Two decades of recipient and donor referrals for heart transplantation to Groote Schuur Hospital, Cape Town, South Africa: A retrospective study

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Background. Heart transplantation in South Africa faces numerous challenges related to organ scarcity and unequal access to advanced heart therapy. There is an urgent need to analyse the current transplant referral pathway to optimise equitable access to transplantation.
Objectives. To provide an audit of heart transplant referrals to Groote Schuur Hospital, Cape Town, over a 23-year period, focusing on patient demographics, indications for referral, waiting-list dynamics, and transplant referral outcomes.
Methods. The study utilised a retrospective patient folder review for the period 1 January 1997 - 31 December 2019 and audited the trends in heart transplant referrals and associated outcomes of the referral at a tertiary academic hospital.
Results. A total of 625 recipients were referred for heart transplantation, with the majority being male (n=412; 65.9%), while gender was undocumented for 69 cases (11.0%). The mean age was 38.1 (14.6) years, and 153 (24.5%) were listed for transplant, while 215 (34.4%) were deemed ineligible for listing. Contraindications for listing included social (n=106; 49.3%), medical (n=83; 38.6%) and psychological (n=26; 12.0%) factors, while 134 patients (21.4%) were considered too well. Poor social circumstances (n=38; 39.6%), poor insight (n=28; 29.2%) and poor compliance (n=21; 21.9%) were the most common non-medical reasons for not listing recipients, while obesity (n=30; 31.3%) and smoking (n=23; 24.0%) were notable medical contraindications. Forty-nine patients (7.8%) died during work-up, while 130 (85.0%) of the listed patients received a heart transplant. Of the 429 donor referrals, 139 (32.4%) were accepted for organ procurement. Reasons for declining donors included unsuitability for transplantation (30.3%), lack of capacity (1.8%), and recipient-donor mismatch (66.9%).
Conclusion. Three-quarters of the referred patients were deemed unsuitable for heart transplantation for medical and/or social reasons. The ratio of referral to listing has decreased over time. However, once listed, the likelihood of receiving a transplant was high.

S Afr Med J 2024;114(3b):e1371. https://doi.org/10.7196/SAMJ.2024.v114i3b.1371

Heart transplantation is the gold-standard treatment for end-stage cardiac failure, which improves both survival and quality of life.[1] This advanced therapy should be considered for all patients who are refractory to goal-directed medical therapy or for whom alternative surgical options are not available or are contraindicated. Indications are also extended to non-heart failure patients with debilitating angina or refractory ventricular arrythmias, where alternative therapies are not suitable.[2] The timing of referral and listing of patients for heart transplant has evolved over time, with the introduction of implantable resynchronisation therapy and durable ventricular assist devices as well as novel medical agents (SLGT2 inhibitors) as bridging therapies.[3] However, these adjuncts should not alter the absolute number of heart transplant candidates referred to an advanced heart failure centre, as they are provided at the same facility.

Groote Schuur Hospital (GSH) is an academic referral hospital that provides tertiary care for the population of Western Cape Province, South Africa (SA), and is a national referral centre for nominated quaternary therapies. As such, GSH is the only provider of heart transplantation in the state sector and accepts cross-provincial referrals for both insured and uninsured patients.[4] Despite its long history of heart transplantation,[5] there has been a notable recent decline in activity at GSH. Although a national moratorium on heart transplantation at the end of the previous century,[6] as well as a simultaneous self-imposed restriction on heart transplant numbers by the hospital administration, is a potential explanation, the recent renewed support for transplants by both hospital and provincial management has not translated into an increase in the number of transplants. A further explanation would be the development of private heart transplant facilities diluting the relative number of transplants since activity peaked at GSH in the mid-1990s. The population has increased by 26% over this period, however, with >50 million citizens without medical insurance in a setting where cardiovascular disease remains the dominant cause of death.[7]

