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Center variation in hospital costs for pediatric heart transplantation: The relationship between cost and outcomes

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Abstract

There are limited published data addressing the costs associated with pediatric heart transplantation and no studies evaluating the variation in costs across centers. We aimed to describe center variation in pediatric heart transplant costs and assess the association of transplant hospitalization costs with patient outcomes. Using a linkage between the Pediatric Health Information System and Scientific Registry of Transplant Recipients databases, hospital costs were assessed for patients (<18 years) undergoing heart transplantation (2007–2016). Severity-adjusted patient costs were calculated using generalized linear mixed-effects models with a random hospital intercept. Center variation in hospital cost was described after adjusting for the predicted risk of in-hospital mortality. Post-transplant survival was compared between low and high-cost centers using Cox proportional hazard models. A total of 2156 patients were included from 24 centers. There was 3.7-fold variation in transplant hospitalization costs across centers, ranging from $329,477-$1,226,507. Patients transplanted at high-cost centers have a higher predicted risk of in-hospital mortality (8.1% vs. 6.1%, p<0.001). Both early (p=0.008) and long-term (p=0.003) post-transplant survival was better in patients transplanted at low-cost centers. Transplant at low-cost

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Disclosures:

The data reported here have been supplied by the Minneapolis Medical Research Foundation as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.

Compliance with Ethical Standards:

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

centers was associated with improved post-transplant survival, independent of patient-specific risk (AHR 0.72; 95%CI 0.57–0.92, p=0.008). There is wide variation in cost for pediatric heart transplant inpatient care among U.S. centers with low-cost centers demonstrating the best patient survival. Differences in patient populations likely contributes to these findings, but cannot account for all the variation seen. This suggests that variability in the delivery of care across centers may influence post-transplant survival.

Keywords

pediatric; heart transplant; cost; survival; quality

Introduction:

In the recent era, there is increasing focus on providing high "value" care, with an emphasis on optimizing patient outcomes while minimizing costs [1,2]. Multiple studies have demonstrated significant variation in costs among centers performing congenital heart surgery [3,4], associated in part to differences in post-operative complications and lengths of stay [5]. More importantly, lower cost hospitals demonstrate the best post-operative outcomes following congenital heart surgery independent of disease severity, suggesting that higher cost is not clearly associated with higher quality care [2]. Heart transplantation is a well-accepted treatment for end stage heart failure in children [6]. However, it is known to be resource intensive with median transplant hospitalization costs exceeding $500,000 in the pediatric population [7]. Despite some overlap in practice patterns among pediatric heart transplant centers [8], there remains significant variability in transplant candidate selection and listing practices [9–11], waitlist times [12], pre-transplant support strategies [13], selection of immunosuppression [6], and post-transplant surveillance [14]. This variation in practice has the potential to impact both costs and patient outcomes; however, the differences in cost among heart transplant centers have not been studied in the pediatric population. This study aimed to utilize a novel linkage of clinical registry and administrative data to report the center-level variation in costs associated with pediatric heart transplantation and to assess the association of center costs with patient outcomes. We hypothesized that there would be significant variation in costs among pediatric heart transplant centers and that low-cost centers would demonstrate better survival, similar to what has been described for non-transplant pediatric cardiac surgery.

Methods:

This study utilized a novel linkage between the Scientific Registry of Transplant Recipients (SRTR, Minneapolis Medical Research Foundation, Minneapolis, MN) and the Pediatric Health Information System (PHIS, Children's Hospital Association, Lenexa, KS) administrative database which has been previously described [7]. The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the U.S., submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. The SRTR

includes data from every organ transplant and waitlist addition since October 1987 [7]. The PHIS database is an administrative database that collects clinical and resource utilization data from 49 tertiary children's hospitals. This includes data from inpatient hospitalizations, observation, ambulatory surgery, and emergency department visits. This database also collects diagnosis and procedural ICD-9 and ICD-10 codes, payer information, along with encounter-level hospital charge data [7].

All patients <18 years of age who underwent heart transplantation between 2007 and 2016 were identified from the linked database for inclusion in the analysis. Patients transplanted at hospitals that performed <15 heart transplant procedures over that timeframe were excluded. This number was chosen to ensure an adequate number of transplants were performed at each included center, allowing a more representative assessment of center-level costs. Patient-level hospital charges for the transplant hospitalization were converted to costs using hospital-specific and year-specific cost-to-charge ratios reported by each hospital. All costs were adjusted for inflation to 2016 U.S. Dollars using the medical component of the Consumer Price Index. Severity-adjusted patient costs were calculated using generalized linear mixed effects models with a random hospital intercept. Since costs are not normally distributed, we modeled the natural log of costs and severity-adjusted the models using independent variables, which were selected *a priori*. Variables selected for inclusion in the severity-adjustment model were patient age, underlying cardiac diagnosis of congenital heart disease or cardiomyopathy, race, blood type, use of extracorporeal membrane oxygenation (ECMO) support pre- or post-transplant, pre-transplant ventricular assist device (VAD) support, pre-transplant ventilator support, pre-transplant inotropic support, and transplant year. Costs were then transformed back to the original scale for subsequent analyses.

