Published in final edited form as:

Am J Transplant. 2013 December ; 13(12): 3262–3268. doi:10.1111/ajt.12507.

Heart Transplantation for Chagas Cardiomyopathy in the United States

E. P. Kransdorf[1], **L. S. C. Czer**[1], **D. J. Luthringer**[2], **J. K. Patel**[1], **S. P. Montgomery**[3], **A. Velleca**[1], **J. Mirocha**[1], **P. C. Zakowski**[4], **R. Zabner**[4], **C. R. Gaultier**[4], **Y. Qvarnstrom**[3], **T. Benedict**[3], **F. Steurer**[3], **E. Bosserman**[3], **C. D. Paddock**[5], **M. Rafiei**[1], **J. A. Kobashigawa**[1,*]

[1]Cedars-Sinai Heart Institute, Los Angeles CA

[2]Department of Pathology, Cedars-Sinai Medical Center, Los Angeles CA

[3]Parasitic Diseases Branch, Centers for Disease Control and Prevention, Atlanta GA

[4]Tower Infectious Diseases Medical Associates, Los Angeles CA

[5]Infectious Disease Pathology Branch, Centers for Disease Control and Prevention, Atlanta GA

Abstract

Since an initial case in 2006, we noted multiple patients undergoing heart transplantation (HTx) for Chagas cardiomyopathy (CC) at our transplant program. The clinical characteristics, laboratory results and outcomes of patients with CC undergoing HTx in the United States have not been reported previously. In 2010, we implemented a systematic screening and management program for patients undergoing HTx for CC. Before HTx, all patients with idiopathic dilated cardiomyopathy who were born in a Chagas disease endemic country were screened for *Trypanosoma cruzi* (TC) infection with serology. After HTx, monitoring for TC reactivation was performed using clinical visits, echocardiography, endomyocardial biopsy and serial whole blood polymerase chain reaction (PCR) testing. Between June 2006 and January 2012, 11 patients underwent HTx for CC. One patient was empirically treated due to the presence of TC amastigotes in explanted cardiac tissue. Two patients experienced allograft dysfunction due to TC reactivation and three patients experienced subclinical reactivation (positive PCR results), which were treated. Chagas disease is a common cause of dilated cardiomyopathy in patients from endemic countries undergoing HTx at a transplant program in the United States. Reactivation is common after transplantation and can cause adverse outcomes.

Keywords

Cardiomyopathy; Chagas disease; heart transplantation; *Trypanosoma cruzi*

*Corresponding author: Jon A. Kobashigawa, jon.kobashigawa@cshs.org.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation.*

Supporting Information

Additional Supporting Information may be found in the online version of this article.

Introduction

Chagas disease is a major cause of end-stage cardiomyopathy in Mexico, South America and Central America, with current estimates of 7.7 million persons infected in 18 countries (1). Patients with Chagas cardiomyopathy (CC) have a higher mortality when compared with other etiologies of cardiomyopathy (2); thus, it is a common indication for heart transplantation (HTx) in endemic countries where this therapy is available. Given the potential for reactivation of the causative agent *Trypanosoma cruzi* (TC) with immunosuppression, CC was initially considered to be a relative contraindication to HTx (3). Subsequently, studies have shown that the outcome after HTx for CC is acceptable (4), and as such it is now performed routinely, but requires close clinical and laboratory monitoring for TC reactivation (5).

The true prevalence of Chagas disease in the United States is unknown. A recent study estimates that there are 300 000 persons with chronic Chagas disease in the United States, resulting in 30 000–45 000 cases of CC (6). Although locally acquired infection continues to be identified in the United States (7), the vast majority of cases occur in patients born in endemic countries who immigrate to the United States (6). Because this population is underserved, and physicians in the United States have a poor awareness of Chagas disease (8), CC is likely underdiagnosed (9). HTx for CC has been previously reported in isolated cases in the United States (3,10). Since an initial case in 2006, we have noted multiple patients undergoing HTx for CC at our program. Given this, as well as recently published recommendations for posttransplant monitoring (5), we performed a comprehensive analysis of our series of patients undergoing HTx for CC at a transplant program in the United States.

