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Reactivation of Chagas disease among heart transplant recipients in the United States, 2012-2016

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Abstract

Background: Heart transplantation has been shown to be a safe and effective intervention for progressive cardiomyopathy from chronic Chagas disease. However, in the presence of the immunosuppression required for heart transplantation, the likelihood of Chagas disease reactivation is significant. Reactivation may cause myocarditis resulting in allograft dysfunction and the rapid onset of congestive heart failure. Reactivation rates have been well documented in Latin America; however, there is a paucity of data regarding the risk in non-endemic countries.

Methods: We present our experience with 31 patients with chronic Chagas disease who underwent orthotopic heart transplantation in the United States from 2012 to 2016. Patients were monitored following a standard schedule.

Results: Of the 31 patients, 19 (61%) developed evidence of reactivation. Among the 19 patients, a majority (95%) were identified by laboratory monitoring using polymerase chain reaction testing. One patient was identified after the onset of clinical symptoms of reactivation. All subjects with evidence of reactivation were alive at follow-up (median: 60 weeks).

Conclusions: Transplant programs in the United States are encouraged to implement a monitoring program for heart transplant recipients with Chagas disease. Our experience using a preemptive approach of monitoring for Chagas disease reactivation was effective at identifying reactivation before symptoms developed.

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AUTHORS' CONTRIBUTIONS

EBG and SPM participated in the conception and design of the project; RML, JSG, and VRH contributed patient summaries for the case series; TB and HR performed serologic and PCR laboratory testing; EBG analyzed data; EBG wrote the manuscript; and RML, JSG, VRH, TB, HR, and SPM critically revised the manuscript.

CONFLICT OF INTEREST

The authors of this manuscript have no conflicts of interest to disclose. The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Keywords

Chagas disease; heart transplant; reactivation; *Trypanosoma cruzi*

1 | INTRODUCTION

Heart transplantation (HT) can be lifesaving for patients suffering severe cardiomyopathy due to chronic Chagas disease, a disease caused by the parasite *Trypanosoma cruzi*. Survival after HT for Chagas cardiomyopathy (CC) is comparable to HT performed for other indications.[1] However, these patients are at risk for Chagas disease reactivation (CDR) following immunosuppression.[2–5] Failure to identify patients with CDR has been associated with severe or fatal outcomes.[6,7] The clinical manifestations of CDR, such as myocarditis, can result in allograft dysfunction and the rapid onset of congestive heart failure.[2,5] Other signs and symptoms may include fever, inflammatory panniculitis, and skin nodules.[8–10] Early identification and treatment of CDR can prevent clinical symptoms and allograft injury.[11] Reported rates of reactivation among heart transplant recipients with chronic Chagas disease in Latin America vary widely, from 20% to 90%.[1,4,12,13] When available, reported time from transplant to CDR ranged from 11 to 23 weeks.[13] While most reports of CDR have been published from Latin America, recent cases have been documented in the United States.[14]

Antitrypanosomal treatment is recommended for all patients with CDR.[15] Two drugs, benznidazole and nifurtimox, are effective for treating Chagas disease. As of May 2018, benznidazole is approved by the US Food and Drug Administration (FDA) for use in children 2–12 years of age and is commercially available. Nifurtimox is not currently FDA approved and is available from the CDC Drug Service for use under an investigational protocol. Benznidazole typically is favored over nifurtimox in transplant recipients as it is better tolerated.[2,16]

Based on Chagas disease prevalence in countries of Latin America and US rates of immigration, an estimated 300 000 individuals with Chagas disease live in the United States.[17] Approximately 20%−30% of chronically infected people will develop Chagas disease complications, such as gastrointestinal or cardiac disease.[18] In endemic areas, Chagas disease is a leading cause of cardiomyopathy and sudden cardiac death.[19,20] In two small studies in the United States, *T. cruzi* infections were identified in 13%−19% of Latin American immigrants with non-ischemic cardiomyopathy who resided for at least one year in a country where Chagas disease is endemic.[21,22] The first step to mitigate the potentially devastating effects of CDR in HT recipients is to screen transplant candidates based on epidemiological risk factors such as birth or residence in Latin America.[14]