In the GSH heart and lung transplant unit, which provides healthcare to patients from all socioeconomic strata, psychosocial factors remain a significant burden and a barrier to this advanced therapy. Integration of social support systems within transplant programmes to improve access to solid-organ transplants has been described.[8] The liberalisation of access to therapy at our own institution through updated local guidelines has not resulted in an apparent increase in local transplant activity. A confounder must therefore include the deceased-donor referrals over the same timeframe, which may account for reduced heart transplant activity. The scarce resource of organ donors worldwide, and particularly in SA, is well described as a limiting factor for solid-organ transplantation. SA, with a low donor referral rate of 1.4 per million, also lacks a centralised organ donor organisation.[9] Referral for organ donation is sporadic and dependent on individual healthcare workers referring potential donors to co-ordinators employed by transplant centres.[10]

This retrospective folder review audited recipient referrals for heart transplant as well as the consented donor cohort with a view to documenting the referral-transplant trend over 2 decades. By improving understanding of patient characteristics and transplantation rates, the study aimed to provide valuable insights into the effectiveness of the transplant referral pathway in meeting the needs of patients with end-stage cardiac failure in the SA context.

Methods

Study design

This study utilised a retrospective patient folder review and audit approach to describe trends in heart transplant referrals and associated outcomes at a tertiary academic hospital. The data collection period spanned from 1 January 1997 to 31 December 2019.

Study setting

GSH, located in Cape Town, is the only academic tertiary care facility providing heart transplantation in SA. The hospital primarily serves patients who do not have medical insurance and are from a low socioeconomic background.[11] Suitability for listing was based on the GSH unit guidelines for recipient listing (February 2017 circular, unpublished), which use the International Society for Heart and Lung Transplantation (ISLHT) listing criteria as a backbone reference publication.[12] All patients who meet medical criteria undergo a formal social worker assessment, delivered as a written report and presented independently at a multidisciplinary recipient review meeting. The report has a standardised format evaluating the following domains: family and social network (availability of reliable and supportive caregivers), emotional stability (presence of a support system such as friends, relatives or support groups), financial support, psychosocial suitability (mental health, coping skills, and ability to adhere to the post-transplant treatment plan, triggering referral to mental health services if appropriate), suitability of the home environment (accessibility, safety and hygiene), and commitment (willingness to adhere to the post-transplant medical regimen, avoidance of substance abuse, and lifestyle changes, dietary restrictions and exercise).

Patient inclusion

The review included patients referred for heart transplantation who were >12 years of age. Data on potential and utilised organ donors were also included.

Data collection and management

A standardised data collection form was developed to acquire data on referred patients and donors. Fields for referred recipients included patient demographics (age and gender), diagnosis, and referral indications for heart transplant. The duration of time spent on the waiting list and the outcome or decision following referral were recorded. For patients not listed for transplant, the reasons for exclusion were documented between 2010 and 2019 and are reported in Supplementary Table 1 (available online at https://www.samedical.org/file/2154); this information was not available in the first decade.

Similarly, for donor organ referrals, data collected included the cause of death of the donor, demographics (age, gender, and province of referral), the suitability of the referred organ, and whether the organ was accepted or declined. In cases where the organ was declined, the reasons were recorded if available. Organ referral from a state or private hospital was also documented. The following definitions were applied when categorising brain-dead donors: a potential donor was defined as a patient with a devastating brain injury or lesion; an eligible donor was declared dead, medically suitable and consented for transplant; unsuitable donors were potential donors who were not medically suitable, whereas in recipient-donor mismatch the donor was eligible but declined on the grounds of immunological or size incompatibility; and lack of capacity was defined where there was insufficient staff or hospital bed capacity to undertake a transplant.

Data were de-identified and entered into a secure electronic database (Filemaker version 18; Claris International, USA) hosted by and backed up on the University of Cape Town's server. A one-time pin authentication is required by approved users to protect the confidentiality and integrity of the data.

Data analysis

Descriptive statistics were used to summarise the data. Continuous variables such as age and waiting-list duration were reported as means with standard deviations (SDs). Categorical variables were presented as frequencies and percentages. Temporal trends, referral patterns, recipient and organ decline, and outcomes were illustrated per year over the study period.

Ethical considerations

Prior to commencing the study, ethics approval was obtained from the University of Cape Town's Human Research Ethics Committee (ref. no. HREC 575/2019).

