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Long-term Survival Following Heart Transplantation for Chagas Versus Non-Chagas Cardiomyopathy: A Single-center Experience in Northeastern Brazil Over 2 Decades

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Background. Data on post–heart transplant (HT) survival of patients with Chagas cardiomyopathy (CC) are scarce. We sought to evaluate post-HT survival in patients with CC as compared with other causes of heart failure across different eras of HT. **Methods.** We conducted a retrospective, cohort study of 376 adult HT recipients between October 1997 and November 2019. Participants were classified according to the etiology of heart failure as CC (N = 66), nonischemic cardiomyopathy (N = 214), and ischemic cardiomyopathy (N = 96), and according to the era of HT as early (1997–2009), recent (2010–2014), and current era (2015–2019). **Results.** After a mean follow-up of 5.0 y (0–20.5 y), post-HT survival rates at 1, 5, and 10 y were comparable between groups. One-y survival improved from 70% in the early eras to 80% in the current era (hazard ratio [HR], 0.63; 95% confidence interval [CI], 0.41-0.97; *P* = 0.034). After adjustment for sex, age, and mechanical circulatory support, time-related improvement in survival was observed only in patients without CC (HR, 0.54; 95% CI, 0.32-0.91; *P* = 0.019) but not in those with CC (HR, 0.99; 95% CI, 0.36-2.73; *P* = 0.98). Causes of death were similar between patients with CC and the other etiological subgroups. **Conclusions.** Posttransplant survival is comparable between patients with CC, nonischemic cardiomyopathy, and ischemic cardiomyopathy. Although survival has improved significantly over years for most HT recipients, it has remained unchanged for those with Chagas disease. These trends underscore the importance of scientific research, policy discussions and a collaborative registry of heart transplantation in Chagas cardiomyopathy.

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INTRODUCTION

Nearly 8 million people are infected with *Trypanosoma cruzi* worldwide, mainly in Latin America where Chagas disease causes >10 000 deaths per year.[1] Although the majority of infected individuals reside in parts of Mexico, Central America, and South America, infection has been increasingly detected in nonendemic areas, particularly in the United States and Europe.[2]

Chagas cardiomyopathy (CC) is the most serious manifestation of Chagas disease. Observational studies suggest that heart failure (HF) hospitalization and all-cause mortality are higher in patients with CC than in patients with ischemic cardiomyopathy (ICM) or other types of nonischemic cardiomyopathy (NICM).[3-7] Although CC is usually classified as a type of dilated cardiomyopathy, the combination of segmental fibrotic lesions, lymphocytic infiltration, dysautonomia, and myocyte hypertrophy distinguishes it from other forms of heart disease.[8-10] Orthotopic heart transplant (HT) is safe and effective for patients with end-stage HF because of CC, with short- and long-term outcomes comparable to those reported

in the general HT population.[11-14] Indeed, an earlier cohort study of patients with Chagas disease who underwent HT suggested better survival in patients with CC than in those with idiopathic or ischemic heart disease.[11] However, data on posttransplant survival of patients with CC are scarce in the modern era of immunosuppressive regimens, surgical techniques, and mechanical circulatory support (MCS).[15-17] The objective of this study was to evaluate posttransplant survival in patients with CC, ICM, and NICM across different eras of HT.

MATERIALS AND METHODS

We conducted a retrospective, observational cohort study of consecutive adult recipients of primary heart-alone transplants between October 1997 and November 2019 at a single, high-volume transplant center located in northeastern Brazil. Patient inclusion is shown as a flowchart in Figure 1. Exclusion criteria were pediatric transplantation, repeat transplantation, and missing data. The cohort was categorized into 3 mutually exclusive subgroups according to primary etiology of HF: CC, NICM, and ICM. To identify changes over time, recipients were grouped into 3 time eras according to major disruptive advances in our institution: "early era," defined as the time interval between our first HT (October 1997) and the first application of a short-term MCS as bridge-to-transplant therapy (BTT; December 2009) (N = 166); "recent era," defined as the time interval between the "early era" and the beginning of our activities as a Multidisciplinary Mentoring Program in Transplant Cardiology (from January 2010 to December 2014 [N = 100]); and "current era," from January 2015 to November 2019 (N = 110). "Era" was treated as a 3-level variable and additional analyses were conducted to test for interactions with pretransplant and posttransplant use of MCS by fitting interaction terms (pretransplant MCS × era and posttransplant MCS × era). The study complies with the Declaration of Helsinki and was conducted with the approval of our Institutional Review Board.

