

CONSENSUS STATEMENT PAPER

# ISHLT consensus statement on donor organ acceptability and management in pediatric heart transplantation



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The number of potential pediatric heart transplant recipients continues to exceed the number of donors, and consequently the waitlist mortality remains significant. Despite this, around 40% of all donated organs are not used and are discarded. This document (62 authors from 53 institutions in 17 countries) evaluates factors responsible for discarding donor hearts and makes recommendations regarding donor heart acceptance. The aim of this statement is to ensure that no usable donor heart is discarded, waitlist mortality is reduced, and post-transplant survival is not adversely impacted.

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There are worldwide geographic and programmatic disparities in pediatric donor heart usage. The waitlist mortality is 17% to 30%,<sup>1,2</sup> yet around 40% of offered organs are not utilized.<sup>3</sup> The non-utilization of donors has many contributing factors: the absence of any accepted standards or guidelines for pediatric donor heart assessment and subsequent acceptance; the influence of physician and surgeon preferences; disparate regulatory requirements; variability in program quality indicators and expected benchmarks for success; and regional differences in prioritization schemes and healthcare system economics. Additional factors include waitlist times, number of heart donors, listing criteria, recipient acuity, and the availability of bridging devices.

This consensus statement highlights these differences, evaluates factors responsible for discarding donor hearts,

and makes recommendations regarding donor heart acceptance. The aim of this statement is to ensure that no usable donor heart is discarded, waitlist mortality is reduced, and post-transplant survival is not negatively impacted.

An expert writing group was appointed by the International Society for Heart and Lung Transplantation (ISHLT) Standards and Guideline Committee. There were a total of 62 authors from 53 institutions in 17 countries. The following 6 topics were identified as key to this process:

1. What is the waitlist mortality?
2. What is the current donor discard rate?
3. How much do donor characteristics influence outcomes?
4. Can we improve donor management?
5. How do recipient and donor interactions affect outcomes?
6. Behavioral psychology, programmatic, and regulatory influences

The writing group was divided into task forces to address these topics. Between September and December 2018, they undertook a formal literature search and wrote their review. Drafts were sent to the 4 editors for editing and

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**Table 1** OPO Survey Responses

OPO (Data collection date range)	Population (million)	Listed patients (n)	Removed from waitlist (%) <sup>a</sup>	Death on waitlist (%)	Discarded pediatric donor hearts <sup>b</sup> (%)
Australia (1/1/2005–8/1/2018)	24.6	133	21	13	57
Eurotransplant <sup>c</sup> (1/1/2005–12/31/2017)	136.39	962	29	18	24
Scandiatransplant <sup>d</sup> (1/1/2005–12/31/2017)	30.05	N/A	N/A	15	18
Swisstransplant <sup>e</sup> (1/1/2008–12/31/2017)	8.42	72	N/A	25	N/A
Colombia (1/1/2013–12/31/2017)	45.5	30	55	21	N/A

Abbreviations: N/A, not applicable; OPO, organ procurement organization.

<sup>a</sup>Includes death on waiting list, removal for recovery, and inactive on waiting list.

<sup>b</sup>Percentage of donor hearts reported to OPO but not used/retrieved/procured.

<sup>c</sup>Eurotransplant (<16 years): Austria, Belgium, Croatia, Germany, Hungary, Luxemburg, Netherland, and Slovenia.

<sup>d</sup>Scandiatransplant (<16 years): Denmark, Estonia, Finland, Iceland, Norway, and Sweden.

<sup>e</sup>Swisstransplant: Switzerland.

incorporation into a single document. This document was reviewed by the task forces and underwent further editing, and the conclusions and recommendations were generated. The expert writing group was polled to establish the level of agreement for the conclusions and recommendations with a response rate of 97%, and each recommendation achieved at least 90% endorsement. The document was then distributed to the ISHLT community for comment and discussed at the 2019 ISHLT Annual Meeting. Following these consultations, the document was finalized and underwent independent expert review. This document is in full compliance with the ISHLT Standards and Guidelines regulations. Detailed review articles on each topic were written concurrently and have been published separately.

