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Changes in pediatric heart transplant hospitalization costs over time

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Abstract

Background—Despite significant changes in the past decade for children undergoing heart-transplantation, including the evolution of mechanical circulatory support and increasing patient complexity, costs and resource utilization have not been reassessed. We sought to utilize a novel linkage of clinical-registry and administrative data to examine changes in hospitalization costs over time in this population.

Methods—We identified all pediatric heart transplant recipients in a unique linked PHIS/SRTR dataset (2002–2016). Hospital costs were estimated from charges using cost-to-charge ratios, inflated to 2016 dollars. Severity-adjusted costs were calculated using generalized linear mixed-effects models. Costs were compared across 3 eras (Era-1:2002–2006; Era-2:2007–2011; and Era-3:2012–2016).

Results—A total of 2896 pediatric heart transplant recipients were included; Era-1:649 (22.4%), Era-2:1028 (35.5%), and Era-3:1219 (42.1%). ECMO support at transplant decreased over time, concurrent with an increase in VAD-supported patients. Between Era-1 and Era-2 there was an

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increase in pretransplant hospitalization costs ($343,692 vs. $435,554; p<0.001). However, between Era-2 and Era-3 there was a decline in total ($906,454 vs. $767,221; p<0.001), pretransplant ($435,554 vs. $353,364; p<0.001), and posttransplant ($586,133 vs. $508,719; p=0.002) hospitalization costs.

Conclusions—Concurrent with the increase in utilization of VAD support, there has been an increase in pretransplant costs associated with pediatric heart transplantation. However, in the most recent era, costs have declined. These findings suggest the evolution of more cost-effective management strategies, which may be related to shifts in the approach to pediatric mechanical circulatory support.

Introduction

Heart transplant (HT) has become a widely accepted treatment for end stage heart failure in both children and adults[1,2]. However, it is resource-intensive with reported median hospital charges of $137,679 in adults and mean hospital charges of >$450,000 in children[3,4]. At least one prior report from patients transplanted between 1997 and 2006 suggests that hospital costs associated with pediatric HT have increased over time[3]; however, there have been no publications describing resource utilization in this population from a more contemporary cohort. Additionally, many changes have occurred over time that may impact resource utilization including shifts in the use of mechanical circulatory support and increasing patient complexity.

Ventricular assist device (VAD) use in children has increased significantly over the past 10 years[5], likely impacting the costs associated with HT. Mahle et al reported mean hospital costs of $758,199 for pediatric patients bridged to HT with a VAD between 2002 and 2007[6]. Waitlist survival has also improved over time[7], likely resulting in increased waitlist duration and associated costs. In addition, recent changes in pediatric heart allocation that prioritize donor hearts to the most critically ill candidates, including those with congenital heart disease and those who require VAD support, are likely to further impact waitlist durations and contribute to increases in the costs associated with pediatric HT[8].

This project aimed to describe the changes in hospitalization costs associated with pediatric HT over time. We hypothesized that improvements in waitlist survival and increases in the frequency of VAD utilization would result in increases in cost over time.

Materials and Methods

This study utilized a unique database 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, and has been previously described[9]. The SRTR data system includes data on all donors, waitlisted 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. SRTR data are derived from multiple sources including the OPTN, transplant programs, organ

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procurement organizations, histocompatibility laboratories, the Centers for Medicare and Medicaid Services, and the National Technical Information Service's Death Master File. The SRTR database includes data from every organ transplant and waitlist addition within the U.S. since October 1987[9]. The PHIS database is an administrative database that collects clinical and resource utilization data for hospital encounters from 49 tertiary care children's hospitals. This includes data from inpatient hospitalizations, observation, ambulatory surgery, and emergency department visits. This database accumulates encounter–level diagnosis and procedural ICD-9 and ICD-10 codes, payer information, along with daily encounter-level hospital charge data[9].

