Transplant Outcomes for Congenital Heart Disease Patients Bridged With a Ventricular Assist Device

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Background. **Ventricular assist device (VAD) use as a bridge to transplant (BTT) for children with end-stage heart failure and congenital heart disease (CHD), although challenging, has increased, but its effect on posttransplant outcome is unknown. This study describes posttransplant outcomes of CHD patients BTT with a VAD.**

Methods. **All heart transplant recipients identified in United Network of Organ Sharing database from 2006 to 2015 (n = 21,865) were divided into four groups by those with (+) and without (–) a diagnosis of CHD and with (+) and without (–) VAD support at transplant: +CHD/+VAD, +CHD/–VAD, +VAD/–CHD, and –VAD/–CHD. Posttransplant survival of +CHD/+VAD was compared with +CHD/–VAD, –CHD/+VAD, and –CHD/–VAD in addition to pretransplant characteristics comparison between +CHD/+VAD and +CHD/–VAD.**

Results. **Of 1,871 patients (8.6%) with CHD, 1,348 (72%) were younger than 18 years old, and 143 (7.6%) were BTT with a VAD (+CHD/+VAD). At transplant, +CHD/+VAD compared with +CHD/–VAD were more likely to have worse functional status (<50%: 60% vs 46%, $p = 0.004$), infections (29% vs 14%, $p < 0.001$), to be sensitized (47% vs 30%, $p < 0.001$) and on ventilator support (20% vs 13%, $p = 0.029$) and dialysis (13% vs 2.5%, $p < 0.001$). Overall, 1-year (84% vs 87%) and 5-year (72% vs 75%) survival was similar for +CHD/+VAD and +CHD/–VAD ($p = 0.694$). Survival was also similar when +CHD/+VAD were compared with –CHD/+VAD (n = 7,363; $p = 0.529$) and –CHD/–VAD (n = 12,613; $p = 0.097$).**

Conclusions. **Although more ill pretransplant, CHD patients BTT with a VAD have similar posttransplant survival compared with CHD patients without a VAD and with other non–CHD heart transplant patients. VAD support may mitigate certain risk factors for poor posttransplant outcomes in the challenging CHD cohort.**

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The use of ventricular assist devices (VADs) as a bridge to cardiac transplantation in pediatric patients has become an established therapy with excellent outcomes [1]. Initially, adult devices were selectively applied to appropriate pediatric patients until a pediatric-specific device was developed [2, 3]. As more centers gain experience with the Berlin Heart EXCOR VAD (Berlin Heart Inc, The Woodlands, Texas), the range of pediatric patients that can be supported has greatly expanded [4]. This device, along with adult devices, and the development of the total artificial heart, have given heart failure clinicians a much broader array of technology to treat pediatric patients with end-stage cardiac disease than even 10 years ago [5]. Compared with the historical use of extracorporeal membrane oxygenation, the EXCOR device has proven to be a far superior and efficacious modality for bridging pediatric patients to a heart transplant, although its morbidity profile is higher than that seen in adult durable continuous-flow VADs [6].

Multiple reports have shown that pediatric patients with end-stage congenital heart disease (CHD) are a higher-risk population for cardiac transplantation [7]. Michielon and colleagues [8], for example, showed a 1-year posttransplant survival of 77% in Fontan patients undergoing heart transplantation compared with a 1-year survival of 91% if recipients had a non–CHD diagnosis [8]. From 2009 to 2015, CHD patients accounted for 37% of all pediatric heart transplants. Yet only 16% of CHD patients who had a heart transplant were bridged with a

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Abbreviations and Acronyms

BTT	=	bridged to transplant
CHD	=	congenital heart disease
+CHD/+VAD	=	congenital heart disease cardiac transplant recipients bridged to transplant with a ventricular assist device
+CHD/–VAD	=	congenital heart disease cardiac transplant recipients without a ventricular assist device
–CHD/+VAD	=	noncongenital heart disease cardiac transplant recipients bridged to transplant with a ventricular assist device
–CHD/–VAD	=	noncongenital heart disease cardiac transplant recipients without a ventricular assist device
GFR	=	glomerular filtration rate
HTx	=	heart transplant/transplantation
INTERMACS	=	Interagency Registry for Mechanically Assisted Circulatory Support
PRA	=	panel reactive antibodies
UNOS	=	United Network for Organ Sharing
VAD	=	ventricular assist device