Results

Referred recipients

The mean (SD) age of referred recipients was 38.1 (14.6) years, and the majority were male (65.9%) (Table 1). Dilated cardiomyopathy accounted for nearly half (45.1%) of all recipient referrals. Additionally, nearly a quarter (24.3%) of the referrals were diagnosed with ischaemic

Table 1. Demographic characteristics for recipient referrals (*N*=625)

Characteristic	*n* (%)*
Age (years), mean (SD)	38.1 (14.6)
Sex	
Male	412 (65.9)
Female	144 (23.0)
Undocumented	69 (11.0)
Diagnosis on referral	
Dilated cardiomyopathy	282 (45.1)
Ischaemic cardiomyopathy	152 (24.3)
Documented as unknown	51 (8.1)
Other diagnosis	36 (5.8)
Structural prosthetic valve failure	20 (3.2)
Not documented	16 (2.6)
Restrictive cardiomyopathy	12 (1.9)
Valvular-related heart disease	18 (2.9)
Complex congenital heart disease	10 (1.6)
Peripartum cardiomyopathy	17 (2.7)
Arrhythmogenic right ventricular dysplasia	7 (1.1)
Chronic rejection post-transplant	4 (0.6)
Waiting-list period (days), mean (range)	190 (1 - 916)

SD = standard deviation.
*Except where otherwise indicated.

cardiomyopathy. Only 4 patients were referred for retransplant due to chronic rejection, and the diagnosis was not documented or documented as unknown in 67 (10.7%) of the referrals.

Referred donors

The mean (SD) age of donors at referral was 29.4 (15.0) years, and the majority were male (67.5%). Most donors (54.1%) were referred from Western Cape Province, and 58.3% of all the donors presented at a state facility (Table 2).

The number of recipient referrals generally exceeded the number of organs referred, except for the years 2008 and 2018, when there were more donors referred. On an annual basis, the recipient referral rate was calculated to be 27 patients and the annual donor referral rate was determined to be 19 patients. No apparent association was identified in the trend of referrals between donors and recipients over the years. Analysing the historical data, it was observed that the highest number of recipient referrals occurred in 1997, reaching a peak of 42 patients. Conversely, the lowest number of donor referrals was recorded in 2012, with only 6 patients referred (Fig. 1).

The most frequently reported cause of death among the donors was head trauma, accounting for a significant proportion of cases (*n*=235; 54.8%) (Table 2). Spontaneous cerebral bleeds were the second most prevalent cause of death, representing 26.6% of the cases (*n*=114). Among donors with head trauma as the cause of death, a substantial majority (82.9%) were deemed suitable for organ transplantation. Conversely, the majority of organs donated by individuals who had infection as the cause of death (80.0%) were considered unsuitable for transplantation (Fig. 2).

Table 2. Characteristics of consented donor referrals (*N*=429)

Characteristic	*n* (%)*
Age (years), mean (SD)	29.4 (15.0)
Sex	
Male	282 (67.5)
Female	136 (32.5)
Undocumented	11 (10.0)
Province or country of referral	
Western Cape	232 (54.3)
Gauteng	98 (30.0)
Free State	18 (4.2)
Limpopo	1 (0.2)
Mpumalanga	1 (0.2)
KwaZulu-Natal	17 (4.0)
Eastern Cape	58 (13.6)
Namibia	2 (0.5)
Undocumented	2 (0.5)
Insurance	
Uninsured	250 (58.3)
Private	125 (29.1)
Undocumented	54 (12.6)
Cause of death	
Head trauma	235 (54.8)
Spontaneous cerebral bleed	114 (26.6)
Anoxia	33 (7.7)
Undocumented	22 (5.1)
Embolic stroke	14 (3.3)
Infection	6 (1.4)
Brain tumour	5 (1.2)

SD = standard deviation.
*Except where otherwise indicated.

Transplant activity

Among the 625 recipient referrals, a total of 153 individuals, representing 24.5% of the referrals, were listed for transplant. Of those who were listed, 23 patients (15.0%) died while waiting for a suitable organ to become available. The remaining 130 individuals (85.0%) underwent successful transplantation. A significant number of recipient referrals, totalling 215 (34.4%), were turned down for transplant (Fig. 3). The primary reasons for declining referrals were categorised as social, medical and psychological factors. Social factors were the main exclusion criteria for transplantation and accounted for 106 (49.3%) cases of non-listing; medical causes accounted for 83 cases (38.6%), and psychological contraindications for 26 (12.0%). In the subset analysis of the decade 2010 - 2019, when data were captured with higher-resolution analyses, 265 recipients were referred, of whom 96 were declined for listing. Supplementary Table 1 (https://www.samedical.org/file/2154) outlines the reasons for the decline captured from 2010 to 2019. Poor social circumstances (*n*=38; 39.6%), poor insight (*n*=28; 29.2%) and poor compliance (*n*=21; 21.9%) were the most common non-medical reasons for not listing recipients.

