. Due to the increased population mobility and migration of infected individuals to developed countries, it has become a worldwide problem, mostly in Europe and North America [1–3]. In the last decades, initiatives by Latin America countries to improve disease control and reduce transmission, based on vector and transfusional control and case management, have greatly reduced the number of incident cases. Current official estimates suggest that between 8 million and 10 million people are chronically infected worldwide, 4.6 million of them in Brazil [4–6]. Due to a cohort effect, the disease is now a public health problem among older individuals in the old endemic regions, where ChD is still a major cause of heart disease, stroke, and death, now predominantly in the elderly [7].

Chagas cardiomyopathy is the most severe manifestation of ChD and is associated with high morbidity and mortality [8]. It may affect up to 40% of patients in the chronic phase of the disease [9]. Electrocardiographic abnormalities may precede the signs and symptoms of Chagas cardiomyopathy [8,10], and some abnormalities have prognostic impact [11]. Therefore, the determination of the prevalence of electrocardiographic abnormalities in ChD patients is of major clinical and epidemiological importance. The objective of this study was to identify prevalent electrocardiographic abnormalities and common associated conditions in a large sample of ChD patients evaluated in the primary care setting.

METHODS

This retrospective observational study included all consecutive 12-lead digital electrocardiograms (ECG)

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TABLE 1. Clinical characteristic of the ChD patients and noninfected individuals (Minas Gerais, Brazil; N = 264,324)

	ChD Patients (n = 7,590)	Noninfected Individuals (n = 256,733)
Age, yrs	57.0 ± 13.7	50.4 ± 19.1
Octogenarians	369 (4.9)	12,908 (5.0)
Nonagenarians	46 (0.6)	1,528 (0.6)
Women	4,866 (64.1)	152,677 (59.5)
Hypertension	4,656 (61.3)	80,048 (31.2)
Diabetes	692 (9.1)	13,615 (5.3)
Dyslipidemia	520 (6.9)	6,914 (2.7)
Chronic kidney disease	108 (1.4)	1,123 (0.4)
COPD	99 (1.3)	1,735 (0.7)
Family history of CAD	2,475 (32.6)	37,255 (14.5)
Current smokers	812 (10.7)	17,998 (7.0)
Previous MI	194 (2.6)	1,715 (0.7)

Values are mean ± SD or n (%).
CAD, coronary artery disease; ChD, Chagas disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction.

analyzed by the cardiologists from the Telehealth Network of Minas Gerais, a public telehealth service in Brazil, from January 1 to December 31, 2011. In that time, the service provided support to primary care professionals of 658 cities in the state of Minas Gerais, 85% of them with <14,000 inhabitants, by performing teleconsultation (second opinion), and telediagnosis, including ECG analysis [12].

The digital ECG were performed in the cities using a tele-ECG by Tecnologia Eletrônica Brasileira (São Paulo, Brazil) or Micromed Biotecnologia (Brasilia, Brazil) and sent through the internet to the analysis center, where the exams were immediately directed to a team of cardiologists trained and experienced in analysis and interpretation ECG using standardized criteria [13]. Clinical data (age, sex, comorbidities including ChD, medications) were self-reported and collected using a standardized questionnaire filled out by the referring provider, including hypertension, diabetes, obesity, hyperlipidemia, smoking, family history of coronary disease and previous myocardial infarction, chronic kidney disease, chronic obstructive pulmonary disease, and ChD. Patients who reported having ChD were considered ChD patients, and the ones who did not report having the disease were considered noninfected individuals. For the purpose of this study, the use of a specific medication did not infer a diagnosis of a comorbidity.

All consecutive exams were analyzed. ECG with technical problems, such as interference or lead placement errors, were excluded. For the purpose of this study, when a patient underwent >1 ECG recording during the study period, just the first one was included in the analysis. Atrial flutter was classified as atrial fibrillation, as in other epidemiological studies [14]. To investigate the relation between abnormal ECG and clinical characteristics, logistic regression was performed.