Perioperative Management and Follow-up

Patients requiring continuous inotropic support or temporary MCS were prioritized for organ allocation (equivalent to previous status 1A or 1B in the United Network of Organ Sharing waiting list system). Indications for temporary MCS were BTT or posttransplant graft failure (Interagency Registry for Mechanically Assisted Circulatory Support category 1 or 2). Except for the first 5 cases, all HTs were executed using a bicaval technique. All patients received standard triple-drug immunosuppressive regimen with tacrolimus, mycophenolate (mofetil or sodium), and corticosteroids. Tacrolimus was converted to cyclosporine in 4 recipients with refractory hyperglycemia or persistent rejection. After 6 mo, prednisone was weaned whenever possible. Although mycophenolate-based immunosuppression has been associated with a higher rate of *T. cruzi* reactivation,[18] our protocol does not require routine mycophenolate dose adjustments based on HF etiology. Graft rejection and suspected cases of Chagas disease reactivation were monitored through endomyocardial biopsy (EMB) in accordance with standard clinical. However, although the International Society for Heart and Lung Transplantation (ISHLT) guidelines calls for approximately 14 routine protocol EMBs in the first year after HT, the frequency of EMBs at our center has been significantly lower, around 3 to 5 because of major financial constraints.

Donor Data Collection

Heart donor data were obtained by searching electronic database provided by the Center for Notification, Procurement, and Distribution of Organs. The following data were collected: age, sex, body weight, height, comorbidities, drug abuse, and cause of death. The proportion of donors for whom data were available increased from 1% in the early era, to 84% in the recent era and 100% in the current era.

Statistical Analysis

Baseline characteristics were summarized as mean ± SD or median (range) for continuous variables and as frequency (percentage) for categorical variables. These characteristics were compared between etiological subgroups using analysis of variance for continuous variables, with Bonferroni post hoc tests for multiple comparisons, and χ^2 test for categorical variables. Eligible subjects were followed until death, retransplantation, or the end of the study (July 1, 2020). We estimated overall survival using the Kaplan-Meier method and compared survival between etiological subgroups or eras using the log-rank test. Cox proportional-hazards regression was used to adjust for differences in baseline characteristics. The results of the final Cox models are presented as hazard ratio (HR), 95% confidence interval (CI), and P value. All statistical analyses were performed using Stata software, version 15.0 (Stata Corp).

RESULTS

Baseline Characteristics

We identified 448 patients who underwent HT at our institution between October 1997 and November 2019. We excluded 67 patients who were <18 y of age at the time of transplant or who underwent HT as a repeat transplantation. We excluded an additional 5 patients for not having reached at least 6 mo of follow-up. Accordingly, 376 patients met the study entry criteria and were included in the analysis. Clinical characteristics of the study population are presented in Table 1. The indications for HT were CC in 66 patients (17.5%), NICM in 214 patients (57%), and ICM in 96 patients (25.5%) (Figure 2). The proportion of patients with CC remained constant across the 3 study eras. By contrast, the proportion of patients with ICM increased over time and was significantly higher in the current era than in the early era (P = 0.036).
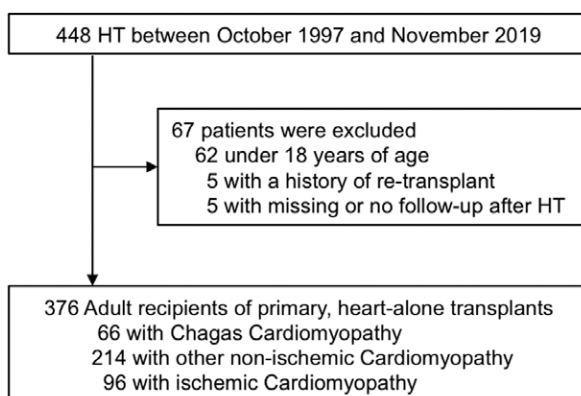
FIGURE 1. Flowchart of patients included into the study. HT, heart transplantation.