Materials and Methods

Study population and design

We identified all patients undergoing a first heart transplant alone at our program between June 26, 2006 (date of transplant for patient 1) and January 10, 2012 (date of transplant for patient 11) with a positive serology result for TC infection. Laboratory follow-up was assessed on May 7, 2012, and clinical follow-up was assessed on September 19, 2012. Patients 3 and 4 were lost to follow-up in the posttransplant period, so clinical and laboratory data are incomplete. This study was performed under protocol #22311 of the Cedars-Sinai Medical Center Institutional Review Board.

Clinical protocol

Detailed methods are available in the Supplemental Materials and Methods section available online. Briefly, maintenance immunosuppression consisted of tacrolimus and mycophenolate mofetil. Prednisone was weaned by month 6 except in patients with sensitization or rejection. Patients who were treated for TC reactivation received nifurtimox or benznidazole as per published recommendations (11).

TC testing

Since 2010, all patients undergoing HTx for idiopathic dilated cardiomyopathy at our program who were born in a Chagas disease endemic country (5) were screened for TC infection with serology as part of a systematic screening and management program. Our strategy for pretransplant screening and posttransplant management of TC infected patients is detailed in Table 1. Serological testing for TC infection was performed on serum using a whole epimastigote immunofluorescence assay (IFA) at Focus Diagnostics (Cypress, CA) or the Centers for Disease Control and Prevention (CDC; Atlanta, GA). CDC also performed an enzyme-linked immunosorbent assay (EIA) to detect antibody to TC (Chagatest ELISA recombinante v.3.0; Wiener Laboratorios, Rosario, Argentina) on samples tested at their facility. After transplantation, clinical monitoring for reactivation comprised of: (1) serial visits with evaluation for symptoms/signs of allograft dysfunction, fever, new skin lesions or arrhythmia; (2) electrocardiography (ECG) with evaluation for new conduction blocks and (3) echocardiography to assess for new left ventricular dysfunction. Changes compatible with Chagas disease in any of these were considered as clinical suspicion of reactivation of TC infection. Laboratory monitoring for reactivation comprised of: (1) microscopy of a buffy coat blood sample for TC; (2) endomyocardial biopsy (EMB) to assess for the presence of amastigotes and (3) whole blood testing by polymerase chain reaction (PCR) for TC at the Reference Diagnostic Laboratory of the Division of Parasitic Diseases and Malaria at CDC (methods described in Ref. (12)). Laboratory-confirmed reactivation was defined as detection of parasitemia on serial samples or parasites in the implanted heart in chronically infected transplant recipients. Patients with positive blood PCR results on serial samples posttransplant but no other symptoms or signs of reactivation were considered suspected reactivation cases. All laboratory-confirmed reactivation cases were treated, while the decision to treat suspected reactivation was made on a case-by-case basis following discussions with the Parasitic Diseases Branch at CDC (SPM, YQ, TB).

Results

Identification of Chagas cohort

Between June 2006 and January 2012, 405 patients received a first heart transplant alone at our program. Of these, 31 patients were born in a Chagas disease endemic country (Figure 1). Eleven of 31 patients had either ischemic or amyloid cardiomyopathy and therefore did not undergo serological testing for TC. The other 20 patients were born in a Chagas disease endemic country, had dilated cardiomyopathy, and underwent serological testing for TC. CC was identified in 11 of these patients by serological testing (Table 2). This group represented 35.5% of the 31 patients who were born in an endemic country and underwent first heart transplant alone during the study period or 55% of the 20 patients from Chagas disease endemic countries who were undergoing transplant for dilated cardiomyopathy. All 11 CC patients were classified as New York Heart Association class IV at the time of evaluation for HTx and none had symptoms or signs of gastrointestinal Chagas disease. Serological testing for TC infection was performed prior to organ donation on 4 of 11 donors; results were negative in all cases.

