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Ventricular Assist Device Support as a Bridge to Transplantation in Pediatric Patients

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ABSTRACT

BACKGROUND Pediatric ventricular assist device (VAD) use has evolved dramatically over the last 2 decades.

OBJECTIVES This study sought to describe the evolution of VAD support to heart transplantation (HTx) in children in a large international multicenter cohort.

METHODS Using data from the Pediatric Heart Transplant Study, comparisons were made between children (<18 years) supported to HTx (January 1, 1993 to December 31, 2015) with VAD or extracorporeal membrane oxygenation (ECMO) to VAD support.

RESULTS Of 7,135 listed patients, 5,145 underwent HTx; 995 (19.3%) were supported by a VAD (113 with congenital heart disease [CHD]). Patients with a VAD as their first device (n = 821) were older, larger, and more likely to have cardiomyopathy (80%) than patients transitioned from ECMO to VAD (n = 164). In the VAD-only cohort, 79% underwent HTx and 14% died, compared with 69% and 24% in the ECMO-to-VAD cohort, respectively. Patients with cardiomyopathy achieved HTx 84% of the time, with a 9% waitlist mortality rate compared with 55% and 36%, respectively, for CHD. Among VAD-treated patients, 79% were age >10 years in the earliest era, a percentage decreasing to 34% more recently, though neonates still represent <1%. Overall, survival at 2 and 20 years showed no difference between VAD and no support (2 years: 75% vs. 80%; 20 years: 55% vs. 54%). Post-HTx outcomes were better for durable versus temporary VADs ($p < 0.01$) and for continuous versus pulsatile VADs ($p < 0.01$) from 2005 onward; timing of VAD had no impact on post-HTx survival ($p = 0.65$).

CONCLUSIONS For one-quarter of a century, major advances have occurred in mechanical support technology for children, thereby expanding the capability to bridge to HTx without compromising post-HTx outcomes. Significant challenges remain, especially for neonates and patients with CHD, but ongoing innovation portends improved methods of support during the next decade. (J Am Coll Cardiol 2018;72:402–15) © 2018 by the American College of Cardiology Foundation.

The clinical course and management of pediatric patients with advanced heart failure have become increasingly complex. The evolution of mechanical support options has opened a myriad of potential paths including temporary versus durable support and bridge to decision, recovery, or transplantation. Complex clinical trajectories allow for crossover among these options

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and make assessment of overall outcomes even more challenging.

Ventricular assist devices (VADs) as a means of mechanical circulatory support in pediatric patients became available in the 1990s (1) but it was not until the Berlin Heart Excor (Berlin Heart, Berlin, Germany) became more widely available in 2005 that VAD support became common, particularly among infants and small children (2,3). Blume et al. (4) reported the early pediatric VAD experience in North America in 99 patients who were supported for a mean of 57 days, with 77% undergoing transplantation. This percentage increased to 86% in the latter era of the study. Investigators in the United Kingdom analyzed 102 patients receiving support with the Excor and reported an 84% survival to transplantation or explantation rate (5).

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The use of VAD as a bridge to transplantation in pediatric patients has continued to increase, with approximately one-third of pediatric patients currently undergoing heart transplantation from VAD support (6). Given the significant morbidity, mortality, resource implications, and gap between donor organ availability and demand, documentation of the spectrum of the use, impact, and relevant outcomes of VADs has become even more crucial. Single-center reports are small in numbers and limited in experience (7–11). The Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS) has been enrolling patients since 2012 and promises to be an important source of data moving forward, but it remains limited to pre-transplantation outcomes in durable VADs (12).

We sought to describe the changing spectrum of VAD use in pediatric heart transplantation candidates, the resultant complex clinical trajectories of patients with end-stage heart failure, and a comparison of post-transplantation outcomes among patients managed pre-transplantation with and without VAD therapy in the largest international multicenter cohort reported to date.

METHODS

PATIENT GROUP AND DATA COLLECTION. This study used data from the PHTS (Pediatric Heart Transplant Study) database, an event-driven, multicenter, prospective registry of children <18 years of age who were listed for primary heart transplantation from 48 pediatric heart transplantation centers in North America, the United Kingdom, and Brazil (Online Table 1). PHTS data collection and management have been described previously; because it is an event-driven database, forms are submitted at the time of listing and then transplantation, death, or removal from the waitlist. If none of these events occur, an annual post-listing follow-up form is submitted (13). Institutional Review Board approval was obtained at the transplantation centers and the data analysis and coordinating center. The study group included all patients who were listed for heart transplantation between January 1, 1993, and December 31, 2015. The first recorded VAD implantation in the registry was on March 28, 1993 (Bio-Medicus BiVAD, Medtronic Bio-Medicus, Inc., Eden Prairie, Minnesota). VADs were classified into 2 types, temporary or durable, as listed in Table 1. Comparisons were made with all patients in the registry who did not have VAD support at any time while listed. Data were analyzed in 3 eras: 1993 to 2004, 2005 to 2009, and 2010 to 2015. Data collected included demographics, United Network for Organ Sharing (UNOS) status at listing, support at listing (intravenous inotropes, ventilator, prostaglandin, extracorporeal membrane oxygenation [ECMO], VAD), timing of ECMO support or VAD placement post-listing, death while waiting, delisting, indications for removal from wait list, transplantation, UNOS status at transplantation, support at time of transplantation (e.g., ECMO, VAD), date of most recent follow-up, death post-transplantation, and cause of death.

STATISTICAL METHODS. Patients who received VAD support at some point while waiting were compared with patients who did not require mechanical support between listing and transplantation. Means and standard deviations were calculated for continuous variables and compared by analysis of variance. Categorical variables were compared using chi-square tests. Alpha was set at 0.05 for significance. For time-related analyses, time 0 was set time of listing for patients who did not receive mechanical circulatory support and at time of first mechanical support for patients receiving ECMO or VAD support. All patients started with time 0 in the listed patients group and were censored at initiation of ECMO or VAD support. Competing-outcomes methods were used to analyze outcome after listing. Standard Kaplan-Meier depictions were generated for survival after transplantation with the log-rank test to compare overall survival between groups.

RESULTS

OVERALL PATIENT GROUP. Patient demographics and clinical characteristics at listing and

ABBREVIATIONS AND ACRONYMS

BiVAD = biventricular VAD

ECMO = extracorporeal membrane oxygenation

LVAD = left ventricular assist device

MCSD = mechanical circulatory support device

PediMACS = Pediatric Interagency Registry for Mechanical Circulatory Support

RVAD = right ventricular assist device

UNOS = United Network for Organ Sharing

VAD = ventricular assist device