## What is the waitlist mortality?

Current waitlist mortality varies by country, region, and institution. Published reports from large national and international datasets have consistently reported waitlist mortality between 17% and 30%. These include Japan (30%),<sup>2</sup> Australia (22% mortality with 7% delisted for clinical deterioration),<sup>4</sup> Eurotransplant (18%),<sup>5</sup> and the United States of America (US, 17%).<sup>1</sup> A contemporary survey of international organ procurement organizations (OPOs) showed waitlist mortality rates of 13% to 25% (Table 1). Differences in waitlist mortality occur within countries. In the US, rates vary from 6.9% to 19.2% despite a national allocation system.<sup>6</sup> There is also significant variability associated with center transplant volume (5% in large centers to 30% in very small volume centers).<sup>7</sup>

Mortality varies by several factors including recipient age, diagnosis, and acuity of illness. Approximately 25% of infants in the US die waiting for a heart, compared with around 15% for children and adolescents.<sup>8</sup> Waitlist mortality for patients with congenital heart disease (CHD, 22%)<sup>1</sup> is higher than in children with cardiomyopathy (8%–14% dependent on the specific type),<sup>9–11</sup> although there are many confounders as the CHD diagnosis may be a surrogate for multiple reoperations, technical surgical challenges, and occult pulmonary vascular disease or coexistent syndromes. Waitlisted patients at higher risk of mortality

include those listed urgently and those on extracorporeal membrane oxygenation (ECMO) or ventilator support.<sup>1,8</sup>

Waitlist mortality has decreased with time, largely because of improved means of supporting patients while waiting, but mortality remains significant.<sup>12,13</sup> We have focused on waitlist mortality, though accruing morbidity is also a significant issue and often responsible for delisting; however, there are no data in the literature.

## What is the current donor discard rate?

There is no standard definition of organ discard across organizations or countries, making it difficult to quantify and make comparisons. Organs may be discarded because potential organ donors were not evaluated for organ donation or were evaluated without assessing the heart, the heart was evaluated but not offered (or not reassessed for suitability to offer), an accepted organ was retrieved but not transplanted, or a donor heart was offered but not accepted for transplantation. The first 3 scenarios are very difficult to quantify as data is lacking; the fourth, although documented, is uncommon, and so only the last scenario will be discussed.

The published pediatric donor heart discard rate, defined as any organ offered by an OPO to a recipient or center and then not used, varies around the world between 34% and 45%.<sup>3,14–16</sup> As part of this project, a survey was sent to 12 OPOs, of which 5 responded, representing 245 million people (Table 1), and their discard rate ranged from 18% to 57%. Reasons for discard are sparse. Australia cited medical reasons (19%) and lack of a suitable recipient (39%). Eurotransplant cited no candidate (20%), donor quality insufficient (38%), or another unspecified reason (42%).<sup>5</sup> In the United Network for Organ Sharing (UNOS) database, reasons were donor age, non-O blood type, Centers for Disease Control high-risk donor status, ejection fraction (EF) <50%, inotropic support, or use of >2 inotropes in the donor.<sup>3</sup>

## How much do donor characteristics affect outcomes?

The impact of donor characteristics and comorbidities on pediatric heart transplant outcomes remains challenging

because of the low quality of available evidence. The literature, however, is consistent in that recipient factors far outweigh donor factors in influencing short- and long-term outcomes. The term marginal donor is often used but donor quality assessment is imprecise,<sup>16</sup> hard evidence lacking, and the variety of criteria used to define a marginal donor for the most part is not evidence-based but enshrined in folklore. They include lower EF, donor death from stroke, Centers for Disease Control increased risk, high inotropic needs, lower glomerular filtration rate, longer ischemic time (IT), and size and age mismatch. The evidence for these is reviewed hereafter.