Of the 11 patients, only 2 were referred for transplantation with a diagnosis of CC (patients 3 and 4), which had been identified in their home country prior to immigration. The other nine cases were identified during the pre- or posttransplant period. Patient 1 was diagnosed with TC infection posttransplant when he presented with clinical signs of reactivation, which prompted serological testing. Patient 2 was identified after transplantation through systematic screening for TC infection, which was instituted after his date of transplant. Patient 5 initially tested negative on pretransplant serology for TC infection, but developed TC reactivation after transplantation. Additional serological testing performed on pretransplant serum at CDC was positive, indicating the initial test result was false-negative.Patients 6–11 were diagnosed via systematic screening during pretransplant evaluation.

Clinical characteristics

The clinical characteristics of the Chagas cohort are summarized in Table 3. As compared to a cohort of 107 patients with CC that underwent HTx in Brazil (4), the Chagas cohort had an older mean age (55 vs. 43 years) and more women (55% vs. 29%). More patients were treated with inotropes or had a ventricular assist device (VAD) in place (73% vs. 47%). All patients in the Chagas cohort had an implantable cardioverter defibrillator (ICD) *in situ* as compared to 10% in the Brazilian cohort.

Echocardiographic characteristics

Mean ejection fraction (EF) was severely depressed at 19%. However, right ventricular function was less severely depressed, with a median value of mild dysfunction. Severe left ventricular dilatation and thinning was present, with an average left ventricular internal diastolic dimension index of 46.2 mm/m^2 and a posterior wall thickness of 8.0 mm. Mitral regurgitation was present in all cases and was severe in 6 of 11 (54.5%). One patient had a left ventricular apical aneurysm by echocardiography (Table 4).

Clinical and laboratory monitoring for TC reactivation

Two patients experienced clinical signs and symptoms of TC reactivation after transplantation (Table 5). Neither of these patients had been diagnosed with TC infection prior to transplant. Patient 1 had an uneventful course until 216 days posttransplant when he presented with symptomatic allograft dysfunction (EF 45%). EMB samples showed the presence of TC amastigotes. He was treated with nifurtimox and has had no further clinical and no PCR evidence of reactivation and is doing well 6 years after transplantation. Patient 5 also had an uneventful course until 100 days posttransplant when he presented with symptomatic high-degree atrioventricular block and underwent pacemaker placement. He then presented 14 days later with symptomatic allograft dysfunction (EF 45%). EMB samples showed the presence of TC amastigotes. Treatment with benznidazole was initiated, but unfortunately, the patient developed cardiogenic shock and died 4 days later.

Patient 3 was empirically treated for TC reactivation with nifurtimox posttransplant due to the presence of TC amastigotes in her explanted cardiac tissue. Patients 3 and 4 were lost to follow-up at 730 and 895 days posttransplant and therefore did not undergo whole blood

PCR testing for TC. Neither patient exhibited clinical or laboratory evidence (assessed by EMB alone) of TC reactivation.

Seven of the patients in the Chagas cohort were followed posttransplant with serial testing of whole blood samples using PCR (Table 5). Three patients had persistently negative PCR results and no evidence of clinical reactivation. Of these, two patients remained healthy as of the end of the follow-up period (patients 2 and 6), and one patient (patient 7) died of sudden cardiac arrest of unknown etiology 45 days posttransplant. Serial PCR testing was initially negative and then turned positive (in at least one sample) in four patients at an average of 22.8 days posttransplant. Based on positive PCR results indicating an increase in parasitemia in serial whole blood samples, treatment with benznidazole was initiated in three of these four patients (patients 8, 9 and 10). These three patients are alive at follow-up with persistently negative PCR results after treatment. Patient 11 had low reactive positive PCR results on one sample and subsequent samples tested negative; therefore, this patient did not have sufficient evidence of reactivation and treatment was not initiated. None of these seven patients developed allograft dysfunction (EF < 50%) by echocardiography in the posttransplant period.

Survival outcome

The median follow-up time for the Chagas cohort was 1.1 years. Overall survival at 30 and 180 days after transplantation was 100% and 82%. Survival in the five patients with, and six patients without, confirmed that TC reactivation was 80% and 83% at clinical follow-up.