Baseline characteristics of heart transplant recipients according to etiological subgroups.

Characteristic	CC, N = 66	NICM, N = 214	ICM, N = 96	P^a, Overall	CC vs NICM	CC vs ICM	NICM vs ICM
Recipient							
Age, y	46.1 ± 10.8	43.2 ± 12.6	55.9 ± 8.9	<0.001	0.23	<0.001	<0.001
Female sex, n (%)	12 (18.2)	49 (22.9)	10 (10.4)	0.034	1.00	0.64	0.028
BMI, kg/m^2	24.5 ± 3.6	24.6 ± 4.1	25.1 ± 3.4	0.76	1.00	1.00	1.00
MAP, mm Hg	76.0 ± 18.0	81.1 ± 14.8	64.4 ± 38.0	0.26	1.00	0.81	0.31
Systolic PAP, mm Hg	55.1 ± 12.0	44.7 ± 12.7	53.8 ± 14.9	0.06	0.07	1.00	0.22
Mean PAP, mm Hg	33.1 ± 8.5	33.1 ± 10.9	38.3 ± 7.9	0.26	1.00	0.44	0.45
CVP, mm Hg	13.6 ± 7.9	10.3 ± 4.4	13.8 ± 4.6	0.33	0.55	1.00	0.66
PVR, Woods units	3.1 ± 1.3	2.6 ± 1.0	3.1 ± 1.2	0.20	0.27	1.00	0.46
Cardiac output, L/min	3.6 ± 1.0	3.8 ± 1.0	3.3 ± 1.0	0.53	1.00	1.00	0.79
Cardiac index, L/min/m^2	2.1 ± 0.6	2.2 ± 0.6	1.8 ± 0.6	0.33	1.00	0.84	0.45
Priority status, n (%)	39 (59.1)	124 (57.9)	45 (46.8)	0.33	1.00	0.76	0.48
Pretransplant MCS, n (%)	8 (12.1)	10 (4.7)	1 (1.0)	0.002	0.039	0.001	0.21
Most recent PRA ≤10%, n (%)	63 (95.5)	200 (93.5)	90 (93.8)	0.84	1.00	1.00	1.00
eGFR, mL/min per 1.73 m^2	66.0 ± 21.5	82.9 ± 25.5	72.8 ± 48.6	0.15	0.15	1.00	0.91
Serum creatinine, mg/dL	1.3 ± 0.4	1.1 ± 0.3	1.5 ± 0.9	0.10	0.34	1.00	0.11
BUN (IQR), mg/dL	24.3 (18.7–31.3)	25.2 (17.8–28.5)	24.8 (22.9–36.4)	0.46	1.00	0.38	0.33
Total bilirubin (IQR), mg/dL	1.1 (0.7–2.2)	0.5 (0.3–1.1)	1.4 (1.0–1.6)	0.12	0.57	1.00	0.59
Transplant							
Ischemic time, min	148.4 ± 40.7	162.7 ± 44.8	170.6 ± 47.3	0.12	0.54	0.17	1.00
Posttransplant MCS, n (%)	1 (1.5)	11 (5.1)	1 (1.0)	0.12	0.48	1.00	0.20
Transplant era							
Early (1997–2009), n (%)	29 (43.9)	101 (47.2)	36 (37.5)	0.28	1.00	1.00	0.34
Recent (2010–2014), n (%)	20 (30.3)	58 (27.1)	22 (22.9)	0.56	1.00	0.89	1.00
Current (2015–2019), n (%)	17 (25.8)	55 (25.7)	38 (39.6)	0.036	1.00	0.17	0.039

^{a}Baseline characteristics were compared between etiological subgroups using ANOVA for continuous variables, with Bonferroni post hoc test for multiple comparisons, and the χ^2 test for categorical variables.

Plus-minus values are means ± SD. Percentages may not add up to total because of rounding.