Median total, pre-, and post-transplant hospitalization severity-adjusted costs were calculated for each center. Variations in center costs were described using standard summary statistics. Transplant centers were ranked based on median adjusted transplant hospitalization cost. Low-cost centers were defined as transplant programs with a median adjusted total cost placing them in the bottom 1/3 compared to all other centers. Patient demographics were compared between low-cost centers and high-cost centers using standard summary statistics. The chi squared test was used for categorical and the Wilcoxon rank sum test was used for continuous variables. Adjusted total, pre-transplant (admission to the day prior to transplant), and post-transplant (day of transplant including transplant surgery costs to hospital discharge) hospitalization costs were compared across cost groups using the Wilcoxon rank sum test. Costs were subdivided into categories including pharmacy, laboratory, imaging, supply, clinical, and other (primarily room and nursing charges) costs and the analysis was repeated.

To account for potential population differences between high and low-cost centers, the predicted risk of in-hospital mortality was calculated for each patient using the risk model developed by Almond et al [15]. While other risk models exist to predict outcomes following pediatric heart transplantation [16], this model was chosen given availability of data. Other risk prediction models were not able to be assessed given lack variables necessary for inclusion in the model. The risk prediction model developed by Almond and colleague's gauges patient risk on the basis of pre-transplant factors including the need for

ECMO support, VAD support, repaired or unrepaired congenital heart disease, and pre-transplant bilirubin and creatinine clearance. Patients with missing data for any variable included in the risk model were excluded from this analysis. The predicted risk of in-hospital mortality was compared between high and low-cost centers using the two-sided Student's t-test. The average predicted risk of in-hospital mortality was calculated for each transplant center. A linear regression was performed to assess the degree of cost variation attributable to differences in center-level risk.

To assess the relationship between center costs and patient outcomes, post-transplant survival curves were constructed for each cost group using the Kaplan-Meier method and compared using the log-rank test. Two separate Cox proportional hazard models were constructed to assess if center cost was independently associated with post-transplant survival. In the first model, patient specific pre-transplant variables with univariate $p<0.2$ were chosen for inclusion in the model. The final model included low-cost vs. high cost centers, cardiac diagnosis, race, use of ECMO pre-transplant, VAD support pre-transplant, and ventilator support pre-transplant. The second model included low-cost vs. high-cost centers and the predicted risk of in-hospital mortality as calculated from the risk-prediction model published by Almond et al [15]. Two separate models were used to provide further evidence of the variation in outcomes, independent of patient risk. Standard error estimates for all models were adjusted for patient clustering within centers.

To assess the potential impact of center transplant volume on costs, a linear regression was performed using the center median adjusted total cost and the average number of pediatric heart transplants performed annually at each center (based on OPTN data). Linear regression was also performed to assess the association of pre- and post-transplant costs.

All statistical analyses were performed in SAS version 9.4 (SAS Institute; Cary, NC) or STATA version 13 (StataCorp LLC; College Station, TX) with two-sided $p<0.05$ considered statistically significant. This project was approved by the Vanderbilt University IRB, PHIS, and SRTR.

Results:

A total of 2,156 pediatric heart transplant recipients from 24 different centers were identified for inclusion in the study. There was a median of 94 patients included from each center (range 18 to 181). The median severity-adjusted total hospitalization cost for all patients was $540,459 (interquartile range [IQR] $393,777 - $789,340), and the median adjusted total cost per center ranged from $329,477 to $1,226,507, representing a 3.7-fold variation among centers (Figure 1). The median pre-transplant adjusted hospital cost was $183,411 (IQR $93,546 - $349,024) with a range from $78,685 to $353,779 (4.5-fold variation) and the median post-transplant adjusted hospital cost was $341,033 (IQR $265,884 - $459,600) with a range from $200,307 to $905,050 (4.5-fold variation).

Eight centers were identified as low-cost, with 705 (32.7%) patients undergoing heart transplant at those centers. Baseline patient demographics comparing patients from low-cost centers to those from high-cost centers are shown in Table 1. There was no difference

between groups based on patient age, diagnosis, sex, blood type, listing status, inotropic support at transplant, and the need for ECMO or VAD support at the time of transplantation. Patients transplanted at high-cost centers were more likely to require ventilator support at the time of transplantation (20% vs. 8.9%, p<0.001) and were more likely to utilize inhaled nitric oxide post-transplant (46.2% vs. 28.6%, p<0.001). Post-transplant complications were similar between groups in terms of the incidence of rejection, stroke, chylothorax, the need for cardiac reoperation or other surgical procedures, and the need for ECMO support post-transplant. However, patients transplanted at high-cost centers were more likely to receive post-transplant dialysis (6% vs. 3%, p=0.003) and have chest tubes in place >2 weeks post-transplant (11.8% vs. 6%, p<0.001). Total, pre-, and post-transplant length of stay were significantly higher at high-cost centers compared to low-cost centers (60, 28, and 22 days vs. 46, 24, and 14 days respectively, p<0.05 for all). This group also demonstrated a longer duration of post-transplant mechanical ventilation (4 vs. 3 days, p<0.001) and longer ICU length of stay (13 vs. 7 days, p<0.001) post-transplant. Despite the differences in length of stay, total waitlist times (inpatient and outpatient) were not significantly different between groups (52 vs. 51 days, p=0.575).

