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Electrocardiographic and echocardiographic abnormalities in residents of rural Bolivian communities hyperendemic for Chagas disease

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Abstract

Background—Chagas disease is a neglected and preventable tropical disease that causes significant cardiac morbidity and mortality in Latin America. Our objective in this study was to describe cardiac findings among inhabitants of rural communities of the Bolivian Chaco.

Methods—The cardiac study drew participants from an epidemiologic study in 7 indigenous Guarani communities. All infected participants 10 years or older were asked to undergo a brief physical examination and 12-lead electrocardiogram. A subset had echocardiograms (ECGs). ECGs and echocardiograms were read by one or more cardiologists.

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Results—Of 1137 residents 10 years or older, 753 (66.2%) had *T. cruzi* infection. Cardiac evaluations were performed for 398 infected participants 10 years or older. Fifty-five (13.8%) participants had one or more ECG abnormality suggestive of Chagas cardiomyopathy. The most frequent abnormalities were bundle branch blocks in 42 (11.3%), followed by rhythm disturbances or ventricular ectopy in 13 (3.3%) and atrioventricular blocks (AVB) in 10 (2.6%) participants. The prevalence of any abnormality rose from 1.1% among those 10-19 years old to 14.2%, 17.3% and 26.4% among those 20-39, 40-59 and older than 60 years, respectively. First degree AVB was seen most frequently in participants 60 years or older, but the 4 patients with 3rd degree AVB were all under 50 years old. Eighteen and two participants had a left ventricular ejection fraction of 40-54% and <40%, respectively. An increasing number of ECG abnormalities was associated with progressively larger left ventricular end-diastolic dimensions and lower left ventricular ejection fraction.

Conclusions—We found a high prevalence of ECG abnormalities and substantial evidence of Chagas cardiomyopathy. Programs to improve access to basic cardiac care (annual ECGs, antiarrhythmics, pacemakers) could have an immediate impact on morbidity and mortality in these highly endemic communities.

Introduction

Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi*, most commonly transmitted to humans by hematophagous triatomine bugs in North, Central and South America. An estimated 8 million people are currently infected with *T. cruzi*, and by far the highest infection prevalence is found in the ecological zone known as the Gran Chaco, shared among Bolivia, Argentina and Paraguay [1]. In rural community surveys in the Bolivian Chaco, infection is found in more than 80% of adults [2, 3].

The most significant clinical sequela of infection is Chagas cardiomyopathy. In the acute phase of the disease, most infected individuals are asymptomatic or have non-specific self-limiting febrile illness [4, 5]. Antitrypanosomal treatment has a high cure rate in the acute phase and is assumed to prevent chronic manifestations. However, acute infection is rarely diagnosed. Left untreated, 20-30% of infected individuals will progress to clinical heart disease, usually decades after the initial infection. Cohort studies in highly endemic areas demonstrate 2-3% annual incidence of cardiac disease [6] and a recent retrospective cohort analysis of Brazilian blood donors estimated a cardiomyopathy incidence rate of 1.85% per year [7].

The early signs of Chagas cardiomyopathy are typically conduction system abnormalities, most commonly right bundle branch block (RBBB), often progressing to bifascicular blocks. Later manifestations include left ventricular systolic dysfunction, apical aneurysms, high-degree atrioventricular block, and sustained and non-sustained ventricular tachycardia [8]. Late cardiac manifestations are associated with high short-term mortality risk [9, 10].

Vector-borne transmission remains the main infection route [5]. Observational data suggest that vector elimination may decrease progression to heart disease in endemic communities [11]. Vector control programs have decreased disease prevalence in many parts of Latin America [5]. However, the Bolivian Chaco continues to have high infestation rates and

extremely high prevalence of *T. cruzi* infection [3]. Our objective in this study was to describe the electrocardiographic and echocardiographic findings among inhabitants of rural communities of the Bolivian Chaco.

Methods

The study took place in the Eity health sector (altitude 800 m), located in Gutierrez municipality, Cordillera province, Santa Cruz department. Data were collected from July 2011 to July 2012. The study site comprised seven neighboring communities with a total population of approximately 2200. The population is almost exclusively of the Native American Guaraní ethnicity, and the local economy is based on subsistence farming and animal husbandry. The study communities were chosen based on Ministry of Health data suggesting high likelihood of active *T. cruzi* transmission. Houses are predominantly constructed of mud and sticks or adobe, with packed dirt floors, and straw or corrugated metal roofs (Figure 1). Serosurvey methods and Chagas disease epidemiology were described in detail in an earlier publication [3]

Ethics statement

The protocol approved by the Institutional Review Boards of the Johns Hopkins University, Hospital Universitario Japonés, Santa Cruz, Bolivia, Asociacion Benefica PRISMA, Lima, Peru and the Centers for Disease Control and Prevention. Adult participants provided written informed consent. Written informed consent was obtained from the parent or guardian on behalf of children, and children older than 7 years provided written assent.