All pediatric (age < 21 years) patients (2002 – 2016) with available hospital charge information in the linked database were included. Hospital charges were converted to costs using hospital-specific and year-specific cost-to-charge ratios. All costs were adjusted for inflation to 2016 U.S. dollars using the medical component of the Consumer Price Index. Costs were assessed for the entire transplant hospitalization, the pretransplant hospitalization period (day of admission to the day prior to HT), and for the post-HT period (day prior to HT to the day of discharge). Adjusted patient costs were calculated with generalized linear mixed effects models using an exponential distribution, and included a random hospital intercept. Variables included in the total and posttransplant cost models were selected a priori and included era, patient age, diagnosis (cardiomyopathy, congenital heart disease, or retransplant), race, the need for ECMO support pre or posttransplant, VAD support, ventilator support, inotropic support, total length of stay, rejection prior to hospital discharge, and the need for dialysis posttransplant. The pretransplant cost model included the same variables but excluded those that were dependent on posttransplant events (posttransplant ECMO, total length of stay, rejection prior to hospital discharge, and the need for dialysis posttransplant). Adjusted costs were expressed as the least squares mean with 95% confidence intervals obtained from the generalized linear mixed models.

Included patients were divided into 3 eras: Era-1 (2002 – 2006), Era-2 (2007 – 2011), and Era-3 (2012 – 2016). Patient demographics were compared across eras using standard summary statistics and either the chi squared or Kruskal-Wallis test, as appropriate. Hospitalization costs were compared across eras using generalized linear mixed effects models. Hospitalization costs were subdivided into categories including pharmacy, laboratory, imaging, supply, clinical, and other costs and the analysis was repeated. Other costs are comprised primarily of room (including operating room) and nursing costs. To assess the impact of VAD support on the changes in hospitalization costs over time, a separate generalized linear mixed effects model was generated to assess the changes in VAD costs across eras, adjusting for the same variables included in the original models. All statistical analyses were performed in SAS version 9.4 (SAS Institute; Cary, NC) or STATA version 13 (StataCorp LLC; College Station, TX) with $p<0.05$ considered statistically significant. This project was approved by the Vanderbilt University IRB, PHIS, and SRTR.

Results

A total of 2896 patients were included in the study with 649 (22.4%) transplanted during Era-1, 1028 (35.5%) transplanted during Era-2, and 1219 (42.1%) transplanted during Era-3.

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Patient characteristics by era are shown in Table 1. Over time there has been a trend towards higher waitlist urgency status with 85.1% of patients listed UNOS status 1A at the time of HT in the 2 most recent eras compared to 74.4% of patients listed UNOS status 1A at HT in Era-1 ($p<0.001$). Fewer patients have been supported with ECMO at HT over time (9.1% vs. 5.4% vs. 3.6% across eras 1, 2, and 3 respectively, $p<0.001$) and VAD use has increased over the same time period (7.1% vs. 17.1% vs. 22.2%, $p<0.001$). There has also been an increase in the use of inhaled nitric oxide following HT and a trend towards fewer patients requiring ventilator support at HT. Between Era-1 and Era-2 there was a significant increase in the total (41 days vs. 52 days, $p<0.001$) and pre-HT (16 days vs. 24 days, $p<0.001$) length of stay but a decrease in the number of days mechanical ventilation was used after HT (mean 16.9 days vs. 9.7 days, $p<0.001$). There has also been a decrease in the incidence of acute rejection prior to hospital discharge (18.4% vs. 13.5%, $p=0.02$) and an increased incidence of chylothorax (1.8% vs. 6.2%, $p<0.001$) between Era-1 and Era-2. There was no difference across eras based on patient age, diagnosis, gender, blood type, need for pre-HT inotropic support, ICU length of stay, the incidence of stroke, and the need for post-HT dialysis or cardiac reoperation.

Adjusted total, pre-, and post-HT costs by era are shown in Table 2. Between Era-1 and Era-2 there was no significant change in total or posttransplant hospitalization costs. Over the same time period, there was a significant increase in pretransplant hospitalization costs ($343,692 vs. $435,554; $p<0.001$). In the most recent era, there was a decline in total ($906,454 vs. $767,221; $p<0.001$), pretransplant ($435,554 vs. $353,364; $p<0.001$), and posttransplant ($586,133 vs. $508,719; $p=0.002$) hospitalization costs.

Total costs based on area of spending are shown in Figure 1. Clinical and other costs represent the largest expenditures for the total hospitalization. The highest cost services in these groups include organ acquisition and procurement, organ transplant service, and intensive care unit charges. Between Era-1 and Era-2 there were no significant changes in total costs across any area of spending (ie, pharmacy, laboratory, imaging, supply, clinical, and other costs). Between Era-2 and Era-3 there were significant decreases in total laboratory, supply, and other costs and a trend towards decreased total pharmacy and clinical costs. Imaging costs did not change during this timeframe.