Of the 429 donor referrals, 139 (32.4%) were accepted for procurement, with less than one-third of the referred donors meeting the criteria for organ procurement. Among the 290 donors who were declined, the most common reason was lack of a suitable recipient due to a recipient-donor mismatch (*n*=194; 66.9%) (Fig. 4). In particular, the years 1998 and 2000 had the highest mismatch of suitability, while 80.0% of the referred organs were deemed unsuitable for transplant in 2012. After recipient-donor mismatch, organ unsuitability was the second most common reason for declining the donor (*n*=88; 30.3%). Eight donors (1.8%) were declined owing to lack of capacity. The mean waiting period for all listed patients in the study was 190 days, with a range of 1 - 916 days. There was a close association between the patients listed, donors referred and patients transplanted (Fig. 1).

Discussion

This study, which reports heart transplant activity from the only public sector programme in SA, has four main findings. Firstly, despite an expanding population with an expected increase in the burden of end-stage cardiac conditions requiring transplantation, we found that the number of recipient referrals remained relatively stable over 2 decades. Secondly, we found that approximately a third of these referrals were turned down because of some disqualifying reason, and although more than one contraindication could be present in the same patient, socioeconomic barriers to transplantation were present in almost half of the declined patients. Thirdly, we found that head injury as the mechanism of brain death was most likely to result in a utilisable donor heart, and that the major reason for a suitable donor heart not being utilised was the absence of a suitable blood group-, size- and/or crossmatched recipient on the waiting list. Lastly, we found that waiting-list mortality was relatively low, with 85% of referrals who were accepted and waitlisted receiving a transplant, a conversion rate that compares favourably with the USA and other countries in the pre-implantable ventricular assist device (VAD) era.[13]

Considering the increasing challenges facing SA society, it should come as no surprise that low social support was a common obstacle to transplantation in the study. Incorporating social support as an important criterion in the transplant evaluation process – based on the principle of utility[14] – is a common practice in solid transplant programmes for different organs around the world.[3,4,15,16] In 2019, a national survey of transplant providers in the USA found that ~20% of transplant candidates were excluded on these grounds.[17] Lower socioeconomic status is also associated with delayed referral for heart transplantation.[18] However, despite being widely used, the social support criterion is considered controversial because of its subjectivity, the lack of standardised assessment tools, and the risk of implicit bias,[19] and because its relationship to post-transplant outcomes has not been consistently demonstrated.[20] A meta-analysis of studies (that included heart, lung, liver and kidney recipients) found that, in the seven high-income countries (HICs) in which the studies were performed, social support was not predictive of post-transplant adherence, and was inconsistently associated with survival and graft loss.[21] Making social support a determining factor for heart transplant eligibility also raises ethical concerns, as it may be seen as discriminatory, disproportionately affects vulnerable patients, and amplifies pre-existing health inequities. It also raises legal and human rights concerns. Countries such as Canada and the European Union have responded to this criticism by removing social support considerations from the list of transplant eligibility criteria, but extrapolating findings from HICs to our setting is clearly not straightforward. In SA, with low donor numbers, limited resources for transplantation and inadequate social support from the state, considering socioeconomic factors when rationing access to transplantation may be a relevant practical necessity, and in part explains the much higher incidence of this contraindication in our study. Transplantation does not take place in a vacuum, and the challenges faced by patients in the transplant system are representative of the limited access to healthcare facilities, shortage of essential resources, and social disparities present in our society as a whole. Consequently, a nuanced approach considering the unique socioeconomic landscape of SA is essential to understand and address the potential barriers that could undermine transplant success in our setting. While socioeconomic factors may be considered in determining eligibility, this should be done carefully and ethically, with a focus on screening for low social support and the offering of assistance, while balancing the need for maximal overall benefit for patients and society. This finding emphasises the need to strengthen the support services around transplantation to ensure that the transplantation process is as equitable as possible.