The benefit of monitoring for CDR after transplantation is well-documented, but there is no consensus or widely recommended standard approach.[23–25] In Latin America, most approaches rely on the identification of trypomastigotes in endomyocardial biopsy or buffy coat, with treatment following the onset of clinical manifestations of CDR.[4,12] Some centers in Latin America have begun using polymerase chain reaction (PCR) for monitoring. PCR testing of whole blood may identify parasitemia days to weeks before clinical evidence of

reactivation can be detected.[2,24] However, even when monitoring by PCR is performed, antitrypanosomal treatment often is not initiated until after clinical signs or symptoms develop.[24] The approach proposed in the United States is to monitor by PCR and microscopic examination of blood smears and fresh buffy coat preparations and to treat on the basis of laboratory evidence of CDR, before the onset of symptoms. The proposed schedule for monitoring for CDR is identical to the frequently recommended schedule for monitoring for donor-derived infections after transplantation: weekly testing for months 1–2, biweekly testing for month 3, monthly testing for months 4–6, and additional testing beyond 6 months in the event of an unexplained febrile episode or an increase in immunosuppression.[15,26]

This report describes the experience monitoring HT patients at risk for CDR in the United States from 2012 to 2016 using the recommended monitoring approach.

2 | METHODS

The Centers for Disease Control and Prevention (CDC)'s Parasitic Diseases Branch (PDB) was notified of heart transplant candidates or recipients with Chagas disease via requests for consultation or testing from healthcare providers or from health departments on behalf of providers in their jurisdictions. As molecular methods for *T. cruzi* laboratory monitoring are not widely available in the United States, the PDB reference laboratory provided *T. cruzi* PCR testing of peripheral blood samples for clinical purposes. Chronic Chagas disease was confirmed first by serologic testing at CDC, and PCR monitoring was initiated following HT in persons with positive serologic results. Heart transplant patients whose infections were confirmed by serology at CDC and who were monitored post-transplant from 2012 to 2016 were included.

Recipient demographic information and country of birth were provided by the transplant center healthcare providers. The activity was approved as a non-research public health program activity by the Office of the Associate Director for Science, Center for Global Health at CDC.

2.1 | Chagas disease testing

Serologic testing for Chagas disease at CDC included three tests: the commercial Chagatest ELISA recombinante v.3.0 (Wiener Laboratorios, Argentina), an in-house immunofluorescence assay (IFA) based on fixed epimastigotes, and a trypomastigote excreted- secreted antigens (TESA) immunoblot.[27] The Chagatest is a qualitative enzyme-linked immunosorbent assay (ELISA) that detects antibodies using five recombinant antigens obtained from the epi- mastigote and trypomastigote stages of *T. cruzi.* The antibody reaction is based on optical density measured using a plate reader. For the in-house IFA, slides coated with *T. cruzi* promastigotes were incubated with serum dilutions of 1:4 to 1:512. The slides were incubated with an anti-human immunoglobulin labeled with fluorescein isothiocyanate (FITC), and the test was considered positive if fluorescence was detected at a titer of 1:32. The *T. cruzi* immunoblot test uses trypomastigote excreted-secreted antigens separated by electrophoresis and transferred onto a nitrocellulose by western blotting. The TESA was performed by incubating a nitrocellulose strip with the

serum sample overnight. The strip was incubated with an anti-human conjugated antibody and developed using a 3'-diaminobenzidine (DAB) substrate. The test was interpreted by the absence (negative) or presence (positive) of the diagnostic band for *T. cruzi.* From 2012 to 2013, recipient infections were confirmed using the ELISA and IFA tests. In 2014, the TESA immunoblot replaced the IFA.[27]

For PCR testing, blood specimens collected in EDTA tubes were sent to CDC where DNA was extracted from whole blood and the buffy coat fraction. The extractions were performed on a QIAcube using the QIAamp blood mini DNA kit (QIAGEN, Valencia, CA). From 2012 to 2013, quantitative real-time PCR was performed using a TaqMan multi-target approach amplifying three different genes: MNC, TCZ, and 18S as described by Qvarnstrom et al.[28] From 2014 to 2016, the 18S gene assay was excluded from the multitarget assay because of poor sensitivity.[28] Positive and negative controls were included in every PCR run. Any specimens that resulted in a signal crossing the threshold and yielding a threshold cycle (Ct) value in both the MNC and TCZ assays were considered positive for the presence of *T. cruzi* DNA. A single positive PCR result may be observed in patients in the absence of CDR.[2] For this summary, we defined laboratory evidence of CDR as either at least two sequential positive PCR test results with decreasing Ct values (indicating an increased presence of parasite DNA) or the identification of trypomastigotes on microscopic examination of whole blood or buffy coat.