Changes in VAD costs over time are shown in Table 3. There was a trend towards decreasing total hospitalization cost for patients supported with a VAD across eras.

Discussion

Our analysis demonstrates that, while pre-HT hospitalization costs increased between Era-1 and Era-2, overall costs have decreased in the most recent era. These improvements were seen during all periods of the transplant hospitalization including total, pretransplant, and posttransplant care. These findings suggest the evolution of more cost-effective management strategies, potentially impacted by advances in pediatric mechanical circulatory support (MCS).

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The early increases seen in pre-HT costs are likely multifactorial; however, shifts in pediatric MCS strategies may play a critical role. VAD use in children has increased significantly over the past 10 years[5]. We also observed this change with VAD use increasing from 7.1% of patients to 22.2% of patients over the 15-year timeframe included in this study. Concurrently, there has been a decline in the use of ECMO for patients undergoing HT. While this shift in MCS strategy may contribute to increases in pre-HT costs, the superior outcomes of VAD support compared to ECMO[10] may offset this added cost. In fact, our analysis demonstrates that the costs associated with HT have decreased in the most recent era. It is possible that the shift in MCS strategy from ECMO to VAD has resulted in patients being better supported prior to HT and leading to a less complicated pre- and post-HT course. Any cost savings associated with VAD support may be outweighed by increased utilization over time. Prior studies have demonstrated that as experience with VAD support increases, costs decrease[11]. We hypothesize that the costs associated with VAD support may be declining as centers gain more experience in successful candidate selection, device management, detection of device complications, and as the use of continuous flow devices expand further in the pediatric population. In fact, our analysis suggests that the total hospitalization costs for VAD supported patients may be decreasing over time. It is also important to note that with each successive era, pediatric heart transplant outcomes have improved.[2] This improvement in early mortality may also influence hospitalization costs over time as early mortality may decrease costs.

The early increase in pre-HT costs may also be impacted by waitlist times. Survival on the waitlist has improved in the recent era[7], which may be directly related to the increased availability of VADs, allowing a longer duration of support. While this likely represents overall improvement in management strategies, this also leads to longer waitlist times and the potential for higher acuity patients undergoing HT. Both of these factors may result in increased costs.

There are limited prior studies addressing the costs associated with pediatric HT and only one that addressed the changes in costs over time. Law et al reported a 160% increase in hospital charges associated with pediatric HT from 1997 to 2006[3]. Our analysis provides more contemporary cost data compared to this prior study, and represents the largest reported U.S. cohort to date. Importantly, while our analysis confirms an increase in pre-HT costs in earlier eras, data from the most recent era suggest the evolution of more cost effective management strategies.

These data demonstrate that areas of cost expenditure have also changed over time. Cost improvements were seen in laboratory, supply, and other costs, while no significant decreases in cost were observed in pharmacy, imaging, and clinical costs. Any potential cost saving strategies for pharmacy and imaging costs may be outweighed by other factors. Pharmacy costs may be influenced by increases in medication costs as well as changes in medication prescribing patterns over time. There has been a shift toward greater utilization of tacrolimus and mycophenolate mofetil over time with fewer patients receiving cyclosporine, azathioprine, or steroids[2,12]. Tacrolimus and mycophenolate mofetil have increased drug acquisition costs compared to cyclosporine and azathioprine respectively, but prior studies indicate that these agents are more cost-effective secondary to improved patient

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outcomes[13–15]. Additionally, there has been an increase in the use of induction therapy, further impacting pharmacy costs[2,12]. In fact, T cell depleting agents are now the most commonly used induction agents following pediatric HT and also represent the most costly alternative compared to IL-2 receptor antagonists or no induction therapy[15]. Additionally, multiple studies have documented a significant increase in the utilization of imaging over time[16,17], which may offset any potential cost savings in this area.

Prior studies have suggested that physicians have little awareness of the costs associated with the therapies they prescribe[18–20]. For this reason, any improvement in costs over time may not be related to physicians becoming more cost conscious, but instead related to improvements in patient management and quality of care. Further improvements in costs may be possible; however, these will likely require increased physician awareness and involvement in selecting the most cost-effective therapies.

