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Cost Analysis of Percutaneous Pulmonary Valve Implantation versus Surgical Pulmonary Valve Replacement

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Abstract

Right ventricular outflow tract (RVOT) and pulmonary valve dysfunction account for roughly 20% of all congenital heart diseases. Over time, these types of dysfunction can lead to right heart failure, which is associated with significant morbidity and mortality. Improvements in RVOT and pulmonary valve function may reverse some of the deleterious effects. Historically, surgical pulmonary valve replacement has been the mainstay method of pulmonary valve repair. In 2010, percutaneous pulmonary valve implantation (PPVI) was introduced in the US. This study analyzed the healthcare costs for 47 and 51 patients that underwent PPVI and surgical pulmonary repair, respectively, at Yale-New Haven Hospital from 2007 to 2014. The analysis included all costs incurred during the hospital admission and follow-up visits within one month of discharge.

The overall total PPVI and surgery costs were $71,966 ± 16,326 and $90,917 ± 22,639, respectively ($p < 0.001$). The difference of $18,951 is largely accounted for by the difference in indirect costs, $24,553 ± 7,018 and $36,195 ± 15,735 ($p < 0.001$). The remaining difference can be attributed to the direct costs, which were broken down by department. Surgery was more costly in nearly all categories, including physician fees, ICU care, and non-ICU care. The only exception was that the PPVI valve ($26,154) cost 3.5 times as much as the surgical valve ($7,556).

A multivariate regression analyses of the overall total cost with patient demographic and clinical characteristics yielded a model consisting of the variable, hospital length of stay, as the only statistically significant predictor of cost ($p = 0.016$, $R^2 = 0.363$).

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Introduction

Right Ventricular Outflow Tract Dysfunction

The prevalence of congenital heart disease ranges from 6 to 13 out of 1000 live births (1). Of all congenital heart diseases, roughly 20% involve right ventricular outflow tract (RVOT) and pulmonary valve dysfunction (2). These defects are present in pathologies including transposition of the great arteries, tetralogy of Fallot, truncus arteriosus, double outlet right ventricle, and others. While surgical techniques exist to modify and improve RVOT and pulmonary valve dysfunction, these methods in general do not result in complete normalization of the RVOT or pulmonary valve function. Thus, patients with these types of congenital heart disease frequently endure life-long RVOT and valve dysfunction to varying degrees.

Both RVOT and pulmonary valve dysfunction can eventually lead to right heart failure. RVOT obstruction results in pressure overload of the right ventricle with resultant muscular hypertrophy, which itself has deleterious effects on systolic and diastolic function. Pulmonary valve regurgitation results in volume overload of the right ventricle. This often leads to progressive chamber dilation with associated tricuspid valve regurgitation and systolic dysfunction.

Studies indicate that severe RVOT dysfunction and pulmonary regurgitation can lead to increased morbidity, such as exercise intolerance, atrial and ventricular arrhythmias, and increased overall mortality (3). Improvements in RVOT and pulmonary valve function may reverse some of the deleterious effects imposed by long-standing dysfunction and thereby decrease morbidity and mortality.

There are currently two pulmonary valve repair methods: surgical pulmonary valve replacement and percutaneous pulmonary valve implantation (PPVI).

Surgical Pulmonary Valve Replacement and Percutaneous Pulmonary Valve Implantation

In the 1950s, the development of open-heart surgery allowed congenital heart diseases to be treated with surgical techniques, which remained the standard treatment for RVOT and pulmonary valve defects for decades. Surgical repair involves the placement of a conduit, a segment of animal jugular vein containing a three-leaf valve, to connect the right ventricle to the pulmonary valve; in other instances, a patch to modify the patients' own conduit is sufficient to repair the defect. Conduit replacement or reconstruction typically uses synthetic, homograft, or autograft tissue, which cannot grow with the host patient. Given the nature of congenital heart diseases that may necessitate surgery in the first days or months of life, patients may require repeat surgeries when they outgrow their prosthetic conduit. With time, RVOT obstruction and pulmonary regurgitation can also recur as the conduit and valve wear out. There is debate regarding the timing of repeat interventions: early intervention in the worsening disease process improves symptoms but would require more frequent re-intervention; later intervention may lead to irreversible deterioration of right ventricular function. Thus, the benefits of improving or maintaining ventricular function must be weighed against the risks and costs of repeat surgeries (4).

In the late 1990s, the first transcatheter pulmonary valve was developed and successfully implanted into animals. In 2000, the first human transcatheter pulmonary valve replacement was performed on a 12-year old boy with stenosis and insufficiency of his prosthetic conduit (5). Transcatheter procedures created the possibility of providing the same, or similar, benefits to ventricular function as surgical replacement did - but without the risks of repeat sternotomies (4).

Further research and commercial development of the transcatheter pulmonary valve was conducted by Medtronic, Inc. Between 2006 and 2010, the Melody® valve was approved for use in the Europe, Canada, and United States. Since 2000, more than 6000 valves have been implanted and a dozen studies of early and mid-term outcomes conducted (3). These studies suggest that PPVI improves RVOT obstruction and regurgitation to reestablish ventricular load within normal range, while sustaining pulmonary valve competence.

Research indicates that percutaneous pulmonary valve implantation (PPVI) is a promising alternative to surgery, providing similar benefits with less procedural morbidity. Statistically, roughly 50% of surgical conduits require replacement after 10 years, with subsequent replacements often having shorter lifespans (3).

Melody® Valve and Its Clinical Use

Figure 1. Melody® valve and Ensemble® transcatheter delivery system (3).

The Melody® valve is composed of a valved bovine jugular venous conduit sutured into a balloon expandable metal stent. At its smallest, the flexible stent can be crimped into a diameter of 7mm. On inflation, the valve can function well from a diameter of 14mm to 22mm;

flexibility and wide range in size were important in the design of this valve, due to the variability in RVOT architecture that different patients may have (4).

The Ensemble® transcatheter delivery system consists of a guide wire and two balloons that facilitate conduit deployment. The delivery system is inserted through the femoral vein into the RVOT. The balloons are then inflated sequentially to deploy the valve. Once the valve is implanted, the balloons are deflated, and the delivery system is removed (4).

The Melody® valve was approved by the FDA under the Humanitarian Device Exemption Program for use as an adjunct therapy to surgery. Guidelines dictate that the adult or pediatric patient must have a RVOT of at least 16mm in diameter, with RVOT dysfunction that requires intervention: either moderate to severe regurgitation or stenosis (mean RVOT pressure gradient ≥ 35mm) (4).

Economic Analyses in Healthcare

Rising healthcare spending in the US has brought increasing scrutiny to its high costs. As such, economic analyses of healthcare services have become increasing relevant and important to many stakeholders, including patients, physicians, administrators, taxpayers, and policymakers. Results of these analyses may have a significant impact on healthcare policy: for example, when presented with multiple options, lawmakers may choose to fund the interventions that are more cost-effective over others. This section provides a brief overview of the main types of economic analyses and their key attributes.

Table 1. Types of economic analyses (6).

Analysis Type	Metric	Description
Cost analysis	$	Evaluates only cost of an intervention.
Cost-effectiveness analysis	$/year	Evaluates cost per additional year of life gained due to an intervention.
Cost-utility analysis	$/QALY* or $/DALY**	Evaluates cost per additional year of life of equivalent quality gained due to an intervention.
Cost benefit analysis	Variable metric	Evaluates all positive and negative consequences of an intervention, converted to a comparable metric. Typically used to evaluate effects of public policies.

*Quality-adjusted life-year. **Disability-adjusted life-year.

Cost analyses evaluate cost only, without regard to the effectiveness of the intervention. Cost-effectiveness, cost-utility, and cost benefit analyses can only be conducted if the effectiveness of the intervention is well-understood and quantifiable.

When calculating costs, it is important to consider the perspective of the analyses.

Table 2. Perspectives of cost analyses.

Perspective	Description
Patient / family	Costs borne by patient and family.
Provider	Costs borne by hospitals, clinics, etc.
Payer	Costs borne by insurance companies, Medicaid, Medicare, etc.
Health system	Costs related to providing health care, including all categories of providers.
Society	All costs, regardless of who bears them.

Other important attributes of economic analyses include types of cost, time horizon, discounting and inflation (7):

Types of cost: direct healthcare costs include physician services, hospital services, medications, etc. Direct non-healthcare costs are those incurred surrounding healthcare, such as transportation to and from care facilities. Indirect costs include healthcare administration, finance, utilities, etc.

Time horizon: this refers to the time frame within which significant health and economic outcomes are captured in the analysis. Depending on the intervention, the time horizon may range from a single disease episode, one patient lifetime, or even multiple generations.

Discounting: discounting accounts for the passage of time and preference for benefits to occur earlier rather than later. This is because costs and benefits that occur in the future are considered to have less value than those that occur today.

Inflation: given that ten years ago, $1 had greater purchasing power than it does today, costs from different years must be adjusted for inflation so that all values are in dollars of one single comparable year.