2.2 | Preemptive monitoring for CDR

As was done previously in an assessment of donor-derived Chagas disease, laboratory monitoring after transplant was categorized by adherence to the recommended schedule.[29] Three criteria were assessed: PCR monitoring initiated within 2 weeks of transplantation, weekly testing performed for the first 2 months after transplantation, and biweekly to monthly testing performed until month 6 or until CDR was identified. We defined adherence to recommended monitoring as "Complete" if all three criteria were met; "Partial" if two of the three criteria were met; and "Incomplete" if only one criterion was met or no testing was performed prior to diagnosis at the time of symptom development in the recipient.[29]

Time from transplant to CDR was calculated using the collection date of the first positive specimen (ie, the earliest evidence of reactivation), although two sequential positive results with decreasing Ct values were necessary to be considered a case of reactivation based on PCR results. Treatment options were discussed at the time of laboratory evidence of CDR. Benznidazole was obtained from CDC through an investigational protocol.

3 | RESULTS

From 2012 to 2016, CDC was notified of 31 heart transplant recipients at risk for CDR. The median age of the transplant recipients was 53 years (range: 31–74 years), and 18 (58%) were male (Table 1). Countries of birth were available for 30 (97%) patients; 47% of these patients were born in El Salvador (n = 14), 23% in Mexico (n = 7), and 13% in Honduras (n = 4) (Table 1). The transplants were performed at hospitals across the United States: California (n = 10), New York (n = 4), District of Columbia (n = 2), Florida (n = 2), New Jersey (n = 2), Texas (n = 2), Virginia (n = 2), Arizona (n = 1), Maryland (n = 1),

Massachusetts (n = 1), Minnesota (n = 1), North Carolina (n = 1), Utah (n = 1), and Wisconsin (n = 1). Screening for chronic Chagas disease by serologic testing at or before the time of HT was conducted for 24 (77%) of the patients. For the seven patients who were not diagnosed with Chagas disease before or at the time of transplant (Table 1, Cases 26–31), PCR testing began a median of 12 weeks post-transplant; information on the reason for the delay in monitoring was not collected.

3.1 | Chagas disease reactivation

Nineteen patients (61%) developed laboratory evidence of CDR. The median time from transplantation to laboratory evidence of CDR was 3 weeks (range: <1–89 weeks). Eighteen patients were diagnosed by PCR monitoring before clinical symptoms (Table 1, Cases 1–18). One additional patient, who had Incomplete PCR monitoring, was diagnosed only after the development of clinical symptoms by the identification of trypomastigotes on blood smear examination (Case 19, Table 1). The median age of patients who had laboratory evidence of CDR was 53 years (compared to 59 years among those who did not have laboratory evidence of CDR). Nine (47%) of the 19 CDR patients were male. Adherence to the monitoring schedule for the 19 recipients who experienced CDR varied: 16 (84%) had received complete monitoring based on the recommended schedule, 1 (5%) received partial monitoring, and 2 (11%) received incomplete monitoring (Table 2). The median time from transplantation to the detection of CDR was shortest for the patients monitored following the recommended schedule: 2 weeks for those with complete monitoring, 46.5 weeks for the patients who were partially monitored, and 8 weeks for the patient who was not monitored.

Treatment with benznidazole was initiated for the 19 patients with evidence of CDR. All patients with laboratory evidence of CDR were alive at follow-up. The median follow-up time was 60 weeks (range: 11–172 weeks) for patients who experienced CDR and 77 weeks for patients who did not experience CDR. One patient died one week after transplant from an intracranial hemorrhage. The patient had no laboratory evidence of CDR and his death was considered unrelated to Chagas disease.

Three cases were selected for inclusion in the below case series to provide a more detailed description of clinical management and outcomes. Routinely collected data do not include information on immunosuppression, rejection events, or other clinical aspects of patient care. These examples highlight the positive outcomes of monitoring.

3.2 | Case Series

3.2.1 | Case 13—The recipient was a 42-year-old Hispanic man from El Salvador, living in the United States since 1990, who was diagnosed with Chagas cardiomyopathy in 2010 with progressive heart failure necessitating implantation of a left ventricular assist device in 2012, leading to HT May 2015 (Table 1). During his transplant evaluation, the diagnosis of Chagas disease was confirmed by serology at CDC. At the time of transplant, the local laboratory prepared to initiate microscopic examination of serial peripheral blood smears and CDC was contacted to optimize the submission of blood samples for PCR testing. The patient received basiliximab as induction immunosuppression, and cyclosporine, mycophenolate, and prednisone as maintenance immunosuppresion. Post-transplant, the

