Modern Outcomes of Mechanical Circulatory Support as a Bridge to Pediatric Heart Transplantation

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Background. **Pediatric patients awaiting orthotopic heart transplantation frequently require bridge to transplantation (BTT) with mechanical circulatory support. Posttransplant survival outcomes and predictors of mortality have not been thoroughly described in the modern era using a large-scale analysis.**

Methods. **The United Network for Organ Sharing database was reviewed to identify pediatric heart transplant recipients from 2005 through 2012. Patients were stratified into three groups: extracorporeal membrane oxygenation (ECMO), ventricular assist device (VAD), and direct transplantation (DTXP). The primary outcome was posttransplant survival.**

Results. **Two thousand seven hundred seventy-seven pediatric patients underwent orthotopic heart transplantation. There were 617 patients who required BTT with mechanical circulatory support (22.2%), of whom there were 428 VAD BTT (69.4%) and 189 ECMO BTT (30.6%). An increase in VAD use was observed during the study period ($p < 0.0001$). Compared with DTXP, patients in the ECMO BTT group had a lower median age (<1 versus 5 years; $p < 0.0001$) and were significantly smaller (8 versus 14 kg; $p < 0.001$), whereas patients in the VAD BTT group were older (8 versus 5 years; $p = 0.0002$) and larger (24 versus 14 kg; $p < 0.001$). Actuarial survival was greater in the DTXP group compared with ECMO BTT, but similar to VAD BTT at 30 days and 1, 3, and 5 years. However, this survival difference was lost after censoring the first 4 months after transplant. In multivariable analysis, when restricted to the first 4 months of survival, independent predictors for mortality were ECMO BTT, age, diagnosis, and functional status, whereas VAD BTT was not.**

Conclusions. **Pediatric patients with DTXP or VAD BTT have equivalent posttransplant survival. However, those requiring ECMO BTT have inferior early posttransplant survival compared with those receiving DTXP.**

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Heart transplantation remains the definitive, gold standard treatment for pediatric patients with end-stage heart failure. Because of the scarcity of available donor organs, in conjunction with a growing number of children diagnosed with end-stage heart failure, the list of pediatric patients awaiting heart transplantation continues to grow, and the waiting list mortality remains the highest of any group in need of solid organ transplantation [1, 2].

To achieve survival to heart transplantation, the use of mechanical circulatory support (MCS) is often required in a bridge to transplantation (BTT) strategy. Patients may be bridged using ventricular assist devices (VADs) or extracorporeal membrane oxygenation (ECMO) [3]. Several large single-center [4–6] and multicenter [7–9] studies, as well as a prospective randomized controlled trial [10], have reported their experience using MCS as a BTT. However, the impact of MCS as a BTT on posttransplant survival has not been thoroughly examined. The primary aim of this study was to estimate differences in posttransplant survival of pediatric patients requiring MCS as a BTT in the modern era compared with patients who underwent direct transplantation (DTXP).

Patients and Methods

The United Network for Organ Sharing (UNOS) database was queried to identify pediatric cardiac transplant patients (≤18 years of age) between January 1, 2005, and December 31, 2012. Patients were categorized as either DXTP or MCS as a bridge to transplant with extracorporeal membrane oxygenation (ECMO BTT) or with a ventricular assist device (VAD BTT). Additionally, we performed a secondary analysis with a fourth level of exposure for patients who were initially placed on ECMO before undergoing a VAD implantation during the listing period ("bridge to VAD"). These patients were identified

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Abbreviations and Acronyms

BTT = bridge to transplantation
CI = confidence interval
DTXP = direct transplantation
ECMO = extracorporeal membrane oxygenation
HR = hazard ratio
MCS = mechanical circulatory support
UNOS = United Network for Organ Sharing
VAD = ventricular assist device

in the UNOS registry as those requiring ECMO support at "time of listing" but VAD support at "time of transplant."

Variables were first investigated for frequency, distribution, and amount of missing data. The primary exposure variable was defined as one of three levels of BTT: DXTP, VAD, or ECMO. The primary outcome variable was 5-year survival. All potential confounders were selected a priori and investigated using a three-step process. First, the crude association between BTT type and survival was estimated. Stratified analyses were then run adjusting for one additional covariate entered as a categorical variable (diagnosis, medical condition at transplant, functional status at transplant based on the Lansky score [11], and age in years). Variables that changed the crude hazard ratio (HR) by more than 10% were considered potential confounders and further investigated in multivariable Cox models. Kaplan-Meier analysis and Cox proportional hazards regression were used for time-to-event analysis. Multivariable Cox models were built by including all potential confounders and then removing one variable at a time and comparing the Akaike's information criterion for nested models. The final model with the best fit was then tested for violations of the proportionality assumption using martingale

Table 1. Baseline Characteristics of Pediatric Heart Transplant Recipients[a]

Characteristic	DTXP (n = 2,160)	ECMO (n = 189)	VAD (n = 428)	*p* Value
Age, y (median and IQR)	5 (0–13)	0 (0–6)	8 (1–14)	<0.0001[b]
Weight, kg (median and IQR)	14 (7–43)	8 (4–21)	24 (11–52)	<0.0001[b]
Female	1007 (47)	85 (45)	191 (45)	0.71[c]
Diagnosis				
Congenital defect, s/p surgery	729 (34)	83 (44)	64 (15)	<0.0001[c]
Idiopathic DCM	514 (24)	32 (17)	200 (47)	
Idiopathic restrictive cardiomyopathy	112 (5)	6 (3)	6 (1)	
DCM s/p myocarditis	49 (2)	12 (6)	42 (10)	
HLHS	74 (3)	7 (4)	1 (<1)	
Other	682 (32)	49 (26)	115 (27)	
Days on waitlist (median and IQR)	46 (16–106)	13 (6–36)	52 (23–102)	<0.0001[b]
Medical condition at transplant				
ICU	951 (44)	173 (92)	317 (74)	<0.0001[c]
Hospitalized, non-ICU	387 (18)	8 (4)	78 (18)	
Not hospitalized	822 (38)	8 (4)	33 (8)	
Previous heart transplant	166 (8)	14 (7)	7 (2)	<0.0001[c]
Functional status at transplant				
10%	98 (5)	46 (24)	72 (17)	<0.0001[c]
20%	60 (3)	4 (2)	24 (6)	
30%	65 (3)	2 (1)	29 (7)	
40%	199 (9)	7 (4)	59 (14)	
50%	124 (6)	1 (1)	23 (5)	
60%	253 (12)	7 (4)	52 (12)	
70%	137 (6)	2 (1)	22 (5)	
80%	175 (8)	3 (2)	29 (7)	
90%	165 (8)	7 (4)	20 (5)	
100%	145 (7)	3 (2)	15 (4)	
N/A (<1 year old)	638 (30)	98 (52)	64 (15)	
Unknown	101 (5)	9 (5)	19 (4)	
Ischemic time (median and IQR) (hours)	3.5 (3–4)	3.8 (3–4)	3.4 (3–4)	0.005[b]

[a] Data are number of patients (%) unless indicated. [b] *p* value by one-way median analysis. [c] *p* value by χ^2 test.

DCM = dilated cardiomyopathy; DTXP = direct transplantation; ECMO = extracorporeal membrane oxygenation; HLHS = hypoplastic left heart syndrome; ICU = intensive care unit; IQR = interquartile range; N/A = not available; s/p = status post; VAD = ventricular assist device.