ANOVA, analysis of variance; BMI, body mass index; BUN, blood urea nitrogen; CC, Chagas cardiomyopathy; CVP, central venous pressure; eGFR, estimated glomerular filtration rate; ICM, ischemic cardiomyopathy; IQR, interquartile range; MAP, mean arterial pressure; MCS, mechanical circulatory support; NICM, other nonischemic cardiomyopathy; PAP, pulmonary artery pressure; PRA, panel-reactive antibody; PVR, pulmonary vascular resistance.
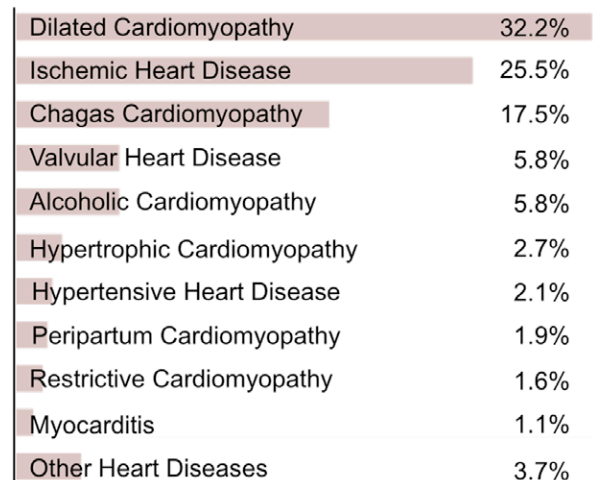
Demographic characteristics were comparable between patients with CC and those with NICM, but patients with CC were more likely to be female and younger than those with ICM. Patients with CC were also more likely to require MCS therapy as a BTT than individuals with other types of HF. Among the 19 patients who underwent MCS therapy as a BTT, support was provided with CentriMag (Thoratec Corp, Pleasanton, CA) in 8 patients (42.1%), AB5000 (ABIOMED Inc, Danvers, MA) in 6 patients (31.6%), and venoarterial extracorporeal membrane oxygenation (Maquet Getinge Group, Rastatt, Germany) in 5 patients (26.3%). There were no differences in allocation prioritization between the CC, NICM, and ICM subgroups. For the entire cohort, the median duration on the waitlist was 45 d (range, 0–481 d), and the median duration of pretransplant MCS was 18 d (range, 0–176 d). There were no significant differences between etiological subgroups for either of these durations.

Donor age, sex, comorbidities, drug abuse, vasopressor support, and cause of death did not differ significantly between CC, NICM, and ICM subgroups. However, the donor-recipient age difference was significantly greater in patients with ICM than in patients with other types of HF. Ischemic time and donor-recipient size or sex mismatches also did not differ significantly between CC, ICM, and NICM subgroups.

Survival Analysis

Survival data were available for all study participants. The mean follow-up was 5.0 y (range, 0–20.5 y), during which 186 deaths occurred. The overall 1-, 5-, and 10-y survival rates were, respectively, 73%, 60%, and 46%, with a median survival of 9.5 y (95% CI, 8.50-10.52). Survival rates were comparable between CC, NICM, and ICM subgroups at 1, 5, and 10 y (respectively, 70%, 62%, and 49% for CC; 73%, 57%, and 46% for NICM; and 75%, 66%, and 40% for ICM; $P = 0.41$) (Figure 3). The risk of death among HT

Dilated Cardiomyopathy	32.2%
Ischemic Heart Disease	25.5%
Chagas Cardiomyopathy	17.5%
Valvular Heart Disease	5.8%
Alcoholic Cardiomyopathy	5.8%
Hypertrophic Cardiomyopathy	2.7%
Hypertensive Heart Disease	2.1%
Peripartum Cardiomyopathy	1.9%
Restrictive Cardiomyopathy	1.6%
Myocarditis	1.1%
Other Heart Diseases	3.7%