patient had complete adherence to laboratory monitoring (peripheral blood *T. cruzi* PCR testing at CDC and local blood smear examination) for CDR. He also underwent monthly endomyocardial biopsies to complement the evaluation for CDR. He was diagnosed with asymptomatic CDR 15.5 weeks after transplant when whole blood PCR results were positive. In addition to *T. cruzi* testing, an endomyocardial biopsy result resembling grade 2 acute cellular rejection (2004 ISHLT classification) and grade 2 pathologic antibody mediated rejection (2013 ISHTL classification) was interpreted as evidence of CDR in the setting of positive whole blood PCR results. Benznidazole at 5 mg/kg/day (200 mg twice daily) was initiated and continued for 8 weeks, immunosuppression was concomitantly reduced (50% reduction of mycophenolate). PCR test results were negative two weeks after the initiation of treatment and have remained negative. Two weeks after discontinuation of benznidazole, the patient developed severe neuropathy, thought to be related to benznidazole treatment, which was non-responsive to maximum dose gabapentin and required treatment with prednisone 1 mg/kg. Other adverse effects attributed to benznidazole included headaches and decreased energy. All symptoms progressively improved and the patient was doing well with excellent allograft function at 53 weeks post-transplantation.

3.2.2 | Case 16—The recipient was a 47-year-old man from El Salvador who was diagnosed and treated for CC in 2011 during evaluation for congestive heart failure (Table 1). Progressive cardiomyopathy developed 17 months after completion of nifurtimox therapy, leading to HT in December 2016. Induction immunosuppression included azathioprine, tacrolimus, and steroids. The early transplant course was complicated by two episodes of acute cellular rejection (ACR) on days 7 and 15 after transplant. The first episode, ACR 2R, was managed with high dose steroids and a change of immunosuppression from azathioprine to mycophenolate. The second episode, ACR 2R/3A, was treated with high dose steroids and thymoglobulin. Screening for CDR began at the time of transplant. *T. cruzi* PCR test results at day 7 were negative, at the time of first rejection, but positive at day 14, and examination of thick blood smears showed low-level parasitemia at day 24 after transplant. In addition to rejection treatment, antitrypanosomal therapy (benznidazole 5 mg/kg/day divided every 12 hours), was initiated on day 25 after transplant and continued for 60 days; benznidazole therapy was tolerated well without side effects. PCR testing results became negative at day 46, three weeks after the initiation of benznidazole. Maintenance immunosuppression consisted of tacrolimus, mycophenolate, and prednisone 5 mg daily. As of 12 months after transplant, the patient continued to do very well with good graft function and no further episodes of rejection.

3.2.3 | Case 17—The recipient was a 54-year-old woman born in Santa Barbara, Honduras, who relocated to an urban area of Honduras at age 18 and immigrated to the United States in 1989 (Table 1). She developed non-ischemic cardiomyopathy in 2014 and presented with persistent orthopnea, paroxysmal nocturnal dyspnea, abdominal distension, and severe fatigue. A transthoracic echocardiogram from June 2014 revealed an ejection fraction <20%, global hypokinesis, and a left ventricular diastolic diameter of 5.7 cm (severely enlarged). Cardiac catheterization showed no significant coronary artery disease. Testing at CDC was positive for antibody to *T. cruzi* by ELISA and TESA immunoblot. Due to progressive heart failure necessitating dobutamine and milrinone, she received an

orthotopic HT in September 2014. Thymoglobulin was used for induction immunosuppression followed by maintenance with mycophenolate mofetil, tacrolimus and prednisone. Monthly myocardial biopsies remained negative for rejection or active *T. cruzi* infection. Peripheral blood *T. cruzi* PCR monitoring performed at CDC was negative between September 2014 and April 2015. PCR results were positive in May 2015 (35 weeks after transplantation) and September 2015, and negative in June and November 2015. The patient remained asymptomatic and ongoing monitoring was continued. In October 2015, mycophenolate mofetil was switched to sirolimus due to leukopenia and nausea, and tacrolimus was continued. *T. cruzi* PCR was consistently positive beginning 20 months after transplant. At that time, serial buffy coat examinations for *T. cruzi* were negative, and the patient remained clinically asymptomatic. Sirolimus dose was reduced and treatment for CDR with benznidazole (5.7 mg/kg/day divided every 12 hours) was initiated after discussion with CDC. Because of a shortage of drug supply, treatment with benznidazole stopped after 3 weeks. After a 1-month interruption, the patient completed a full 60-day course of benznidazole without any significant adverse reactions. Her peripheral blood PCR and buffy coat were closely monitored during her therapy and following completion. All testing remained negative through March 2017. The patient continued to do well 3 years after transplantation.