A total of 2,057 patients (95%) had complete data allowing estimation of in-hospital mortality risk. Ninety-nine patients were excluded due to missing data (27 from low-cost and 72 from high-cost centers, 3.8% vs. 5.0%, p=0.239). The average predicted risk of in-hospital mortality across all patients was 7.4% (95% confidence interval [CI] 7.0% - 7.9%). Patients transplanted at high-cost centers demonstrated a higher predicted risk of in-hospital mortality compared to patients transplanted at low-cost centers (8.1% vs. 6.1%, p<0.001). Predicted patient risk accounted for approximately 23% (linear regression $R^2 = 0.227$, p = 0.022) of the observed variation in cost across centers in our model (Figure 2). One center was an outlier (>3 standard deviations from mean) for total adjusted cost and this center was excluded from linear regression analysis.

Total, pre-, and post-transplant severity-adjusted costs are shown in Table 2. Median adjusted total hospitalization cost for low-cost centers was $388,114 compared to $642,798 for high-cost centers, with persistent differences for pre-transplant ($119,007 vs. $224,212) and post-transplant ($259,359 vs. $397,886) periods (p<0.001 for all). High-cost centers also demonstrated significantly higher costs in all resource groups including pharmacy, laboratory, imaging, supply, clinical, and other costs, with up to 15-fold variation across centers based on the specific area of spending (Table 3). Center transplant volume was not associated with median total severity-adjusted cost per center (R^2=0.003, p=0.795) (Figure 3), nor with pre-transplant (R^2=0.02, p=0.499) or post-transplant (R^2=0.001, p=0.918) hospitalization costs. However, there was a correlation between pre-transplant and post-transplant costs (R^2=0.404, p<0.001).

Patients transplanted at low-cost centers demonstrated improved survival compared to patients transplanted at high-cost centers (log rank p = 0.003) (Figure 4). This difference remained significant when early (<1 year) post-transplant survival was assessed (log rank p = 0.008). When assessed in separate multivariable models, undergoing transplant at a low-cost center was independently associated with improved post-transplant survival after accounting for patient risk factors directly as covariates in the model and when adjusting for

the predicted risk of in-hospital mortality (adjusted hazard ratio [AHR] 0.74; 95% CI 0.58 – 0.93, p=0.011 and AHR 0.72; 95% CI 0.57 – 0.92, p=0.008, respectively).

Discussion:

This multicenter analysis represents the first report describing the variation in hospitalization costs across U.S. pediatric heart transplant centers. In addition to providing benchmark cost data for pediatric heart transplantation (in 2016 U.S. Dollars), we demonstrate wide variation in costs that is independent of transplant center volume and only partially explained by underlying patient-severity / predicted risk of in-hospital mortality after transplantation. These findings suggest that there may be variation in the delivery of cost-effective care among transplant programs.

There are multiple factors that likely contribute to variation in costs across U.S. transplant centers; some of which may not be modifiable. Centers vary in their thresholds to pursue transplantation in high-risk patients and therefore it is likely that patient populations vary by center. In fact, our analysis suggests that high-cost centers transplant higher risk patients. Patients from high-cost centers more frequently required ventilator support at the time of transplantation, were less likely to be outpatient at the time of transplant and demonstrated an increased risk of in-hospital mortality based on a previously validated risk-prediction model. Linear regression analysis demonstrated that the predicted risk of in-hospital mortality correlated with median total cost at the center level, however only a portion of total costs could be attributed to variations in pre-transplant risk. While the risk prediction model implemented has inherent limitations, this suggests that other factors independent of patient complexity and risk may also contribute to the center variation in costs.

Similar to patients undergoing congenital heart surgery [3,5,2,17], post-transplant complications and resulting length of stay may play a role in the variation in heart transplant costs across centers. Low-cost centers demonstrated significantly shorter total, pre-, and post-transplant length of stay compared to high-cost centers. In addition to this, patients transplanted at high-cost centers were significantly more likely to require post-transplant dialysis, have treated rejection, prolonged chest tube drainage, and more likely to require non-cardiac surgical procedures.