Overall, only about a third of donor heart referrals to our hospital resulted in a transplant, meaning that ~70% of donor hearts were either unused or referred to the private sector. Even countries such as the USA, with centralised organ allocation systems maximising donor-recipient matching, the non-utilisation rate of donor hearts is still ~50% (despite the use of

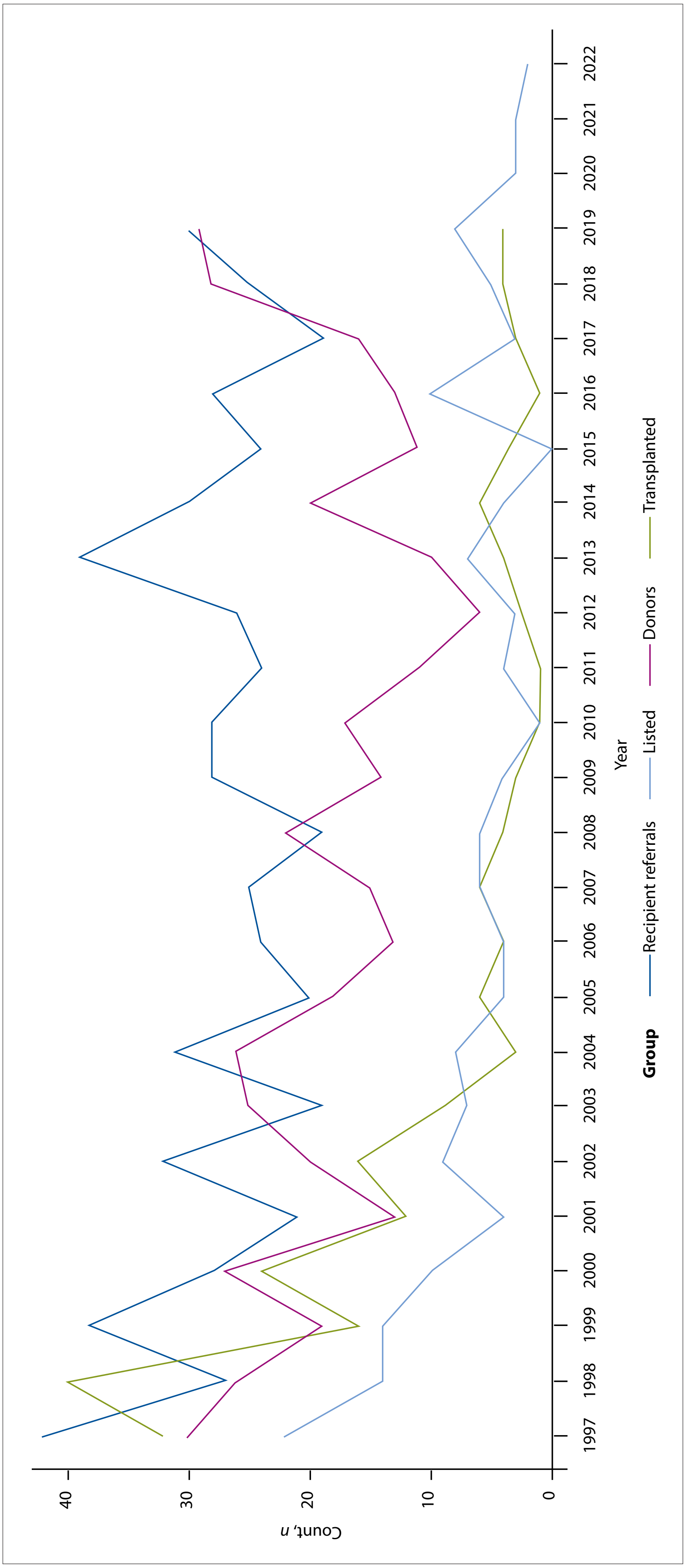

Fig. 1. Merged data representing absolute recipient referrals and consented donor referrals against listed recipients and transplants.