## Size

Donor recipient weight ratio 0.6 through 3.0 has not been reported to be associated with adverse outcomes.<sup>17,18</sup> There is no advantage to using height alone for size matching.<sup>19</sup>

## Age

In the ISHLT registry, most donors for pediatric recipients are  $\leq 18$  years old (donors  $> 18$  years, 24%), although notable geographic differences exist, with  $< 1\%$  of donors over 35 years of age in North America compared with 19% in Europe.<sup>20</sup> Analysis of the UNOS database showed that there is some evidence that there is a difference in mortality and the development of cardiac allograft vasculopathy, especially in adolescents who receive a donor organ  $> 5$  years older than their chronological age, especially if the donor is  $> 25$  years of age.<sup>21</sup>

## Donor heart function

A number of pediatric and adult studies have demonstrated comparable recipient outcomes following transplantation of hearts with EF  $< 50\%$ <sup>6,22–25</sup> and/or evidence of segmental wall motion abnormalities.<sup>6,25</sup> Despite this, multiple studies have demonstrated decreased utilization of potential donor hearts with echocardiographic evidence of EF  $< 50\%$ .<sup>16,22,23,26,27</sup> There may, however, be a lower limit that is acceptable. ISHLT guidelines recommend refusal of donor hearts with EF  $< 40\%$ ,<sup>28</sup> and this practice is supported by several pediatric<sup>27,29</sup> and adult<sup>30</sup> studies.

## Donor-derived infections

Donor-derived infections (DDIs) may influence outcomes, but they are uncommon. An analysis of all solid organ transplants by the Organ Procurement and Transplantation Network database demonstrated that out of 199,050 transplants, only 45 (0.02%) recipients died from a DDI.<sup>31</sup>

### Bacteria

Donors with a variety of bacterial infections, including any culture positivity and meningitis, have been reported without significant impact on outcomes in pediatrics, and the

use of such organs is supported by the American Society of Transplantation Infectious Disease Community of Practice.<sup>32–35</sup> Transmission of *Mycobacterium tuberculosis* from a donor has been reported in an adult and successfully treated.<sup>36</sup>

### Viruses

Cardiac transplantation from donors dying from influenza has been successful.<sup>37</sup> The risk of transmitting hepatitis B, hepatitis C, or human immunodeficiency virus can be reduced by a thorough donor history combined with serological testing, although donor infection can still be transmitted despite negative serology and nucleic acid testing because of a window period. However, the risk is significantly reduced when both serology and nucleic acid testing are negative.<sup>38,39</sup> Dengue virus has been transmitted to recipients causing clinical illness post-transplant without deaths,<sup>40</sup> but transmission of West Nile Virus from donor to recipients has been reported to cause neuroinvasive disease in up to 70% of recipients and death in 30%.<sup>41</sup> DDI has not yet been reported with Zika virus.<sup>42</sup>

### Parasites

The literature regarding parasitic infections with toxoplasmosis is controversial.<sup>43</sup> Strongyloides can be managed with recipient prophylaxis or preemptive treatment for donor-positive serology.<sup>44,45</sup> In contrast, *Trypanosoma cruzi* donors (Chagas disease) should not be used.<sup>46</sup>

### Fungi

Fungal infections in donors pose a risk with significant mortality if unrecognized and untreated in the recipient, but prophylaxis and early therapy decreases the risk of mortality.<sup>47,48</sup>

### Non-bacterial meningoencephalitis

Non-bacterial meningoencephalitis has been reported to transmit a variety of infections,<sup>42,49</sup> and it is recommended by the Ad Hoc Disease Transmission Advisory Committee of UNOS that extreme caution be used in determining the suitability of donors with meningoencephalitis of unknown etiology or because of a pathogen without available treatment.<sup>50</sup>

### Comorbidities

There are no pediatric studies on the influence of donor diabetes, hypertension, or transmission of anaphylaxis, but adult data suggest little influence on outcomes except for hypertension.<sup>51–54</sup> Donor malignancy has not been shown to have an increased risk of early death or graft loss overall in solid organ transplant recipients, although hematologic and otolaryngologic tumors have been associated with decreased survival following heart transplant.<sup>55</sup> The Organ

Procurement and Transplantation Network has issued a consensus statement on donor malignancy.<sup>56</sup> There are only case reports of genetic syndromes in donors and no conclusions can be drawn.<sup>57</sup>

### Donor cardiopulmonary resuscitation (CPR)

A history of donor CPR should not preclude transplantation of an otherwise acceptable donor,<sup>58–61</sup> although the upper limit of donor CPR duration is not known.<sup>60,62–64</sup>