Discussion

Here we report the clinical characteristics and survival outcomes of our series of patients undergoing HTx for CC in the United States. As a result of instituting systematic screening, we found Chagas disease to be a common cause of dilated cardiomyopathy in patients from endemic countries undergoing HTx at our program. This high prevalence may be attributable to the large immigrant Hispanic population in Southern California and the relatively high rate of infection in persons from certain endemic countries, such as El Salvador (6). Given the potential for reactivation after transplantation (13), universal screening for TC infection in all patients born in a Chagas disease endemic country and undergoing transplant evaluation for dilated cardiomyopathy is indicated.

Serological testing methods for chronic TC infection, such as the whole epimastigote IFA and Chagatest ELISA used in this study, have a sensitivity and specificity of 95% or greater (14), but are imperfect. We observed that patient 5 had a single negative whole epimastigote IFA for TC infection at a commercial laboratory before transplantation, and then developed fulminant TC reactivation after transplantation. Repeat serological testing performed on pretransplant serum at CDC was positive for TC infection. This diagnostic failure highlights the importance of following guidelines that clinical diagnosis utilize two serological assays with different formats and TC antigen preparations (15). It is important to note that the reagents for whole epimastigote IFA are not standardized, and therefore the sensitivity of this assay is variable (16).

Testing of potential organ donors for chronic TC infection is of paramount importance due to the risk of donor-transmitted infection. In our series, 4 of 11 organ donors underwent testing for TC infection. Given a seroprevalence of TC infection of approximately 0.02% in blood donors and 0.2% in organ donors in Southern California (17,18), universal testing is necessary to prevent donor-transmitted TC infection, which led to the death of two heart transplant recipients in 2006 (19). The most common reason for omission of TC testing in our cohort was that the Organ Procurement Organization (OPO) did not routinely perform TC testing, even on at-risk donors. Recent data indicate that only 19% of OPOs in the US perform TC testing (20).

We found that CC patients in our cohort had clinical characteristics that differed from those of a cohort of patients with CC undergoing HTx in the Chagas disease endemic country of Brazil. Our Chagas cohort had higher utilization of inotropes/VADs, ICDs, as well as a lower mean EF. We surmise that our Chagas cohort had more advanced CC than the Brazilian cohort. We speculate that this may be due to the high utilization of electrical (ICDs and cardiac resynchronization therapy) and ventricular support devices in our Chagas cohort that provided cardiac support until the time of HTx.

Reactivation of TC infection is a major concern after HTx for CC because of the risk of allograft dysfunction (13). We identified reactivation in five patients (45%), detected by clinical signs of reactivation with accompanying allograft dysfunction by echocardiography in two cases, and whole blood PCR testing in three patients. The TC reactivation rate in our cohort is higher than the rates of 21–39% that have been reported by transplant centers in Brazil (4,13,21). This difference is likely due to the use of the more potent immunosuppresive agents tacrolimus and mycophenolate mofetil in the United States, as compared to predominant use of cyclosporine and azathioprine in Brazil. Mycophenolate mofetil in particular has been associated with a higher rate of TC reactivation (21,22), which was used in all patients in the Chagas cohort.

Given the high frequency of TC reactivation after HTx for Chagas disease, both in our study and in those from Brazil, a strategy of universal “prophylactic” treatment with antitrypanosomal therapy after transplantation seems appealing. However, several pieces of data indicate that universal treatment is neither necessary nor appropriate. First, not all patients undergoing HTx for Chagas disease will experience TC reactivation posttransplant, as demonstrated by our data. Next, the currently available PCR test is sufficiently sensitive to detect TC reactivation before complications such as allograft dysfunction develop. In our series, in the three cases where TC reactivation was detected by PCR testing of whole blood samples, no clinical symptoms were apparent at the time of detection and no further TC-related complications occurred. Both antitrypanosomal agents have significant side effects and are poorly tolerated (23), so treatment should only be undertaken when indicated. Finally, it is important to note that treatment does not result in “cure” of chronic TC infection (23), and as such transplant recipients will continue to require lifelong TC monitoring.