Procedures

Demographic data and serum specimens were collected during the community survey during house-to-house visits [3]. All sera were tested by the indirect hemagglutination test (Chagas Polychaco, Lemos Laboratories) and a whole parasite lysate enzyme-linked immunosorbent assay (Wiener Laboratories, Rosario, Argentina). Discordant specimens were tested by a third assay (Recombinante 3.0, Wiener Laboratories, Rosario, Argentina). Specimens with positive results by at least two assays were considered to have confirmed *T. cruzi* infection [12].

Cardiac study

The cardiac study focused on seropositive participants 10 years and older; we were unable to include an age-comparable seronegative control group, because nearly all adults had *T. cruzi* infection. All eligible participants were asked to come to the health center for evaluation. Height, weight, blood pressure and heart rate were recorded. A resting 12-lead electrocardiogram (ECG) and a 10-second multi-lead rhythm strip were performed using a portable ECG machine (Welch Allyn CardioPerfect Workstation Software, Welch Allyn Inc, Skaneateles Falls, NY). Two (in cases of discordancies, three) cardiologists blinded to the participant's serologic status interpreted each ECG. Interpretation and coding were based on those developed by the Pan American Health Organization for use in epidemiological studies of Chagas heart disease[13]. The ECG findings assessed included rhythm, atrial and ventricular ectopy, ventricular and supraventricular arrhythmias, atrio-ventricular blocks,

right bundle branch block (RBBB), left anterior fascicular block (LAFB), left bundle branch block (LBBB), left posterior fascicular block (LPFB), non-specific intraventricular conduction delay, ST segment and T wave abnormalities, low voltage, right and left ventricular hypertrophy [13].

We categorized ECG abnormalities characteristic of Chagas cardiomyopathy into 3 categories: bundle branch blocks, atrioventricular blocks, and rhythm disturbances (including complex ventricular ectopy) [14]. An abnormal ECG suggestive of Chagas cardiomyopathy was defined as an ECG with complete RBBB, LAFB, LPFB, LBBB or bifascicular block; any degree of atrioventricular block; atrial fibrillation/flutter, junctional rhythm, sinus bradycardia with heart rate <50 beats per minute (bpm), or complex ventricular ectopy. Incomplete right bundle branch block was not included, as we and others have found this pattern can occur as a normal variant in physically active young adults [15]. Atrial ectopy, nonspecific ST T wave changes, low voltage, right or left ventricular hypertrophy were considered to be relatively non-specific and were not included in our definition of an ECG suggestive of Chagas cardiomyopathy.

Echocardiograms

An echocardiographer (AF) performed examinations during a 2-week field visit. Participants with abnormal ECGs, plus as many of those with normal ECG as could be examined in available appointment times, were invited to undergo a 2-dimensional and Doppler echocardiogram at the Eity Health Center using a MicroMaxx Ultrasound machine (SonoSite, Inc. Bothell, WA). Patients were examined in the left lateral recumbent position using standard parasternal and apical views. Two-dimensional measurements of the left ventricle (LV) were obtained following standard guidelines. [16] LV regional wall motion was based on the 17-segment model. Segments were classified as normal, hyperkinetic, hypokinesis, akinesis or dyskinesis and aneurysmal. Mitral, tricuspid, aortic and pulmonary regurgitations were qualitatively evaluated. The presence of pericardial effusion was evaluated. Left ventricular end diastolic diameter (LVEDD) is presented both as measured (considering 57 mm or above as dilatation) and corrected for body surface area (BSA) using this formula: For the corrected LVEDD, a result ≥ 31 mm was considered abnormal [16]. We considered LV ejection fractions of 40-54% as moderately decreased and <40% as severely decreased [15, 17]. The completion of echocardiograms was limited to the number of individuals able to reach the health center from the community during the echocardiographer's field visit. Some older adults who had not yet had an ECG were brought to the health center for echocardiogram by vehicle. Therefore, not all patients with abnormal ECGs had echocardiographic data, and vice versa. Only those with ECG data were included in the analysis of the echocardiographic data.