IBM SPSS Statistics for Windows (version 20.0, Armonk, NY) was used for statistical analysis. Categorical data were reported as counts and percentages; continuous variables were reported as means ± SD or medians (interquartile ranges [IQR]), as appropriate. To assess the association between abnormal ECG and clinical characteristics, univariate and multivariate odds ratios (OR) and 95% confidence intervals (CI) were estimated by logistic regression. The multivariate model included all clinical characteristics. A 2-tailed p value of 0.05 was considered statistically significant.

This study was approved by the Research Ethics Committee of the Universidade Federal de Minas Gerais.

TABLE 2. Prevalence of ECG with no abnormalities in patients with and without ChD according to age distribution (N = 264,324)

	ChD Patients (n = 7,590; Mean Age 57.0 ± 13.7 yrs)		Noninfected Individuals (n = 256,733; Mean Age 50.4 ± 19.1 yrs)		
Age Group, yrs	n	Prevalence n (%)	n	Prevalence n (%)	p Value
0–19.9	40	24 (60.0)	18,960	14,910 (78.6)	<0.001
20–29.9	88	49 (55.7)	23,073	18,126 (78.6)	<0.001
30–39.9	685	302 (44.1)	32,577	24,938 (76.6)	<0.001
40–49.9	1,608	622 (38.7)	45,244	31,651 (70.0)	<0.001
50–59.9	2,051	687 (33.5)	50,607	30,489 (60.3)	<0.001
60–69.9	1,718	446 (26.0)	42,408	20,975 (49.5)	<0.001
70–79.9	1,027	197 (19.2)	29,322	11,254 (38.4)	<0.001
80–89.9	323	52 (16.1)	11,379	3,189 (20.0)	<0.001
≥90	46	6 (13.0)	1,528	361 (23.6)	<0.001
Missing	4	2 (50.0)	1,635	1,019 (62.3)	—

The dash indicates that the value could not be determined.
ChD, Chagas disease; ECG, electrocardiogram(s).

RESULTS

During the study period, 264,324 patients underwent ECG, 7,590 of them (2.87%) reported having ChD. The mean human development index of the cities where the patients lived was 0.664 ± 0.057, ranging from 0.529 to 0.810, and the median population was 9,671 inhabitants (IQR: 5,537, 17,739), ranging from 815 to 1,967,913. The median population of the cities where the ChD patients were located was 10,737 inhabitants (IQR: 5,940, 28,315). Clinical characteristics of ChD patients and noninfected individuals are shown on Table 1.

Regarding the ECG analysis, 31.45% of the ECG had no abnormalities versus 61.15% in noninfected individuals ($p < 0.001$). The prevalence of normal ECG decreased with aging (Table 2, Figure 1) and was significantly lower than for noninfected individuals in all age groups. The association between abnormal ECG and clinical characteristics in ChD patients is shown on Table 3.

In ChD patients who had abnormalities, the median number of electrocardiographic abnormalities was 2 (IQR: 1, 3; maximum number 9). Patients who exhibited >1 abnormality represented 40.9% of the study sample, and 20.3% had ≥3 abnormalities.

The most frequent electrocardiographic abnormalities are shown in Table 4. Pacemaker rhythm (OR: 13.29, 95% CI: 11.47 to 15.40), right bundle branch block (RBBB) (OR: 10.73, 95% CI: 10.10 to 11.41), especially in association with left anterior hemiblock (LAH) (OR: 12.09, 95% CI: 11.20 to 13.04), second atrioventricular block (OR: 4.05, 95% CI: 2.47 to 6.63), and third atrioventricular block (OR: 13.29, 95% CI: 11.47 to 15.40) were strongly related to ChD. Atrial fibrillation was seen in 5.35% of ChD subjects, and its prevalence was greater in octogenarians, reaching 16.26% of patients: 15.47% of women and 17.95% of men.

