Identifiable Risk Factors and Miscalculations During Listing for Pediatric Heart Transplantation

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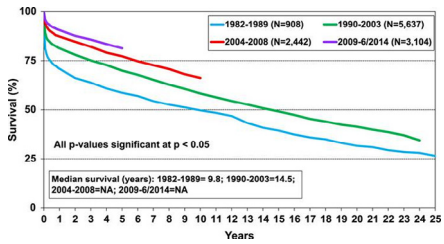
The objective of this study is to describe identifiable risk factors, complications, and pitfalls while listing pediatric patients for heart transplantation, which is the standard of care for end-stage heart disease in children. Since the introduction of cyclosporine in the 1980s, the management in pediatric heart transplantation has shown consistent improvement, mainly because of technological advances and the integration of multidisciplinary teams in the field. However, the complexity of this patient population makes medical providers vulnerable to complications as a result of undesirable mistakes. Transplant survival is impacted negatively when mistakes from health-care providers compound the high-risk status of the patient. The identification of multiple risk factors and undesirable miscalculations may help transplant teams make decisions before allocating organs, intervene or minimize morbidity, and provide the best quality of life to recipients.

Keywords: listing, heart failure, pediatric heart transplant, high-risk factors and mistakes

Introduction

Pediatric heart transplantation (PHT) is a therapeutic option for those with end-stage heart failure. Since Dr. Kantrowitz performed the first pediatric heart transplant in 1967, enormous strides have been made in surgical approach, organ preservation, and immunosuppressive management; yet, pitfalls to heart transplantation (HT) remain.[1] Contemporary 1- and 3-year pediatric survivals exceed 90% and 80%, respectively (Fig).[2] Common preventable mistakes that can influence outcomes include patient selection, organ allocation, and judgment errors in listing too early (especially in the case of reversible causes of heart failure) or too late (after the disease process has progressed to systemic or pulmonary involvement).

Since the initial transplants in 1967, over 10,000 transplants have been performed in patients <18 years of age around the world, with the greatest numbers being from North America and Europe.[3] The experience gathered over the past decades in this field has been instrumental for the process of listing candidates and the management of transplanted patients. Clinical and surgical advances by the pediatric heart transplant community have increased the survival rate considerably. Despite this tremendous progress, optimal outcomes have not yet been achieved and the field continues to be challenged by preventable mistakes, shortage of organ donors, the lack of balanced immunology therapies, and pre- and post-transplant complications.



Kaplan-Meier survival by era.

Central Message

The identification of undesirable risk factors may help transplant teams minimize morbidity and improve the quality of life of recipients.

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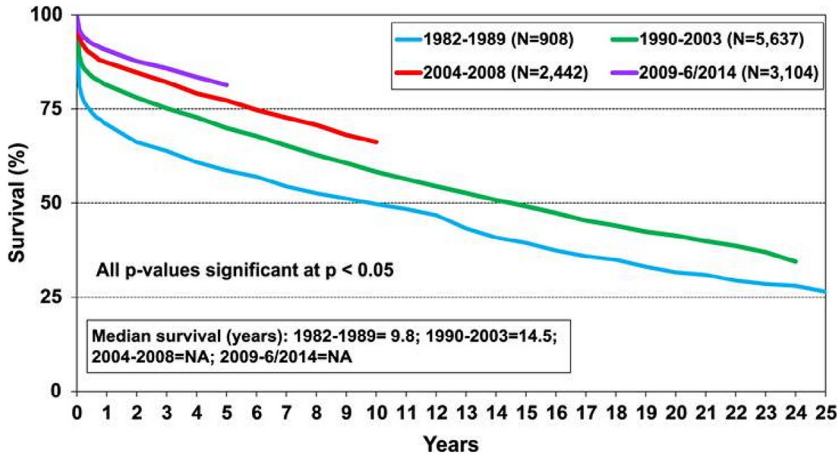

Figure Kaplan-Meier survival by era (transplants: January 1982-June 2014).[2] (Color version of figure is available online.)