FIGURE 2. Percent of heart transplant recipients according to heart failure etiology (adult heart transplants between October 1997 and November 2019).
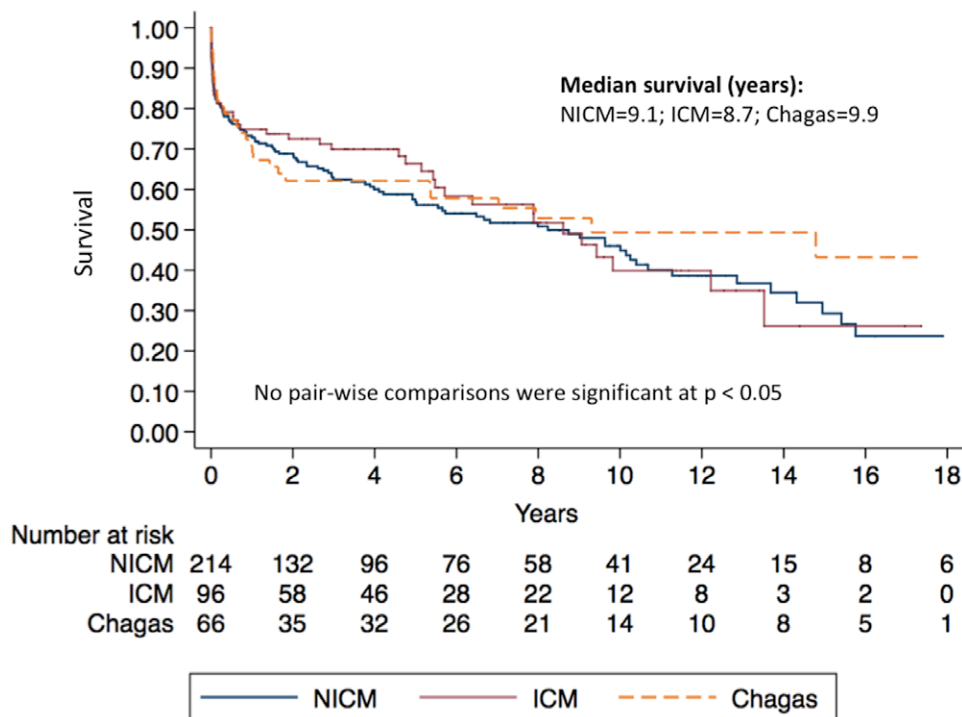
FIGURE 3. Kaplan-Meier survival curves of heart transplant recipients according to etiology (adult heart transplants between October 1997 and November 2019). Chagas, Chagas cardiomyopathy; ICM, ischemic cardiomyopathy; NICM, other non-ICM

recipients with CC was similar to that of HT recipients with other types of HF, even after adjustments for age, sex, MCS, and era (CC versus non-CC: HR, 0.86; 95% CI, 0.57-1.28; $P = 0.46$).

Survival rates improved over time for the entire cohort, with 1-y survival increasing from 70% in the early and recent eras to 80% in the current era (current versus previous eras: HR, 0.63; 95% CI, 0.41-0.97; $P = 0.034$) (Figure 4A). However, in a multivariable model adjusting for sex, age, and MCS, time-related improvement in survival was observed only in patients without CC (HR, 0.54; 95% CI, 0.32-0.91; $P = 0.019$) but not in those with CC (HR, 0.99; 95% CI, 0.36-2.73; $P = 0.98$) (Figure 4B and C).

Posttransplant mortality in the entire cohort was significantly associated with posttransplant use of MCS (HR, 2.37; 95% CI, 1.09-5.17; $P = 0.030$) and pretransplant central venous pressure (HR, 1.13; 95% CI, 1.01-1.26; $P = 0.023$). Although the magnitude of effect was greater in the current era, there was no statistically significant interaction between pretransplant

and posttransplant MCS use and the 3 study eras. Although elevated pulmonary vascular resistance, advanced donor and recipient ages, and prolonged ischemia time are known risk factors for adverse outcomes after HT, survival was not associated with any of these variables in the present analysis.

