

Epidemiological Profile of Donation Candidates at a Pediatric Heart Transplant Reference Center

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ABSTRACT

Introduction: Heart transplantation is the standard treatment for end-stage heart disease. This therapy is limited by factors related to both the donor and the recipient, in addition to peculiarities inherent to its implementation in the pediatric population. Due to the disparity between organ supply and demand, heart transplant waiting list mortality is high in this age group, ranging from 17 to 30% worldwide. Even so, around 40% of listed hearts are not used worldwide. High refusal rates are due to the lack of uniformity in assessment, as well as in the acceptance and refusal of organs in pediatric heart transplantation. It is known that donor and recipient factors interact with each other in a complex way, requiring a joint analysis to determine whether the organ available at that time is suitable for the patient in question. **Objectives:** To identify the epidemiological profile of candidates for heart donation offered to a pediatric heart transplant center in southern Brazil. **Methods:** This is an observational, descriptive, and retrospective study. The sample consisted of medical records from potential donors offered from January 2021 to December 2023. **Results:** There were 205 organs offered during this period, eight of which were excluded from the analysis due to a lack of data. The average age of the patients was 19.5 years and 67.5% of them were male. Chest radiography or tomography was not available in 38.6% of cases. A total of 56.3% of cases had an electrocardiogram available, but 45% of them were abnormal, and 29.4% of patients had no echocardiogram. Of the echocardiograms, 22.3% showed dysfunction. A total of 88.8% of patients were receiving vasoactive drugs and 61.9% had an active infection. Of the available organs, 92.9% were refused. **Conclusion:** The refusal rate was higher than the global estimate, which may result from the lack of relevant donor-related information at the time of the offer. Moreover, there is a prevalence of data suggesting some degree of cardiac dysfunction in potential donors.

Descriptors: Heart Transplantation; Organ Transplantation; Tissue Donors; Descriptive Epidemiology.

Perfil Epidemiológico de Candidatos à Doação em um Centro de Referência de Transplante Cardíaco Pediátrico

RESUMO

Introdução: O transplante cardíaco (TxC) é o tratamento-padrão para doença cardíaca em estágio terminal. A adoção dessa terapêutica é limitada a fatores relacionados ao doador e ao receptor, além de haver peculiaridades inerentes à sua realização na população pediátrica. Devido à disparidade entre oferta e demanda de órgãos, a mortalidade durante a espera por um TxC é alta nessa faixa etária, variando de 17 a 30% no mundo. Mesmo assim, cerca de 40% dos corações listados não são utilizados em nível mundial. A alta taxa de recusa se explica pela falta de uniformidade na avaliação, no aceite e na recusa das ofertas no TxC em pediatria. Sabe-se que os fatores do doador e do receptor interagem entre si de forma complexa, exigindo uma análise conjunta para definir se o órgão disponível naquele momento é adequado ao paciente em questão. **Objetivos:** Identificar o perfil epidemiológico de candidatos à doação de coração ofertados a um centro de referência de TxC pediátrico do sul do Brasil. **Métodos:** Trata-se de um estudo observacional, descritivo e retrospectivo. A amostra foi formada por prontuários de potenciais doadores ofertados de janeiro de 2021 a dezembro de 2023. **Resultados:** Foram 205 órgãos ofertados no período, sendo oito excluídos da análise devido à falta de dados. A média de idade dos pacientes foi de 19,5 anos, sendo 67,5% do sexo masculino. Radiografia ou tomografia de tórax não foi disponibilizada em 38,6% dos casos. O total de 56,3% tinha eletrocardiograma, dos quais 45% apresentavam alteração, e 29,4% não tinham ecocardiograma. Dos ecocardiogramas, 22,3% apresentavam disfunção. O total de 88,8% dos pacientes estava em uso de

droga vasoativa e 61,9% apresentavam infecção ativa. Foram recusados 92,9% dos órgãos. **Conclusão:** Verificou-se uma taxa de recusa superior à estimativa mundial, o que pode ser resultado da ausência de informações sobre parâmetros relevantes relacionados ao doador no momento da oferta. Também se nota a prevalência de dados que sugerem algum grau de disfunção cardíaca nos potenciais doadores.