While post-operative complications may contribute to differences in post-transplant length of stay, this does not account for the differences in pre-transplant length of stay. Prior studies have demonstrated significant regional variation in waitlist times [12], which may contribute to this finding. Despite this, there was no significant difference in waitlist times in our analysis. This may indicate differences in listing strategies among transplant programs in terms of timing of listing as well as determination of listing status. In fact, prior studies support the notion that transplant centers vary in their application of listing criteria [10,11]. These differences may become even more significant with recent updates to the pediatric listing criteria [18], which are expected to result in increased utilization of status exceptions and may alter waitlist support strategies across centers. In addition to the potential for varying waitlist times, geographic factors may influence costs in other ways. The cost of organ procurement varies widely [19]. Geography likely contributes to this based on the size

of the potential organ donor pool as well as the associated travel expenses for organ acquisition. In addition to this, reimbursement rates vary based on geography, potentially impacting our analysis [20].

There are limited prior studies addressing the costs associated with pediatric heart transplantation. A prior single center study reported a mean cost of $221,897 for pediatric heart transplants performed between 1997 and 2004 [21]. Subsequently, Law and colleagues reported mean hospital charges ranging from $279,399 in 1997 to $451,738 in 2006 from a large administrative database [22]. These results are comparable to the current analysis, accounting for inflation. A more recent study, which also utilized the PHIS database, highlighted the potential for variation in resource utilization across pediatric heart transplant centers dependent on center volume [23]. Our analysis provides contemporary high-quality cost data from the largest cohort of pediatric heart transplant recipients to date. The linkage of PHIS and SRTR also enables the first analysis addressing the association between costs and pediatric heart transplant outcomes.

In our analysis, low-cost centers demonstrated improved post-transplant survival compared to other centers. While differing patient risk contributes to this finding, improved survival at low-cost centers remained significant when multiple adjustments were made to account for varying patient risk. This finding is comparable to prior studies which have shown that low-cost centers have the best post-operative outcomes following congenital heart surgery, independent of disease severity [2]. Additionally, multiple prior adult studies have associated low cost with higher “quality” care [24–26]. These findings indicate that the same relationship exists between cost and survival in pediatric heart transplantation and suggests that there may be underlying differences in the delivery of care across centers.

Limitations:

There are inherent limitations to our analysis. We were only able to adjust for population differences based on variables contained in the linked dataset. Given the inherent lack of data granularity it is possible that there are population differences between centers that were not captured by our analysis. Centers vary in their thresholds to pursue transplantation in high-risk patients and there are notable population differences between high and low-cost centers. It is possible that low-cost centers are more conservative with listing patients perceived as high-risk. However, our analysis demonstrates that variation in pre-transplant risk only accounts for a fraction of the variation in costs observed. Despite this, the use of risk prediction models also has limitations. The pediatric heart transplant population is extremely heterogeneous. Therefore, developing a model to fully encompass risk across this diverse group can be challenging. Alternate risk prediction models also exist, but were unable to be assessed in our analysis due to lack of data availability. To ensure an adequate number of transplant patients at each center from which to estimate costs, the smallest volume centers were excluded, representing a potential limitation. In addition to this, PHIS data does not include physician professional fees, resulting in an expected underestimation of costs. Lastly, as with any large dataset, there is the potential for missing or erroneous data.

Conclusion:

This multicenter analysis demonstrates wide variation in costs among pediatric heart transplant centers with up to 3.7-fold differences in median severity-adjusted cost per center. Low-cost centers demonstrate fewer post-transplant complications, shorter length of stay, and improved post-transplant survival compared to other centers. Patients transplanted at high-cost centers are higher risk; however, differences in pre-transplant risk only account for a portion of the cost variation observed, suggesting that there may be inherent differences in the delivery of care among pediatric heart transplant programs.