Over 22 y, the leading cumulative causes of death after HT were infection (n = 67, 35.8%), rejection (n = 51, 27.2%), and cardiac allograft vasculopathy (n = 38, 20.3%). Figure 5 depicts the breakdown of the leading causes of death in adult HT recipients between October 1997 and July 2020. Within the first 30 d after HT, infection accounted for 30 (50.8%) deaths, followed by graft failure (primary and nonspecific) (n = 19, 32.2%) and acute rejection (n = 7, 11.8%). From 31 to 365 d, acute rejection accounted for 21 (50%) deaths, followed by infection (n = 18, 42.8%). After the first year, cardiac allograft vasculopathy accounted for 37 (43.5%) deaths, followed by rejection (n = 23, 27.1%) and infection (n = 19, 22.3%). Causes of death were comparable between patients with CC and the other etiological subgroups (Table 2).
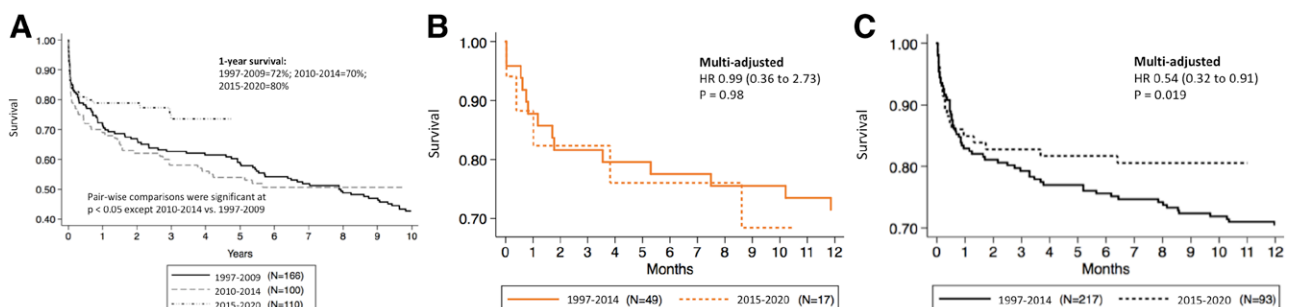
FIGURE 4. Kaplan-Meier survival curves of heart transplant recipients according to era (adult heart transplants between October 1997 and November 2019). A, Curves for the entire cohort, including patients with Chagas cardiomyopathy, ischemic cardiomyopathy, and other nonischemic cardiomyopathy over the 3 study eras (early, recent, and current). B and C, Curves for the cohorts with Chagas and non-Chagas cardiomyopathies, respectively (early and recent eras were merged into 1 single category). HR, hazard ratio.
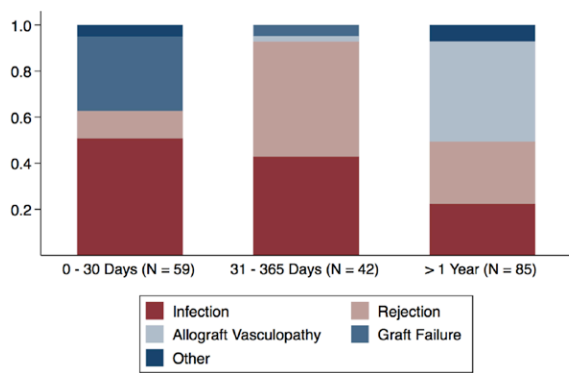
FIGURE 5. Leading causes of death in adult heart transplant recipients between October 1997 and July 2020.

Infection, rejection, and cardiac allograft vasculopathy rates in patients with CC, NICM, and ICM were, respectively, 15.1%, 12.1%, and 10.6% for CC; 19.2%, 17.3%, and 8.9% for NICM; and 16.7%, 6.3%, and 12.5% for ICM. There was a trend toward fewer episodes of rejection in patients with ICM than in those with NICM. One patient died from *T. cruzi* reactivation during the follow-up period, but there were no other specific Chagas-related posttransplant complications between the current and previous eras in CC patients.

DISCUSSION

Heart transplantation is a well-established therapeutic option for patients with end-stage HF caused by Chagas disease.[8,12,15,19-21] We report our 22-y experience with HT for patients with CC compared with other types of HF in an economically deprived region of Northeast Brazil. Among 376 adult recipients of primary heart-alone transplants, CC remained the third-leading indication for HT from October 1997 to November 2019. The proportion of patients undergoing HT for CC in our study is consistent with previous reports.[11,22-24] Moreover, the demographic and clinical characteristics of patients were similar to those observed in other studies comparing CC with NICM or ICM, including a retrospective analysis of 2552 Latin Americans from the Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure and The Aliskiren Trial to Minimize Outcomes in

