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Commentary: Crawling toward heart transplantation and beyond

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CENTRAL MESSAGE

Should we change our expectations in high risk pediatric heart transplantation?

The composition of pediatric patients undergoing heart transplantation evolves over time. Primary transplantation for infants with a diagnosis of hypoplastic left heart syndrome (HLHS) or pulmonary atresia with intact ventricular septum was considered as the best option in the 1990s. With the maturation of the surgical techniques, perioperative management and other factors, surgical palliation is the standard approach, with only a minority of cases being considered for primary transplantation.

However, a subset of this population experiences early failure following surgical palliation.¹ These result in inter-stage mortality or consideration for heart transplantation, whereas some of these patients can accumulate significant morbidity related to suboptimal results from initial the palliation. Prolonged hospital stay and intensive care unit stay, need for ventilatory support, nutritional assistance, acquired infections, and liver and renal dysfunction are some of these comorbidities common to this cohort of patients.^{2,3}

In this issue of the *Journal*, Riggs and colleagues⁴ present their analysis of UNOS data with the idea of presenting incremental risk attributed to comorbidities pretransplantation toward early post-transplantation mortality. They separated the cohort of pediatric transplantations between 2000 and 2017 into those with modifiable risk factors and those with nonmodifiable risk factors. The proposed modifiable risk factors include the need for mechanical ventilation, liver dysfunction, and renal dysfunction, whereas the nonmodifiable factors were age <1 year at the time of listing and a diagnosis of congenital heart disease (CHD). Using regression analysis, they found that the addition of modifiable risk factors to a reference patient of an infant with CHD led to a significant

decrease in post-transplantation survival at 1 year. The addition of mechanical ventilation and renal dysfunction resulted in almost 40% lower survival at 1 year compared with the reference patient. The greatest incremental risk appears to come from concurrent mechanical ventilation and renal dysfunction. They propose using such analyses in setting expectations of post-transplantation outcomes. The authors are to be commended for their attempt to address a significant challenge in decision making for these patients.

These data are similar to those from previously published risk prediction models.^{2,3} For example, in the model presented by Almond and colleagues,³ patients with repaired CHD on mechanical ventilation would have mortality between 19% and 55% depending on the degree of renal and hepatic dysfunction.

These analyses are educating us about the risk factor profiles of patients undergoing heart transplantation in the current era and the impact of these factors on post-transplantation survival. Trends suggest improving survival post-transplantation in patients with CHD with palliated HLHS over the longer term^{5,6}; however, perioperative mortality is an Achilles heel both for high-risk pediatric patients with CHD and for adults with CHD undergoing transplantation. Therefore, as a community, we may ask ourselves 2 questions: are we allowing the risk factors to accumulate before listing?, and are some patients just too high risk for transplantation? Patients with CHD who are considered for transplantation during infancy (the reference group) have by default experienced early failure of surgical palliation. Clinical observations will demonstrate that this group shows a slow and steady decline with obvious heart failure symptoms along with nutritional, respiratory, and renal decline. Recognition of this group of patients early in the process may potentially allow for earlier listing before comorbidities add up. Early consideration may modify some of this risk.

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The authors raise the issue of ventricular assist device (VAD) use in modification of the renal dysfunction and liver dysfunction in listed patients. However, these data are mainly for patients with cardiomyopathy and not necessarily for the highest-risk patients, such as infants with CHD. As the experience with VAD matures, this may change over time, particularly at large-volume centers. For patients with significant renal or hepatic dysfunction, the results of dual-organ transplantation may be superior to heart-only transplantation and merit increasing consideration. This analysis does not address perioperative and other transplantation-related factors that have shown to impact early mortality, such as graft selection, preservation, and bypass time, which are potentially modifiable risk factors.

Finally, considering the second question of when the risk is too high, as a community, should persistence in the face of such sobering results be the proper approach? As Riggs and colleagues suggest, some of these analyses should naturally be factored in during discussions with the families for listing. Taking an “informed risk” may be acceptable to

go along with the current UNOS listing status strategy of prioritizing patients at highest risk for waitlist mortality.

We congratulate and thank the authors for their important contribution.

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Commentary: Providing a “leg up” for those who “limp” to heart transplantation

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In this issue of the *Journal*, Riggs and colleagues² sought to quantify known risk factors associated with short-term mortality after pediatric heart transplantation (HTx). Their specific focus was on modifiable risk factors (MRFs) that

The growth of pediatric heart transplantation over the last 33 years is indicative of the need for evolving clinical care.¹

CENTRAL MESSAGE

Survival after pediatric heart transplantation is significantly influenced by preoperative modifiable risk factors. Identifying the impact of these factors will help guide management and resource utilization for these children.

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