Minimizing the Risk of Severe Primary Graft Dysfunction in Infant Heart Transplant Recipients: Time for a Paradigm Shift

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Infants undergoing heart transplantation have the highest risk of early mortality compared with all other pediatric age groups.1 Despite this, those who survive the first posttransplant year demonstrate the best long-term survival. Therefore, developing strategies to improve pretransplant support, donor optimization and selection, and posttransplant management in this age group is critically important to minimize the risk of early mortality. One important cause of early mortality in infant heart transplant recipients is severe primary graft dysfunction, a potentially devastating posttransplant complication that is more common in this population.1–5

In this issue of the Journal of the American Heart Association (JAHA), Singh et al examined risk factors for severe primary graft dysfunction in infant heart transplant recipients, defined as requiring extracorporeal membrane oxygenation support within 2 days of transplantation.6 Although the Organ Procurement and Transplantation Network database does not collect data pertaining to posttransplant use of extracorporeal membrane oxygenation, the authors leveraged a unique linkage with the ELSO (Extracorporeal Life Support Organization) registry, providing a highly novel and robust method to achieve their study aims. The authors demonstrate that despite evolution in management strategies over time, the incidence of severe primary graft dysfunction has not changed over the 20-year timeframe included in their analysis. Importantly, the authors highlight a number of risk factors independently associated with the development of severe primary graft dysfunction including a diagnosis of congenital heart disease, extracorporeal membrane oxygenation or biventricular mechanical support at the time of transplantation, use of an undersized donor, and a donor ischemic time >4 hours. Notably, support with a left ventricular assist device was not associated with an increased risk of severe primary graft dysfunction and in fact appeared to have a protective effect in patients with congenital heart disease.

Use of ventricular assist devices has been shown to mitigate pretransplant risk in patients with congenital heart disease. In a study by Bryant and colleagues, posttransplant survival was no different in those with congenital heart disease supported with a ventricular assist device as compared to patients with and without congenital heart disease not requiring ventricular assist device support.7 The results of the analysis by Singh et al suggests that ventricular assist device support may also help to mitigate risk in infants with congenital heart disease, representing a potential strategy to reduce the incidence of severe primary graft dysfunction.8 However, there are notable challenges associated with ventricular assist device support in the infant population. In the landmark paper by Almond and Morales et al, lower recipient weight was independently associated with early mortality following placement of a Berlin

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In prior studies, patients with severe primary graft dysfunction demonstrated acceptable long-term survival, contingent upon survival to hospital discharge. In contrast, the impact of severe primary graft dysfunction on posttransplant survival in the infant population appears distinct. The analysis by Singh et al demonstrates continued attrition of patients who experienced severe primary graft dysfunction well beyond the early posttransplant period. This finding underscores the importance of preventing primary graft dysfunction in the infant population, as it not only influences early posttransplant outcomes but has implications for long-term patient survival.

The findings of Singh and colleagues provides a critical foundation to help advance our understanding of severe primary graft dysfunction in infant heart transplant recipients. Developing strategies to mitigate the risk of early mortality attributable to primary graft dysfunction has significant implications for both short- and long-term patient survival and would represent an important step forward in pediatric heart transplantation.

Heart EXCOR ventricular assist device. Morrability was also significant in this cohort, with nearly 1 in 3 patients experiencing a neurologic event and 44% with a major bleeding event. Fortunately, with increasing use of direct thrombin inhibitors, the safety profile of ventricular assist device support in the pediatric population has greatly improved. These advances are largely attributable to focused efforts from the Advanced Cardiac Therapies Improving Outcomes Network, which provides a learning health system to promote collaboration and accelerate progress in the care of children with advanced heart failure. In light of these recent advances, it may be time for a paradigm shift whereby the benefits of ventricular assist device support in the infant population outweigh the risks. This holds especially true in infants with congenital heart disease as increased use of left ventricular assist devices may help to reduce the risk of severe primary graft dysfunction.

The results of this analysis have significant implications for the selection of donors in infant heart transplant candidates. Singh and colleagues effectively demonstrate the additive effect of multiple risk factors in the development of severe primary graft dysfunction. Although some risk factors are not modifiable, careful consideration to avoid an undersized donor or donors with an anticipated prolonged ischemic time in recipients with existing risk factors may be important to minimize the risk of severe primary graft dysfunction. However, these factors must be weighed with the knowledge that the limited number of infant donor hearts may preclude declining an otherwise acceptable heart based on these factors in a critically ill infant awaiting transplantation.

ARTICLE INFORMATION

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Disclosures
None.

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