### Donor inotropes

The 2017 ISHLT registry report cites donor inotrope use as being associated with increased 1-year mortality but does not define the dose or number of inotropes.<sup>20</sup> In all other studies, donor inotrope use has either not been associated with post-transplant outcomes<sup>25,61,65–67</sup> or has been associated with improved recipient outcomes.<sup>68–70</sup> Historically, impaired myocardial function as assessed by the use of high dose inotropes or vasopressors or multiple inotropes have been considered contraindications for heart donation or acceptance of an offered organ.<sup>3,71–73</sup> In recent studies, however, no difference in clinical outcomes was associated with inotrope use.<sup>67,73</sup> Increasingly, use of vasopressors and inotropes are not considered contraindications to organ donation.<sup>70,74</sup>

### Mode of death

Concern surrounding the mode of death on long-term myocardial function following heart transplantation is largely focused on the heart's tolerance of the catecholamine surge that occurs following a rise in intracranial pressure.<sup>75</sup> Some pediatric studies have demonstrated slightly higher 1-year mortality rates utilizing donors from cerebrovascular accidents,<sup>29,76</sup> whereas others have not.<sup>22,27,77</sup> A small study demonstrated that donors from sudden infant death syndrome with a normal EF have graft survival comparable with non-sudden infant death syndrome donors.<sup>78</sup>

### Donor cardiac testing

#### *Echocardiogram*

Donor function is often reduced on the initial echocardiogram after brain death because of the autonomic storm. Recovery of function usually occurs with time.<sup>22,69,79</sup> If the initial echocardiogram demonstrates decreased function, then it should be repeated to assess for recovery. Both pediatric and adult studies have demonstrated concerning disparity in image interpretation in the evaluation of left ventricular function between the donor and recipient site.<sup>80,81</sup> Considering the importance of echocardiographic measures of function in the decision to accept or decline a potential heart, it is reasonable for recipient sites to request direct visualization of echocardiographic images.

#### *Electrocardiogram (ECG)*

There is a paucity of adult studies and no pediatric data addressing the utility of donor ECG information in donor heart selection. ECG findings are often abnormal after brain death and, aside from an association between pathological Q waves and decreased ventricular function, have not been predictive of outcomes.<sup>25,82–84</sup>

#### *Troponin, creatinine kinase, and natriuretic peptides*

An elevated troponin or creatine kinase-muscle/brain, regardless of its value, in both adult and pediatric studies has not shown any adverse graft outcomes when there was normal donor heart function.<sup>24,59,69,85–88</sup> Use of donor B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide has also failed to predict recipient outcomes.<sup>89–92</sup>

### IT

Donor ITs >4 hours have been associated with increased intensive care unit (ICU) and hospital stays<sup>20,93</sup> and early phase graft failure,<sup>11,20,64,94–96</sup> but not long-term graft or recipient survival.<sup>11,61,76,94,95,97</sup> Some studies suggest that recipients >10 years of age are at higher risk,<sup>64,95</sup> but others suggest this is more of an issue in infant recipients.<sup>20,94</sup> It has been one of the main parameters used to determine outcomes in the first year after heart transplant. The largest cohort of pediatric heart transplant patients ( $n = 4,716$ ) retrospectively evaluated over 2 decades showed that an IT <3.5 hours was associated with the best outcome. The 2017 ISHLT registry report<sup>20</sup> focused on IT that varied by geographic region, recipient age, diagnosis, mechanical support, and acuity. An IT >4 hours, compared with 2 to 4 hours, was independently associated with decreased survival at 1 year (87% vs 92%) and 5 years (77% vs 82%), but there was no long-term effect on mortality. IT is composed of several components that may confound the data; for example, explant time in CHD may be increased because of unforeseen technical challenges, leading to a prolonged IT, and the survival difference actually may be because of the CHD recipient factors rather than issues surrounding donor distance or travel time. Despite long IT and travel distances, good outcomes can be achieved both in pediatric and adult recipients particularly using pediatric donors.<sup>14,97,98</sup>

