Brief Report

Outcomes of Adult Patients With Congenital Heart Disease After Heart Transplantation: Impact of Disease Type, Previous Thoracic Surgeries, and Bystander Organ Dysfunction

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ABSTRACT

Background: Adults with congenital heart disease (CHD) are at increased risk for adverse outcomes after heart transplantation (HT). However, small cohorts have constrained the identification of factors associated with poor prognosis. We hypothesized that number of sternotomies and bystander organ dysfunction would be associated with an increased risk for early death after HT.

Methods and Results: We performed a retrospective observational study of all adult CHD patients who underwent HT at our institution from January 1997 to January 2014. Forty-eight adult CHD patients were followed for a mean of 5 years. Diagnoses included tetralogy of Fallot/pulmonary atresia/double-outlet right ventricle in 15 (31%), D-transposition of the great arteries (TGA) in 10 (21%), tricuspid atresia/double-inlet left ventricle in 9 (19%), ventricular or atrial septal defect in 4 (8%), heterotaxy in 3 (6%), congenitally corrected TGA in 2 (4%), and other diagnoses in 5 (10%). Survival at both 1 and 5 years was 77%. According to multivariate analysis, ≥3 sternotomies (hazard ratio [HR] 8.5; $P = .02$) and Model for End-Stage Liver Disease Excluding International Normalized Ratio (MELD-XI) score >18 (HR 6.2; $P = .01$) were significant predictors of mortality. Failed Fontan surgery was not a significant predictor of death ($P = .19$).

Conclusions: In our cohort of adult CHD patients undergoing HT, ≥3 sternotomies and MELD-XI score >18 were significantly associated with death. These findings may be important in patient selection and decision regarding tolerable number of CHD surgeries before considering HT. (*J Cardiac Fail 2016;22:578−582*)

Key Words: Congenital heart disease, heart transplantation, mortality.

Survival of adult patients with congenital heart disease (CHD) continues to increase secondary to improvements in medical and surgical care.[1] With increasing survival, it is estimated that up to 10%−20% of adult CHD patients will ultimately require heart transplantation (HT) for improved quality of life and longevity.[2−4] However, patient-specific risk factors for early mortality remain poorly defined.[5,6]

Increasingly, the Model for End-Stage Liver Disease Excluding International Normalized Ratio (MELD-XI) score has been used to quantify bystander organ dysfunction to predict outcomes in the general HT population and specifically in adult CHD patients listed for HT.[7,8] To aid in defining a methodology for patient selection, we sought to identify patient-specific risk factors for early mortality in adult CHD patients after HT, including number of earlier sternotomies and degree of bystander organ dysfunction as quantified with the use of the MELD-XI score.

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Methods

Study Population

We performed a retrospective observational study of all patients aged ≥18 years with CHD who underwent HT at Columbia University Medical Center (CUMC) from January 1997 to January 2014. Approval from the CUMC Institutional Review Board was obtained before data acquisition. Patient and survival data were extracted from medical records, the United Network from Organ Sharing (UNOS) database, and an institution-specific database.

Risk Factors

Variables of interest were defined before data collection. These included patient diagnosis, age at HT, earlier surgeries, number of sternotomies, systemic right ventricle, significant thoracic collateral circulation, recurrent arrhythmias, and a composite of hepatic and renal dysfunction, measured by means of the MELD-XI score. MELD-XI was calculated as $5.11 \times \ln(\text{total bilirubin}) + 11.76 \times \ln(\text{creatinine}) + 9.44$, where total bilirubin and creatinine are equal to 1 if the raw laboratory values are <1.[9] Patients were categorized as "failed Fontan" if the indication for referral to HT was refractory heart failure and end-organ damage related to long-term effects of earlier Fontan surgery.

UNOS Exception Status

We recorded all patients who required a UNOS exception. These are patients whose medical urgency warranted immediate listing, but who did not meet UNOS criteria 1A for HT and require regional board review to receive 1A exception status.[10]

Primary Outcome

The primary outcome was prespecified as death after HT. Time to the event was defined as time from HT to death or last known date of patient status.