Acknowledgments

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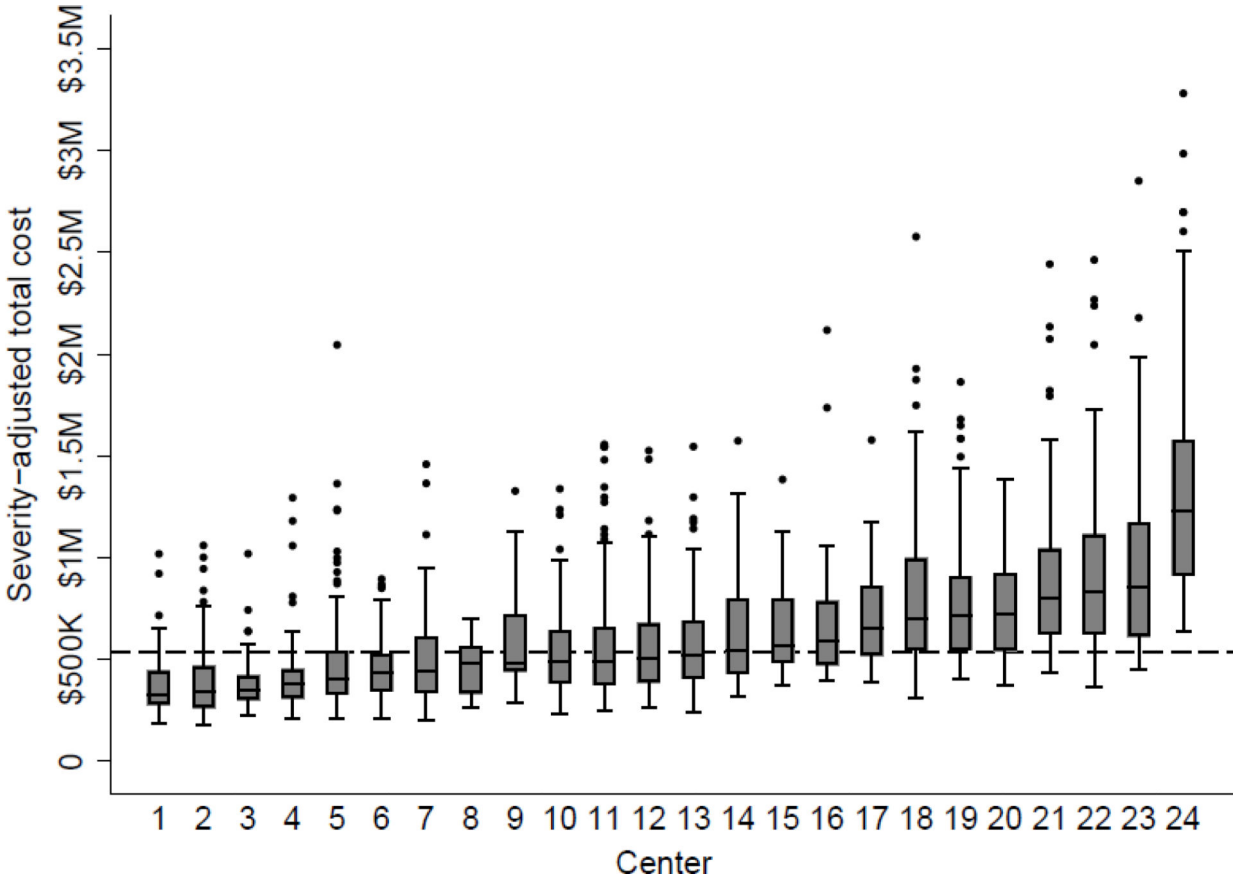

Figure 1.

Variation in pediatric heart transplant hospitalization costs by center. Dashed line represents the median total cost across all centers, adjusted for patient characteristics and severity of illness.

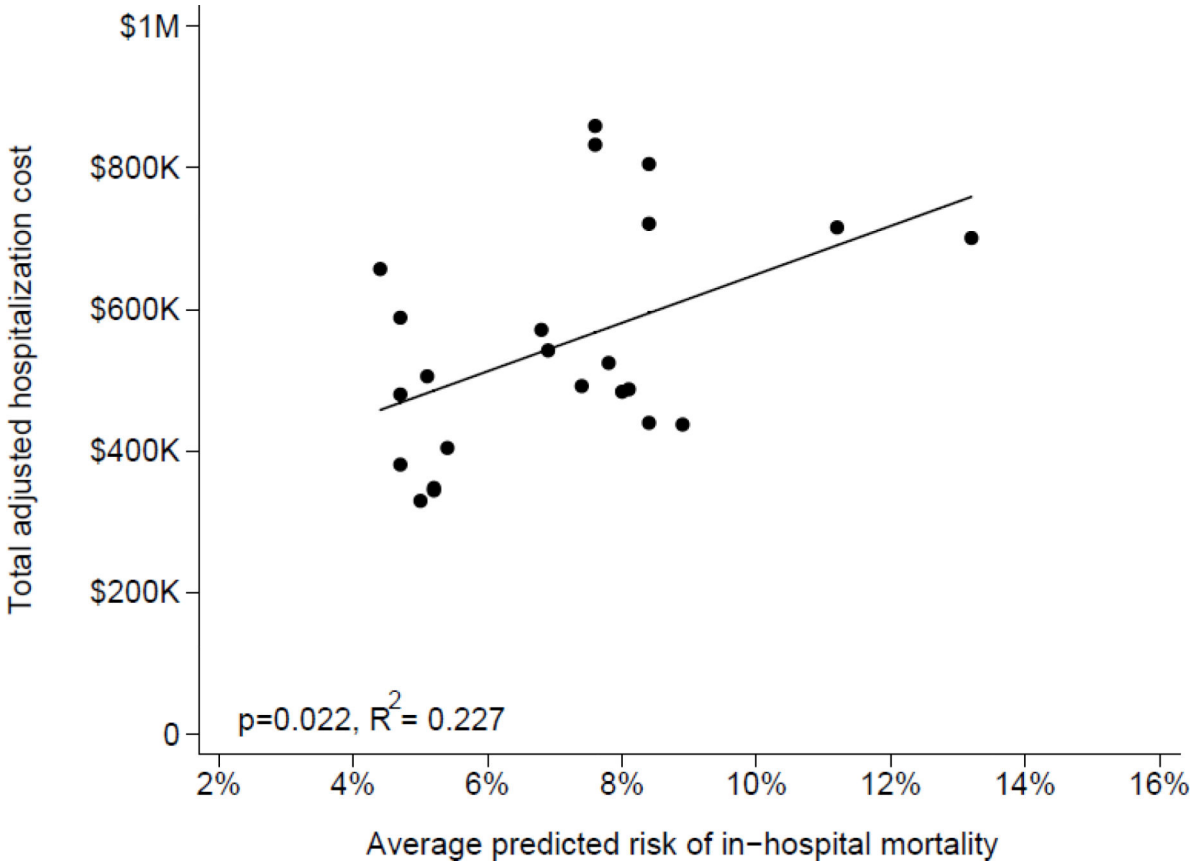

Figure 2.