Limitations

Our analysis has inherent limitations. Given the expected positive skewed distribution of cost data[21], outliers may exist that overestimate the true cost. However, the use of generalized linear mixed effects models with an exponential distribution (to model skewed data) and reporting of least squares means represents the most statistically appropriate methodology. The linked PHIS and SRTR database only includes transplanted patients and therefore excludes patients who were listed but not transplanted. This may result in underestimation of costs, but is unlikely to significantly impact assessment of the changes in cost over time. Patients who were not hospitalized at the time of HT had negligible pre-HT costs, potentially resulting in underestimation of these costs. Additionally, we are only able to report data from hospitals that contribute to both databases. While this unique linkage has allowed an in-depth assessment of HT costs over time, the etiology for the changes remains unclear. There may be significant regional variation in costs, potentially impacting our analysis. To address this, a study investigating the differences in costs across HT centers is underway. As with any large dataset, there is the potential for missing or erroneous data. However, we believe that the merger of these 2 databases increases data granularity and helps to minimize this limitation.

Conclusion

The costs associated with pediatric HT have decreased in the most recent era, suggesting the evolution of more cost effective management strategies. These changes may be in part related to shifts in pediatric mechanical circulatory support.

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Abbreviations

ECMO	extracorporeal membrane oxygenation
HT	heart transplant
MCS	mechanical circulatory support
OPTN	Organ Procurement and Transplantation Network
PHIS	Pediatric Health Information System
SRTR	Scientific Registry of Transplant Recipients
VAD	ventricular assist device

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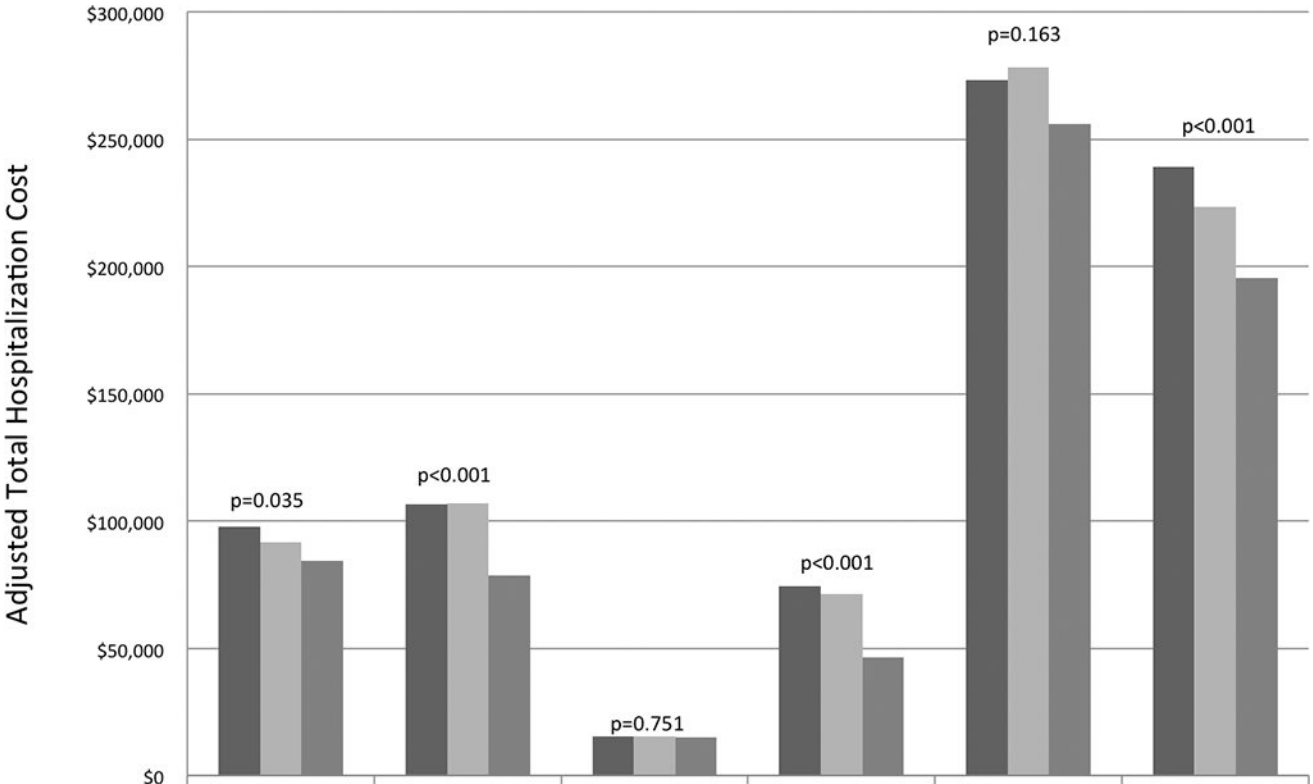