Statistical analysis

Data were analyzed in SAS 9.0 (SAS Institute Inc., Cary, NC, 2005) and SPSS version 18.0 (SPSS Inc, Chicago 2009). Continuous variables were compared using the Wilcoxon Rank Sum test or Kruskal Wallis test. Categorical variables were compared using the Mantel-Haenszel Chi square (or 2-tailed Fisher Exact test if expected cell values were <5).

RESULTS

Characteristics of the study population

The overall study population comprised 1580 participants, corresponding to 72% of the total estimated population of the villages. Of these, 1137 were 10 years or older, 753 (66.2%) with *T. cruzi* infection and 384 (33.8%) without infection (Table 1). The infection prevalence rose steeply with increasing age, reflecting intense sustained vector-borne *T. cruzi* transmission over past decades [3]. Overall, 398 infected participants (53% of those in the eligible age range) reported to the health center for an ECG. Women were significantly more likely than men to join the cardiac substudy (59% vs 44%; $p < 0.001$), and participation was higher among older age groups (49% of 10-19-year-olds, 46% of 20-39-year-olds, 63% of 40-59-year-olds and 57% of those older than 60 years).

ECG data

The mean QRS duration was 98.2 ± 20.5 ms and mean PR interval was 150.3 ± 26.0 ms. The mean PR interval increased with increasing age (Figure 2). A total of 55 (13.8%) participants had ECG findings suggestive of Chagas cardiomyopathy (Table 2). Abnormalities fell into three categories, rhythm disturbances or ventricular ectopy, bundle branch blocks and atrioventricular blocks (AVB). The most common abnormalities were bundle branch blocks, found in 42 (11.3%) participants, followed by rhythm disturbances or ventricular ectopy in 13 (3.3%) and atrioventricular blocks in 10 (2.6%) participants. Ten of the 55 participants with abnormal ECGs had findings in more than one category (Table 3). The group with multiple abnormalities on ECG included 4 patients in need of pacemakers (patients 1, 2, 4 and 5).

The prevalence of abnormalities rose with increasing age, from 1.1% among those 10-19 years old to 14.2%, 17.3% and 26.4% among those 20-39, 40-59 and older than 60 years, respectively (Figure 3). Bundle branch blocks comprised most of the abnormalities seen in younger individuals. First degree AVB was seen most frequently in participants 60 years or older, but the 4 patients with 3rd degree AVB were 30, 39, 46 and 47 years old.

Echocardiographic data

Echocardiography data were available from 97 *T. cruzi*-infected participants. The median LV enddiastolic diameter was 44 mm [interquartile range 40, 49] while the median LV ejection fraction was 60% [55, 65] (Table 4). Only two participants had LVEDD ≥ 57 mm; 13 had LVEDD corrected for body surface area above the published cut-off of 31 mm. Eighteen and two participants had LVEF 40-54% and $<40\%$, respectively. An increasing number of abnormalities on ECG was associated with progressively higher LVEDD and lower LV ejection fraction ($p = 0.004$ and $p = 0.02$ by Kruskal-Wallis test). Four individuals were found to have valvular heart disease, one with a combination of aortic and mitral valve disease, probably due to rheumatic heart disease, one with moderate mitral regurgitation, and two with aortic stenosis.

Discussion

Chagas disease remains a major cause of morbidity and mortality in Latin America [18]. Despite progress in vector control [19], communities with intense transmission remain, especially in the Gran Chaco [1, 2, 3]. Our study took place in one such area, where the majority of houses were still infested at the time of our survey and the force of infection was estimated at 4% per year [3]. We found ECG abnormalities suggestive of Chagas cardiomyopathy in nearly 15% of community residents aged 20-39 years, and more than 25% of those 60 or older, figures consistent with the estimate that 20-30% of infected individuals eventually develop heart disease [5]. Signs of dilated cardiomyopathy by echocardiogram were most frequent in the group of individuals with multiple abnormalities on ECG, a group that included four patients who needed pacemakers [20].