### Donor preservation

A published review provides information on the biochemical comparison of common preservation solutions and relevant preservation studies; however, there have been no new developments in this area for a considerable time.<sup>99</sup> Hypothermia alone is unable to abolish all cellular damage, as metabolism persists at approximately 5% to 10% of normal. Normothermic donor heart perfusion is a potential solution<sup>100</sup>; however, it is currently only suitable for older

teenagers because of instrumentation size. It allows for extended out-of-body time of the donor heart for up to 8 hours, potentially expanding geographic zones for organ procurement, reducing explant timing pressures, enhancing functional assessment of marginal hearts, and reducing out of hours operating times and retrieval team transport fatalities.<sup>101–103</sup>

### Effect of multiple donor factors

The effects on outcome do not seem to be additive when multiple variables in the same donor occur,<sup>64,73</sup> although this does not seem to be widely known or accepted, as the magnitude of donor non-utilization based on marginal characteristics is significant—60% of donors with  $\geq 1$  marginal characteristics were not used compared with 20% with no marginal characteristics.<sup>6,16,61,94</sup>

### Can we improve donor management?

Management of pediatric donors primarily focuses on measures to mitigate the pathophysiologic responses to brain death.<sup>104–106</sup> A recent consensus statement by the Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations made recommendations for both adult and pediatric donors.<sup>105</sup> Early, targeted management of the potential donor can increase the number of available donor hearts without a deleterious effect on post-transplant outcomes.<sup>107</sup> A number of studies demonstrate improved organ donation rates after a longer period of donor stabilization.<sup>108–111</sup>

A dedicated team in an ICU setting should manage the pediatric cardiac donor to maximize the probability of successful transplantation.<sup>105</sup> The Japan Organ Transplant Network dispatches dedicated medical consultants (usually cardiothoracic surgeons) to the donor hospital to assess and intensively manage the potential donor and provide advice during the procurement operation.<sup>112</sup>

Invasive monitoring is necessary for hemodynamic optimization. Brain stem death is associated with severe autonomic and inflammatory responses that result in early catecholamine release and later hypotension because of cardiac dysfunction and/or vasoplegia associated with inflammatory activation and loss of vascular tone from spinal cord ischemia.<sup>113</sup> Hypovolemia may further exacerbate management because of diabetes insipidus.<sup>109</sup> Hemodynamic management includes some combination of volume resuscitation, inotropic and/or vasopressor administration, and hormonal replacement.<sup>105,114</sup> These should be titrated to achieve the goals of adequate central venous pressure, normalization of blood pressure, urine output, and markers of adequate tissue oxygen delivery. Most donors have significantly reduced arginine vasopressin, corticosteroids, and thyroid hormone levels.<sup>105,115</sup> Hormonal replacement may mitigate endocrine abnormalities, but there is no consensus whether hormonal replacement therapy should be given prophylactically or only in those donors with significant hemodynamic and electrolyte derangement.<sup>105</sup> A pediatric registry study noted that hormonal replacement therapy

**Table 2** One-Year Survival (%) Stratified by Donor and Recipient Risk (Adapted from Trivedi et al.<sup>118</sup>)

1-year survival (%) stratified by donor and recipient risk		
Donor risk	Very low risk recipient	Very high risk recipient
Low	94	80
Intermediate	92	75
High	89	62

(defined as thyroid hormone, vasopressin, and/or glucagon) was associated with improved recipient survival.<sup>64</sup>

### How do recipient and donor interactions affect outcomes?

Limited data exist on the interplay between the recipient and donor variables but do suggest there is likely a combination of factors at play.<sup>25,116–119</sup> Recipient factors appear to influence transplant outcomes more<sup>64</sup> and has been clearly shown in adults (Table 2).<sup>118</sup> Despite this evidence, it is common for physicians to accept marginal donors for recipients who are at higher risk. Examples are a patient deemed too sick to continue to wait, for example, on ECMO, not a ventricular assist device candidate or progressive end organ injury. The marginal organ is used with the view that there is nothing to lose and that such an organ is unlikely to be used elsewhere. The poor results of such decisions may well validate the impression that marginal donors have worse outcomes.