	Pharmacy costs	Lab costs	Imaging costs	Supply costs	Clinical costs	Other costs
Era 1: 2002 - 2006	$97,851	$106,585	$15,554	$74,493	$273,323	$238,962
Era 2: 2007 - 2011	$91,762	$106,849	$15,604	$71,491	$278,386	$223,295
Era 3: 2012 - 2016	$84,397	$78,430	$15,110	$46,301	$255,831	$195,576

Figure 1.
Adjusted total cost based on area of spending by era

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Transplantation. Author manuscript; available in PMC 2019 October 01.

Table 1

Population differences by era

	Total N=2896		Era 1 (2002 – 2006) N=649 (22.4%)		Era 2 (2007 – 2011) N=1028 (35.5%)		Era 3 (2012 – 2016) N=1219 (42.1%)		p–value[a]
Age									
<1 year	896	(30.9%)	216	(33.3%)	328	(31.9%)	352	(28.9%)	
1–5 years	688	(23.8%)	152	(23.4%)	239	(23.2%)	297	(24.4%)	
6–10 years	407	(14.1%)	94	(14.5%)	131	(12.7%)	182	(14.9%)	0.458
11–17 years	829	(28.6%)	174	(26.8%)	302	(29.4%)	353	(29.%)	
18–21 years	76	(2.6%)	13	(2.%)	28	(2.7%)	35	(2.9%)	
Diagnosis									
Cardiomyopathy	1330	(46.5%)	284	(44.4%)	496	(48.6%)	550	(45.7%)	
Congenital Heart Disease	1373	(48.%)	313	(48.9%)	466	(45.7%)	594	(49.4%)	0.2
Retransplant	160	(5.6%)	43	(6.7%)	58	(5.7%)	59	(4.9%)	
Race									
Caucasian	1701	(58.7%)	381	(58.7%)	622	(60.5%)	698	(57.3%)	
African-American	535	(18.5%)	143	(22.%)	184	(17.9%)	208	(17.1%)	0.013
Hispanic	493	(17.%)	94	(14.5%)	162	(15.8%)	237	(19.4%)	
Other	167	(5.8%)	31	(4.8%)	60	(5.8%)	76	(6.2%)	
Male Gender	1585	(54.7%)	346	(53.3%)	556	(54.1%)	683	(56.%)	0.465
Blood Type									
O	1310	(45.2%)	286	(44.1%)	469	(45.6%)	555	(45.5%)	
A	1087	(37.5%)	260	(40.1%)	379	(36.9%)	448	(36.8%)	0.619
B	376	(13.%)	74	(11.4%)	133	(12.9%)	169	(13.9%)	
AB	123	(4.2%)	29	(4.5%)	47	(4.6%)	47	(3.9%)	
Status at Transplant									
1A	2395	(82.7%)	483	(74.4%)	875	(85.1%)	1037	(85.1%)	
1B	320	(11.%)	80	(12.3%)	98	(9.5%)	142	(11.6%)	<0.001
2	181	(6.3%)	86	(13.3%)	55	(5.4%)	40	(3.3%)	
ECMO at Transplant	158	(5.5%)	59	(9.1%)	55	(5.4%)	44	(3.6%)	<0.001
VAD at Transplant	493	(17.%)	46	(7.1%)	176	(17.1%)	271	(22.2%)	<0.001