Published Cost Analyses of Transcatheter Valvular Procedures

Cost analyses of transcatheter valvular procedures have primarily focused on aortic and mitral valve implantations in adults. Due to the immaturity of the field of mitral valve implantation and its research, only the cost studies on aortic valve replacement are discussed here.

Transcatheter aortic valve replacement (TAVR) is approved to treat symptomatic aortic stenosis in patients unsuitable or at high risk for surgical correction. Without treatment, symptomatic aortic stenosis has a mean survival duration of only 1.8 years and a high 5-year mortality rate of 88% (8). Since its first use in 2002, more than 100,000 procedures have been performed around the world (9). It is estimated that the prevalence of severe aortic stenosis is 3.4% in the elderly (>75 years old), accounting for 27,000 new TAVR candidates in Europe and North America annually (10).

Given the significant patient population and relatively longer history of TAVR (compared to PPVI), studies have focused on two issues: cost effectiveness of TAVR versus medical therapy in nonsurgical candidates, and cost effectiveness of TAVR versus surgical aortic valve replacement (SAVR). Two cost studies were based on the randomized controlled clinical study, Placement of Aortic Transcatheter Valves (PARTNER) trial. In cohort A, high risk patients were randomized to TAVR and SAVR. In cohort B, nonsurgical patients were randomized to TAVR and medical management.

Cost comparisons of TAVR versus SAVR in high-risk patients have yielded inconsistent results. One was based on a randomized controlled trial, and the others were based on hypothetical patient population models. Among the six studies across North America and Europe, half found TAVR to be more cost-effective than SAVR. When TAVR was found to be more cost-effective, it was due to shorter hospital lengths of stay and/or decreased follow-up medical costs (11, 12). When TAVR was less cost-effective, it was attributed to the significantly higher cost of the TAVR valve (11, 13, 14). Three of the studies differentiated between transapical (TA) and transfemoral (TF) TAVR, because the different access sites are thought to affect procedural risk and recovery. The studies concluded that TF-TAVR was more cost-effective than SAVR, but TA-TAVR was less cost-effective than SAVR (11, 13, 15).

Table 3**.** Cost-effectiveness studies comparing TAVR and SAVR in high-risk patients (8).

Authors	**Location**	**Study Method**	**Time Horizon**	**Result**
Reynolds et al.	US	Based on PARTNER trial.	1 year	TF[1] >[3] SAVR
				SAVR > TA[2]
Gada et al.	US	Hypothetical patient population model. TF vs. SAVR.	Lifetime	TF > SAVR
Gada et al.	US	Hypothetical patient population model. TA vs. SAVR.	Lifetime	SAVR > TA
Doble et al.	Canada	Hypothetical patient population model.	20 years	SAVR > TAVR
Neyt et al.	Belgium	Hypothetical patient population model.	1 year	SAVR > TAVR
Fairbairn et al.	UK	Hypothetical patient population model.	10 years	TAVR > SAVR

[1] TF transfemoral TAVR. [2] TA transapical TAVR. [3] x > y indicates x is more cost-effective than y.

The only cost analysis based on the randomized controlled trial PARTNERS was conducted by Reynolds et al. In cohort A of the PARTNERS trial, high risk patients anatomically suitable for transfemoral access (n = 492) were randomized to TF-TAVR or SAVR. Those that were not suitable (n = 207) were randomized to TA-TAVR or SAVR. The trial found that TAVR or SAVR had similar 1- and 2-year survival rates. Quality of life was greater in TAVR patients at 1 month after the procedure, but similar at 6- and 12-month follow-up (16).

Reynolds et al. also broke down the cost analysis by access site, but limited the analysis to the first 12 months, rather than lifetime time horizon (11). Of note, they assumed physician fees for TAVR and SAVR were identical; in contrast, the costs of the TAVR and SAVR valves were $5,277 and $30,000, respectively. TF-TAVR and SAVR had similar admission costs ($73,219 vs. $74,067), because the higher valve cost was offset by shorter hospital stay (6 days). TA-TAVR patients similarly had shorter hospital stays (1-2 days), but it was insufficient to offset the higher valve cost and resulting overall admission cost ($90,919 vs. $79,024). Follow-up costs were nearly identical for all groups. TAVR and SAVR cohorts as a whole were similar in cost-effectiveness; however, when the TAVR cohort was broken down by access site, TF-TAVR was found to be more cost-effective than SAVR, while TA-TAVR was less cost-effective.

The seven cost studies comparing TAVR and medical therapy in nonsurgical candidates have been fairly consistent: all but one concluded that TAVR significantly increases survival, as well as healthcare costs. While TAVR may not be more cost-effective than medical management, the increased survival renders TAVR cost-effective. The studies were conducted in Europe and North America, with cost projections based on time horizons ranging from 3 year to lifetime. One was based on patient data from a randomized controlled trial; the remaining are based on hypothetical patient populations with projected medical outcomes based on published literature and standardized medical costs within that country. The cost per quality-adjusted life-year ranged widely, from $25,000 in the UK, to four times that amount in the US (8).

Table 4**.** Cost-effectiveness studies comparing TAVR and medical therapy in nonsurgical candidates (8).

Authors	**Location**	**Study Method**	**Time Horizon**	**Result**
Reynolds et al.	US	Based on PARTNER trial.	Lifetime	TAVR >[1] MM[2]
Gada et al.	US	Hypothetical patient population model.	Lifetime	TAVR > MM
Doble et al.	Canada	Hypothetical patient population model.	20 years	MM > TAVR
Neyt et al.	Belgium	Hypothetical patient population model.	Lifetime	TAVR > MM
Watt et al.	UK	Hypothetical patient population model.	10 years	TAVR > MM
Hancock et al.	Canada	Hypothetical patient population model.	3 years	TAVR > MM
Simon et al.	US	Hypothetical patient population model.	Lifetime	TAVR > MM

[1] x > y indicates x is more cost-effective than y.

[2] MM medical management.

The cost study conducted by Reynolds et al. is considered to be the most definitive, because it is the only one based on data from the PARTNER randomized controlled clinical trial. Cohort B of the trial randomized nonsurgical patients with severe aortic stenosis to TAVR (n = 179) or medical treatment (n = 179) in 21 centers (17 US, 3 Canadian, 1 European) (17). Reynolds et al. used medical and hospital billing data from the first 12 months after the procedure to project cost-effectiveness over the patient lifetime. Quality-adjusted life-years were derived by administering health status questionnaires at 1, 6, and 12 months (18).

Compared to patients undergoing medical treatment, TAVR patients had lower 12-month follow-up costs ($29,289 versus $53,621) due to lower hospitalization rates. However, TAVR increased life expectancy by 1.6 years (1.3 quality-adjusted life-years), so the associated medical follow-up resulted in an incremental cost of $79,837. This translates to an incremental cost-effectiveness ratio of $50,200 per year of life gained, or $61,889 per quality-adjusted life-year gained. Given that the accepted incremental cost-effectiveness ratio in Western countries is typically taken to be $50,000 per quality-adjusted life-year gained, the authors concluded that TAVR is a cost-effective option for nonsurgical candidates (18).

PPVI Cost Analyses

Unlike aortic valve replacement studies, economic analyses of pulmonary valve replacement is limited to cost analyses only. This is because cost-effectiveness can only be evaluated when there is sufficient data on the effectiveness of an intervention, which is not yet available for PPVI due to its recent introduction and relatively small patient population.

Table 5**.** Cost analyses of PPVI versus surgical replacement.

Authors	**Location**	**Study Method**	**Time Horizon**	**Result**
Gatlin et al.	US	Based on clinical data of 39 patients.	5 years	PPVI >[1] SM[2]
Vergales et al.	US	Based on clinical data of 34 patients.	5, 10 years	SM > PPVI
Raikou et al.	Canada	Hypothetical patient population model.	25 years	PPVI > SM

[1] x > y indicates x costs more than y.
[2] SM surgical management.

The first study comparing the costs of PPVI versus surgical pulmonary valve replacement was conducted at the Children’s Healthcare of Atlanta in 2011. The cohort included 33 surgical and 6 PPVI patients, who underwent procedures between 2004 and 2010. The study calculated the total 5-year hospital cost: this included direct hospital costs and labor costs; nurse and other ancillary personnel costs were estimated from hourly wages, and physician fees were estimated from Medicare reimbursement rates. The 5-year cost also included reintervention costs: the freedom from reintervention rates were derived from data published in three reintervention studies (53% for percutaneous pulmonary valves and 90% for surgical conduits), and the cost of each additional intervention was assumed to be the same as that of the first procedure (19).

While the cost of the transcatheter valve and delivery system ($30,500) was greater than that of the surgical conduit ($8,700), the total procedural costs were nearly identical ($50,000 per procedure). Due to the higher rate of reintervention for transcatheter valves, the study concluded a cost savings for surgical cases of $20,000 per patient at 5 years. However, the study acknowledges that the high cost of transcatheter pulmonary valves may be associated with the initial learning curve of the new technology; reintervention rates, and therefore total cost, may decrease in the future as experience with the device increases. Finally, the study recommends future analysis of costs to society: given that patients undergoing transcatheter procedures typically have hospital stays that are two days shorter than those undergoing surgery, the cost to families due to lost wages during the recovery period should be considered as well (19).

