The Prevalence of Chagas Disease among Latin American Immigrants with Pacemakers in Los Angeles, California

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Abstract. Chagas disease (CD), with associated conduction abnormalities, is a common indication for pacemaker implantation in Latin America. The prevalence of CD in Latin American immigrants with pacemakers residing in the United States has never been studied. This single-center cross-sectional study included pacemaker patients who were aged 18 years or more with a previous residence in Latin America for at least 6 months. Patients with an implantable cardioverter-defibrillator, cardiac resynchronization therapy, or iatrogenic and/or congenital heart block were excluded. Serological testing for *Trypanosoma cruzi* was performed at enrollment. A total of 80 patients were enrolled, and CD was diagnosed in six patients (7.5%). Patients with CD were more likely to be from El Salvador ($P = 0.001$). Other clinical, therapeutic, electrocardiographic, and echocardiographic variables were similar between the CD and non-CD groups. There is a high prevalence of CD among Latin American immigrants with pacemakers in Los Angeles.

Chagas disease (CD), caused by the parasite *Trypanosoma cruzi*, has both an acute and chronic phase. Most chronically infected patients remain asymptomatic indefinitely; however, approximately one-third will develop cardiac manifestations 10–30 years after the initial infection. Conduction abnormalities, dysrhythmias, apical aneurysms, and cardiomyopathy have all been attributed to CD.^{1,2} Bradyarrhythmias from CD are related to chronic inflammation and fibrosis of the myocardial conduction system that results in sinus node, atrioventricular node, and Purkinje fiber conduction abnormalities.^{3,4} CD is responsible for nearly 25% of all pacemaker implants in Brazil, where it is the most frequent indication for implantation.^{5,6}

The World Health Organization estimates that 7–8 million people worldwide are infected with *T. cruzi*, though primarily in Latin America.⁷ Because of immigration patterns, there is a growing recognition of CD in nonendemic countries including the United States where an estimated 300,000 individuals are infected.^{2,8} Los Angeles County has more than 2 million residents born in Chagas-endemic countries,⁹ and Los Angeles blood banks have estimated seroprevalence rates of CD to be nearly one in 2000 among blood donors.¹⁰ There have been no studies to date, which have examined the burden of bradyarrhythmias related to CD in the United States.

This study is a cross-sectional survey with a retrospective chart review of patient data. This research was approved by the local Institutional Review Board, and all participants provided written, informed consent before study enrollment. Participants were sought from the pacemaker clinic at Olive View-UCLA Medical Center from March 2014 to March 2015. Patients were included if they were 1) at least 18 years of age, 2) had a pacemaker, and 3) had lived in Latin America for at least 6 months continuously at any time. Since the goal of the study was to find patients with early cardiac involvement from CD, patients with an implantable cardioverter-defibrillator, cardiac resynchronization therapy, or iatrogenic and/or congenital heart block were excluded. There were a total of

237 patients in the pacemaker clinic (Figure 1). A total of 113 patients met inclusion criteria. Of these, 33 did not give consent or were not reachable.

At the time of study enrollment, participants were interviewed to assess basic demographic information and country of origin. In addition, a chart review was performed to gather information on indications for pacemaker placement, history of cardiac surgery, past medical history, medication use, and smoking history. We were unable to obtain medication history for one patient. Because of low counts, response categories for country of origin were collapsed into three categories: Mexico, El Salvador, and other (Argentina, Chile, Ecuador, Guatemala, Honduras, Nicaragua, Peru, and Uruguay).

Blood samples were screened serologically to establish infection with *T. cruzi*. The Ortho *T. cruzi* enzyme-linked immunosorbent assay (Ortho Clinical Diagnostics Inc., Raritan, NJ) was initially performed on all samples. Additional testing performed by the U.S. Centers for Disease Control and Prevention included the trypomastigote excreted or secreted antigen immunoblot. A 12-lead electrocardiogram (ECG) and transthoracic echocardiogram were performed at our institution. ECG abnormalities were classified according to the Minnesota Code Manual of Electrocardiographic findings.¹¹ ECGs of nonpaced rhythms were available in 71 patients. Echocardiography, available in 74 patients, was used to determine left ventricular ejection fraction (LVEF) by visual estimation and left ventricular end-diastolic diameter (LVEDD) from the standard parasternal long axis view.¹² ECGs and echocardiograms were interpreted by two board-certified cardiologists; discrepancies were resolved by a third board-certified cardiologist with consensus opinion.