In our population, right bundle branch blocks, alone or in combination with LAFB, were the most frequent abnormalities consistent with Chagas cardiomyopathy. These findings are consistent with results of other community-based studies conducted in other parts of Bolivia and in Brazil [21, 22, 23]. In our data, the prevalence of ECG abnormalities rose steadily with age. A Brazilian study from the 1980s found the highest rate of ECG abnormalities in participants 25-44 years old, and interpreted this finding as suggestive of excess mortality due to Chagas cardiomyopathy among older residents [21]. However, more recent studies show steadily increasing prevalence of abnormalities with age, perhaps due to better survival of affected individuals in recent decades [22, 23, 24]. While we found the highest rates of bundle branch blocks and 1st degree AVB in the oldest age group, 3rd degree AVBs were found only among participants younger than 50, possibly reflecting premature mortality among those who had high grade AVBs for longer periods of time.

Direct comparisons of the prevalence of ECG abnormalities are impeded by the fact that each study used different criteria [21, 22], and some studies fail to specify the precise definitions used and the age groups surveyed [23]. We attempted to use rigorous criteria for defining ECG abnormalities. For the sake of higher specificity, we excluded incomplete right bundle branch blocks, intraventricular conduction delays, low QRS voltage and non-specific ST-T wave changes from our definition of abnormal ECGs, and we defined sinus bradycardia as heart rate < 50 beats per minute. We may have therefore excluded some individuals with changes due to *T. cruzi* infection. However, in recent publications from Brazil, low QRS voltage and ST-T wave changes were equally frequent among *T. cruzi*-infected and uninfected adults [24, 25]. Especially in the absence of a seronegative comparator group, we considered specificity more important than sensitivity.

The direct linear relationship between PR prolongation and age in our study is intriguing. One of the Brazilian community studies demonstrated significantly longer mean PR interval among *T. cruzi* – infected study participants compared to uninfected participants, but apparently without age adjustment [23]. Among *T. cruzi*-infected blood donors, PR interval prolongation was significantly associated with left ventricular dysfunction [25]. In another endemic area of Brazil, PR prolongation among Chagas disease patients was associated with a higher mortality risk [26]. Without an age-matched seronegative control group, we cannot

unequivocally attribute this finding to Chagas cardiomyopathy, but further investigation may confirm PR interval as a useful prognostic parameter.

As expected in a community-based study, most of the abnormalities we found were relatively mild and the vast majority of our participants reported no cardiac symptoms. Because the evolution of Chagas cardiomyopathy occurs over multiple decades, a snapshot survey of the prevalence of cardiac abnormalities, especially in a young population, will reveal relatively few severe cases [8, 21]. We found few participants with high grade conduction system disease or dilated cardiomyopathy, and these abnormalities tended to occur in the same individuals. Those with multiple abnormalities on ECG were also those mostly likely to have a dilated left ventricle and/or depressed LV ejection fraction, a finding consistent with the natural history of Chagas cardiomyopathy and with earlier studies comparing ECG and echocardiogram results [27].

It is important to note that our findings may underestimate the prevalence of severe disease, because severely ill community residents may have been unable to report to the health center for evaluation. Indeed, two seropositive patients with advanced cardiomyopathy, a 69-year-old woman with an apical aneurysm, ejection fraction of 30%, and severe right and left systolic dysfunction and a 72-year-old man with a left ventricular aneurysm with thrombus, ejection fraction of 25% and severe LV dysfunction, were excluded from the analysis because they lacked ECGs. These patients were brought to the health center by vehicle during the echocardiographer's visit, but likely were unable to walk to the health center later for their ECGs. Other limitations of our study are related to the absence of an appropriate seronegative control group. We assume that our ECG and echo findings were related to *T. cruzi* infection, but despite using the most specific definitions we could design, some of the findings may still have been related to other cardiovascular disease.

In summary, we found a high prevalence of ECG abnormalities and substantial evidence of Chagas cardiomyopathy in these highly endemic communities, with rates and patterns similar to those seen in community studies from other areas in the Southern Cone. We found at least four participants with sustained or intermittent complete heart block who could benefit from pacemaker implantation. However, access to pacemakers and other advanced cardiac interventions is severely limited in rural southern Bolivia. Programs to improve access to basic cardiac care (annual ECGs, antiarrhythmics, pacemakers) could have an immediate impact on morbidity and mortality in these hyperendemic villages.

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Highlights

- The prevalence *T. cruzi* infection in survey participants was 52% overall and 94% among those 40 years or older
- Among infected participants, 13.8% had at least one abnormality on ECG suggestive of Chagas heart disease, most commonly right bundle branch block, with or without left anterior hemiblock
- The prevalence of ECG abnormalities rose with age from 1.1% among those 10-19 years old to 14.2%, 17.3% and 26.4% among those 20-39, 40-59 and older than 60 years, respectively
- An increasing number of abnormalities on ECG was associated with progressively higher left ventricular end diastolic diameter and lower ejection fraction.
- Programs to improve access to basic cardiac care could have an immediate impact on morbidity and mortality in these highly endemic communities.