4 | DISCUSSION

The approach of monitoring for laboratory evidence of CDR and treating before the onset of clinical manifestations is intended to prevent severe symptoms and damage to the transplanted heart. [25,30,31] Among the patients we reviewed who were monitored and treated promptly following laboratory evidence of CDR, outcomes were good. In the immunosuppressed host, development of CDR can lead to significant allograft dysfunction with resultant morbidity and mortality. Active infection could also be mistaken for rejection resulting in enhanced immunosuppression and detrimental outcomes. A single positive PCR result in a chronically infected patient may not indicate the presence of live parasites or CDR. We considered at least two sequential positive PCR results of increasing intensity (ie, decreasing Ct values) to be indicative of worsening parasitemia. Although testing tissues collected by endomyocardial biopsy after transplantation has been proposed by some centers,[4] defining the clinical utility of biopsy vs monitoring by PCR of whole blood specimens warrants further research.

Most cases of CDR in solid organ transplant recipients have been reported by transplant centers in Latin America, and various approaches to managing CDR have been considered including prophylactic treatment[32] and treatment following the development of clinical symptoms.[24,25,30,31] Prophylactic treatment before or after transplantation is not currently recommended as treatment in chronically infected patients may not be curative, and patients could still experience reactivation.[2] Also, the prolonged course of treatment (60 days for benznidazole) and the incidence of side effects may delay or impede HT.[15,33,34] As has been observed in Latin America, prophylactic treatment with nifurtimox before transplantation did not prevent reactivation for one of the patients described here (Case 16).[3,5] Additionally, *T. cruzi* specific antibody may persist for years after successful treatment, and currently there is no test of cure. Because of these concerns, patients who receive prophylactic

treatment may remain at risk for CDR and monitoring after transplantation should be considered regardless of treatment status.

The rate of reactivation observed in this US case series (61%) was within the broad range reported from Latin America (19.6%−90%).[1,4,12,35] The detection of CDR in our cases was based on laboratory evidence (primarily, positive PCR results) and not clinical manifestations. CDR was detected earlier in this case series than in studies from Latin America, likely because of differences in how CDR was defined based on laboratory monitoring. Because cases were identified and treated early, it is not known how many of these patients would have gone on to develop symptomatic CDR. One patient (Table 1, Case 9) was not monitored by PCR after transplant and was identified following the development of clinical manifestations at week 8.

Most published reports of CDR focus on HT recipients; however, CDR may occur during immunosuppression from other causes, such as HIV/AIDS, stem cell transplantation, and other solid organ transplantation but perhaps to a lesser extent.[36–38] Although other organ type transplants may have occurred in patients with chronic Chagas disease, CDC was not notified of transplants of other organ types in patients with chronic Chagas disease during 2012–2016.

This series had several limitations. Patients were identified passively, when providers or health departments contacted CDC for consultation, and may not be representative of the general US population of heart transplant recipients or individuals with chronic Chagas disease. Additional transplant recipients with chronic Chagas disease may have gone undiagnosed or unreported, and their outcomes are unknown. Although the patients who experienced CDR did well clinically during the period of follow-up (median: 60 weeks), the long-term outcomes for these patients are not known. We were not able to assess potential risk factors for CDR including specifics of patient clinical management and immunosuppressive therapy, transplant outcomes, adverse reactions to Chagas treatment, or other outcome measures.

Our experience suggests that HT recipients with a prior history of chronic Chagas disease can achieve excellent outcomes when the risk of CDR is managed as described: Screening before transplantation in patients with epidemiological risk factors for Chagas diseases and clinical and laboratory monitoring for CDR immediately after transplant, when immunosuppressive therapy has greatest impact.[39] Monitoring does not prevent CDR; however, it does allow for the prompt identification and treatment to prevent adverse outcomes. Transplant programs in the United States are encouraged to implement their monitoring program for *T. cruzi* infection in coordination with the CDC Parasitic Diseases Branch.