The limited follow-up time in this study makes comparison to other series difficult. However, 82% of our Chagas cohort was alive at 6 months posttransplant, as compared

to about 70% at 1 year posttransplant in the study by Fiorelli et al (24). In our series, one patient died of TC reactivation and one patient without suspected reactivation died suddenly 45 days posttransplant. We cannot rule out arrhythmia due to TC reactivation in this case, as no autopsy was performed. As compared to the series of 117 and 107 cases of HTx for CC from Brazil reported by Fiorelli et al (4) and Bocchi and Fiorelli (25), our cohort had lower perioperative mortality but a higher incidence of TC reactivation and TC-related mortality.

This study is limited by several factors inherent to a small case series. First, the patients in the Chagas cohort were all referred for HTx, and therefore are not likely to be representative of patients with less severe Chagas heart disease in the community. Second, the limited follow-up time and lack of a control group in our study precluded a comparison of long-term survival and other complications, such as non-TC infection and rejection between patients undergoing heart transplant for CC as compared to other etiologies. Analysis of these complications in the future will be important in order to improve the outcome of patients undergoing HTx for CC.

In conclusion, Chagas disease is a common cause of dilated cardiomyopathy in patients in the United States who were born in a Chagas disease endemic country and are referred for HTx. Systematic screening of all patients with dilated cardiomyopathy who were born in a Chagas disease endemic country is imperative. Reactivation is common after transplantation and unless detected and treated appropriately is likely to cause adverse outcomes. Routine clinical and laboratory monitoring is therefore essential to reduce the risks of reactivation in this group of patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The findings and conclusions are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Abbreviations:

CC	Chagas cardiomyopathy
CDC	Centers for Disease Control and Prevention
ECG	electrocardiography
EF	ejection fraction
EIA	enzyme-linked immunosorbent assay
EMB	endomyocardial biopsy
HTx	heart transplantation
ICD	implantable cardioverter defibrillator

IFA	immunofluorescence assay
OPO	Organ Procurement Organization
PCR	polymerase chain reaction
TC	*Trypanosoma cruzi*
VAD	ventricular assist device

References

1. Rassi A Jr., Rassi A, Marin-Neto JA. Chagas disease. Lancet 2010; 375: 1388–1402. [PubMed: 20399979]
2. Freitas HF, Chizzola PR, Paes ÂT, Lima AC, Mansur AJ. Risk stratification in a Brazilian hospital-based cohort of 1220 out-patients with heart failure: Role of Chagas' heart disease. Int J Cardiol 2005; 102: 239–247. [PubMed: 15982491]
3. Kirchhoff LV. American trypanosomiasis (Chagas' disease)—A tropical disease now in the United States. N Engl J Med 1993; 329: 639–644. [PubMed: 8341339]
4. Fiorelli AI, Santos RHB, Oliveira JL, et al. Heart transplantation in 107 cases of Chagas' disease. Trans Proc 2011; 43: 220–224.
5. Chin-Hong PV, Schwartz BS, Bern C, et al. Screening and treatment of Chagas disease in organ transplant recipients in the United States: Recommendations from the Chagas in Transplant Working Group. Am J Transplant 2011; 11: 672–680. [PubMed: 21401868]
6. Bern C, Montgomery SP. An estimate of the burden of Chagas disease in the United States. Clin Infect Dis 2009; 49: e52–e54. [PubMed: 19640226]
7. Cantey PT, Stramer SL, Townsend RL, et al. The United States *Trypanosoma cruzi* Infection Study: Evidence for vector-borne transmission of the parasite that causes Chagas disease among United States blood donors. Transfusion 2012; 52: 1922–1930. [PubMed: 22404755]
8. Stimpert KK, Montgomery SP. Physician awareness of Chagas disease, USA. Emerg Infect Dis 2010; 16: 871–872. [PubMed: 20409389]
9. Bern C, Kjos S, Yabsley MJ, Montgomery SP. *Trypanosoma cruzi* and Chagas' disease in the United States. Clin Microbiol Rev 2011; 24: 655–681. [PubMed: 21976603]
10. Blanche C, Aleksic I, Takkenberg JJ, Czer LS, Fishbein MC, Trento A. Heart transplantation for Chagas' cardiomyopathy. Ann Thorac Surg 1995; 60: 1406–1408. [PubMed: 8526639]
11. Bern C, Montgomery SP, Herwaldt BL, et al. Evaluation and treatment of Chagas disease in the United States: A systematic review. JAMA 2007; 298: 2171–2181. [PubMed: 18000201]
12. Qvarnstrom Y, Schijman AG, Veron V, Aznar C, Steurer F, da Silva AJ. Sensitive and specific detection of *Trypanosoma cruzi* DNA in clinical specimens using a multi-target real-time PCR approach. PLoS Negl Trop Dis 2012; 6: e1689. [PubMed: 22802973]
13. Godoy HL, Guerra CM, Viegas RF, et al. Infections in heart transplant recipients in Brazil: The challenge of Chagas' disease. J Heart Lung Transplant 2010; 29: 286–290. [PubMed: 19783174]
14. Ramírez JD, Guhl F, Umezawa ES, et al. Evaluation of adult chronic Chagas' heart disease diagnosis by molecular and serological methods. J Clin Microbiol 2009; 47: 3945–3951. [PubMed: 19846646]
15. WHO Expert Committee on the Control of Chagas Disease. Control of Chagas disease: Second report of the WHO expert committee. Geneva, Switzerland: World Health Organization, 2002, pp. 25–28.
16. Malan AK, Avelar E, Litwin SE, Hill HR, Litwin CM. Serological diagnosis of *Trypanosoma cruzi*: Evaluation of three enzyme immunoassays and an indirect immunofluorescent assay. J Med Microbiol 2006; 55: 171–178. [PubMed: 16434709]
17. Leiby DA, Herron RM Jr., Read EJ, Lenes BA, Stumpf RJ. *Trypanosoma cruzi* in Los Angeles and Miami blood donors: Impact of evolving donor demographics on seroprevalence and implications for transfusion transmission. Transfusion 2002; 42: 549–555. [PubMed: 12084162]