Median severity-adjusted cost per transplant hospitalization based on the average predicted risk of in-hospital mortality. Note: One center was an outlier (median cost >3 standard deviations above the mean) and was excluded from this analysis.

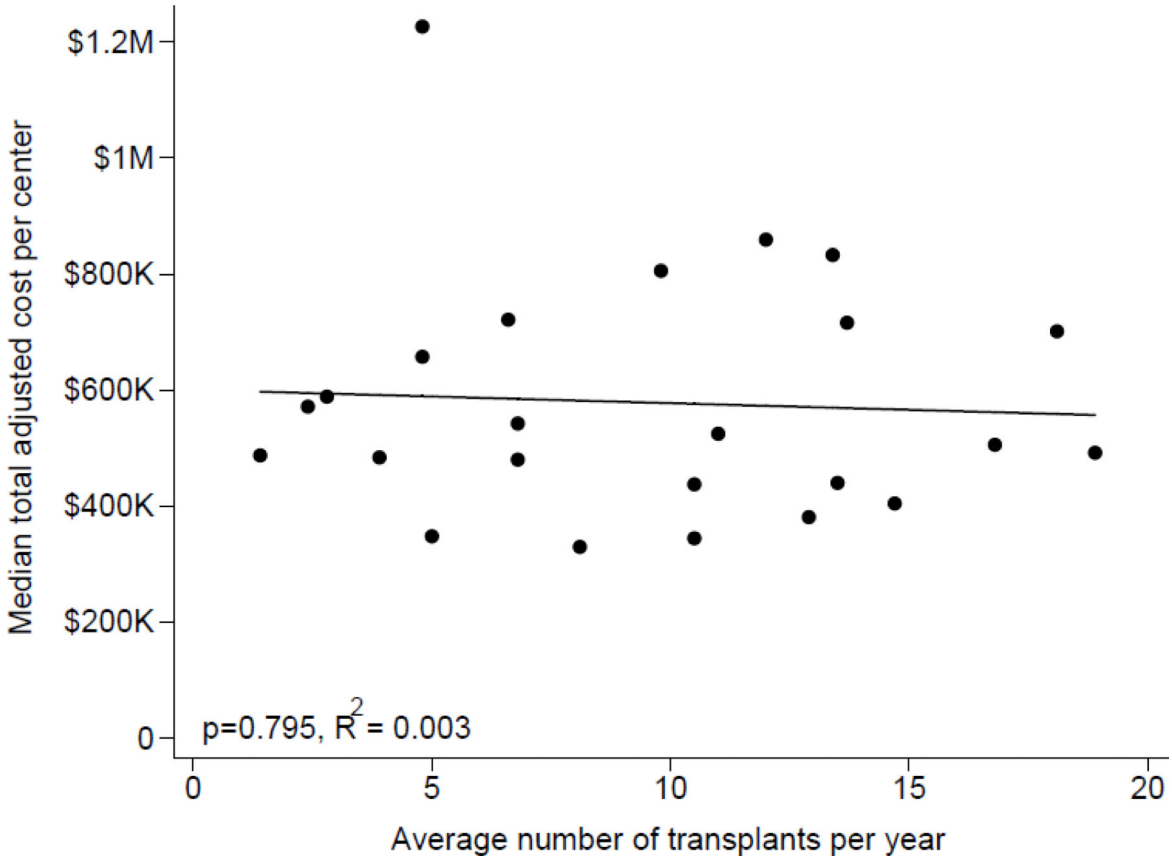

Figure 3.
Median severity-adjusted cost per transplant hospitalization by center volume.