A similar study was conducted in 2013 at the University of Virginia. The first 17 patients who had undergone PPVI were compared to 17 patients who had undergone surgery during the same time period. Both 5-year and 10-year economic estimates were made. Instead of costs, however, the data on actual hospital charges were obtained, then converted to hospital costs using a standard overall ratio of cost to charge specific to each department. Similar to the first study, charges and costs included only those associated with the admission for the procedure, and not those before or after discharge. Societal costs were also accounted for: wage loss was calculated by summing the patient’s hospital length of stay with recommended recovery time before returning to work. Wages were based on average, gender-specific earnings reported by the U.S. Department of Labor and U.S. Bureau of Labor Statistics. It was assumed that the mothers of patients under the age of 18 were out of work for the recommended patient recovery time. The authors also conducted a sensitivity analysis to model the degree to which the reintervention charges of the two procedures would need to change in order to result in equivalent costs (20).

The study found that the mean hospital charges for surgery patients ($126,406 ± $38,772) were significantly higher than those for PPVI patients ($80,328 ± $17,387), which is largely due to shorter length of stay (1 day ± 0 vs. 5.7 ± 2.2 days) without use of intensive care services. Furthermore, cost to society was lower for transcatheter patients due to shorter length of stay and recovery time, which resulted in wage loses of $611 versus $3,113. Sensitivity analyses showed that transcatheter implantation failure rates would need to be 17% per year, significantly higher than the published revision rate of 6%, before it lost its cost benefit. Thus, the authors concluded that transcatheter procedures have a clear cost advantage over surgical procedures (20).

Outside the United States, a British study drew opposite conclusions. The study conducted at the Great Ormond Street Hospital in London compared the cost of treating patients with right ventricular outflow tract dysfunction when PPVI is available, and the cost of treating patients when only surgical replacement is available. There are several important differences between this and the American studies: first, the authors here excluded the first 50 PPVI patients to omit the effect of the learning curve; this resulted in 141 patients who had undergone PPVI. Second, the study used the average costs of these patients to project 25-year costs for a hypothetical population of 1,000 patients. In the study group with only surgery as a treatment option, the model assumes that a certain proportion of this group will undergo surgical re-operation, another proportion will die, and the remaining proportion will be free of re-operation. In the cohort with PPVI as an option, a proportion will receive a second PPVI, another proportion will undergo surgical replacement, a third proportion will die, and the remaining will not need another procedure. The study concluded that PPVI is more costly than surgical management over 25 years, by £2,041 ($3,076) to £3,913 ($5,894) (21).

Study Methodology

This study analyzed the clinical and financial records of PPVI patients and a comparable cohort of surgical patients who have undergone pulmonary valve replacement or implantation at Yale-New Haven Hospital between 2007 and 2014.

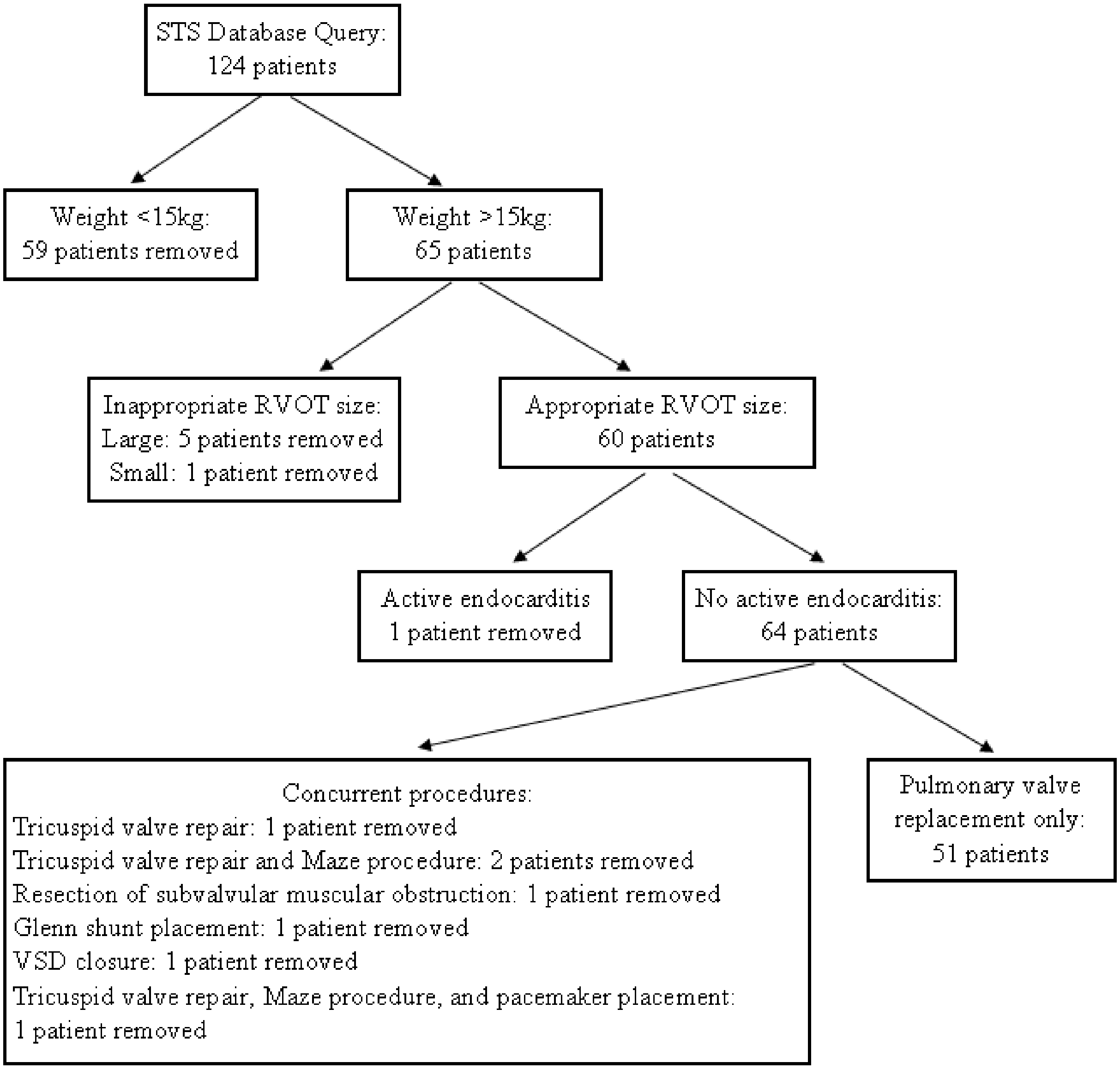
PPVI Patients

PPVI patients were identified from existing clinical databases. All patients who were reported to have undergone transcatheter pulmonary valve implantation at Yale-New Haven Hospital were included in the initial cohort. Additional clinical data were obtained through the Improving Pediatric and Adult Congenital Treatment (IMPACT) Registry. The initial group included 52 patients. One patient was excluded, because she had a Sapien, rather than Melody valve implant. Two patients were excluded, because PPVI was attempted but unsuccessful due to technical reasons, and surgical replacement was performed instead. One patient was excluded, because the Melody placement was part of a staged procedure with subsequent surgical tricuspid valve replacement during same admission. One patient was excluded, because the indication for PPVI was endocarditis. The remaining 47 patients, all of whom received Melody valves, were analyzed in this study.

Surgical Patients

The initial cohort of surgical patients was obtained from querying the surgical database of the Society of Thoracic Surgeons (STS) for all patients who had undergone pulmonary valve replacement at Yale-New Haven Hospital between January 1 2007 and December 31st, 2014 (Figure 2). Additional clinical information was obtained through electronic medical records. The query returned 124 patients: 59 were excluded for weighing less than 15kg, the lower bound of patients eligible for PPVI. Six patients were excluded, because their right ventricular outflow tracks were too large or too small. One patient was excluded, because the indication for pulmonary valve replacement was endocarditis. Seven patients were excluded for having additional concurrent procedures performed. The remaining surgical cohort analyzed in this study included 51 patients.

Figure 2: Surgical cohort selection



Financial Records

Hospital cost data were obtained from the Yale-New Haven Hospital Department of Analytic Strategy and Financial Planning. The data included itemized direct medical costs (excluding physician fees) for each patient’s hospital admission, indirect costs (administration, medical records, finance, utilities, etc.), and costs of outpatient and inpatient follow-up visits within one month after admission. Actual physician fees for each procedure were not able to be obtained from Yale Medical Group. Instead, physician fees were derived from current procedural terminology codes and standard Medicare reimbursement rates: $8,500 for PPVI and $11,040 for surgical replacement.