VAD compared with non–CHD patients, of whom more than 40% were bridged to transplant with a VAD [9]. When assessing pediatric patients of all diagnoses bridged with a VAD to cardiac transplant, their overall survival was similar to patients undergoing a transplant without a VAD [9]. However, whether this is true for those with CHD bridged to transplant with a VAD is unknown. The purpose of this study was to assess the posttransplant outcomes of pediatric patients with CHD disease who are bridged to cardiac transplantation with VADs.

Patients and Methods

Data Source

The Standard Transplant Analysis and Research data set, from the United Network for Organ Sharing (UNOS) database, was used in this study. This data set contains records of all transplants performed in the United States. UNOS is a private, nonprofit organization that is responsible for managing the transplant system of the United States under a federal contract.

Study Population

All heart transplant patients, listed and who received a transplant from January 1, 2006, to June 30, 2015, were identified and divided into two groups based on the presence (+) or absence (–) of CHD as the primary diagnosis for transplant. From the two cohorts that received a transplant, four subgroups were created based on being bridged to transplant with or without a ventricular assist device (VAD):

- +CHD patients bridged to transplant with a VAD: +CHD/+VAD
- +CHD patients without a VAD: +CHD/–VAD
- –CHD patients bridged to transplant with a VAD: –CHD/+VAD
- –CHD patients without a VAD: –CHD/–VAD

The primary study end point of the study was posttransplant survival. Secondary end points included freedom from retransplantation, rejection events, and posttransplant dialysis or stroke. For the primary study groups (+CHD/+VAD, +CHD/–VAD), patient baseline characteristics and posttransplant outcomes were compared. Risk factors associated with 1-year and overall mortality were also analyzed for the primary study population, +CHD. Posttransplant survival between +CHD/+VAD and +CHD/–VAD was also compared. A matched cohort was created by propensity score analysis (ratio 1:1) based on factors at the time of transplant that are known to affect transplant outcomes: age, transplant year, ventilator support, higher total bilirubin (>1.2 mg/dL), and poor renal function (glomerular filtration rate <60 mL · min^{-1} · 1.73 m^{-2}). Five +CHD/+VAD patients were removed during propensity score matching process due to missing data for one or more variables needed for matching. A cohort of high-risk recipients was also created. High-risk recipients were defined as patients who, at the time of transplant, had a clinical infection, ventilator support, dialysis support, or panel reactive antibodies exceeding 10%.

Posttransplant survival comparison between +CHD/+VAD and +CHD/–VAD was performed for matched and high-risk recipient cohorts, and posttransplant survival of +CHD/+VAD was compared with the subgroups –CHD/+VAD and –CHD/–VAD. The outcome of CHD patients on the waiting list who did not undergo cardiac transplantation was also assessed.

Statistical Analysis

Summary statistics are presented as medians (interquartile ranges) and counts (percentages). Characteristics and outcomes at listing, at the time of transplant, and after transplant were analyzed using the Student *t* test for normally distributed continuous data, the Mann-Whitney *U* test for skewed continuous data, and the χ^2 test for categoric data, where appropriate. Posttransplant survival curves were calculated by the Kaplan-Meier method, and the log-rank test was used to determine the equality of curves. Multivariate analysis was performed to determine risk factors that were independently associated with mortality. Variables for the model were selected based on clinical significance for affecting 1-year or overall mortality. Logistic regression was performed to determine risk factors associated with 1-year mortality. The Cox proportional hazard model was used to determine risk factors associated with overall mortality. Data analysis was performed with IBM SPSS 24 software (IBM, Armonk, NY), and propensity score matching was performed with IBM SPSS 24 PS matching extension with R 3.2.1 software (The R Foundation for Statistical Computing, Vienna, Austria).