Descritores: Transplante de Coração; Transplante de Órgãos; Doadores de Tecidos; Epidemiologia Descritiva.

INTRODUCTION

Heart transplantation (HTx) is the standard treatment for end-stage heart disease in children and adults¹, with cardiomyopathies and complex congenital heart diseases being the main indications for this procedure in the pediatric age group². However, pediatric HTx has unique and peculiar characteristics that differentiate it from pediatric cardiac surgery in general and HTx in adults³.

Adoption of this therapy is limited by factors related to the donor, including availability, eligibility, and complex anatomy in the case of complex heart diseases, as well as by factors related to the recipient⁴. As there is a significant disparity between supply and demand for organs, mortality while waiting for an HTx remains high in the pediatric age group, ranging from 17 to 30% around the world⁵, despite the advent and implementation of ventricular assist devices³. Even so, on a global level⁵, approximately 40% of the hearts listed are not used.

This high rate of organ rejection is explained by the lack of uniformity in evaluating, accepting and rejecting offers in the context of HTx in pediatrics⁶. No risk assessment score establishes a good relationship with prognosis based on data available at donation acceptance⁷, much less a validated score for donor evaluation⁸. Furthermore, there is no consensus on the definitions of a high-risk recipient, one who, theoretically, would have greater surgical and post-transplant risks, or a borderline donor, who would not be the ideal choice⁸. This context makes it difficult to standardize scientific production and compare the data obtained.

It is known that donor and recipient factors interact in a complex and unique way, requiring that the parameters be analyzed together to determine whether the donor available at that time is suitable for the recipient in question⁸. Some donor characteristics are notably related to a worse prognosis, although there is no well-established cutoff point. These are:

- Older donor age – The International Society for Heart and Lung Transplantation (ISHLT) suggests that organs from patients up to 45 years of age are eligible⁵. However, Westbrook et al.⁹ demonstrated an increase in mortality and incidence of allograft vascular disease in adolescents who received hearts from individuals more than 5 years older than their chronological age, especially when the donor was over 25 years old.
- Altered cardiac function – The ISHLT suggests rejecting organs with a left ventricular ejection fraction (LVEF) of less than 40%⁵. The 3rd Brazilian Guideline for Heart Transplantation sets an LVEF cutoff of less than 45%, which would determine the need for more intensive management of the donor until conditions are reached that allow the use of the organ¹⁰. It is also possible to evaluate changes in the electrocardiogram (ECG), but there is still no consensus on which findings would be acceptable or not^{5,8}. In our service, the protocol for patients waiting in the non-priority queue is to accept organs with LVEF equal to or greater than 55%. In comparison, hearts with LVEF below 55% are accepted only in prioritized patients, according to prioritization criteria, and with low doses of vasoactive drugs (VAD).
- Donor-to-recipient weight ratio – ISHLT recommends 0.7 to 2 for adults⁵. Still, there is evidence that these values can be extrapolated with relative safety in pediatrics, reaching up to 2.5 to 3 times the weight of the recipient, depending on their physical structure and degree of cardiomegaly⁴.
- Ischemic time – Related to higher mortality after 6 months of transplantation when it is longer than 3.5 hours¹¹.

Cardiopulmonary arrest (CPA) time, use of VAD and cause of death should not be assessed in isolation, but there is no definition of what would be tolerable^{12,13}. Few donor infections are an absolute contraindication for transplantation⁴, these being: infection by the human immunodeficiency virus, in the case of a recipient who is not a carrier, Chagas disease^{4,5} and central nervous system infections (viral or bacterial meningitis)¹⁴. Bacteremia and sepsis alone do not contraindicate transplantation. However, it is not recommended to use hearts from donors in septic shock¹⁵. However, serological testing and, if possible, polymerase chain reaction testing for hepatitis B and C are also recommended⁴.