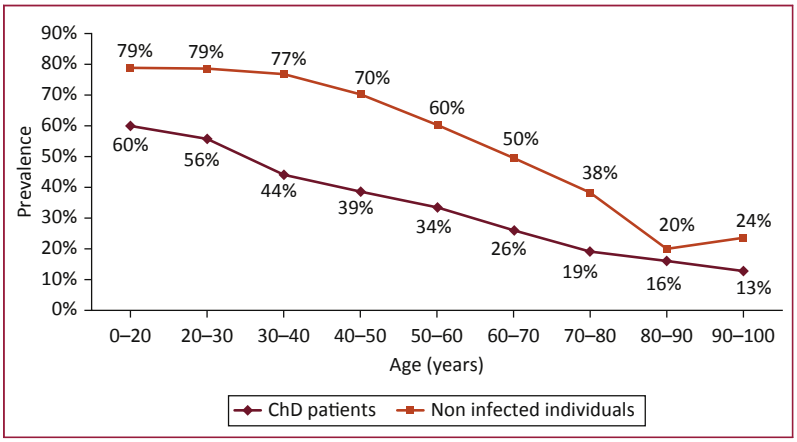

FIGURE 1. Prevalence of electrocardiograms with no abnormalities in patients with and without Chagas disease (ChD) according to age distribution.

DISCUSSION

This study included a large database of ECG of ChD patients evaluated in the primary care setting and showed a high prevalence of ECG abnormalities: 68.55% of the patients had ≥1 abnormality, almost the double of patients who did not reported having ChD.

Poverty is closely associated with the prevalence of neglected tropical diseases, including ChD, and increased vulnerability to these diseases [15]. Although the burden of these diseases is falling, and ChD transmission is considered to be eliminated in Brazil, this study showed that ChD is still prevalent, accounting for 2.87% of patients who performed ECG in the primary care setting of cities with a mean human development index of 0.664, which is ranked as a medium human development index [16]. This is due to the operation of a cohort effect: although the transmission was eradicated, patients who were infected in the past survived [17]. However, this study showed that ChD is not restricted to elderly or even adult patients, as 40 of 19,000 patients (0.21%) in the age group 0 to 20 years who reported having the disease. This finding of infection of younger patients is intriguing and requires further investigation. One hypothesis for this is the possibility of alternative forms of transmission in this population, such as oral transmission or maternal-fetal transmission [18,19], or even residual vectorial transmission.

Most previous studies in ChD patients showed a lower prevalence of electrocardiographic abnormalities [10,20,21] that is probably related to lower mean age or to the fact that, in these studies, patients were enrolled in the community [20,21] or among asymptomatic blood donors [10]. In the present study, patients were enrolled in the primary care setting, and they already knew about the diagnosis. Therefore, our hypothesis is that those patients already had symptoms and then they were diagnosed with ChD, so probably the disease was more advanced when compared with that of asymptomatic blood donors.

There was an increase in the proportion of ECG abnormalities with increasing age. It may be a nonspecific finding, because older individuals tend to have other concomitant comorbidities beyond ChD, such as hypertension, that are primarily responsible for the repercussions in the ECG. However, the proportion of ECG with no abnormalities reduced more rapidly in patients with ChD (Table 2, Figure 1), especially in younger patients (<60 years). So, it may reflect the progression of the disease, observed even in the adult population: a large 10-year retrospective cohort study observed a moderate rate of progression to cardiomyopathy (1.85%/year) among adult persons infected with *Trypanosoma cruzi* but without cardiomyopathy at baseline [22]. Indeed, the established concept that elderly patients with ChD tend to have a lower degree of cardiac dysfunction caused by disease and that

TABLE 3. Association between abnormal ECG and clinical characteristics of ChD patients (n = 7,590)

	Univariate	Multivariate*
Age	1.03 (1.03–1.04)	1.03 (1.03–1.03)
Male sex	1.63 (1.47–1.81)	1.72 (1.55–1.92)
Current smokers	0.92 (0.79–1.08)	0.90 (0.76–1.06)
Hypertension	1.66 (1.50–1.83)	1.39 (1.24–1.55)
Diabetes	0.91 (0.77–1.07)	0.79 (0.66–0.94)
Dyslipidemia	0.96 (0.79–1.16)	0.85 (0.69–1.04)
Chronic kidney disease	0.61 (0.42–0.90)	0.62 (0.41–0.93)
COPD	1.44 (0.91–2.29)	1.38 (0.84–2.25)
Previous MI	1.00 (0.74–1.36)	1.02 (0.73–1.42)
Family history of CAD	1.21 (1.09–1.34)	1.16 (1.04–1.29)

Values are odds ratio (95% confidence interval).
Abbreviations as in Table 1.
*Adjusted for all clinical characteristics.