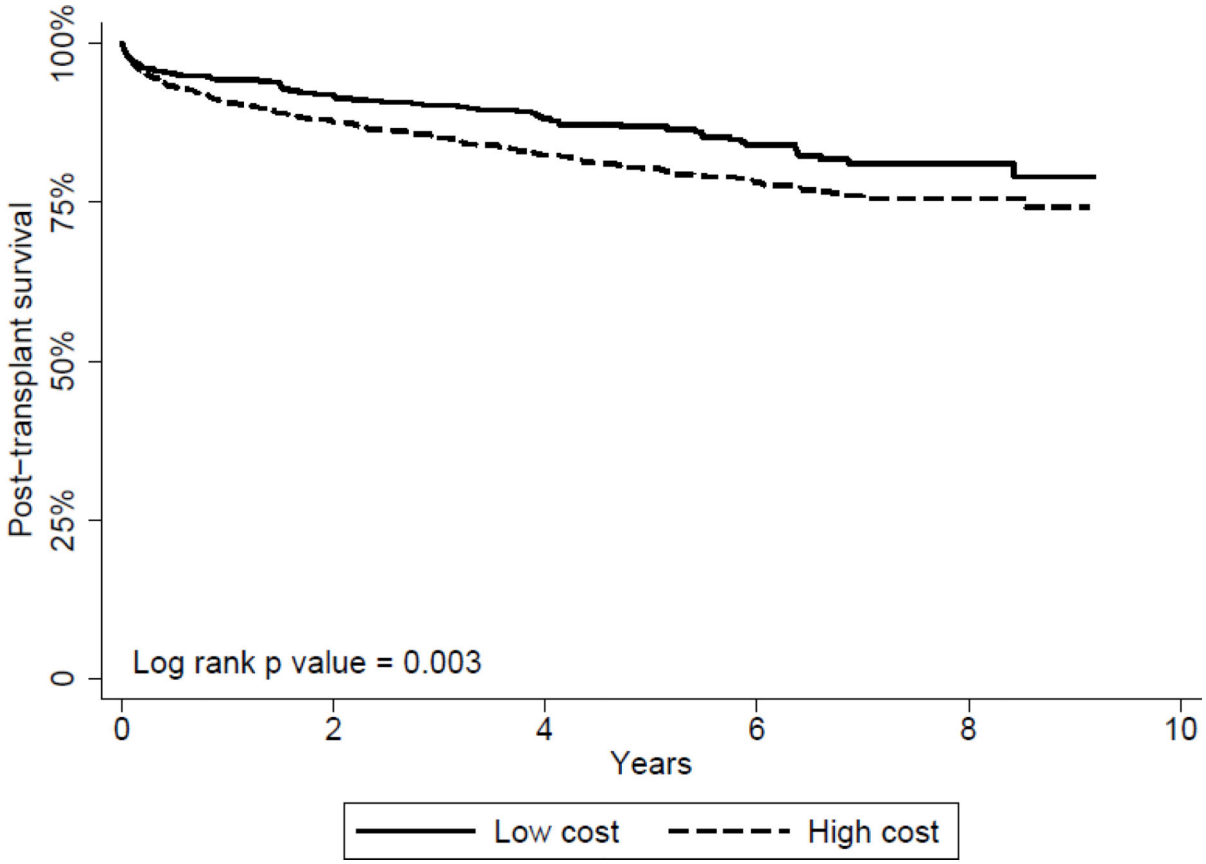

Figure 4.
Post-transplant survival based on center cost.

Table 1.

Population differences by center cost

	Center Cost Groups			
	Low Cost	**High Cost**	**Total**	**p-value**
	N=705 (32.7%)	**N=1451 (67.3%)**	**N=2156**	
Age				
<1 year	210 (29.8%)	462 (31.8%)	672 (31.2%)	
1–5 years	179 (25.4%)	349 (24.1%)	528 (24.5%)	0.562
6–10 years	95 (13.5%)	213 (14.7%)	308 (14.3%)	
11–17 years	221 (31.3%)	427 (29.4%)	648 (30.1%)	
Diagnosis				0.122
Cardiomyopathy	332 (47.4%)	665 (46.4%)	997 (46.7%)	
Congenital Heart Disease	323 (46.1%)	703 (49.1%)	1026 (48.1%)	
Single ventricle lesion	132 (40.9%)	309 (44%)	441 (43%)	0.353
Retransplant	45 (6.4%)	65 (4.5%)	110 (5.2%)	
Race				
Caucasian	469 (66.5%)	796 (54.9%)	1265 (58.7%)	
African-American	111 (15.7%)	263 (18.1%)	374 (17.3%)	<0.001
Hispanic	89 (12.6%)	300 (20.7%)	389 (18%)	
Other	36 (5.1%)	92 (6.3%)	128 (5.9%)	
Male Gender	396 (56.2%)	786 (54.2%)	1182 (54.8%)	0.381
Blood Type				
O	324 (46%)	655 (45.1%)	979 (45.4%)	
A	242 (34.3%)	551 (38%)	793 (36.8%)	0.213
B	109 (15.5%)	184 (12.7%)	293 (13.6%)	
AB	30 (4.3%)	61 (4.2%)	91 (4.2%)	
Status at Transplant				
1A	601 (85.2%)	1251 (86.2%)	1852 (85.9%)	
1B	72 (10.2%)	141 (9.7%)	213 (9.9%)	0.81
2	32 (4.5%)	59 (4.1%)	91 (4.2%)	
ECMO at Transplant	24 (3.4%)	70 (4.8%)	94 (4.4%)	0.13
VAD at Transplant	128 (18.2%)	301 (20.7%)	429 (19.9%)	0.158
Ventilator at Transplant	63 (8.9%)	290 (20%)	353 (16.4%)	<0.001
Inotropes at Transplant	349 (49.5%)	746 (51.4%)	1095 (50.8%)	0.405
Post-transplant iNO	201 (28.6%)	670 (46.2%)	871 (40.4%)	<0.001
Total Length of Stay (Days)	46 (17 – 91)	60 (25 – 116)	54 (22 – 106)	<0.001
Pre-transplant Length of Stay (Days)	24 (1 – 66)	28 (1 – 74)	26 (1 – 71)	0.03
Post-transplant Length of Stay (Days)	14 (10 – 25)	22 (14 – 36)	19 (12 – 33)	<0.001
Waitlist time	52 (22 – 106)	51 (19 – 120)	52 (20 – 114)	0.575
Outpatient prior to transplant	227 (32.2%)	402 (27.7%)	629 (29.2%)	0.031
Post-Transplant ICU Days	7 (5 – 14)	13 (7 – 26)	10 (6 – 22)	<0.001
Post-Transplant Days on Ventilator	3 (2 – 6)	4 (2 – 11)	3 (2 – 9)	<0.001