Patients with Heart Failure trials.[5,7,24-27] Evidence suggests that individuals with HF because of CC have worse outcomes than those with other types of HF.[7,27-29] Notably, we found that patients with CC were more likely to require MCS therapy as a BTT than those with NICM or ICM, which supports prior reports of a worse prognosis in patients with CC among HT candidates categorized as high priority.[3,30,31]

Previous Brazilian reports of HT in patients with CC have shown 1-y survival rates ranging from 25% to 83%.[11,12,22,24,32,33] The largest Brazilian cohort of HT patients, with 720 patients who underwent HT in 16 Brazilian transplant centers between 1984 and 1999, reported 1-y survival rates of 59% and 71% for ischemic and chagasic patients, respectively.[11] In the present study, posttransplant survival was similar to that observed in most regional centers,[12,22,23,33] but lower than the survival reported by the ISHLT Registry and other South American transplant centers.[34-36] This difference can be explained by the higher incidence of infection and rejection during the first year after HT in Brazilian cohorts reflecting characteristics of a developing country, with unavailability of MCS, use of marginal donors, and lack of bioptomes for routine surveillance EMBs.[12] Data from the largest transplant program in the country indicate that the probability of freedom from rejection and infection for patients with CC within 30 d after HT is 53% and 57%, respectively.[22] Similar to our findings, their leading causes of death in adult HT recipients were infection (31.5%), graft dysfunction (31.5%), rejection (21.1%), and sudden death (10.5%) >25 y of experience.[24] Another high-volume transplant center also reported high rates of infection (31.7%) and rejection (28.5%) as the leading causes of death in their first posttransplant year, with no differences between patients with CC and those with other types of HF after 5 y of follow-up.[32] In the United States, socioeconomic disparities have been associated with posttransplant outcomes.[37,38] However, the impact of these disparities in a universal healthcare system is controversial. Brazil is a large country, marked by socioeconomic inequalities that could influence posttransplant rates of infection and rejection.[39-42] A small single-center Brazilian study of 44 HT recipients between 2000 and 2005 found no association between socioeconomic status and posttransplant survival, but no risk-adjusted analysis was presented.[43] Conversely, a larger retrospective study of 2384 HT recipients using data

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TABLE 2.

Causes of death after heart transplantation according to etiological subgroups

Causes of death	CC, N = 66	NICM, N = 214	ICM, N = 96	*P*[a], Overall	CC vs NICM	CC vs ICM	NICM vs ICM
Causes of death, n (%)							
Infection	10 (15.1)	41 (19.2)	16 (16.7)	0.89	1.00	1.00	1.00
Rejection	8 (12.1)	37 (17.3)	6 (6.3)	0.06	1.00	0.77	0.052
Allograft vasculopathy	7 (10.6)	19 (8.9)	12 (12.5)	0.30	1.00	1.00	0.40
Graft failure	3 (4.5)	9 (4.2)	8 (8.3)	0.17	1.00	1.00	0.19
Malignancies[b]	1 (1.5)	5 (2.3)	0 (0.0)	0.37	1.00	1.00	0.49
Cerebrovascular	1 (1.5)	1 (0.5)	0 (0.0)	0.40	0.80	0.56	1.00
Trypanosoma cruzi reactivation	1 (1.5)	0 (0.0)	0 (0.0)	0.09	0.11	0.20	1.00
Multiple organ failure	0 (0.0)	0 (0.0)	1 (1.0)	0.19	1.00	0.53	0.23
Total	31 (47.0)	112 (52.3)	43 (44.8)				

[a]Baseline characteristics were compared between etiological subgroups using ANOVA for continuous variables, with Bonferroni post hoc test for multiple comparisons, and the χ^2 test for categorical variables.
[b]Both posttransplant lymphoproliferative disease and nonhematologic malignancies.
ANOVA, analysis of variance; CC, Chagas cardiomyopathy; ICM, ischemic cardiomyopathy; NICM, other non-ICM.

from the United Kingdom Transplant Registry between 1995 and 2014 showed that median overall and conditional posttransplant survival was significantly 3.4 y shorter in the most deprived socioeconomic quintile.[44] Therefore, despite recent advances in transplant care, we believe that socioeconomic factors and environmental exposures may determine the ultimate outcome of HT recipients.