Statistical Analysis

Data were expressed as n (%) or median (interquartile range [IQR]) where appropriate. Univariate analyses comparing discrete clinical variables were performed with the use of a χ^2 test or Fischer exact test. Continuous variables of interest were analyzed with the use of standard t tests as required. Prespecified dichotomized values for continuous variables were based on previous studies and included MELD-XI score >18 and ≥3 sternotomies.[8,9,11] Cox proportional hazards regression was used to assess univariate predictors of the primary outcome. On the basis of the univariate analysis, multivariate linear regression models were constructed such that any covariates reaching $P < .20$ in univariate analysis were included in the model.[12] Statistical analysis was performed with the use of Stata statistical software (version 13.1; Stata Corp, College Station, Texas).

Results

Patient Characteristics

We identified 48 patients who met the inclusion criteria. Demographic and historical data are presented in Table 1. Over a mean follow-up period of 5 years after HT, 14 patients (30%) died with 9/14 (64%) deaths occurring within 30 days after HT. Table 2 presents patient-specific data for cause of death.

Table 1. Patient Characteristics (n = 48)

Characteristic	n (%)
Sex (female)	18 (38%)
Age at transplant, y, median (IQR)	35.4 (21)
Age at first congenital surgery, y, mean ± SD	8 ± 1.2
Diagnosis	
Single ventricle	10 (21%)
D-TGA	10 (21%)
ccTGA	2 (4%)
TOF/PA/DORV	15 (31%)
Heterotaxy	3 (6%)
ASD/VSD	4 (8%)
Ebstein anomaly	1 (2%)
Other	4 (8%)
Earlier procedures	
TOF repair	7 (15%)
Rastelli/LV-PA conduit	5 (10%)
Mustard/Senning	9 (19%)
Classic Fontan	10 (21%)
Lateral tunnel Fontan	2 (4%)
Atrial septal defect closure	2 (4%)
Ventricular septal defect closure	1 (2%)
Glenn (without Fontan completion)	1 (2%)
Blalock Taussig shunt (only)	3 (6%)
Konno	1 (2%)
Other	3 (6%)
None	5 (10%)
UNOS status at transplantation	
1A	29 (60%)
1B	13 (27%)
2	6 (13%)
Donor age, y, median (IQR)	29 (14)
Granted an exception	9 (19%)
Number of sternotomies, mean ± SD	2.3 ± 0.2
Significant collaterals	4 (8%)

IQR, interquartile range; D-TGA, D-transposition of the great vessels; ccTGA, congenitally corrected transposition of the great vessels; TOF, tetralogy of Fallot; PA, pulmonary atresia; DORV, double-outlet right ventricle; ASD, atrial septal defect; VSD, ventricular septal defect; UNOS, United Network for Organ Sharing.

Univariate and multivariate predictors of overall mortality are listed in Table 3. Risk factors for mortality according to univariate analysis included MELD-XI score >18 ($P = .02$) and ≥3 sternotomies ($P = .01$). In a multivariate model that included ≥3 sternotomies, MELD XI score >18, heterotaxy, history of a failed Fontan, and history of a Rastelli or other conduit, MELD-XI score >18 (hazard ratio [HR] 6.27; $P = .01$) and ≥3 sternotomies (HR 8.52; $P = .02$) remained significant predictors of mortality. Heterotaxy was associated with increased risk for early death in multivariate analyses (HR 9.8; $P = .01$), but there were only 3 patients in this subcohort. Notably, although 5 patients (42%) with a failed Fontan died, history of a failing Fontan was not associated with overall mortality according to univariate ($P = .19$) or multivariate ($P = .10$) analyses.

UNOS Status and Year of Transplant

In this study, patients transplanted after 2006 were older at the time of transplant (42.2 vs 31 years; $P = .001$) and required more exceptions ($P < .001$). Patients transplanted