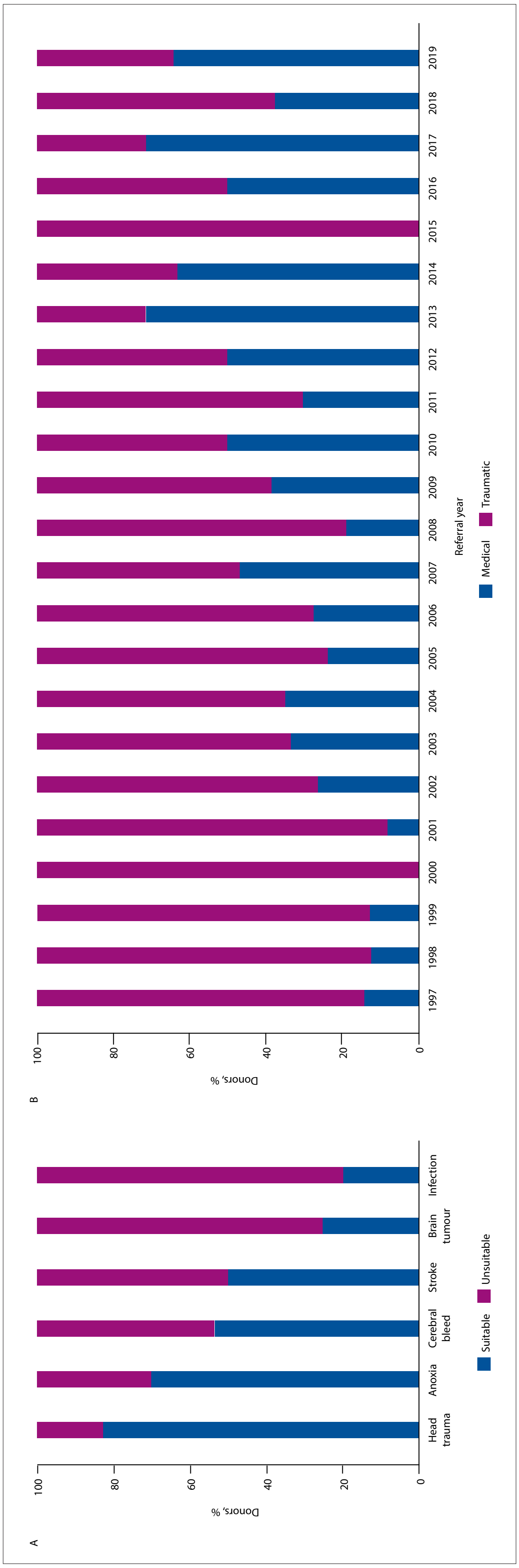

Fig. 2. Suitability of consented organ referral by pathological cause of death. (A) Suitability of heart for transplantation categorised by cause of death, and (B) consented donor referrals by year based on medical or traumatic aetiology.

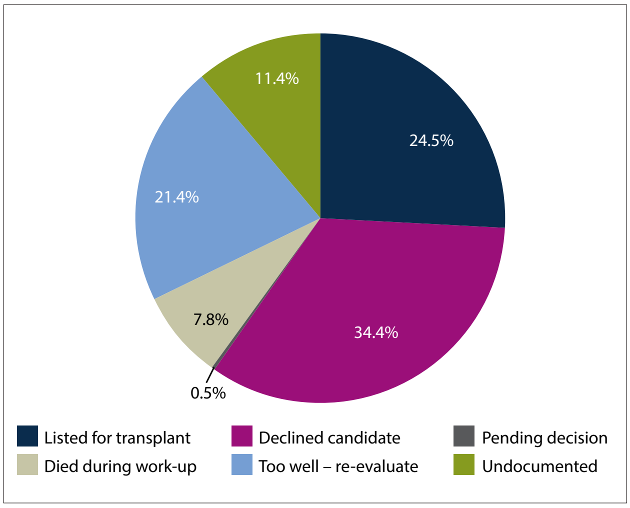

Fig. 3. Recipient referral outcome.

so-called extended-criteria hearts such as those from donors with diabetes and hypertension, or from donors who have hepatitis C or have abused illicit drugs),[22] but these hearts are usually declined because of either undesirable patient-related factors or adverse haemodynamic or echocardiographic findings.[23] In our study, however, the major reason for donor heart non-utilisation was the lack of a suitable blood group-, size- and/or crossmatched recipient. This finding emphasises the urgent need to expand the recipient pool. A limited recipient pool and a shortage of donor organs lead to lengthy waiting lists for heart transplantation. (In our study, the average waiting period after being listed for transplant was just over 6 months, which is about the same as reported in the United Network Organ Sharing database in the USA in the era before implantable VADs.[24]) In addition, with a larger recipient pool, there is a higher likelihood of matching a donor heart with a suitable recipient, and it also allows for a more comprehensive evaluation of potential matches based on factors such as severity of illness, medical urgency and compatibility. This approach ensures that donor organs are allocated to those patients who will benefit the most from the transplant, maximising the use of available organs.