Methods of Analysis

The baseline characteristics of PPVI and surgical cohorts were analyzed to compare their demographic and clinical features. Demographic data included: age, gender, height, weight, and insurance status. Clinical data included: cardiac diagnosis, indication for pulmonary valve procedure, pre-operative factors, and other comorbidities. Echocardiographic and MRI data were also obtained to compare right ventricular ejection fraction (RVEF), degree of tricuspid regurgitation, right ventricular outflow tract maximum instantaneous gradient (RVOT MIG) and right ventricular end diastolic volume (RVEDV). Two-tailed t-tests and two-proportion z-tests were used to identify any statistically significant differences in demographic and clinical features between the PPVI and surgery groups.

Cost Analysis

This analysis examines cost only, because there is insufficient clinical data to conduct a cost-effectiveness analysis. The overall total costs was broken down into direct and indirect hospital costs, inpatient, and outpatient follow-up costs. There was no discounting necessary in this analysis, because discounting is necessary for projection of future costs, but we only analyzed costs incurred in the past.

Annual inflation rates specific for medical services were obtained from the US Bureau of Labor Statistics for the years 2007 to 2014. The annual rates were then compounded to convert costs from 2007-2013 to 2014 dollars. All costs are analyzed in 2014 dollars.

Table 6: Annual inflation rate of medical services (22).

Year	Inflation Rate
2007-2008	3.7%
2008-2009	3.2%
2009-2010	3.4%
2010-2011	3.0%
2011-2012	3.2%
2012-2013	2.0%
2013-2014	3.0%

The cost analyses examined the direct and indirect costs associated with the valve procedure, including the associated hospitalization, any hospital readmissions, and outpatient follow-up visits within one month of discharge. The direct costs were further broken down by department to identify sources of variation. Multivariate regression analyses were conducted to identify any statistically significant differences in the total costs between the PPVI and surgical groups, as well as any demographic or clinical characteristics that affect the overall total cost. Similar analyses were also conducted to look for patient characteristics that affect variations in cost within each group. All statistical analyses were performed using STATA 12.1.

Limitations of the Study

This study is limited to hospital healthcare costs and does not include other costs to society, such as patient lost wages or home nursing services. In addition, the study is limited to the costs incurred during the procedure and follow-up costs in the one month after discharge. We did not predict costs over a long term time horizon.

The study is also limited by the quality of the financial data we were able to obtain. When we began analyzing the hospital detailed charges, we noticed that there were many errors. For example, some patients were missing charges for services like anesthesia, which were required for every procedure. In addition, the indirect costs were not further broken down. Lastly, we were unable to obtain actual physician fees, so standard Medicare reimbursements were used.

Results

Patient Demographics

The cohorts of PPVI and surgery patients had similar demographics, with no statistically significant differences in their gender, age, weight or height (Table 7). The PPVI cohort had slightly lower percentage of males (51%) than the surgery group (65%). The patient ages ranged from 4 to 56 years old. They had similar types of insurance coverage, with private insurance and Medicaid combining to cover more than 90% of both cohorts (Table 8).

Table 7. Demographics.

Demographics		PPVI (n = 47)	Surgery (n = 51)	P-value
Male		51%	65%	0.175
Age (years)	Mean ± SD	22.2 ± 13.2	21.6 ± 14.3	0.834
	Range	4.7 - 55.3	4.0 - 56.8	
Height (cm)	Mean ± SD	152.4 ± 20.8	150.7 ± 27.2	0.719
	Range	107.0 - 183.0	46.6 - 185.4	
Weight (kg)	Mean ± SD	59.2 ± 29.2	53.2 ± 25.0	0.268
	Range	18.0 - 161.2	15.4 - 106.0	

Table 8. Insurance status.

Insurance	PPVI (n = 47)	Surgery (n = 49)	P-value
Private	48.9%	57.1%	0.426
Medicare	2.1%	4.1%	0.587
Medicaid	46.8%	38.8%	0.432
State[1]	6.4%	4.1%	0.616
None	2.1%	2.0%	0.977

[1] State refers to Connecticut state-sponsored insurance, which is not Medicare or Medicaid, for government employees.

Clinical Characteristics

There are three indications for pulmonary valve replacement: pulmonary insufficiency, pulmonary stenosis, and the combination of both conditions. In the PPVI group, the patients were roughly evenly split across the three indications. In contrast, 86% of surgical patients had pulmonary insufficiency (Table 9).

Table 9. Indication for pulmonary valve replacement or implantation.

Indication	PPVI (n = 47)	Surgery (n = 51)	P-value
Pulmonary insufficiency (PI)	31.9%	86.3%	< 0.001
Pulmonary stenosis (PS)	34.0%	7.8%	0.001
PI and PS	34.0%	5.9%	<0.001

Tetralogy of Fallot was the most common cardiac condition in the PPVI (46.8%) and surgical group (58.8%). However, the PPVI group had a high proportion of patients with pulmonary atresia with VSD (27.7%) and aortic stenosis (13.5%), while the surgical cohort had a high proportion of patients with pulmonary stenosis (23.5%).

Table 10. Cardiac diagnosis.

Diagnosis	PPVI (n = 47)	Surgery (n = 51)
Aortic Stenosis	13.5%	0.0%
DORV	4.3%	3.9%
DTGA	4.3%	0.0%
LTGA	2.1%	0.0%
PA/IVS	0.0%	10.2%
PA/VSD	27.7%	3.9%
Pulmonary Stenosis	0.0%	23.5%
TOF	46.8%	58.8%
Truncus Arteriosis	4.3%	0.0%

Abbreviations: DORV Double Outlet Right Ventricle, DTGA Dextro-Transposition of the Great Arteries, LTGA Levo-Transposition of the Great Arteries, PA/IVS Pulmonary Atresia with Intact Ventricular Septum, PA/VSD Pulmonary Atresia with Ventricular Septal Defect, TOF Tetralogy of Fallot

Prior to the pulmonary valve replacement procedure, patients were evaluated for degree of tricuspid regurgitation and right ventricular outflow tract maximum instantaneous gradient (RVOT MIG) by echocardiography, and right ventricular end diastolic volume (RVEDV) and right ventricular ejection fraction (RVEF) by MRI. While all patients had echocardiography data, only 91 patients had reports that explicitly stated the parameters we compared. MRI data was limited to 68 patients, because patients with pacemakers cannot undergo MRIs, and some patients had MRIs in other healthcare facilities, where medical records were not accessible to us.

There were no statistically significant differences in the right ventricular ejection fraction and degree of tricuspid regurgitation between the two groups. Most patients had trivial to mild tricuspid regurgitation and an average right ventricular ejection fraction of 43-44% (Table 11). There were statistically significant differences in the RVOT MIG and RVEDV. RVOT MIG was greater in the PPVI group (51.1 ± 21.8 mmHg) than in the surgery group (27.6 ± 23.4 mmHg), while RVEDV was greater in the surgical group (170.3 ± 59.1 cc) than in the PPVI group (127.5 ± 42.1 cc).

Table 11. Right ventricle disease characteristics.

Degree of TR	PPVI (n = 41)	Surgery (n = 50)	P-value
None	0.049	0	0.117
Trivial	0.341	0.38	0.707
Mild	0.488	0.44	0.653
Moderate	0.122	0.18	0.451

RVOT MIG	PPVI (n = 41)	Surgery (n = 41)	P-value
Mean ± SD	51.1 ± 21.8	27.6 ± 23.4	< 0.001
Range	13 - 120	6 - 100	

RVEF	PPVI (n = 28)	Surgery (n = 40)	P-value
Mean ± SD	44.1% ± 10.5%	43.2% ± 9.0%	0.712
Range	27.0% - 72.0%	24.0% - 63%	

RVEDV	PPVI (n = 28)	Surgery (n = 41)	P-value
Mean ± SD	127.5 ± 42.1	170.3 ± 59.1	0.002
Range	71.2 - 278.2	49.6 - 472.8	

Of the three main types of right ventricular outflow tracts, the majority of surgical patients had transannular patches. In contrast, PPVI patients had a nearly even split between bioprosthetic valve, homograft, and transannular patch.

Table 12. Type of pre-existing right ventricular outflow tract.

RVOT Type	PPVI (n = 47)	Surgery (n = 51)
Bioprosthesis	17	1
Homograft	17	7
Transannular Patch	11	37
Other	2[1]	6[2]

[1] 1 Hancock, 1 REV. [2] 4 valvotomy, 1 valvectomy, 1 valvuloplasty.

A small number of patients in both cohorts had other conditions, with Noonan Syndrome and DiGeorge Syndrome being the most common (Table 13). A shared feature of these syndromes is cardiac defects, including pulmonary stenosis in Noonan Syndrome and tetralogy of Fallot in DiGeorge Syndrome.

Table 13. Coexisting conditions.

Condition	Number of Patients	
	PPVI	Surgery
Noonan Syndrome	0	5
DiGeorge Syndrome	3	0
Down Syndrome	2	0
Diabetes	1	2
Hypercoagulability Disorder	1	0
Hypocoagulability Disorder	2	0

Hospital Admission

There were statistically significant differences in the total length of hospital stay and length of Intensive Care Unit (ICU) stay. On average, surgery patients had ICU and overall hospital stays that were 2 and 3 days longer, respectively, than PPVI patients. PPVI patients rarely stayed in the ICU (Table 14).