Patient Selection

After a patient is considered for transplantation, a series of comprehensive assessments by multiple disciplines allow medical providers to evaluate for suitability. First, a complete collection of the patient's medical records should be available to the transplant team. Second, a thorough physical examination is necessary not only to delineate end-stage heart failure, but also to identify any potential contraindications to transplantation including active infections or manifestations of systemic diseases that may impact the recipient's life expectancy.[4] Oncologic disorders should be analyzed individually. Transplantation in the context of a history of a known cancer diagnosis may be justified particularly if the interval between diagnosis of malignancy and evaluation for listing for transplantation exceeds 5 years.[5] A complete cardiac catheterization should be obtained, especially in those with congenital heart disease (CHD) or who are suspected to have elevated pulmonary vascular resistance (PVR). For individuals with more complex anatomical anomalies, a cardiac magnetic resonance or computed tomography angiography can be more informative. Historically, an indexed PVR (PVRi) greater than 6 Wood units has been considered a major contraindication for transplant when the pulmonary vascular bed is nonreactive to medical therapy.[6] This concept is even more important in patients with single ventricle physiology, in whom the accuracy of obtaining PVRi is challenging. The risk involved in underestimation of PVRi is the potential of right heart failure in the post-transplant period.[7] Annual right heart catheterization is advised until transplantation, especially when there is a concern for PVRi. Evaluation of end-organ damage should be routinely assessed in all patients as immunosuppressant medications can adversely manifest renal and hepatic toxicity, representing an avoidable risk factor when addressed early. If significant hepatic or renal dysfunction is present, combined organ transplant may be considered, dependent upon the expertise and level of coordination of multiple transplant teams at that particular institution.[8] The inclusion of the evaluation of infectious disease allows identification of the presence of dormant or active viral, bacterial, or parasitic infections, which could be reactivated or disseminated when immunosuppressive therapy is initiated. The use of antiviral medications should be contemplated as prophylactic and therapeutic methods to avoid viral inflammatory reactions causing graft failure or death.[9]

Cardiac transplantation in patients with preformed antibodies against human leukocyte antigens (HLAs) can be problematic. HLA sensitization is associated with cellular and antibody-mediated rejection, increasing patient morbidity and mortality.[10] A common measure of sensitization is the use of the panel reactive antibody (PRA). When elevated to a level greater than or equal to 10%, patients are considered at higher risk for post-transplant rejection and mortality when compared with nonsensitized recipients.[11] Hence, it is important for the transplant team to be aware of those situations prone to develop anti-HLA antibodies. Risks include transfusion of blood products (especially platelets), the presence of cryopreserved tissue valves or allograft conduits, the use of mechanical circulatory support, and history of previous organ transplants.[11] The management of sensitized patients remains controversial but as immunosuppression strategies for PHT evolve, more aggressive protocols should be implemented to expand donor organ usage.[11]

Candidates for transplantation may die on the wait list due to problems with a limited organ donor pool. HLA sensitization places further restrictions on this limited donor pool, with higher wait list mortality for those with unacceptable antigens listed as "donor avoids." Thus, knowledge of HLA sensitization and how antibodies cause damage have important implications to a transplant center's approach to organ acceptance. One commonly used test to detect for antibodies utilizes individual beads coated with single HLA antigens. The single antigen bead assay (SAB) is more sensitive and specific for antibody detection compared with previous methodologies.[12] The evolution in SAB technology includes specific detection of antibodies capable of binding the first component of complement (C1q).[13] Utilization of the C1q SAB assay may allow for acceptance of a wider range of potential organ donors and reduce wait list mortality.[14,15]

Behavioral and psychosocial assessments are commonly employed to evaluate for stressors in patients and caregivers and identify individuals who may require additional surveillance and support. Patient and family compliance following organ transplantation can be limiting factors for long-term outcome, especially among teenagers.[16,17] The complexity of high-risk behaviors and