TABLE 4. Prevalence of ECG abnormalities in patients with and without ChD

	ChD Patients (n = 7,590)	Noninfected Individuals (n = 256,733)	Adjusted for Age and Sex	Fully Adjusted Model*
Rhythm				
Atrial fibrillation	406 (5.35)	4,231 (1.65)	2.49 (2.24–2.77)	3.15 (2.83–3.51)
Pacemaker rhythm	265 (3.49)	614 (0.24)	12.04 (10.38–13.96)	13.29 (11.47–15.40)
Ectopic atrial rhythm	23 (0.30)	574 (0.22)	1.40 (0.92–2.13)	1.43 (0.94–2.17)
Junctional rhythm	20 (0.26)	244 (0.10)	2.53 (1.60–4.00)	2.63 (1.66–4.16)
Multifocal atrial rhythm	3 (0.04)	32 (0.01)	2.47 (0.75–8.10)	2.77 (0.85–9.06)
Premature ventricular beats	412 (5.43)	5,747 (2.24)	1.99 (1.79–2.21)	2.21 (1.99–2.46)
Premature supraventricular beats	192 (2.53)	4,569 (1.78)	1.11 (0.96–1.29)	1.26 (1.09–1.46)
Intraventricular block				
RBBB	1,723 (22.70)	6,503 (2.53)	10.17 (9.57–10.81)	10.73 (10.10–11.41)
Incomplete RBBB	507 (6.68)	8,901 (3.47)	2.08 (1.89–2.28)	2.10 (1.92–2.31)
LBBB	233 (3.07)	3,935 (1.53)	1.48 (1.29–1.70)	1.74 (1.52–2.00)
Incomplete LBBB	108 (1.42)	3,978 (1.55)	0.70 (0.54–0.85)	0.78 (0.64–0.94)
LAH	1,709 (22.52)	14,380 (5.60)	4.49 (4.05–4.56)	4.68 (4.41–4.97)
RBBB + LAH	1,043 (13.74)	3,136 (1.22)	11.10 (10.29-11.98)	12.09 (11.20–13.04)
Left posterior hemiblock	55 (0.72)	1,026 (0.40)	2.21 (1.68–2.91)	2.35 (1.79–3.09)
Atrioventricular block				
First degree	370 (4.87)	4,294 (1.67)	2.42 (2.18–2.71)	2.71 (2.43–3.03)
Second degree	18 (0.24)	136 (0.05)	3.64 (2.22–5.98)	4.05 (2.47–6.63)
Third degree	18 (0.24)	132 (0.05)	3.51 (2.14–5.77)	4.08 (2.49–6.69)
Hypertrophy/enlargement				
Left atrial hypertrophy	192 (2.53)	6,628 (2.58)	0.81 (0.70–0.94)	0.87 (0.75–1.00)
Left ventricular hypertrophy	275 (3.62)	8,512 (3.32)	0.88 (0.78–1.00)	0.97 (0.86–1.10)
Right atrial enlargement	10 (0.13)	460 (0.18)	0.67 (0.36–1.25)	0.68 (0.36–1.28)
Right ventricular enlargement	21 (0.28)	231 (0.09)	3.46 (2.20–5.44)	3.59 (2.28–5.64)
Ischemic				
Poor R-wave progression	281 (3.70)	5,721 (2.23)	1.40 (1.24–1.58)	1.51 (1.34–1.71)
Pathological Q waves	117 (1.54)	2,563 (1.00)	1.29 (1.06–1.56)	1.38 (1.15–1.67)
ST-segment elevation†	13 (0.17)	462 (0.18)	0.88 (0.65–1.20)	0.87 (0.50–1.51)
ST-segment depression‡	18 (0.24)	927 (0.36)	0.70 (0.50–0.98)	0.56 (0.35–0.89)
Other				
Nonspecific repolarization abnormalities	2,628 (34.62)	50,315 (19.60)	1.84 (1.75–1.94)	1.89 (1.80–1.98)
Early repolarization	40 (0.53)	2,535 (0.99)	0.71 (0.52–0.98)	0.74 (0.54–1.02)
Brugada pattern	3 (0.04)	40 (0.02)	2.98 (0.92–9.65)	2.92 (0.90–9.52)
Wolff-Parkinson-White	9 (0.12)	474 (0.18)	0.72 (0.37–1.40)	0.73 (0.38–1.41)