SPSS 20 software was used for all analyses (SPSS Inc., Chicago, IL). Data were compared using χ^2 tests for categorical variables and *t* tests for continuous variables. Fisher exact tests were used in 2×2 categorical comparisons with cell counts less than five. Differences between groups were considered statistically significant if they attained a *P* value of < 0.05 .

A total of 80 patients were included in this study (Table 1), and six (7.5%) were diagnosed with CD. As a group, 60.0% of participants were female. The mean age at the time of pacemaker placement was higher in the CD versus non-CD group, though this difference was not significant ($70.3 \pm$

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FIGURE 1. Patient enrollment.

11.3 years versus 63.0 ± 12.1 years, $P = 0.177$; Table 1). Patients who were diagnosed with CD were more likely to be from El Salvador ($P = 0.001$). Clinical variables, such as the prevalence of hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease, tobacco use, and prior cardiac surgery, were not different between CD and non-CD groups. Therapeutic variables including the use of beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors ("statins"), and aspirin were not different between the CD and non-CD groups.

Electrocardiographic and echocardiographic characteristics of the study group are shown in Table 2. There were no significant differences for electrocardiographic variables including left bundle branch block, right bundle branch block, intraventricular conduction delay, left anterior fascicular block, left posterior fascicular block, or prior infarct. Similarly, there were no significant differences for the echocardiographic variables LVEF or LVEDD.

This is the first study to examine the prevalence of CD in Latin American patients with pacemakers in the United States. Our data demonstrate that in this population, nearly one in 13 patients (7.5%) have chronic CD. This result is inconsistent with studies conducted in Latin America, where a 25–72% prevalence of the disease is found among patients with pacemakers.^{5,13,14} Some of these studies enrolled patients with CD from the outset however, making comparisons between studies difficult.¹⁴ The difference in prevalence surely reflects the fact that CD is not endemic to the United States, but there may be another factor at play. Since the immigrant population in the United States has been removed from

TABLE 1
Study population characteristics

	CD (N = 6)	Non-CD (N = 74)*	All (N = 80)	P value†
Demographic variables				
Male, n (%)	4 (66.7)	28 (37.8)	32 (40.0)	0.211
Mean age in years ($\pm$ SD)	73.5 ($\pm$ 12.6)	68.3 ($\pm$ 11.7)	68.7 ($\pm$ 11.8)	0.303
Mean age at PPM insertion in years ($\pm$ SD)	70.3 ($\pm$ 11.3)	63.0 ($\pm$ 12.1)	63.5 ($\pm$ 12.1)	0.153
Country of origin				0.001
Mexico, n (%)	1 (16.7)	49 (66.2)	50 (62.5)	
El Salvador, n (%)	4 (66.7)	8 (10.8)	12 (15.0)	
Other, n (%)	1 (16.7)	17 (23.0)	18 (22.5)	
Clinical variables				
Hypertension, n (%)	4 (66.7)	52 (70.3)	56 (70.0)	1.000
Hyperlipidemia, n (%)	2 (33.3)	32 (43.2)	34 (42.5)	1.000
Diabetes mellitus, n (%)	2 (33.3)	30 (40.5)	32 (40.0)	1.000
Coronary artery disease, n (%)	1 (16.7)	12 (16.2)	13 (16.3)	1.000
Tobacco use, n (%)	3 (50.0)	20 (27.0)	23 (28.7)	0.347
Prior cardiac surgery, n (%)	0 (0.0)	16 (21.6)	16 (20.0)	0.340
Therapeutic variables				
Beta-blocker, n (%)	2 (33.3)	22 (30.1)	24 (30.4)	1.000
ACEI/ARB, n (%)	2 (33.3)	40 (54.8)	42 (53.2)	0.411
Statin, n (%)	0 (0.0)	30 (41.1)	30 (38.0)	0.078
Aspirin, n (%)	2 (33.3)	29 (39.7)	31 (39.2)	1.000
Indication for PPM placement				
AV block, n (%)	4 (66.7)	41 (55.4)	45 (56.3)	0.691
SSS, n (%)	4 (66.7)	46 (62.2)	50 (62.5)	1.000
Atrial fibrillation, n (%)	2 (33.3)	27 (36.5)	29 (36.3)	1.000

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; AV = atrioventricular; CD = Chagas disease; PPM = permanent pacemaker; SD = standard deviation; SSS = sick sinus syndrome.

*N = 73 for therapeutic variables in the non-CD column.