Table 14. Length of hospital and ICU stay.

Admission		PPVI (n = 47)	Surgery (n = 51)	P-value
LOS (days)	Mean ± SD	1.2 ± 0.7	4.3 ± 2.4	< 0.001
	Median	1	4	
	Range	1 - 5	2 - 16	
ICU stay (days)	Mean ± SD	0.3 ± 0.5	2.5 ± 1.2	< 0.001
	Median	0	2	
	Range	0 - 2	1 - 7	

Surgical replacements were performed by five surgeons: Drs. Gary Kopf, Paul Kirshbom, Toshiharu Shinoka, Richard Kim, and Mohsen Karimi; they each performed 22, 17, 9, 2, and 1 case(s), respectively.

All PPVI procedures were performed by Dr. Jeremy Asnes. The access site for almost all patients was the right femoral vein (Table 15).

Table 15. PPVI access site.

Access Site	Number of Patients
Right Femoral	35
Left femoral	8
Right Jugular	3
Transthoracic	1

Eight PPVI patients experienced either arrhythmia or bleeding as post-procedural complications (Table 16). Ten surgery patients experienced complications that varied in severity, from bleeding and wound dehiscence to hypertensive crisis and pericardial effusion (Table 17).

Table 16. PPVI complications.

Number of Patients	PPVI Complication
2	Arrhythmia
6	Bleeding

Table 17. Surgical complications.

Patient	Surgical Complication
1	Arrhythmia, pneumothorax
2	Pericardial effusion requiring drainage
3	Systemic vein obstruction
4	Postoperative respiratory insufficiency requiring reintubation, pneumothorax, bleeding requiring reoperation
5	Arrhythmia requiring electrical cardioversion or defibrillation
6	Wound dehiscence
7	Cardiac dysfunction resulting in low cardiac output
8	Arrhythmia requiring drug therapy
9	Pulmonary hypertensive crisis (PA pressure > systemic pressure), pneumonia
10	Pneumothorax

Cost Analysis

There were statistically significant differences in the overall total, indirect, and outpatient follow-up costs between the PPVI and surgical group. The average overall total costs for PPVI and surgery patients were $71,966 and $90,917, respectively ($p < 0.001$). The indirect costs were $24,553 and $36,195 for the PPVI and surgical groups, respectively ($p < 0.001$). The direct costs were $46,850 and $55,756 for the PPVI and surgical groups, respectively ($p = 0.008$). Post-procedure readmission costs were also higher in the surgical group, but this difference did not meet statistical significance ($p = 0.889$).

The overall total cost is the sum of the direct and indirect hospital costs incurred during the admission, and the subsequent readmission and outpatient follow-up costs. The direct cost is composed of the detailed charges and physician fees from patients' hospital admissions; these detailed charges were assorted into 16 categories to compare the differences in cost for the two cohorts with greater granularity. The 16 categories include procedure costs, ICU and non-ICU care, and ancillary services, like laboratory and pharmacy.

Table 18. Cost analysis.

	PPVI (n = 47)	Surgery (n = 51)	Difference	P-value
Direct Cost				
Mean ± SD	$ 46,850 ± 11,630	$ 55,756 ± 19,365	$ 8,906	0.008
Range	$ 21,577 - 77,012	$ 31,156 ± 137,634		
Indirect Cost				
Mean ± SD	$ 24,553 ± 7,018	$ 36,195 ± 15,735	$ 11,642	< 0.001
Range	$ 9,327 - 45,174	$ 16,311 - 124,420		
Readmission Cost				
Mean ± SD	$ 267 ± 2,033	$ 354 ± 2,018	$ 58	0.889
Range	$ 0 – 13,935	$ 0 - 13,883		
Outpatient Follow-up				
Mean ± SD	$ 267 ± 352	$ 418 ± 320	$ 151	0.029
Range	$ 0 – 1,512	$ 0 – 1,063		
Overall Total Cost				
Mean ± SD	$ 71,966 ± 16,326	$ 90,917 ± 22,639	$ 18,951	< 0.001
Range	$ 31,995 - 118,209	$ 60,441 - 172,688		

Of note, the category of cardiac lab includes all direct medical costs incurred during the PPVI procedure, excluding the physician fee, Melody valve, and its delivery system. Similarly, the operating room category includes all medical costs incurred during the pulmonary valve replacement surgery, excluding the physician fee and pulmonary valve implant. Not all patients used services from all categories – for example, no PPVI patients utilized rehabilitation services - so two average costs for each category were calculated: the average cost across only those patients that utilized the services, and the average cost across all patients of each cohort.

There are several cost differences that are of note. Looking at averages across all patients, the costs in nearly all categories were higher for surgical patients compared to PPVI patients. Cardiac lab cost was $9,473, compared to $10,736 for the operating room. The total cost of ICU care was 14 times higher for surgical patients ($9,409) than for PPVI patients ($659). Non-ICU care for surgical patients ($2,794) was almost 2.6 times as expensive as that for PPVI patients

($1056). This pattern holds true for less costly departments as well, from diagnostic radiology ($1,325 vs. $278) to respiratory care ($502 vs. $66).

The notable exception to the trend of higher surgery costs is the pulmonary valve cost. The Melody valve and delivery system cost $26,154, which is 3.5 times the cost of the surgical valve ($7,556).

The higher cost of the PPVI valve becomes pronounced when we compare the largest slices of the cost pie for the two groups. The Melody valve and delivery system accounts for 36.3% of the overall total PPVI cost, compared to just 8.2% of the overall total cost that the surgical valve makes up. Cardiac lab cost is also a higher proportion of the PPVI overall total cost (15.2%) than the operating room is of the surgery overall total cost (11.7%). The indirect cost for PPVI ($24,553) is much lower than that for surgery ($36,195), but it makes up about the same percentage of the total cost, 34.1% and 39.4%, respectively. The four categories, cardiac catheterization lab, pulmonary valve, physician fees, and indirect cost, account for more than 95% of the total cost for PPVI. In contrast, the cost of surgery is spread across many more categories of services.

Figure 3. Average cost across all patients

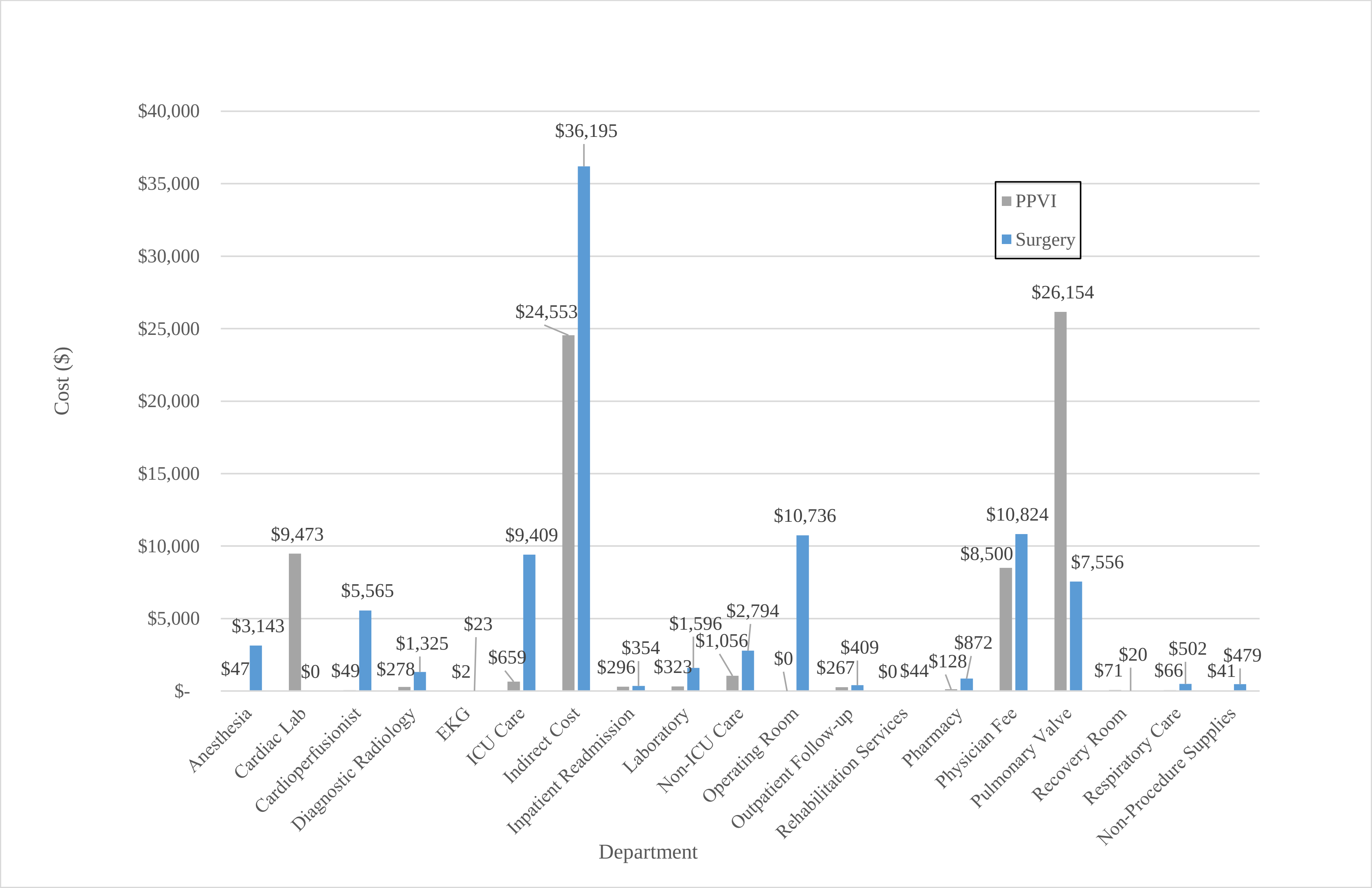


Figure 4. Average cost across service-utilizing patients.