Values are n (%) or odds ratio (95% confidence interval).
LAH, left anterior hemiblock; LBBB, left bundle branch block; RBBB, right bundle branch block.
*Adjusted for age and sex.
†Excludes early repolarization.
‡Excludes strain pattern.

they usually die from other causes [23] has been challenged with studies showing that *T. cruzi* infection remains an important cause of death in infected elderly patients [7].

RBBB and LAH were very frequently observed in this sample of ChD patients, and they had a strong association with ChD, reinforcing previous studies in different populations [10,11,20,21]. RBBB is the most characteristic abnormality, as it is highly prevalent, fairly specific, and of great positive predictive value for *T. cruzi* infection [10,11,20,21,24]. There is evidence that RBBB is related to more severe cardiac damage [10] and is an independent risk factor for death in patients with ChD [11,25].

ChD is an important cause in Latin America countries of atrioventricular blocks and sinus node dysfunction, which are usually caused by widespread and distal fibrosis of the conduction system [8]. Those patients are frequently candidates for the implantation of pacemakers and, in our study, second and third atrioventricular block and pacemaker rhythm were strongly related to ChD. Chagas pacemaker patients have more severe disease than

pacemaker patients without Chagas disease, with a lower left ventricular ejection fraction and more frequent ventricular arrhythmia during Holter monitoring, than pacemaker patients without Chagas disease do [26].

Ventricular repolarization abnormalities were the most common finding in ChD patients, affecting more than one-third of patients. Indeed, as this study did not differentiate more pronounced ST-T wave abnormalities from minor repolarization abnormalities, and most patients have concomitant diseases, it is difficult to attribute these abnormalities to the *T. cruzi* infection. However, it should be stressed that this finding was significantly more frequent in ChD patients than in noninfected individuals (34.62% vs. 19.60%), and that repolarization abnormalities in ChD may be related to the presence of left ventricular dysfunction [6] and may have prognostic importance [27].

In this study, 5.35% of ChD patients had atrial fibrillation versus 1.65% in noninfected individuals. In ChD, it usually develops in patients with advanced heart involvement and severe ventricular dysfunction, as occurs in other heart diseases [1,8]. In patients with chagasic cardiomyopathy, atrial fibrillation may be associated with further systolic function deterioration due to both shortening of the systolic interval and loss of the atrial contraction-mediated Frank-Starling mechanism [28]. This arrhythmia has been considered a marker of poor prognosis of death in ChD patients [11,29] and constitutes an independent risk factor for the occurrence of embolic stroke [30].

Although the main goal of the study was to evaluate the prevalence of electrocardiographic abnormalities in ChD patients, this study also provided information about the prevalence of ECG abnormalities in a large sample of noninfected primary care patients. Nonspecific repolarization abnormalities, LAH, left ventricular and left atrium hypertrophy, incomplete or complete RBBB, premature ventricular beats, and poor R-wave progression were the most common findings.

Study limitations

As ChD was self-reported, screening tests for confirmed ChD were not performed routinely, so the prevalence estimates in this study should not be considered population-based estimates. Furthermore, ECG abnormalities in patients with ChD may not be specific and may be attributed to other causes. Finally, although standardized criteria were used to recognize ECG abnormalities, ECG were not coded in a central Reading Center and were not coded by a pair of cardiologists, as is the standard for epidemiologic studies. So, some interobserver variation among cardiologist readers should be expected.

CONCLUSIONS

This study demonstrates that despite successful eradication programs, ChD remains prevalent in Brazilian adults. Pacemaker rhythm, RBBB, especially in association with LAH, second and third atrioventricular block, and atrial fibrillation were strongly related to ChD, and the prognostic significance of ECG abnormalities over the life course deserves further study.

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