18. Nowicki MJ, Chinchilla C, Corado L, et al. Prevalence of antibodies to *Trypanosoma cruzi* among solid organ donors in Southern California: A population at risk. Transplantation 2006; 81: 477–479. [PubMed: 16477238]

19. Kun H, Moore A, Mascola L, et al. Transmission of *Trypanosoma cruzi* by heart transplantation. Clin Infect Dis 2009; 48: 1534–1540. [PubMed: 19400748]

20. Schwartz BS, Paster M, Ison MG, Chin-Hong PV. Organ donor screening practices for *Trypanosoma cruzi* infection among US organ procurement organizations. Am J Transplant 2011; 11: 848–851. [PubMed: 21426487]

21. Campos SV, Strabelli TMV, Amato Neto V, et al. Risk factors for Chagas' disease reactivation after heart transplantation. J Heart Lung Transplant 2008; 27: 597–602. [PubMed: 18503957]

22. Bacal F, Silva CP, Bocchi EA, et al. Mychophenolate mofetil increased Chagas disease reactivation in heart transplanted patients: Comparison between two different protocols. Am J Transplant 2005; 5: 2017–2021. [PubMed: 15996254]

23. Bern C Antitrypanosomal therapy for chronic Chagas' disease. N Engl J Med 2011; 364: 2527–2534. [PubMed: 21714649]

24. Fiorelli AI, Stolf NAG, Honorato R, et al. Later evolution after cardiac transplantation in Chagas' disease. Trans Proc 2005; 37: 2793–2798.

25. Bocchi EA, Fiorelli A; First Guideline Group for Heart Transplantation of the Brazilian Society of Cardiology. The Brazilian experience with heart transplantation: A multicenter report. J Heart Lung Transplant 2001; 20: 637–645. [PubMed: 11404169]