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	Total N=2896		Era 1 (2002 – 2006) N=649 (22.4%)		Era 2 (2007 – 2011) N=1028 (35.5%)		Era 3 (2012 – 2016) N=1219 (42.1%)		p–value[a]
Ventilator at Transplant	493	(17.%)	129	(19.9%)	177	(17.2%)	187	(15.3%)	0.045
Inotropes at Transplant	1438	(49.7%)	297	(45.8%)	513	(49.9%)	628	(51.5%)	0.059
Post-transplant iNO	1452	(50.2%)	217	(33.4%)	494	(48.1%)	741	(61.1%)	<0.001
Total Length of Stay (Days)	50	(20–98)	41	(18–77)	52	(23–97)	54	(20–111)	<0.001
Pre-transplant Length of Stay (Days)	23	(1–62)	16	(1–41)	24	(1–63)	26	(1–77)	<0.001
Post-transplant Length of Stay (Days)	18	(12–32)	18	(10–31)	18	(12–33)	19	(12–33)	0.016
Post-Transplant ICU Days	9	(4–20)	8	(4–18)	9	(5–21)	9	(5–21)	0.103
Post-Transplant Days on Ventilator	2	(1–8)	3	(1–11.75)	2	(1–8)	2	(1–7)	<0.001
Post-Transplant Complications									
Dialysis	161	(5.6%)	48	(7.4%)	49	(4.8%)	64	(5.3%)	0.063
Rejection Prior to Discharge	360	(13.6%)	74	(18.4%)	139	(13.5%)	147	(12.1%)	0.006
Stroke	99	(3.4%)	18	(2.8%)	37	(3.6%)	44	(3.6%)	0.585
Chylothorax	147	(5.1%)	12	(1.8%)	64	(6.2%)	71	(5.8%)	<0.001
Cardiac Reoperation	188	(8.3%)	50	(7.8%)	83	(9.%)	55	(7.9%)	0.63

[a] p-values from the chi square test for categorical and Kruskal Wallis test for continuous variables

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Table 2

Unadjusted and adjusted hospitalization costs based on era

	Era 1 (2002 – 2006) N=649 (22.4%)		Era 2 (2007 – 2011) N=1028 (35.5%)		Era 3 (2012 – 2016) N=1219 (42.1%)		p-value[a]		
							Overall	Era 1 vs. Era 2	Era 2 vs. Era 3
Unadjusted costs									
Total cost	$680,831	($587,849– $788,521)	$730,861	($636,746– $838,885)	$670,273	$587,527– $764,673)	0.12	0.170	0.048
Pre-transplant costs	$182,311	($154,509– $215,117)	$280,286	($239,387– $328,173)	$279,555	($240,160– $325,412)	<0.001	< 0.001	0.953
Post-transplant costs	$476,947	($407,388– $558,383)	$429,596	($370,058– $498,711)	$385,713	($334,151– $445,231)	<0.001	0.043	0.014
Adjusted costs[b]									
Total cost	$913,390	($604,342– $1,380,480)	$906,454	($599,850– $1,369,776)	$767,221	($508,211– $1,158,237)	<0.001	0.899	<0.001
Pre-transplant costs	$343,692	($270,794– $436,214)	$435,554	($344,417– $550,805)	$353,364	($281,608– $443,404)	<0.001	<0.001	< 0.001
Post-transplant costs	$586,298	($385,560– $891,550)	$586,133	($385,650– $890,837)	$508,719	($334,998– $772,526)	0.003	0. 0.996	0.002

[a] p-values from generalized linear mixed models

[b] Cost expressed as least squares mean (Lower and Upper 95% confidence interval), inflated to 2016 dollars

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Table 3

Unadjusted and adjusted hospitalization costs based on VAD Utilization

	Era 1 (2002 – 2006) N=649 (22.4%)		Era 2 (2007 – 2011) N=1028 (35.5%)		Era 3 (2012 – 2016) N=1219 (42.1%)		p-value*		
							Overall	Era 1 vs. Era 2	Era 2 vs. Era 3
Unadjusted costs									
No VAD	$661,353	($566,546– $772,024)	$663,489	($572,798– $768,540)	$596,058	($517,596– $686,415)	0.056	0.953	0.029
With VAD	$986,549	($723,476– $1,345,283)	$1,096,136	($917,845– $1,309,061)	$917,043	($788,634– $1,066,360)	0.197	0.533	0.072
Adjusted costs									
No VAD	$721,882	($471,513– $1,105,194	$721,813	($470,717– $1,106,853	$612,681	($399,713– $939,119)	0.002	0.999	< 0.001
With VAD	$1,273,933	($542,009– $2,994,241)	$1,176,332	($512,326– $2,700,933)	$975,842	($425,680– $2,237,049)	0.108	0.672	0.068

*p-values from generalized linear mixed models

Cost expressed as least squares mean (Lower and Upper 95% confidence interval), inflated to 2016 dollars