	Center Cost Groups			
	Low Cost	**High Cost**	**Total**	**p-value**
	N=705 (32.7%)	**N=1451 (67.3%)**	**N=2156**	
Post-Transplant Complications				
Dialysis	21 (3%)	87 (6%)	108 (5%)	0.003
Rejection Prior to Discharge	80 (11.3%)	200 (13.8%)	280 (13%)	0.114
Stroke	25 (3.6%)	53 (3.7%)	78 (3.6%)	0.881
Chylothorax	41 (5.8%)	87 (6%)	128 (5.9%)	0.868
Cardiac Reoperation	42 (8.3%)	93 (8.7%)	135 (8.6%)	0.813
Other Surgical Procedures	60 (12%)	166 (15.7%)	226 (14.5%)	0.054
Chest tube >2 weeks	30 (6%)	122 (11.8%)	152 (9.9%)	<0.001
Post-transplant ECMO	41 (5.8%)	114 (7.9%)	155 (7.2%)	0.085

* p-values from the chi square test for categorical and the Wilcoxon rank sum test for continuous variables

Abbreviations: ECMO - Extracorporeal membrane oxygenation, iNO - inhaled nitric oxide, VAD - Ventricular assist device

Table 2.

Total, pre-, and post-transplant hospitalization costs

	Adjusted Costs			
	Low Cost	**High Cost**	**Total**	
Centers	**N=8**	**N=16**	**N=24**	**p-value***
Patients	**N=705 (32.7%)**	**N=1451 (67.3%)**	**N=2156**	
Total cost	$388,114 ($307,145 – $505,929)	$642,798 ($476,205 – $890,401)	$540,459 ($393,777 – $789,340)	<0.001
Pre-transplant costs	$119,007 ($65,521 – $227,147)	$224,212 ($115,754 – $398,185)	$183,411 ($93,546 – $349,024)	<0.001
Post-transplant costs	$259,359 ($217,936 – $305,586)	$397,886 ($312,355 – $503,825)	$341,033 ($265,884 – $459,600)	<0.001

* p-values from the Wilcoxon rank sum test

Cost expressed as median (interquartile range), inflate to 2016 dollars

Table 3.

Adjusted total costs based on area of spending

	Low cost	High cost	Total		Range		Ratio
Centers	**N=8**	**N=16**	**N=24**	**p-value***	**Minimum**	**Maximum**	**Max/Min**
Patients	**N=705 (32.7%)**	**N=1451 (67.3%)**	**N=2156**				
Pharmacy costs	$32,067 ($24,746 – $46,996)	$57,851 ($39,553 – $92,312)	$47,561 ($31,788 – $76,439)	<0.001	$25,014	$183,088	7.3
Lab costs	$25,506 ($18,295 – $38,999)	$46,405 ($30,969 – $76,515)	$38,406 ($24,860 – $64,510)	<0.001	$11,883	$86,478	7.3
Imaging costs	$7,753 ($4,534 – $12,607)	$15,739 ($9,579 – $25,113)	$12,497 ($6,924 – $21,580)	<0.001	$2,419	$31,581	13.1
Supply costs	$12,982 ($7,166 – $26,101)	$26,715 ($14,278 – $51,650)	$21,324 ($10,985 – $43,379)	<0.001	$3,530	$55,876	15.8
Clinical costs	$154,025 ($113,877 – $194,001)	$237,408 ($160,270 – $313,364)	$199,927 ($136,490 – $275,670)	<0.001	$78,569	$613,638	7.8
Other costs	$113,694 ($79,976 – $169,980)	$180,973 ($119,708 – $266,289)	$156,859 ($102,020 – $241,452)	<0.001	$76,712	$311,475	4.1

* p-values from the Wilcoxon rank sum test

Cost expressed as median (interquartile range), inflated to 2016 dollars