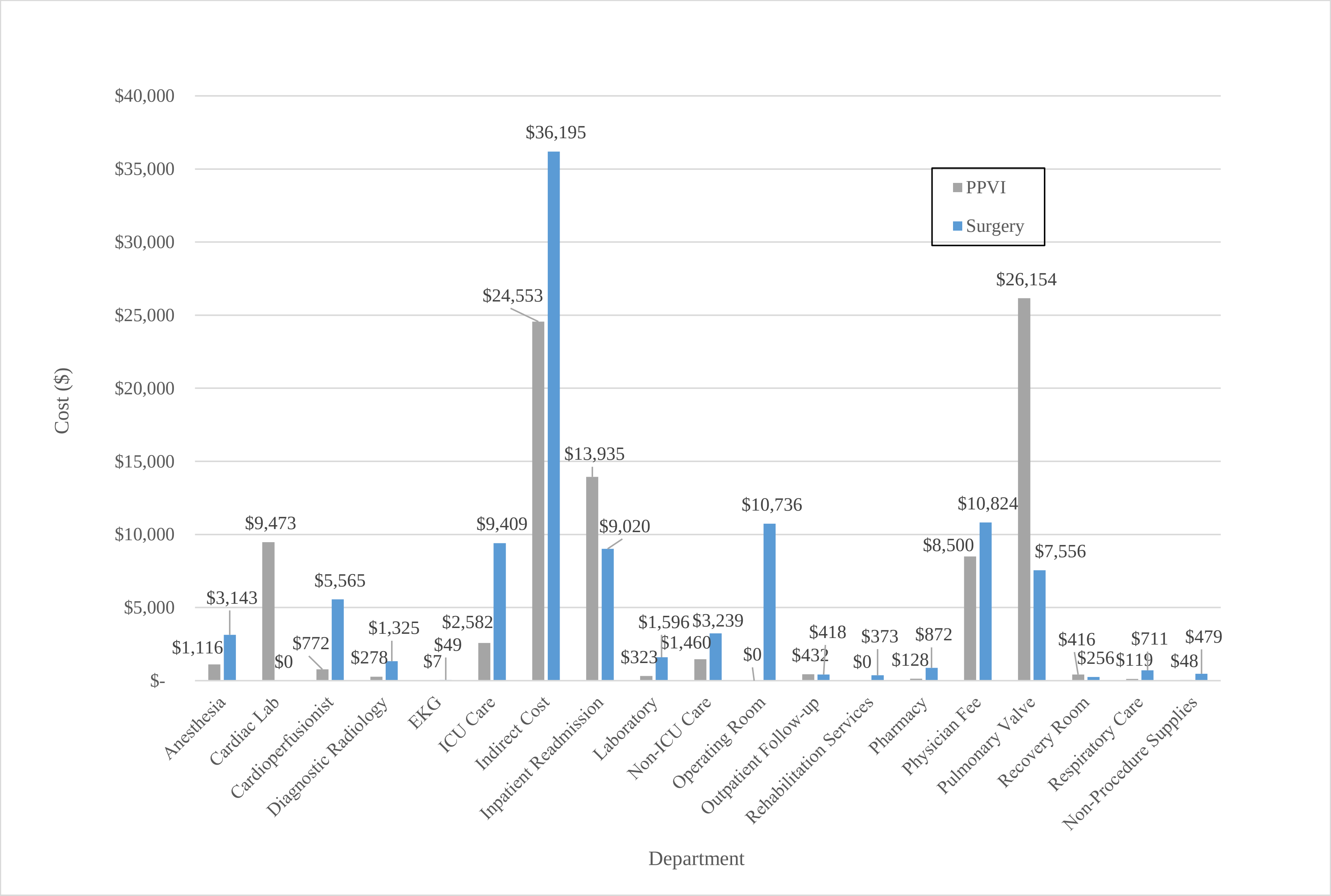


Figure 5. PPVI cost breakdown.

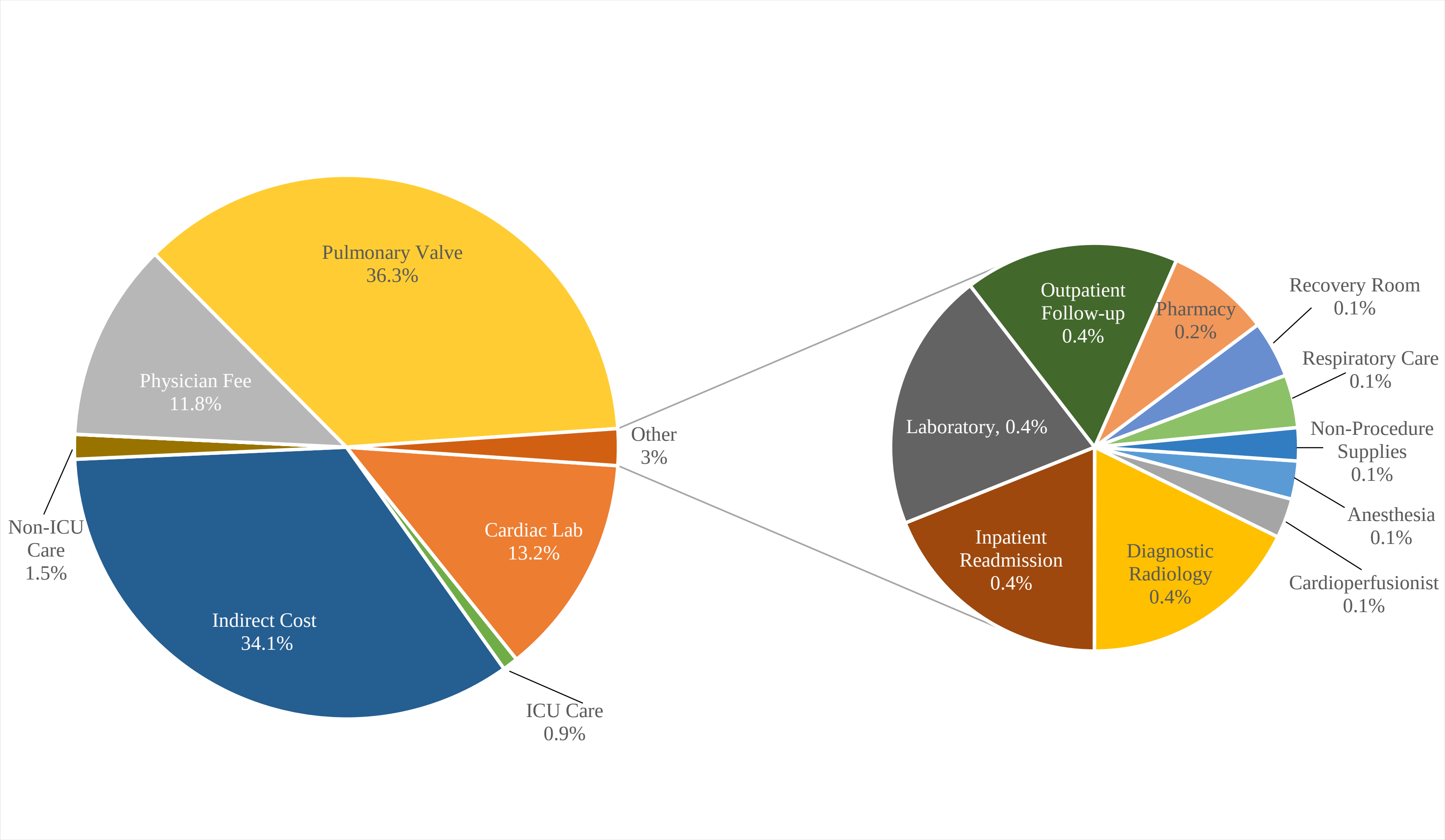
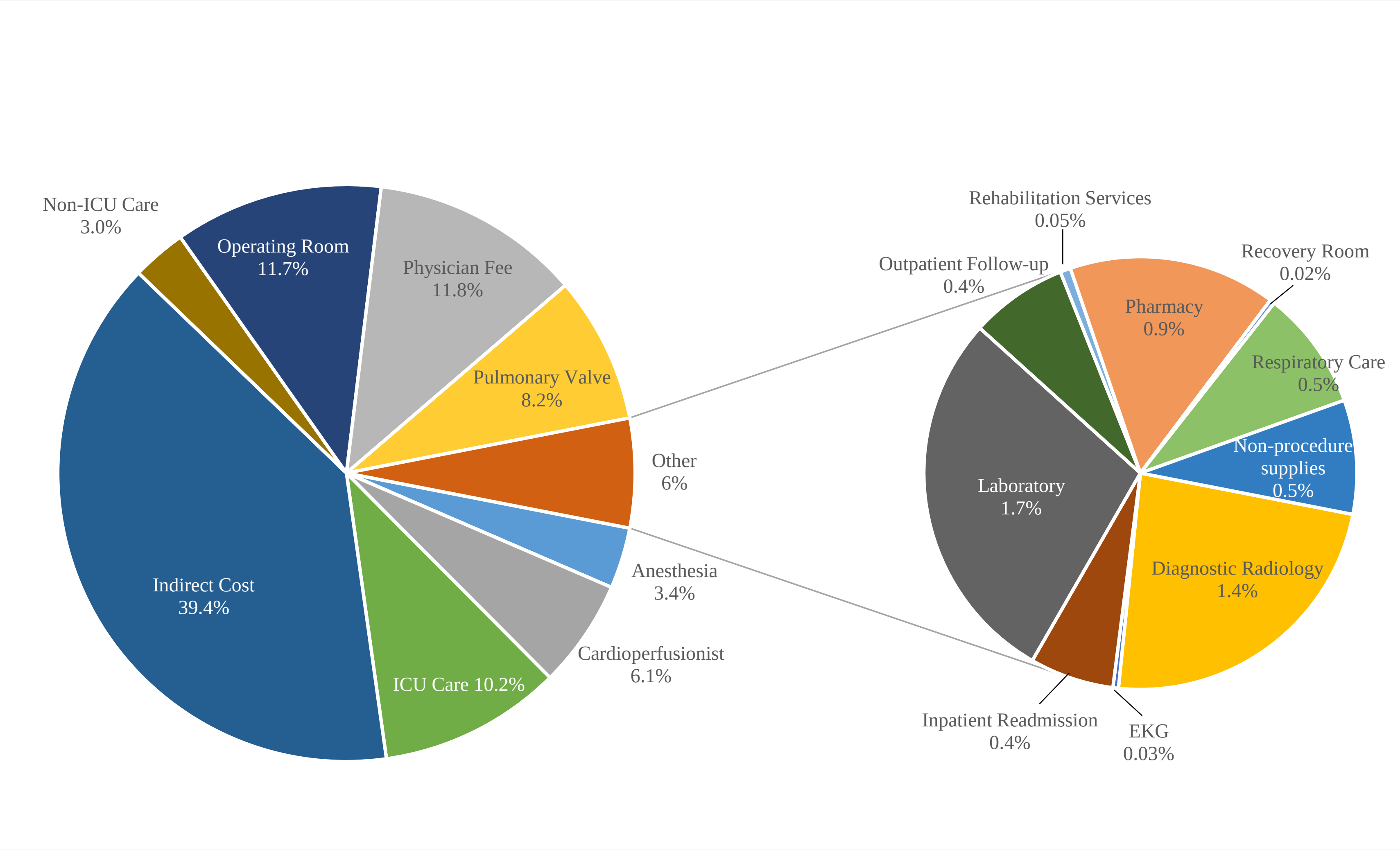