Donor risk calculators are available for several organ groups and predominantly attempt to correlate with post-transplant outcomes. They thus ignore the waitlist morbidity and mortality. A review of existing heart donor risk prediction models identified only 1 published pediatric donor heart score, which was developed using UNOS data to predict post-transplant mortality at 1 year.<sup>29</sup> It was based on the following 5 factors: stroke as cause of death, donor-to-recipient height ratio, EF, glomerular filtration rate, and cold IT. However, the score showed poor model discrimination, with a C-statistic of 0.62. There may also be unintended consequences of the use of donor calculators. In the US renal community, the introduction of a granular Kidney Donor Profile Index to predict graft outcomes increased the discard rate of high-risk kidneys, despite the fact that recipients of these kidneys were at much lower risk of death (relative risk 0.77 at 2 years post-transplant) compared with those who remained waiting for low-Kidney Donor Profile Index kidneys on dialysis.<sup>120</sup>

Special consideration is often given to subgroups of patients. In highly sensitized recipients, recent data suggests that there is no standardized approach to transplantation.<sup>121,122</sup> The requirement for a negative prospective crossmatch in this group has been demonstrated to result in longer waitlist times and inferior outcomes following listing.<sup>123</sup> Decision model analysis favors acceptance of the first organ regardless of sensitization, but this might not be

true of all recipients, some of whom may be able to safely wait for a matched donor.<sup>121</sup> ABO blood group incompatible donors have increased the donor pool for appropriate pediatric recipients with no difference in post-transplant outcomes compared with recipients with an ABO-compatible graft.<sup>124</sup>

## Behavioral science, programmatic, and regulatory influences

Behavioral science and the psychology of decision making provide insights into human behavior and explain why choices often deviate from rational predictions.<sup>125–127</sup>

There are several key concepts in behavioral economics and decision psychology that apply to decision making in transplantation.

### Risk aversion

Centers who are concerned about their outcome statistics may be risk averse and refuse a less than straightforward transplant to avoid risking a transplant mortality, as the impact of a single mortality is greater than the impact of a single additional patient surviving. As an example, if 10 transplants have already been done with 1 death, the survival rate is 90% and mortality rate 10%. If the next transplant is successful, then the survival rate increases from 90% to 91%, but if unsuccessful, the mortality rate rises from 10% to 18%.

### Omission and commission

People tend to rate harmful omissions as less immoral than harmful commissions even when outcome severity, information, and intentions are held constant.<sup>128</sup> Accepting an organ for transplant produces an outcome of commission, whereas declining an organ produces an outcome of omission. Thus, a post-transplant death (harmful commission) is seen as worse than a waitlist death (harmful omission).<sup>129</sup>

### Loss aversion

One further reason to expect omission bias is loss aversion; gains are weighed less heavily than losses of the same magnitude.<sup>130</sup> The action of declining a heart (foregone gain) is weighted less than accepting a heart that leads to post-transplant death (loss).

### Information cascade behavior

Allocation systems have been developed to allow the equitable distribution of organs and so impact decisions to accept an organ. The role of information cascade behaviors provides an example of how approaches are used globally.<sup>128,130</sup> In the US and Spain, providers are able to see the decisions made by the centers that have already been offered a particular donor organ (including their justifications or reasons for making that decision); if 4 previous centers declined a donor

for quality, the fifth center may automatically conclude that the donor quality must be low and decline too. The Spanish National Transplant Organization, however, discourages information cascade behavior. If a Spanish team rejects a heart offer and the following team in the list accepts it, the first team will be demoted to last priority position for the next available donor. This demotion does not occur in the case of an emergency transplant code. Thus, teams are incentivized to comply with the consensus criteria.<sup>131</sup>

### Outcome bias

Good decisions are more likely to lead to good outcomes than bad decisions, and consequently outcomes provide a proxy for decision quality. However, there is a tendency to overweigh the outcome (success or failure) when evaluating a decision.<sup>132</sup> Regulatory bodies and families primarily evaluate the quality of a transplant center based on outcomes rather than the decision process; therefore, they may be overly swayed by occasional bad outcomes despite the decision-making process being valid. Knowing this, transplant centers may be reluctant to risk having a bad outcome and thus be incentivized to take a conservative approach.