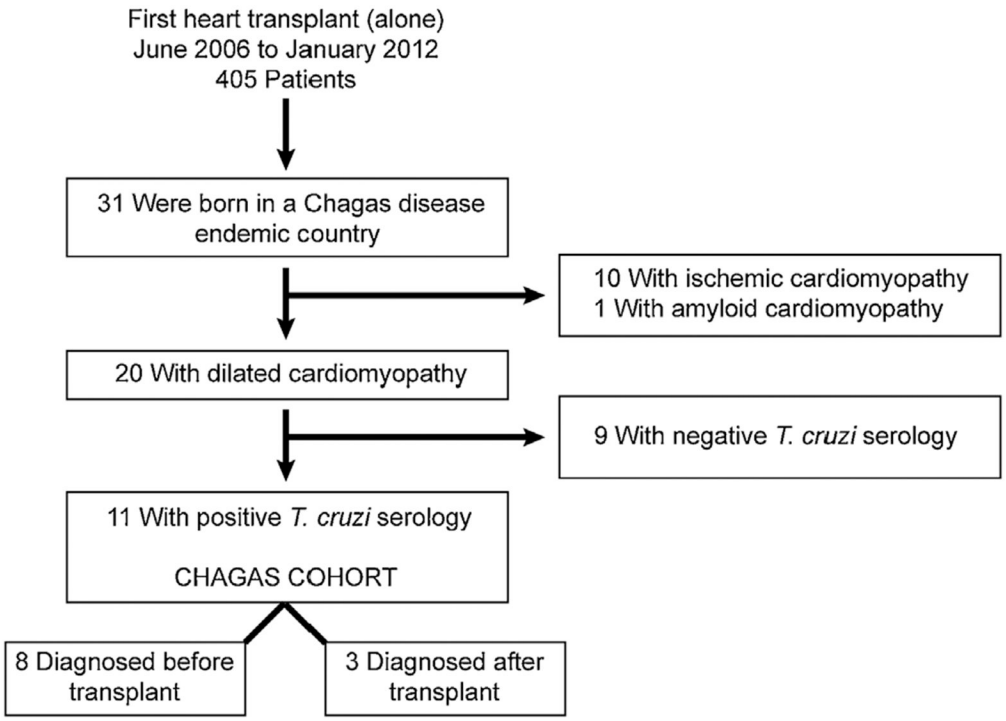

Figure 1: Flowchart for identification of the Chagas cohort.

Four hundred five patients received a first heart transplant alone at our program between June 2006 and January 2012. Thirty-one patients were born in a Chagas disease endemic country. Twenty patients were identified as having dilated cardiomyopathy. Eleven of these 20 (55%) were found to have a positive serology for TC. Of the 11 patients, 8 were diagnosed with TC infection prior to HTx and 3 were diagnosed after HTx (patients 1, 2 and 5).

Table 1:

Strategy for pretransplant screening and posttransplant management of TC infection in heart transplant recipients

Before heart transplantation	
Screen all patients with idiopathic dilated cardiomyopathy born in a Chagas disease endemic country for TC infection	
Perform serological testing using two serological assays with different formats and TC antigen preparations	
After heart transplantation	
Examine cardiac explant by microscopy for presence of TC amastigotes and myocarditis	
Examine paraffin blocks of explanted tissue by (1) IHC for TC and (2) tissue PCR for TC	
Perform serial clinical evaluation for signs/symptoms of allograft dysfunction and arrhythmia (including ECG and 2D echocardiogram)	
Perform serial laboratory evaluation using (1) microscopy of blood buffy coat with attention to TC organisms, (2) EMB with attention to the presence of TC amastigotes and (3) whole blood PCR testing for TC at CDC per schedule:	
Posttransplant months 1 and 2	Weekly
Posttransplant months 3–6	Every 2 weeks
Posttransplant months 6–12	Monthly
Posttransplant months 13–24	Every 3 months
Posttransplant months 25 and greater	Every 6 months

TC, *Trypanosoma cruzi*; IHC, immunohistochemistry; PCR, polymerase chain reaction; ECG, electrocardiogram; 2D, two-dimensional; EMB, endomyocardial biopsy; CDC, Centers for Disease Control and Prevention.