† χ^2 or Fisher exact test (categorical variables); t test (continuous variables).

the endemic region by definition, the risk of reinfection with subsequent progression of the disease has been significantly reduced. Murine models have validated this hypothesis, and others have queried whether the declining morbidity of chronic CD seen in South America could be related to the absence of reinfection vis-à-vis vector control programs.^{15,16}

The majority of the patients diagnosed with CD in this study were from El Salvador (66.7%); however, this finding is likely prone to bias and should only be considered hypothesis-generating. Multiple factors may be contributing to the difference in country of origin: first, among Latin American countries El Salvador is second only to Mexico in terms of number of immigrants present in Los Angeles; second, according to the World Health Organization, El Salvador has a higher rate of *T. cruzi* infection compared with Mexico (1.30% versus 0.78% of the total population, respectively); and third, geographical variations in *T. cruzi* infection are known to exist within a country with the poorer and more rural areas disproportionately affected.^{2,7,9}

There are important clinical implications of this study. Kuschnir and others clinically classified patients who tested

TABLE 2
Electrocardiographic and echocardiographic characteristics

	CD (N = 6)	Non-CD (N = 74)	All (N = 80)*	P value†
Electrocardiographic				
LBBB, n (%)	0 (0.0)	6 (8.1)	6 (7.5)	1.000
RBBB, n (%)	2 (33.3)	13 (17.6)	15 (18.8)	0.313
IVCD, n (%)	0 (0.0)	3 (4.5)	3 (4.3)	1.000
LAFB, n (%)	1 (16.7)	7 (9.5)	8 (10.0)	0.480
LPFB, n (%)	0 (0.0)	2 (2.7)	2 (2.5)	1.000
Prior infarct, n (%)	0 (0.0)	6 (9.2)	6 (8.7)	1.000
Echocardiographic				
Mean LVEDD in mm (±SD)	43.0 (±3.5)	47.5 (±6.5)	47.1 (±6.4)	0.101
Mean LVEF in % (±SD)	55.8 (±11.8)	57.4 (±9.7)	57.3 (±9.8)	0.708

CD = Chagas disease; IVCD = intraventricular conduction delay; LAFB = left anterior fascicular block; LBBB = left bundle-branch block; LPFB = left posterior fascicular block; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; RBBB, right bundle-branch block; SD = standard deviation.

*Two nonpaced electrocardiograms were unavailable for CD, seven electrocardiograms were unavailable for non-CD, and six echocardiograms were unavailable for non-CD.

†Fisher exact test (categorical variables); t test (continuous variables).

serologically positive for *T. cruzi* into four groups (0, I, II, or III) based on the presence or absence of an abnormal ECG, cardiac enlargement by chest X-ray, and clinical signs of heart failure.¹⁷ By this classification scheme, the patients enrolled into the present study would be considered Kuschner group I or II. Previous work has demonstrated a benefit of benznidazole treatment in chronic CD patients in these Kuschner groups.¹⁸ In contrast to these findings, the largest, randomized trial of trypanocidal therapy to date showed no reduction in clinical outcomes in patients with chronic Chagas cardiomyopathy.¹⁹ Importantly, however, this trial included patients with symptoms of heart failure, reduced LVEF, and wall-motion abnormalities by echocardiography. Taken together, the available data suggest that screening Latin American immigrants with pacemakers in the United States may help identify a group of chronic CD patients who would benefit from trypanocidal therapy.

A considerable limitation of this study is the assumption that seropositivity for *T. cruzi* meant that the parasite infection had caused the conduction abnormality. Since it is possible that CD and another etiology for the bradyarrhythmia may coexist in the same person, the conduction disease seen in our study group may not accurately reflect the true percentage of conduction disease caused by CD among Latin American patients with pacemakers in Los Angeles. Indeed, since only 113 out of 237 potential patients qualified for the study our exclusion criteria may have been too stringent. Furthermore, by excluding patients with Chagas cardiomyopathy (i.e., reduced LVEF), the electrocardiographic and echocardiographic findings are skewed. In addition, this study was limited to a single hospital in Los Angeles and the results may not accurately reflect the prevalence in the United States as a whole.

This is the first study to examine the prevalence of CD among Latin American immigrants with pacemakers in the United States. The relatively high prevalence of undiagnosed CD (nearly one in 13) among this population argues for screening all Latin American immigrants with pacemakers in Los Angeles, if not the entire United States. Screening this group should help identify patients with chronic CD that would benefit from early diagnosis and treatment, potentially sparing them the considerable morbidity and mortality associated with Chagas cardiomyopathy.

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