Patients listed in the queue for HTx are prioritized according to the higher risk of death during this wait: those using mechanical circulatory assistance devices, inotropic support and/or mechanical ventilation¹⁰. Due to the unsatisfactory response to currently available treatments, cases of restrictive cardiomyopathy may also be prioritized¹⁰. Some patients do not fit the prioritization guidelines, such as those with complex cyanotic heart disease with or without malnutrition, who have a higher mortality rate in the queue¹⁰.

This study aims to profile the heart donors offered to recipients listed in a pediatric HTx referral center in southern Brazil, allowing an assessment of the viability of the available organs. Given the complexity of accepting organs for transplantation, as previously discussed, the aim is to foster a chain of improvement in the procurement process, which begins with the clinical management of potential donors. The rate of organ rejection by the service was also analyzed, aiming to optimize the performance of heart transplants and reduce the waiting time and mortality of children who are candidates for the procedure.

METHODS

The present study is an observational, descriptive, and retrospective study approved by the Research Ethics Committee of Hospital Pequeno Príncipe, under opinion 70608723.6.0000.0097. The sample consisted of candidates for heart donation offered from January 2021 to December 2023 to the pediatric HTx service of Hospital Pequeno Príncipe in Curitiba, Paraná, Brazil.

Secondary data provided by the State Transplant Center at the time of the offer were collected. All information on candidates for donation in the referred period was included, and the exclusion criteria were incomplete patient information.

The following information was collected: state of origin of the offer, sex, age, weight, height, chest imaging exam (X-ray or CT scan), ECG, echocardiogram, use of VAD with the respective drug used and dose, presence of active infection and focus of infection, occurrence and time of CPA, cause of death and acceptance or rejection of the organ.

The data were tabulated and subsequently submitted to descriptive analysis with the computer program SPSS v.26.0. The results were expressed as means, medians, minimum values, maximum values and standard deviations (quantitative variables) or as frequencies and percentages (qualitative variables).

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RESULTS

A total of 205 organs were offered during the period, of which eight were excluded from the analysis due to lack of data, totaling a sample of 197 potential donors analyzed. The offers originated from all regions of Brazil except the North. The states with the highest number of offers were Paraná (31.97%, n = 63), Santa Catarina (22.33%, n = 44) and Rio de Janeiro (10.66%, n = 21). Hearts were also offered from Minas Gerais, São Paulo, Mato Grosso, Mato Grosso do Sul, Espírito Santo, Distrito Federal, Goiás, Bahia and Rio Grande do Sul.

The average age was 19.5 years, and 67.5% (n = 133) were male. Just over a third of the patients (34%) were over 25 years old, and only one potential donor was over 45. The average height was 148.98 centimeters (cm), and the weight was 54.75 kilograms (kg) (Table 1).

Table 1. Sample characteristics.

Sample characteristics	Mean	Medium	Minimum-maximum
Age (years)	19.5	20	0.5-51.0
Weight (kg)	54.75	65	7.0-110.0
Height (cm)	148.98	164	60.0-190.0

Source: Elaborated by the authors.

Chest imaging (radiography or tomography) was not available in 38.6% of cases (n = 76). Of the 56.3% who had an ECG available (n = 111), almost half had some alteration (45%; n = 50). 29.4% (n = 58) did not undergo echocardiogram. Of the potential donors who had an echocardiogram available, 22.3% (n = 31) had some degree of dysfunction. The mean LVEF was 63.05%, with only two patients (1.6%) having LVEF below 40% (Table 2).

88.8% (n = 175) were using VAD, of which 85.14% (n = 149) used noradrenaline alone or in combination with other VAD. The mean dose of noradrenaline was 0.2 mcg/kg/min, while 59.1% (n = 88) used doses above 0.1 mcg/kg/min. Other VADs used were vasopressin (37.14%; n = 65), adrenaline (8.6%; n = 15) and dobutamine (1.71%; n = 3) (Table 3).

Table 2. Complementary exams available.