Table 2:

Characteristics and serological testing results of the Chagas cohort

Patient	Age	Gender	Country of origin	Year of transplant	Method of Chagas disease diagnosis	Focus IFA titer[1]	CDC IFA titer	CDC EIA titer
1	37	M	Belize	2006	CR, S	NP	1:64	1.099
2	61	M	Mexico	2008	S	NP	1:32	1.603
3	52	F	El Salvador	2009	S	1:64	NP	NP
4	58	F	El Salvador	2009	S	1:128	NP	NP
5	57	M	El Salvador	2010	CR, S	Negative	1:256	3.281
6	61	F	El Salvador	2011	S	1:128	1:64	2.433
7	69	M	Mexico	2011	S	1:128	1:128	2.627
8	52	M	El Salvador	2011	S	1:64	1:512	2.612
9	55	M	Mexico	2011	S	NP	1:256	3.124
10	53	F	El Salvador	2011	S	NP	1:128	3.268
11	50	F	Mexico	2012	S	NP	1:256	2.581

[1] An IgG IFA titer of ≥1:16 (Focus Diagnostics) or 1:32 (CDC) was considered positive.

CR, clinical reactivation; S, serology; IFA, immunofluorescence assay; CDC, Centers for Disease Control and Prevention; EIA, enzyme-linked immunosorbent assay; NP, not performed.

Table 3:

Clinical characteristics of the Chagas cohort[1]

	Chagas cohort (n = 11)
Mean age at transplant	55.4 ± 7.8 (55.6)
Female	6 (55%)
Mean body mass index (kg/m^2)	21.3 ± 3.8 (21.3)
History of hypertension	2 (18%)
History of diabetes mellitus	3 (27%)
ICD device *in situ*	11 (100%)
CRT device *in situ*	8 (73%)
Sudden cardiac death or VT requiring device therapy	5 (46%)
History of VT ablation	2 (18%)
Mean duration of heart failure at transplant (years)	6.3 ± 2.8 (6.3)
Inotropic support at transplant	5 (45%)
VAD in place at transplant	3 (27%)
Mean ischemic time (h)	3.9 ± 1.4 (3.3)
PRA > 10%	3 (27%)
Mean donor age (years)	34.6 ± 12.1 (33.5)

[1]Values are mean plus/minus standard deviation (median) for continuous variables or number (percentage) for categorical variables.

ICD, implantable cardioverter defibrillator; CRT, cardiac resynchronization device; VT, ventricular tachycardia; VAD, ventricular assist device; PRA, panel reactive antibody.

Table 4:

Pretransplant echocardiographic parameters[1]

Parameter	Chagas cohort (n = 11)
Ejection fraction (%)	19 ± 5
Right ventricular dysfunction (0–4)	1 (0, 2)
LVID dimension (mm)	72.4 ± 9.4
LVID dimension index (mm/m^2)	46.2 ± 5.6
Interventricular septal thickness (mm)	7.2 ± 2.1
Left posterior wall thickness (mm)	8.0 ± 1.7
Left atrial dimension (mm)	44.7 ± 7.4
Tricuspid regurgitation severity (0–6)	2 (1, 4)
Right ventricular systolic pressure (mmHg)	37.0 ± 22.2
Mitral regurgitation severity (0–6)	6 (2, 6)
Left ventricular apical aneurysm	1 (9%)

[1]Values are mean plus/minus standard deviation except for the ordinal variables of right ventricular function, tricuspid regurgitation severity and mitral regurgitation severity, which are median (interquartile range).

LVID, left ventricular internal diastolic.

Table 5:

Trypanosoma cruzi (TC) reactivation, treatment status and follow-up in nine patients

Patient	CR	Monitoring results[1]	Time to reactivation (days)	Treatment	Follow-up time (days)	Status at follow-up
1	+	NP	216	Nifurtimox	2270	Alive
2	−	−		None	1448	Alive
3	−	NP		Nifurtimox	730	Alive
4	−	NP		None	895	Alive
5	+	NP	100	Benznidazole	125	Expired
6	−	−		None	412	Alive
7	−	−		None	45	Expired
8	−	+	5	Benznidazole	414	Alive
9	−	+	17	Benznidazole	399	Alive
10	−	+	42	Benznidazole	333	Alive
11	−	±[2]		None	253	Alive

[1] Using whole blood polymerase chain reaction testing for TC.

[2] Patient 11 had low reactive PCR results on one sample; subsequent samples tested negative.

CR, clinical reactivation; NP, not performed.