### Programmatic factors

Donor decisions may be influenced by center transplant volume, donor call responsibilities, geographic factors, resource availability, and overall risk tolerance. A recent international survey of donor acceptance practices suggested that small volume transplant centers consider the risk of programmatic restrictions more frequently than large centers do when accepting a marginal donor.<sup>125</sup> In fact, listing for transplantation at a low volume center has been associated with inferior waitlist outcomes.<sup>7</sup> Decisions may also be impacted by recent programmatic mortalities. In the same survey, 55% of providers reported that they would be less likely to accept a marginal donor in the face of recent programmatic mortalities.<sup>125</sup> Donor call responsibilities also vary and the criteria used to gauge a potential donor vary depending on provider background (i.e., surgeon vs cardiologist). Some centers have instituted a retrospective review of all donor offers,<sup>15</sup> potentially increasing transparency of donor acceptance practices within a center that may help to offset omission bias that exists. Geography likely plays a significant role in donor acceptance. Geographic location impacts waitlist time,<sup>133,134</sup> competition from other centers,<sup>135</sup> and donor availability<sup>136,137</sup> and may impact IT.

### Center management strategies

A marginal donor is more likely to be accepted for a recipient on ECMO support than for a recipient with better health status.<sup>138</sup> However, centers that utilize ventricular assist device support more frequently or do not bridge to transplant with ECMO may be less inclined to proceed with a marginal donor given the perception of waitlist stability.

## Regulatory oversight

The intended purposes of regulatory oversight include transparency to facilitate informed consumer choices, recognize and emulate excellence, and provide identification and potential remedies for programs with inferior outcomes. As in other areas of medicine, there can be unintended consequences as well. Although these reported outcomes are risk-stratified to attempt to compare centers controlling for patient mix and identify high- and low-performing centers, it is very difficult to account for all risk factors on a truly equitable basis or to accurately stratify the summation risk from a combination of factors. As a consequence, centers may well consider the public relations and potential financial implications of accepting donors that may have inferior post-transplant outcomes. In a recent anonymous survey of pediatric heart transplant specialists, 48% explicitly acknowledge that concerns about regulatory bodies affect their donor decision-making.<sup>122</sup>

## Conclusions and recommendations

1. The most important donor information is the echocardiographic measurement of EF. When normal, most other donor factors become irrelevant.
2. It is reasonable to consider donor hearts when the EF is abnormal and/or with focal segmental wall motion abnormalities, but no strong recommendations can be made. Consideration of other factors may play a role in decision making, including the wishes of the recipient or family.
3. There are notable differences in echocardiographic interpretations between local and transplant center cardiologists, so every effort should be made to allow direct echocardiographic image evaluation by recipient sites.
4. Although some studies have demonstrated comparable outcomes following heart transplantation with donor ischemic times >6 hours, others have demonstrated increased early mortality. Minimizing ischemic time is thus advisable, though the literature does not support a discrete cutoff.
5. There is no evidence to show that using donors with medical comorbidities compromises outcomes. Few donor infections are absolute contraindications to heart transplantation in children.
6. Increasing the acceptability of donor hearts can be achieved by appropriately managing the potential donor, and giving time if necessary for recovery of heart function, to maximize the opportunity for acceptance. Dedicated teams with the necessary knowledge and expertise or training of current ICU teams in donor management can help to achieve this.
7. Instituting a process in each center to retrospectively review donor offers (especially if declined) may help to standardize donor selection and improve consistency of donor acceptance.
8. Potential biases may impact donor acceptance decisions and are predictable by behavioral economics and decision-making psychology. Understanding how allocation systems, regulatory oversight, and programmatic biases influence decision making can improve utilization of potentially viable pediatric donor hearts.
9. It is critical that regulatory bodies understand and consider how human decision-making behavior influences donor acceptance, because improving utilization of pediatric donors requires changes to allocation systems and programmatic oversight.
10. Centers and regulatory authorities should audit potential donor identification, referrals to OPOs, and offers to and refusals by transplant centers to promote and achieve transparency and peer review.

It is clear that being too selective in donor heart utilization results in worse pre-transplant survival and does not necessarily lead to better post-transplant outcomes.<sup>139,140</sup> Therefore, as long as children in need of heart transplant are dying on the waitlist, being removed from the waitlist because of deterioration, or developing morbidity while waiting for transplant, there is an obligation for clinicians, OPOs, administrators, and regulators to do their utmost to minimize the discard of potentially viable organs.

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