Figure 1.
A typical house in one of the study villages in Cordillera Province, Santa Cruz Department, Bolivia.

Figure 2.
Mean PR interval in milliseconds among 398 *T. cruzi* infected participants by age group.
Error bars represent standard deviations.

Figure 3.

Age-specific prevalence of ECG abnormalities among 398 *T. cruzi*-infected participants: (A) Right bundle branch block (RBBB), left anterior and posterior fascicular blocks (LAFB, LFPB); (B) atrioventricular blocks (AVB); (C) abnormal rhythms; (D) one or more abnormalities suggestive of Chagas cardiomyopathy (see text and Table 2).

Characteristics of the serosurvey population 10 years or older and cardiac substudy participants, Cordillera Province, Santa Cruz Department, Bolivia.

Table 1

	Serosurvey participants		10 years old ^{1,2}		Electrocardiograms ¹		Echocardiograms ²	
	Uninfected (N=384)	<i>T. cruzi</i> -infected (N=753)	<i>T. cruzi</i> -infected (N=398)	<i>T. cruzi</i> -infected (N=97)				
Male [n (column %)] ³	188 (49.0)	292 (38.8)	128 (32.2)	37 (38.1)				
Female [n (column %)] ³	196 (51.0)	461 (61.2)	270 (67.8)	60 (61.9)				
Age group [n (column %)] ⁴								
10-19	346 (90.1)	187 (24.8)	92 (23.1)	4 (4.1)				
20-39	33 (8.6)	264 (35.1)	120 (30.2)	24 (24.7)				
40-59	5 (1.3)	210 (27.9)	133 (33.4)	42 (43.3)				
>=60	0 (0)	92 (12.2)	53 (13.3)	27 (27.8)				
Median [interquartile range]								
Age ⁵	13 [11, 15]	34 [20, 49]	38 [22, 51]	50 [38, 61]				
Body mass index (kg/m ²)	--	--	24.4 [21.9, 28.2]	26.2 [23.0, 30.0]				
Respiratory rate (per minute)	--	--	20 [16, 20]	20 [16, 20]				
Heart rate (per minute)	--	--	67 [61, 73]	66 [58, 71]				
Systolic blood pressure (mm Hg)	--	--	110 [100, 120]	120 [110, 130]				
Diastolic blood pressure (mm Hg)	--	--	80 [70, 84]	80 [70, 90]				

Comparisons by Chi Square for sex, by Wilcoxon rank sum for continuous variables

¹ Participants with ECG data were more likely to be female (p<0.0001) and were older (p<0.05) than other seropositive survey participants.

² Echocardiogram patients were older (p<0.0001), had higher BMI (p<0.01), lower heart rate (p<0.01), higher systolic (p<0.01) and diastolic BP (p<0.05) compared to seropositive survey participants. They were also older (p<0.0001), had higher BMI (p<0.01), lower heart rate (p<0.01), higher systolic (p<0.01) and diastolic BP (p<0.05) compared to seropositive ECG recipients; there was no difference between ECG and echocardiogram recipients by sex.

³ Females were more likely than males to be seropositive (p<0.01) but this difference was no longer significant (p=0.73) when controlled for age.

⁴ Seropositive participants were significantly more likely to fall into older age categories than seronegative participants (p<0.05)

⁵ Seropositive participants were significantly older than seronegative participants (p<0.0001).

Table 2

Electrocardiogram (ECG) findings among 398 *T. cruzi*-infected study participants 10 years or older.