Figure 6. Surgery cost breakdown.



Multivariate Regression Analyses of Cost

Multivariate regression analyses of the total cost was conducted to identify demographic and clinical characteristics that create variations in cost. The following variables were regressed against the total cost: procedure (PPVI vs. surgery), age, gender, height, weight, year, length of stay, ICU stay, insurance, indication for pulmonary valve replacement, cardiac diagnosis, degree of tricuspid regurgitation, RVOT MIG, RVEF, and RV EDV.

The only variables that yielded statistically significant results when regressed individually with total cost were procedure type, year, total length of hospital stay, and ICU stay. However, ICU stay lost its significance when regressed with total length of stay, due to the high collinearity between them ($r = 0.57$); length of stay remained statistically significant. Procedure type also lost statistical significance when regressed with total length of stay due to collinearity ($r = 0.66$). Lastly, year of procedure lost statistical significance when run with length of stay.

One regression model we built controls for the baseline characteristics (age, gender, year, height, weight) to see if the clinical characteristics of procedure, length of stay, ICU stay, indication, RVEF, and RVEDV can account for any statistically significant difference in cost. The only variable that remained statistically significant was length of stay (Table 19). Based on the coefficient of the length of stay variable, the model tells us that each additional day of hospital stay increases cost by $4,498.50. This regression model accounts for 31.2% of the variation in overall total cost.

Table 19. Total cost regression model.

Variable	Coefficient	Std. Error	t	P > t	β
Procedure	6978.26	10141.57	0.69	0.494	0.152
Age	82.04	337.68	0.24	0.809	0.047
Gender	1644.60	5923.51	0.28	0.782	0.036
Year	1180.76	1565.77	0.75	0.454	0.108
Height	175.70	207.45	0.85	0.401	0.171
Weight	-61.87	172.62	-0.36	0.721	-0.074
ICU	-564.21	3604.39	-0.16	0.876	-0.036
LOS	4498.50	1808.55	2.49	0.016	0.505
PI	1378.80	8678.28	0.16	0.874	0.029
PS	2876.40	9422.76	0.31	0.761	0.045
RVEF	-42.02	675.52	-0.06	0.951	-0.008
RVEDV	-16.81	36.82	-0.46	0.65	-0.062
Constant	-2331844.00	3152572.00	-0.74	0.463	
R^2 = 0.312					
Adjusted R^2 = 0.162					

We conducted a similar analysis of the total costs for the PPVI and surgery patients individually. For the PPVI group, none of the variables listed in Table 19 maintained statistical significance when run together. Instead, the strongest regression model consisted of the procedure indication of pulmonary insufficiency, but did not have high R^2. This model suggests that, compared to the indication of pulmonary insufficiency, versus pulmonary stenosis or pulmonary stenosis with insufficiency, the cost decreases by $11,303.

Table 20. PPVI total cost regression model.

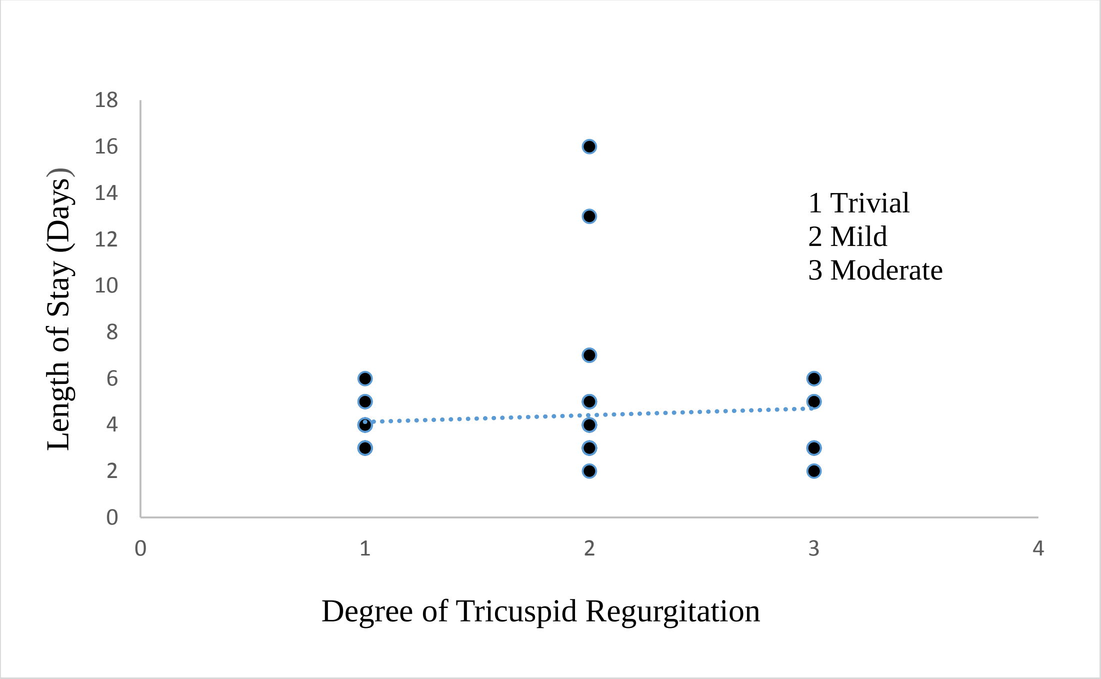
Variable	Coefficient	Std. Error	t	P > t	β
PI	-11303.15	4882.58	-2.31	0.025	-0.326
Constant	75573.08	2758.33	27.40	0.000	
R^2 = 0.106					
Adjusted R^2 = 0.087					

Finally, the regression of costs for surgical patients yielded statistical significance with the variables, length of stay and moderate tricuspid regurgitation. To see if there is a correlation between length of stay and tricuspid regurgitation, a scatter plot of the two variables was created. There was no correlation found between these two variables (Figure 7). Of note, regression of total cost with the different surgeons was not statistically significant.