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Abbreviations:

ACR	acute cellular rejectíon
CC	Chagas cardiomyopathy
CDC	Centers for Disease Control and Prevention
CDR	Chagas disease reactivation
CT	threshold cycle
ELISA	enzyme-linked immunosorbent assay
HT	heart transplantation
IFA	immunofluorescence assay
PCR	polymerase chain reaction

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Table 1

Solid organ recipients monitored for CDRin the United States, 2012–2016

No.	Transplant year	State	Age	Sex	Country of birth	Screened for Chagas disease at or before transplant	Monitoring adherence	Chagas disease reactivation	Time from transplant to reactivation (weeks)	Treated	Status	Time from transplant to status update (weeks)
1	2012	NJ	62	Female	Brazil	Yes	Complete	Reactivation	<1	Yes	Alive	172
2	2012	NJ	58	Male	El Salvador	Yes	Complete	Reactivation	2	Yes	Alive	71
3	2013	FL	58	Female	Honduras	Yes	Complete	Reactivation	2	Yes	Alive	167
4	2013	CA	53	Female	El Salvador	Yes	Complete	Reactivation	2	Yes	Alive	91
5	2014	VA	51	Female	Honduras	Yes	Complete	Reactivation	<1	Yes	Alive	155
6	2014	NY	53	Female	El Salvador	Yes	Complete	Reactivation	3	Yes	Alive	28
7	2015	MD	54	Male	El Salvador	Yes	Complete	Reactivation	2	Yes	Alive	98
8	2015	FL	51	Female	Honduras	Yes	Complete	Reactivation	3	Yes	Alive	75
9	2015	NC	61	Female	Brazil	Yes	Complete	Reactivation	2	Yes	Alive	75
10	2015	CA	31	Female	Mexico	Yes	Complete	Reactivation	6	Yes	Alive	60
11	2015	NY	52	Female	El Salvador	Yes	Complete	Reactivation	1	Yes	Alive	11
12	2016	MA	55	Male	El Salvador	Yes	Complete	Reactivation	1	Yes	Alive	53
13	2016	TX	42	Male	Guatemala	Yes	Complete	Reactivation	13	Yes	Alive	52
14	2016	DC	46	Male	El Salvador	Yes	Complete	Reactivation	1	Yes	Alive	49
15	2016	DC	59	Male	El Salvador	Yes	Complete	Reactivation	2	Yes	Alive	24
16	2016	MN	46	Male	El Salvador	Yes	Complete	Reactivation	2	Yes	Alive	19
17	2014	AZ	54	Female	Honduras	Yes	Partial	Reactivation	89	Yes	Alive	130
18	2016	CA	43	Male	Mexico	Yes	Partial	Reactivation	4	Yes	Alive	21
19	2014	Wl	45	Male	Mexico	No	Incomplete	Reactivation	8	Yes	Alive	21
20[a]	2012	CA	50	Female	Mexico	Yes	Complete	No Reactivation	-	-	Alive	184
21	2012	CA	47	Male	El Salvador	Yes	Complete	No Reactivation	-	-	Alive	55
22	2014	UT	61	Male	Mexico	Yes	Complete	No Reactivation	-	-	Alive	134
23	2015	VA	40	Female	Bolivia	Yes	Complete	No Reactivation	-	-	Alive	78
24	2015	NY	69	Male	El Salvador	Yes	Complete	No Reactivation	-	-	Alive	44
25	2015	TX	52	Male	El Salvador	Yes	Complete	No Reactivation	-	-	Died (Intracranial hemorrhage)	1
26	2012	CA	56	Male	El Salvador	No	Incomplete	No Reactivation	-	-	Alive	210 (approx)
27	2014	CA	65	Male	Mexico	No	Incomplete	No Reactivation	-	-	Alive	119
28	2014	CA	67	Female	Mexico	No	Incomplete	No Reactivation	-	-	Alive	83
29	2014	CA	53	Male	El Salvador	No	Incomplete	No Reactivation	-	-	Alive	59
30	2015	CA	61	Male	Unknown	No	Incomplete	No Reactivation	-	-	Alive	77

No.	Transplant year	State	Age	Sex	Country of birth	Screened for Chagas disease at or before transplant	Monitoring adherence	Chagas disease reactivation	Time from transplant to reactivation (weeks)	Treated	Status	Time from transplant to status update (weeks)
31	2015	NY	74	Male	Ecuador	No	Incomplete	No Reactivation	-	-	Alive	62 (approx)

[a]Case described in a previous publication.[14]

Table 2

Reactivation by adherence to monitoring schedule

Monitoring adherence	Total no. of recipients	No. of recipients with evidence of reactivation (%)	Median time from transplant to reactivation (weeks)	Range (weeks)
Complete	22	16 (73%)	2	1–13
Partial	2	2 (100%)	46.5	4–89
Incomplete	7	1 (14%)	8	8–8
Total	31	19 (61%)	2	1–89