Finding	
PR interval in ms (mean $\pm$ standard deviation)	150.3 $\pm$ 26.0
QRS interval in ms (mean $\pm$ standard deviation)	98.2 $\pm$ 20.5
Rhythm	N (%)
Sinus bradycardia < 50 bpm	5 (1.3)
Junctional rhythm	4 (1.0)
Atrial fibrillation or flutter	2 (0.5)
Normal sinus rhythm	387 (97.2)
Ectopy	N (%)
Complex ventricular premature contractions ¹	2 (0.5)
Simple ventricular premature contractions	2 (0.5)
Atrial ectopic beats	4 (1.0)
Bundle branch blocks	N (%)
Isolated right bundle branch block (RBBB)	11 (2.8)
Isolated left anterior fascicular block (LAFB)	17 (4.3)
RBBB and LAFB	13 (3.3)
RBBB and LPFB	1 (0.3)
Incomplete RBBB	3 (0.75)
No block	353 (88.7)
Atrioventricular blocks	N (%)
1 st degree AVB	7 (1.8)
3 rd degree AVB	4 (1.0)
None	387 (97.2)
Any ECG abnormality suggestive of Chagas cardiomyopathy ^{2,3}	55 (13.8)

ECG interpretation and coding followed methods in Lazzari et al [13].

¹ One multiform PVCs, one ventricular bigeminy.

² Includes RBBB, LAFB, LPFB, bifascicular blocks, AVBs and these abnormal rhythms: junctional, Atrial fibrillation/flutter, sinus brady with HR <50, multiform PVCs, ventricular bigeminy. The following were not considered ECG abnormalities suggestive of Chagas cardiomyopathy: atrial ectopy, simple PVCs, incomplete RBBB [14].

³ Nine participants had abnormalities in two categories and one had abnormalities in three categories (see Table 3).

T. cruzi-infected participants with ECG abnormalities in more than one category (AVBs, BBBs, rhythm, ventricular ectopy)

Table 3

Patient	Age	Sex	Bundle branch blocks	AV blocks	Arrhythmias	LV ejection fraction
1	30	Female	RBBB	3 rd degree AVB	Junctional rhythm (43 bpm)	40 to 45%
2	39	Female	None	3 rd degree AVB	Junctional rhythm (40 bpm)	35%
3	45	Male	LAFB	1 st degree AVB	None	45 to 50%
4	46	Female	None	3 rd degree AVB	Junctional rhythm (47 bpm)	Not done
5	47	Female	None	3 rd degree AVB	Junctional rhythm (45 bpm)	Not done
6	48	Female	RBBB plus LAFB	None	Ventricular bigeminy	Not done
7	58	Male	LAFB	None	Sinus bradycardia (49 bpm)	65%
8	63	Female	RBBB plus LAFB	None	Atrial fibrillation /flutter	40%
9	65	Male	RBBB plus LAFB	1 st degree AVB	None	Not done
10	74	Female	LAFB	1 st degree AVB	None	50%

Abbreviations: RBBB, right bundle branch block; AVB, atrioventricular block; LAFB, left anterior fascicular block; bpm, beats per minute; LV, left ventricular.

Table 4

Echocardiogram findings among 97 *T. cruzi*-infected study participants 10 years or older.

Echocardiogram Findings	All tested N=97	Electrocardiogram findings		
		Normal (N=66)	Single abnormality (N=25)	Multiple abnormalities (N=6)
Left ventricular end-diastolic diameter				
Median (interquartile range) (mm)	44 [40, 49]	43 [40, 45] ¹	47 [41, 51] ¹	54 [49, 56] ¹
N (%) 57 mm	2 (2.1%)	0 (0%)	1 (4.0)	1 (16.7)
LVEDD/BSA ²				
Median (interquartile range) (mm)	27 [25, 30]	26 [24, 29]	27 [25, 30]	31 [29, 34]
N (%) 31 mm	13 (13.4)	7 (10.6)	3 (12.0)	3 (50.0)
Left ventricular ejection fraction				
Median (interquartile range) (%)	60 [55, 65]	60 [55, 65] ³	60 [55, 60] ³	45 [40, 50] ³
N (%) with LVEF 40 – 54%	18 (18.6)	9 (13.6)	5 (20.0)	4 (66.7)
N (%) with LVEF < 40%	2 (2.1)	0 (0)	1 (4.0)	1 (16.7)

Abbreviations: LVEDD/BSA, Left ventricular end diastolic diameter/body surface area; LVEF, Left ventricular ejection fraction

¹ Data missing for two participants with normal ECG. Increasing number of ECG abnormalities associated with decreasing LVEDD, p=0.004 by Kruskal-Wallis test.

² Left ventricular end diastolic diameter/body surface area, calculated as follows: BSA (in m²) = 0.007184 × Height(cm)^{0.725} × Weight(kg)^{0.425}. Cutoff of 31 mm based on reference 16.

³ Data missing for one participant with normal ECG. Increasing number of ECG abnormalities associated with decreasing LV ejection fraction, p=0.02 by Kruskal-Wallis test.