Table 21. Surgery total cost regression model.

Variable	Coefficient	Std. Error	t	P > t	β
LOS	4677.08	1163.87	4.02	< 0.001	0.496
Moderate TR	14296.82	7213.88	1.98	0.053	0.24
Constant	68341.87	6001.04	11.39	< 0.001	
$R^2 =$ 0.2884					
Adjusted $R^2 =$ 0.2581					

Figure 7. Scatter plot of length of hospital stay vs. degree of tricuspid regurgitation.



Discussion

Patient Demographics

The two patient groups had similar demographics, which assured us that age, gender, height, and weight differences would be unlikely confounding factors in the cost analysis. Otherwise, if one cohort had a higher proportion of older patients who have more comorbidities, for example, age differences may lengthen their recovery time and hospital stay, which would skew that group to have higher costs.

Insurance coverage was also analyzed, because healthcare providers typically receive lower reimbursements from government-sponsored insurance than from private entities. The costs we obtained were derived by multiplying charges on patient invoices by cost-to-charge ratios, and patients with private insurance are charged higher rates. Thus, having similar assortments of insurance types in the two cohorts decreased the likelihood that insurance type would be a confounding factor.

Clinical Characteristics

There were significantly more surgery patients who had pulmonary insufficiency as their indication for valve replacement. This is because pulmonary stenosis is not frequently an indication for surgery. Prior to the introduction of the PPVI, patients with pulmonary stenosis could have their right ventricular outflow tract dilated in the catheter lab, rather than undergo surgery. Furthermore, patients with severe pulmonary insufficiency were more likely to have transannular patches and large RVOTs that would render them ineligible for the Melody valve.

There were more patients with pulmonary stenosis in the PPVI group: patients who would have undergone RVOT dilation in the catheter lab in the past, were now able to have a RVOT implanted via PPVI.

Nearly all surgical patients had free pulmonary insufficiency on cardiac echocardiography. Greater severity of pulmonary insufficiency results in right ventricular dilation, which accounts for the higher RVEDV in surgical patients (170.3 ± 59.1 cc) than in the PPVI group (127.5 ± 42.1 cc) that was statistically significant ($p = 0.002$).

Conversely, pulmonary stenosis drives up RVOT pressure, which explains the statistically significant difference in RVOT MIG between the two groups. In the PPVI group, 68% of the patients had pulmonary stenosis (the sum of patients with pulmonary stenosis only and those with both pulmonary stenosis and pulmonary insufficiency) compared to only 13.7% in the surgery group. As such, the average RVOT MIG in the PPVI cohort (51.1 ± 21.8 mmHg) was nearly twice that of the surgery cohort (27.6 ± 23.4 mmHg, $p = 0.000$).

The right ventricular ejection fraction can be considered a surrogate marker for right ventricular function. Tricuspid valve regurgitation may adversely affect venous hemodynamics and lead to venous and organ dysfunction. Since there were no statistically significant differences in these measures, right ventricular systolic function and tricuspid function in the two groups are similar. In other words, the surgery group did not have more severe cardiac disease that could lengthen hospital recovery time.

Hospital Admission

The ICU and total length of stay were significantly higher in the surgery group. This is understandable, considering open thoracic surgery is more traumatic than minimally-invasive transcatheter procedures. The longer recovery time and more severe complications in the surgery group thus account for the longer hospital stays.

Cost Analysis

The overall total cost associated with surgery was $18,951 higher than that with PPVI. This difference is largely due to the $11,642 difference in indirect cost. The indirect cost includes the non-medical hospital costs that are associated with providing care, such as administration, finance, utilities, security, etc. Indirect costs were not broken down into detailed charges in the same way that direct costs were. Instead, they are a proportion of the direct cost.

What determines the exact magnitude of the indirect cost is nebulous: as one staff member of the YNHH Financial Planning and Budget office described, “The indirect costs are a bit of a mix of art and science.” In general, indirect costs are higher for departments that have higher capital costs. For example, operating rooms have high capital costs associated with the maintenance of space, equipment, utilities, etc. As such, operating rooms have higher indirect costs than cardiac labs do.

The second largest source of the cost difference, $8,906, is the direct healthcare cost. As noted in the results section, the average cost of nearly every category was higher for surgery than for PPVI patients. For example, the care for both ICU and non-ICU were several fold higher for surgery than PPVI patients. Inpatient hospital care accounts for just 2.4% of the total cost for the PPVI group, compared to 13.2% in the surgery group. However, this is because surgery patients have longer hospital and ICU stays, not because they are charged more per day. This is elucidated when we compare the average costs distributed across only the utilizing patients: the average ICU cost for the surgery patients is 3.6 times that of the average cost for PPVI patients. However, surgical patients tended to stay in the ICU for 2-3 days longer than PPVI patients, which means the ICU cost per day is nearly equivalent for the two groups.

Because the overall total cost is lower for PPVI patients, the relatively more expensive valve ($26,154 vs. $7,556) makes up a much larger component of the total cost: 36.3% in PPVI versus 8.2% in surgery group.

We can sum up all the average costs associated directly with the pulmonary valve procedure to derive the total procedure cost (sum of cardiac lab or operating room, physician fee, valve, cardioperfusionist, and anesthesia): the average total procedure cost is $44,224 for PPVI and $38,040 for surgery. The percentage of the overall total cost that the procedure accounts for, is lower in surgery (41.2%) than PPVI (61.5%).

Smaller categories of cost are also higher for surgery patients because longer hospital stays require more services – more medications, laboratory tests, supplies, respiratory care, etc.

We did not analyze other costs to society here, such as patient lost wages. Patients are typically recommended to take three weeks for recovery time after surgery and one week after PPVI, so inclusion of this cost would have increased the cost gap between the two groups.

In published economic analyses, the higher overall total cost associated with PPVI has been attributed to the higher cost of the transcatheter valve. It was stated that PPVI will eventually become more economical once the cost of the valve decreases. However, we see that in YNHH, the cost of PPVI is already lower than surgery. When the cost of the transcatheter valve decreases in the future, the cost differential between PPVI and surgery will continue to increase at YNHH.

Multivariate Regression Analyses of Cost

The strongest regression model for the overall total cost found that the length of stay was the only statistically significant variable that explains variation in cost. As discussed in the cost analyses above, longer lengths of stay result in higher costs due to higher usage of hospital resources (eg. supplies and medications) and services (eg. nursing and respiratory care). It is also important to note that none of the demographic or clinical characteristics of the cohorts had statistically significant associations with cost. In other words, patient age, indication for pulmonary valve replacement, and cardiac diagnosis have little effect on the overall total cost. What matters most is how long a patient stays in the hospital.

When examining the factors that affect cost among PPVI patients, it is noteworthy that the indication of pulmonary insufficiency was the only statistically significant variable identified and decreases cost. This may be because patients with pulmonary stenosis tend to have multiple angioplasties and multiple stents placed prior to PPVI. As a result, patients with pulmonary insufficiency, who have fewer RVOT treatments before PPVI, incur lower costs.

In the regression model for the overall total cost for surgery, length of stay and moderate tricuspid regurgitation were the statistically significant variables affecting cost. The length of stay is an understandable predictor of cost. More severe tricuspid regurgitation is an indicator of poorer tricuspid function, which we hypothesized may increase recovery time and therefore, length of stay. However, the scatter plot of length of stay versus tricuspid regurgitation showed no correlation between the two variables, so it is unclear how moderate tricuspid regurgitation increases cost.

Conclusions

This study found that surgery is more costly than PPVI, because surgery is associated with longer ICU and hospital stays due to the trauma of open thoracic surgery. The largest component of total overall cost for both groups was the indirect cost, consisting of 34.1% and 39.4% of the total for PPVI and surgery, respectively. Surgery costs were higher in every category except for the pulmonary valve. The multivariate regression analyses of demographic and clinical characteristics yielded length of hospital stay as the only statistically significant predictor of cost.

Economic analyses in healthcare are increasingly important in this era of rising costs. In the future, if PPVI and surgical replacement are found to be clinically equally effective and PPVI is shown to be consistently more economical, healthcare payers may choose to only pay for PPVI when patients are eligible for both procedures – as they have already done with numerous other treatment options. Future economic studies comparing PPVI and surgery should include larger populations and examine cost-effectiveness, once there are sufficiently large patient populations who have had transcatheter pulmonary valves for longer periods of time to compare their relative clinical effectiveness.

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