Complementary exams	Absolute frequency (n)	Relative frequency (%)
Chest image		
Exams available	76	38.6
ECG		
Exams available	111	56.3
Presence of alteration	50	45.0
Echocardiogram		
Exams available	139	70.6
Presence of dysfunction	31	22.3
LVEF < 40%	2	1.6
Average LVEF		63.5

Source: Elaborated by the authors.

Table 3. Vasoactive drugs.

	Absolute frequency (n)	Relative frequency (%)
VAD	175	88.5
Noradrenaline		
Patients in use	149	85.1
Average dose, mcg/kg/min	0.2	
Patients with dose > 0.1 mcg/kg/min	88	59.1
Adrenaline		
Patients in use	15	8.6
Vasopressin		
Patients in use	65	37.1
Dobutamine		
Patients in use	3	1.7

Source: Elaborated by the authors.

The prevalence of active infection was 62.4% (n = 123) in potential donors. The main focus of infection was the respiratory tract (52%, n = 64), followed by the central nervous system (7.1%, n = 14). In 22% of cases (n = 27), it was impossible to determine the focus of infection according to the information provided (Table 4).

Table 4. Frequency of infections and infectious foci.

Infection	Absolute frequency (n)	Relative frequency (%)
Infection	123	62.4
Respiratory tract	63	52.0
Central nervous system	14	11.4
Musculoskeletal	6	4.9
Urinary tract	5	4.1
Others	8	6.5
Undetermined focus	27	22.0

Source: Elaborated by the authors.

58 patients (29.4%) presented CPA, with an average time of 15.05 minutes. The leading cause of death was traumatic brain injury, totaling 40.1% (n = 79), followed by intracranial hemorrhage (15.7%; n = 31) (Table 5).

The refusal rate was 92.9% (n = 183). The main reasons for refusal given by the service were issues inherent to the donor, which included older age in relation to the recipient, comorbidities, use of legal and/or illegal drugs, changes in ECG, changes in echocardiogram, absence of ECG and/or echocardiogram, use of VAD in high doses, presence of active infection and long CPA time. In only 14 cases (7.6%), unfavorable transport logistics determining an excessive ischemia time were given as a reason for non-acceptance. Of the organs accepted, five were destined for another institution. Among the diagnoses of patients listed as recipients in the service, we have cardiomyopathies (dilated, restrictive, hypertrophic, non-compacted), anatomical congenital malformations (Uhl's anomaly, Ebstein's anomaly, aortic insufficiency, tricuspid atresia) and acquired malformations (post-traumatic interventricular communication with acute myocardial infarction, myocarditis). Despite the high refusal rate, of the 24

patients listed for HTx in the period studied, six died while waiting for an organ, which constitutes a mortality rate of 25% in the waiting list, compatible with that observed worldwide.⁵

Table 5. CPA and cause of death.

	Absolute frequency (n)	Relative frequency (%)
CPA	58	29.4
Average time (minutes)	15.05	
Cause of death		
Traumatic brain injury	79	40.1
Ischemic stroke	5	2.5
Hemorrhagic stroke	31	15.7
Polytrauma	18	9.1
Intracranial hypertension	14	7.1
Anoxia	13	6.6
Meningitis	10	5.1
Sepsis	7	3.6
Others	20	10.1

Source: Elaborated by the authors.

DISCUSSION

The profile of potential heart donors in the service studied is young adults, with an average age of 19.5 years. This fact may limit the acceptance of organs for younger recipients, especially up to 2 years, since the most recent evidence suggests that a difference in donor-recipient age of more than 5 years results in higher post-transplant mortality⁹.

The average weight was also found to be 54.75 kg. The primary way to assess heart size compatibility is still the donor-recipient weight ratio¹⁶. Therefore, this average may also suggest a shortage in the supply of organs compatible with younger patients. Even so, it has already been demonstrated that the use of larger organs, with a donor-recipient weight ratio between 2-3, does not negatively impact mortality or reduce long-term survival after transplantation, despite the increased risk of hyperperfusion syndrome in the immediate postoperative period¹⁶.