Traumatic brain injury was the cause of death in the majority of our donor referrals, reflecting the local context in SA, where incidents of violence and road accidents contribute to a high prevalence of head injuries.[25] This finding is in sharp contrast to the data from Europe, where the pathological cause of death in most donors is spontaneous intracranial haemorrhage.[26] There was, however, a temporal increase during the study period in the number of non-traumatic or so-called 'medical' causes of brain death, reflecting the international trend to expand indications for cardiac donation,[26] for example including donors who have died of poisonings, overdoses and intoxications.[27] We also showed that donors who had head trauma as the cause of death were most likely to be suitable for transplantation; anoxic brain injury donors have been shown to have lower utilisation rates (presumably owing to a greater global injury due to the effects of tissue hypoxia),[28] and there has historically been a reluctance to accept donors with primary brain tumours and infection as causes of brain death because of concerns about metastatic spread and donor-derived infection, although newer studies suggest that these risks may be overstated.[29-31] Although we did not collect these data, we surmise that lower utilisation rates in patients with intracranial haemorrhage or cerebral infarcts are related to unfavourable donor demographics and donor heart characteristics (older age, smoking history, history of hypertension and/or ischaemic heart disease, or echocardiographic features of left ventricular hypertrophy or regional wall motion abnormalities, to

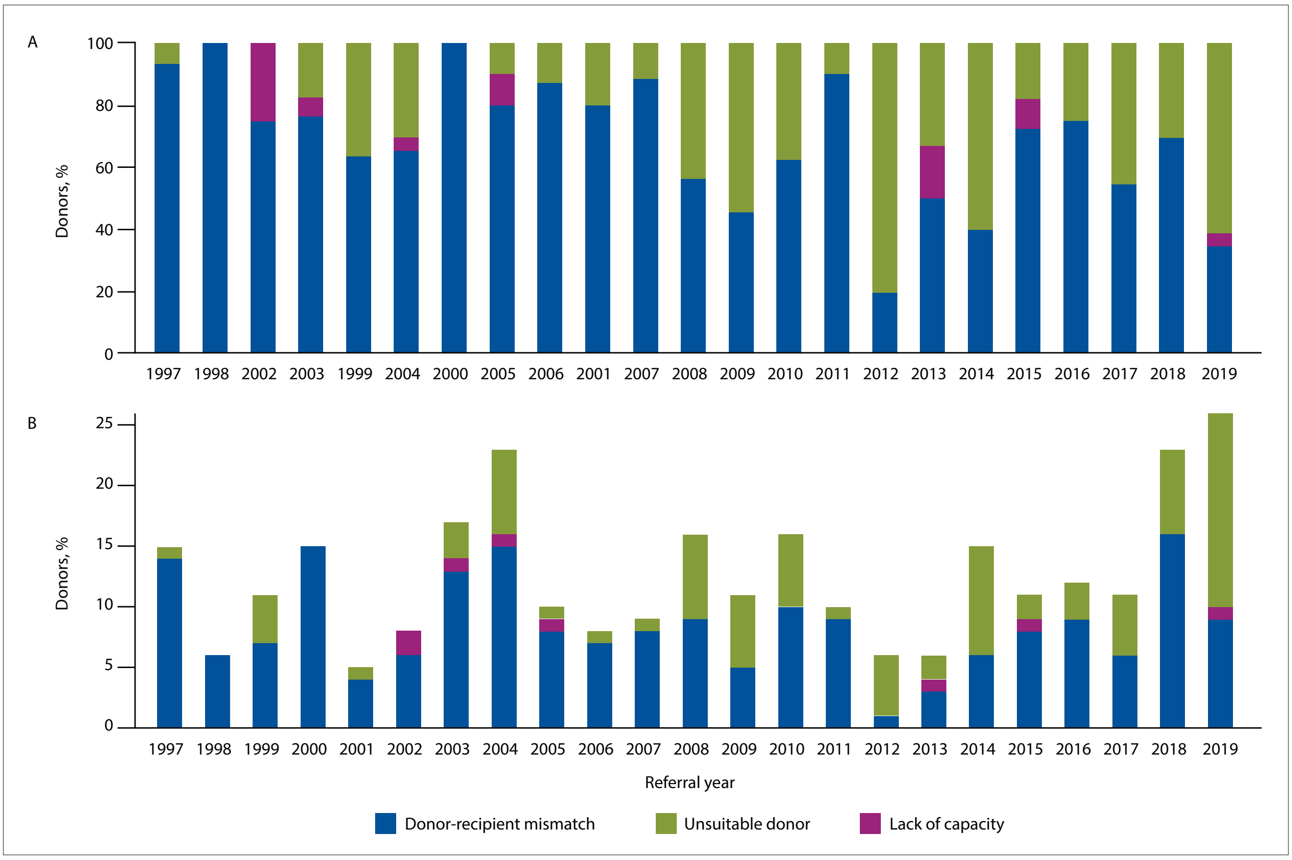

Fig. 4. Reasons for declining consented donors for heart transplant, expressed as (A) ratios and (B) absolute numbers.

name a few) resulting from the underlying cardiovascular risk factors that have predisposed to the intracranial event, as has been shown in other studies.[32-34]

Some limitations of this study deserve emphasis. While all assessments were performed by senior social workers with experience in transplantation, and staff turnover during the study period was low, the lack of a formal scoring system to assess social support may have led to some variation and subjectivity in the assessments of candidacy. Objective psychosocial assessment tools for heart transplantation, such as the Stanford Integrated Psychosocial Assessment for Transplantation, Psychosocial Assessment of Candidates for Transplantation and Transplant Evaluation Rating Scale, have been developed,[35-37] but there is inconsistent evidence demonstrating their prediction of post-transplant outcomes, and they have not been validated in resource-constrained settings.