We found no significant difference in survival rates between HT recipients with CC and those with other types of HF, when treated at the same transplant center. These findings contrast with the results of an earlier multicenter cohort study that showed better survival in patients with CC compared with those with NICM or ICM.[11] Several explanations for the conflicting findings are possible. In the previous study, all patients were treated with an azathioprine-based immunosuppression and many centers performed <9 transplants per year. It is possible that patients with CC have undergone HT at higher-volume centers, which is associated with better survival rates.[45,46] Furthermore, differences in immunosuppressive protocols may have different impacts on the risk of posttransplant mortality.[47-49] Brazilian transplant centers determine immunosuppressive regimens based on their specific patient population, experience, and cost of therapy, which explains differences between institutional protocols.[50] Because the incidence of *T. cruzi* reactivation appears to be higher with mycophenolate than with azathioprine,[18] some transplant centers routinely use azathioprine-based immunosuppression in HT recipients with CC.[21] However, that strategy has not been tested in randomized trials. In our center, all patients receive mycophenolate-based immunosuppression plus conventional doses of tacrolimus and prednisone.

In our study, the overall posttransplant survival improved significantly over time. This result is consistent with data from the ISHLT Registry.[34] However, among patients with CC, there was no trend toward survival improvement across the 3 study eras. These findings suggest that the time-related improvement in survival of HT recipients may be largely because of improvements in HF management for NICM and ICM, but not for CC.[51-53] Chagas disease is a systemic infection with chronic gastrointestinal involvement resulting from peristaltic dysfunction in about 15% of patients.[51] Severe megaesophagus and/or megacolon are a consequence of neuronal destruction of the enteric nervous system and constitute a contraindication for HT. Thus, as patients with CC and gastrointestinal involvement were not considered candidates for HT in our program, the absence of other specific Chagas-related complications that could affect posttransplant outcomes in the current or previous eras is not surprising. Although advances in immunosuppressive regimens, donor procurement, surgical techniques, and postoperative care were introduced into clinical practice during the study period, there is no consensus on the optimal management of patients with CC following HT. Moreover, there have been few anecdotal reports on the outcomes of MCS, either pretransplantation or posttransplantation, in this population.[51] Therefore, it is also not surprising that survival among HT recipients with CC did not change significantly over the study period.

Finally, it is important to carefully address possible reasons for the improved survival observed in the most recent era. Despite the current economic and political crisis in Brazil, our group was able to conceive the first National Multidisciplinary Mentoring Program in Transplant Cardiology, which trained other teams from all over Brazil in the art of HT. Mentoring is central to academic medicine and its purposes and has long played a critical role in the training and career development of healthcare professionals. Successful mentoring programs leave academic medical centers better prepared to advance their missions, accelerate learning, and mature leadership. Another positive impact of a mentoring program is to enhance the skills of mentors, improving the learning curve through teaching. If nothing else, the Hawthorne effect establishes that individuals' productivity increases dramatically to their awareness of being watched.[54] It is possible that a continuous Hawthorne effect caused by the Mentoring Program initiated in 2015 could have induced a permanent change in the culture, behavior, and attitudes of our entire healthcare team. This study is limited by several factors inherent to retrospective studies, including unknown and unmeasured confounding variables. Moreover, all events were recorded at the same institution, and our findings may not be generalizable to other centers. However, we draw attention to the fact that the baseline characteristics and overall survival rates of our cohort are quite similar to those reported in other regional studies. Furthermore, although we believe that socioeconomic factors may have influenced the outcomes, our data does not reflect secular trends among patients with different racial, regional, or socioeconomic backgrounds. Another important limitation relates to missingness, especially for donor data from the early era. However, since all patients were treated at the same transplant center, it is unlikely that differences in donor data would explain our findings.

CONCLUSIONS

In a high-volume HT center, posttransplant survival in patients with CC was comparable to that of patients with ICM and NICM. However, although survival rates improved significantly over a 22-y period for most HT recipients, it remained unchanged for those with Chagas disease. Our results contrast with a larger multicenter cohort study published 20 y ago. These trends underscore the importance of scientific research, policy discussions and a collaborative registry of heart transplantation in CC.

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