Even with almost a quarter of echocardiograms showing dysfunction, this alteration in complementary examination should not be used in isolation as a criterion for organ rejection. Firoz et al.¹⁷ demonstrated that left ventricular dysfunction in the donor's heart was associated with higher post-transplant mortality only when associated with more than 3 hours of ischemic time. However, it is noteworthy that almost 30% of potential donors did not have an echocardiographic evaluation available. Added to this is the prevalence of 38.6 and 43.7% absence at the time of offering chest imaging and ECG, respectively, which compromises the analysis of donor-recipient compatibility, which is already so complex in the context of HTx in pediatrics.

A high prevalence of VAD use in potential donors was also observed, with norepinephrine being the drug of choice. Although it is not an absolute contraindication, the most current recommendations are to consider patients using low doses of norepinephrine, up to 0.1 mcg/kg/min, as potential donors in the absence of other available organs¹⁴. Since it was demonstrated that more than half of the patients offered had doses above this value, it is possible to infer that this is an essential factor for the high rate of refusal of the service.

Most of the potential donors offered had some active infection. The main recommendations to be followed currently include the exclusion of sepsis-induced cardiac dysfunction, obtaining consecutive negative blood cultures before the procedure, and avoiding patients who died after 96 hours of hospital admission¹⁸. Some centers accept organs from patients with bacteremia as long as antibiotic therapy has been used for at least 48 hours with some clinical response and an echocardiogram has been performed to exclude endocarditis¹⁹. However, such analyses may have been hampered by the lack of relevant data regarding the potential donor. This would justify the rejection of organs in the presence of active infection, contributing to the high rejection rate. A total of 14 patients had infections focusing on the central nervous system, which should be rejected according to current recommendations¹⁹.

Regarding CRA, a study by Galeone et al.²⁰ assessed its impact on post-transplant morbidity and mortality and found no relevant difference in the outcome regardless of the time of CRA in the case of preserved LVEF at the time of organ use. Therefore, the importance of a complete assessment of cardiac function for decision-making is noted.

The cause of death of the potential donor can also impact post-transplant survival⁴. Hammond et al.²¹ identified that in their service, recipients who received hearts from people who died from intracranial hemorrhage had a higher frequency of death

related to cardiovascular disease. In our service, the leading cause of death among potential donors was traumatic brain injury, which typically affects young patients without comorbidities⁴. However, intracranial hemorrhage was the second most frequent cause of death.

Concerning mortality during the transplant waiting list, it is worth noting that five of the six patients who died had this outcome less than 30 days after registering for the transplant waiting list and had not been previously followed up with the service. These patients were admitted to our service during acute decompensation and would be the ones who would benefit most from accepting organs from marginal donors.

Since this is a secondary data analysis, there is a limitation in that the information must be correctly recorded and made available. Furthermore, as in any cross-sectional study, it is impossible to determine causality; one can only infer justifications for the high refusal rate. However, more studies with different designs are needed to confirm this relationship.

CONCLUSION

The analysis of donor-recipient compatibility in HTx is complex in the pediatric population, mainly due to the absence of well-established criteria for this assessment and the lack of a complete cardiovascular evaluation and better care for the potential donor. This may explain the high rates of organ rejection worldwide, which would be in agreement with data from other studies conducted in Brazil¹⁵.

An epidemiological analysis of heart donations to the Pequeno Príncipe Hospital was carried out, which showed a refusal rate higher than the global rate of 92.9%. It is possible to infer that this fact may be partly justified by the lack of more complete information about the donor. Still, this hypothesis may be confirmed based on further studies with different designs.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Sturm ALC, Silva BHS; **Conception and design:** Sturm ALC, Silva BHS; **Data analysis and interpretation:** Sturm ALC, Silva BHS; **Article writing:** Sturm ALC, Silva BHS; **Critical revision:** Sturm ALC, Silva BHS; **Final approval:** Sturm ALC.

DATA AVAILABILITY STATEMENT

All data were generated/analyzed in this study.

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