[38] Recognising the critical importance of the psychosocial assessment and the need for standardisation, the ISLHT released a consensus statement in 2018 to promote consistency of evaluation,[35] but this document was only published at the end of our study period and had limited influence on our practice. In addition, it lacks specific recommendations, does not include a scoring system, represents expert opinion from high-volume centres in the Global North, and is not an evidence-based guideline. The development of an objective psychosocial evaluation tool for determining eligibility for heart transplantation in SA is an attractive objective, but the profound discrepancies in healthcare equity in our system and the heterogeneity of the social problems of our patients present a formidable obstacle to this undertaking.

Conclusion

Heart transplantation in SA faces numerous challenges. Addressing these challenges requires a multifaceted approach, including increasing public awareness about organ donation, improving access to cardiac care services and expanding the referral base, and investing in transplant infrastructure and patient support services. Collaboration between the government, healthcare institutions, non-governmental organisations and the public will be vital in overcoming these challenges and improving heart transplantation access in the public sector in SA. Fortunately, opportunities for improvement exist at every link on the chain of transplantation, and even small advances are likely to see commensurate increases in transplant activity. By identifying these bottlenecks and evaluating barriers, we hope to stimulate research and quality improvement to facilitate timely and equitable access to transplantation for all patients in need.

Declaration. The research for this study was done in partial fulfilment of the requirements for RK's MMed degree in cardiothoracic surgery at the University of Cape Town.

Acknowledgements. The authors acknowledge the transplant co-ordinators who make organ transplantation possible, as well as the gift of life given by donors.

Author contributions. Study conception and design: PZ, JB, TP. Analysis and interpretation: PH, RK, TP, GC. Collected data: KS, TP, MM, AR. Wrote article: RK, TP, GC. Refinement of article: JS, AB, CO, NdS, BC. All authors reviewed the results and approved the final version of the manuscript.

Funding. Chris Barnard Division of Cardiothoracic Surgery Research Fund, discretionary MMed grant.

Conflicts of interest. None.

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Accepted 26 October 2023.