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EDITORIAL

Heart transplantation in South America: Risk factors, challenges, and opportunities

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The literature on heart transplantation originates predominantly from centers in the United States, Europe, and Australia. In contrast, there is relative paucity of data on heart transplant from other regions of the world. Disease etiologies, logistical and financial challenges, risk factors, management strategies and outcomes are different but less well studied.

Latin America comprises many countries, peoples and diverse geography, with an estimated around 650 million inhabitants. Heart transplantation started in Latin America in 1968, and a registry reported 12,374 heart transplants in 16 countries from 1968 to 2022.[1] Brazil, with a population of around 215 million, is the highest contributor to heart transplants in Latin America. Brazil's population is approximately 65% of that of the United States. However, the number of transplants performed in Brazil is approximately around 10% of those performed in the United States. The number of patients receiving heart transplant in Brazil has been steady for the last decade with an average of around 350 patients per year, with most of the heart transplants being performed in Sao Paulo.[2]

Many factors-donor-related, recipient-related, and systems-related influence the low rates of transplantation. Delayed recognition of brain death, legal issues regarding donation and recognition of circulatory death, lack of public awareness and willingness by families to donate, and lack of widespread infrastructure for appropriate donor management, including limited availability of tests such as echocardiograms and catheterization in areas with potential donors limit the number of donors. Many patients are referred late, which combined with limited availability of circulatory support devices as a bridge to transplant limits the number of recipients. Low transplant volumes in many centers and countries also means that it is not practical to have cardiologists or surgeons exclusively dedicated to heart transplant. Limited health budgets and lack of organization structures that facilitate transplant also limit growth.[3,4]

Aulicino and colleagues from the Universidad de Sao Paulo present an analysis of the risk factors associated with post-transplant survival in 299 adults transplanted between 2013 and 2019 in the largest heart transplant center in Brazil.[5] Prior to any data analysis, it is interesting to compare their cohort to others described in United States or western Europe. The current cohort was younger, had lower BMI, lower frequency of DM as comorbidity, and only 16% had ischemic cardiomyopathy. Importantly, the most common cause of end-stage heart failure was Chagas disease (36%). Analysis of Chagas cardiomyopathy patients receiving heart transplant has lessons and implications beyond Latin America. For example, autochthonous cases have been described in the United States, specifically in the southern states.[6] With global warming and changes in the residence of the triatomines that carry T. Cruzi, autochthonous cases may be seen outside of the above-described regions.[7] Other insect-borne diseases can similarly affect solid-organ recipients with significant morbidity and mortality.[8] In 2022 the Center for Disease Control and Prevention (CDC) estimated that 288,000 individuals were living with Chagas disease in the US between 2014 and 2018, of which 57,000 were estimated to have cardiomyopathy.[9] In this report, there was no difference in 1-year survival by etiology of cardiomyopathy. The risk of re-activation of Chagas disease is important and requires serial monitoring post-transplantation.[10] Reactivation of Chagas disease was observed in 25 patients, but reactivation did not correlate with 1 year mortality.

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Another important consideration is the organ allocation system. As the authors describe, the Brazilian heart transplant allocation incorporates a 4-tiered system designed to enhance transplant access for the sickest patients. Status 1 is reserved for patients in on extracorporeal membrane oxygenation (ECMO) support, status 2 is assigned to those who are supported by intra-aortic balloon pump (IABP). Inotrope dependent patients or those with durable mechanical circulatory support (dMCS) complications as well as those with hypertrophic and restrictive cardiomyopathy are status 3, and the remaining patients are condition 4.

Most patients were transplanted while hospitalized in cardiogenic shock (INTERMACS profile 1: 7.4%; profile 2: 50%, profile 3: 37%, with the majority of circulatory support being IABP (56.2%) or ECMO (5.3%). Similar to the previous allocation system in the US, this system may not necessarily provide the granularity to differentiate patients at higher risk of poor outcomes on the waitlist. Of the initial cohort of 384 listed patients, 74 (19%) were excluded because they died before transplantation. The lack of coverage of dMCS in the Brazilian public insurance system may have profound implications both in survival in the waitlist as well as in post-transplant survival. This is likely a significant difference between Brazil and other countries where LVAD support is commonly used as a bridge to transplantation, particularly in patients with higher risk profiles.[11] There have been philanthropic and other efforts to increase access to LVAD therapy in Brazil, but the numbers of patients impacted remains very small, at only 10–20 per year.[12,13]

Taking into account all these differences, the overall 1-year survival post-transplantation for the entire cohort was 72.3%, a value that is lower than what has been reported from European and North American centers, highlighting the challenges that our colleagues face in the Latin America region.[14] The most common causes of death within the first year post-transplantation were infection (38.5%), and primary graft dysfunction (PGD) (19.2%), whereas rejection was the cause of death in 8.4%. The PGD rates were in the setting of strict low-risk donor selection criteria, high rates of recipient amiodarone use > 400 mg/day (48%), low rates of induction therapy (13%) and median ischemic time of 3.6 hours. More details about organ procurement, preservation, and transport were not available. Donation after circulatory death for heart transplantation has not been utilized in Brazil due to legal and other restrictions.[15] The use of controlled hypothermia devices, specialized procurement teams, and organ care systems have increased organ availability and decreased the frequency of PGD in other countries and may be areas of future development or implementation.

The authors then embarked in the development of a predictive score to identify patients at the highest risk of mortality after transplantation. Markers of severity of disease and inflammation (SOFA score, creatinine clearance, C-reactive protein, and leukocytes) were independent predictors of 1-year mortality. A risk score was developed, which was able to adequately stratify patients into low risk (1-month mortality 7.9%, 1-year mortality 14.6%) and high-risk (1-month mortality 27.6%, 1-year mortality 44%).

In summary, this report provides us with a glimpse of the current state and opportunities in heart transplantation in one of the largest countries and transplant programs in the Latin American region. Their score, if externally validated, may provide a region-specific risk stratification tool to guide candidate selection and management. A high score should not be used to necessarily restrict access to transplantation as over one third of the cohort qualified as high-risk, but rather to advocate for investigation into and provision of alternative management strategies (eg. Impella 5.5, durable MCS, expanded organ procurement, distribution changes etc.), or structural adjustments to allocation systems to positively impact waitlist and post-transplant outcomes. Individual center studies such as these as well as larger regional registries from regions historically under-reported are thus crucial to better understand transplant practices and limitations, define recommended approaches, identify opportunities, and positively influence health policies.

Disclosure statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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