Percutaneous Versus Surgical Pulmonic Valve Implantation for Right Ventricular Outflow Tract Dysfunction

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ABSTRACT

Background/purpose: Percutaneous pulmonic valve implantation (PPVI) is an alternative treatment strategy to surgical pulmonic valve implantation (SPVI) for right ventricular outflow tract (RVOT) dysfunction. This study sought to compare outcomes of both treatment strategies.
Methods: The study population was extracted from the 2014 Nationwide Readmissions Database (NRD) using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for PPVI and SPVI. Study outcomes included all-cause in-hospital mortality, length of index hospital stay (LOS), post-procedural bleeding, mechanical complications of heart valve prosthesis, vascular complications (VC), infective endocarditis (IE), total hospitalization charges, and 30-day readmission rates.
Results: A total of 975 patient discharges (176 in PPVI and 799 in SPVI group) were identified (average age 25.7 years; 57.5% male). PPVI was associated with significantly shorter median LOS (1 versus 5 days, $p < 0.01$), lower risk of bleeding (4.6% versus 26.4%, $p < 0.01$), and lower total hospitalization charges ($169,551.7 versus $210,681.8, $p = 0.02$). There was no significant difference between both groups in terms of all-cause in-hospital mortality (0% versus 1.4%, $p = 0.12$), mechanical complications of heart valve prosthesis (1.7% versus 2.0%, $p = 0.78$), VC (2.3% versus 2.0%, $p = 0.82$), IE (1.7% versus 3.1%, $p = 0.31$), or 30-day readmission rates (4.4% versus 7.6%, $p = 0.16$).
Conclusion: Compared with SPVI, PPVI was associated with shorter LOS, lower bleeding, and lower total charges. There was no significant difference between the two strategies in terms of all-cause in-hospital mortality, mechanical complications of heart valve prosthesis, VC, IE, or 30-day readmission rates.

1. Introduction

It is estimated that 20% of pediatric patients with congenital heart diseases have right ventricular outflow tract (RVOT) dysfunction (obstruction and/or regurgitation) requiring surgical reconstruction, and frequently redo surgical interventions for degenerated bioprostheses later in life [1]. The number of patients older than 16 years of age who will require surgical interventions for congenital heart diseases, including RVOT dysfunction, is expected to increase [2]. The RVOT dysfunction can be classified based on site of the defect into sub-valvular, valvular, or supra-valvular, in both native (i.e., unoperated) and postoperative (i.e., operated) congenital anomalies [2].

After the first in human percutaneous pulmonic valve implantation (PPVI) was reported in 2000, both balloon-expandable, and more recently self-expandable, PPVI systems have emerged as alternative treatment options to surgical pulmonic valve implantation (SPVI) [3,4]. The very first application of the PPVIs was to extend the life of surgically implanted right ventricle-to-pulmonary artery conduits in order to decrease the need for redo surgical interventions. Subsequently, the applications have been expanded to operated and unoperated RVOT dysfunction (e.g. tetralogy of Fallot and degenerated bioprosthetic valves) meeting the criteria for severe RVOT obstruction or severe pulmonic regurgitation in the absence of contraindications [5–7]. There are limited data that directly compare periprocedural clinical outcomes of PPVI to SPVI.

2. Methods

2.1. Data source

The Nationwide Readmissions Database (NRD) is a part of Healthcare Cost and Utilization Project (HCUP) databases which were developed through a Federal-State-Industry partnership and sponsored

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by the Agency for Healthcare Research and Quality (AHRQ). HCUP databases include the largest collection of de-identified longitudinal hospital care data in the United States from 35 states, including all-payer and encounter-level information. NRD is a unique data subset designed to support various types of analyses including national readmission rates with safeguards to protect the privacy of individual patients, physicians, and hospitals. The NRD contains discharges from >20 states, from all HCUP Partner hospitals. The NRD contains more than a hundred clinical and nonclinical variables for each hospital stay, including unique record identifiers that can be used to combine data elements from different NRD files, verified patient linkage numbers for linking hospital visits for the same patient across hospitals, International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) for principal procedure and diagnosis, and for secondary procedures and diagnoses (including comorbidities and complications), age, sex, length of stay (LOS), and charges of the index hospitalization [8].

2.2. Study cohort

The principal or secondary procedure fields of the NRD database were searched using ICD-9-CM codes of PPVI and SPVI to identify discharges who had these procedures during the index hospitalization. The patients' demographics, baseline characteristics, comorbidities and periprocedural complications were identified and extracted using the ICD-9-CM codes as well (Supplemental Table 1). The NRD excludes discharges from patients with missing age, missing or questionable linkage numbers or from hospitals with >50% of their discharges excluded because of these criteria, because patients treated at these hospitals may not be reliably tracked over time, it excludes rehabilitation and long-term acute care hospitals because of inconsistent data capture from these facilities and their special patient population with longer stays. We excluded all patients who had both PPVI and SPVI during the same admission.

The HCUP databases do not have a present-on-admission indicator, which could potentially limit the ability to distinguish comorbid conditions from post-procedural complications. Therefore, we used the recommended algorithms developed by AHRQ to identify the comorbid conditions (by using the Medicare diagnosis-related groups and comorbidity indices codes which are specific for comorbid conditions) and to identify the post-procedural complications (by using the patients' safety indicators version 4.4, March 2012, which have been established by AHRQ to monitor preventable adverse events during hospitalization, and the secondary codes that are specific for post-procedural complications) from secondary diagnoses' fields (Supplemental Tables 1&2) [9–12]. We followed all of HCUP's recommendations and best practices methodology to use HCUP databases highlighted by Khera et al. [13].

The NRD database also provides the number of chronic conditions and the number of diagnoses reported on discharge. A chronic condition is a condition that lasts 12 months or longer and meets one or both of the following criteria: (1) limits self-care, independent living, and social interactions; (2) needs ongoing intervention with medical products, services, and special equipment. The number of diagnoses is defined as the total number of ICD-9-CM diagnoses coded on the discharge record, including principal and secondary diagnoses, up to 15 diagnoses [14].

2.3. Study outcomes

Study outcomes included all-cause in-hospital mortality, median LOS of index hospitalization, post-procedural bleeding, mechanical complications of heart valve prosthesis, vascular complications (VC), infective endocarditis (IE), total charges of index hospitalization and 30-day readmission rates. The NRD 2014 reports all-cause in-hospital deaths, LOS, and the total charges of index hospitalization, which represents how much the hospital billed for the service but not necessarily the actual cost or the amount the hospital actually received. The actual cost was calculated by multiplying the total charges by the cost/charge

ratio based on the NRD recommendations [15]. The other outcomes were defined by either patient safety indicator codes or ICD-9-CM codes that are specific for post-procedural complications, as follows: (1) bleeding included any new post-procedural bleeding of anemia (that was not present before the procedure), or any blood or blood product transfusion post-procedure; (2) mechanical complications of heart valve prosthesis included paravalvular leak, valve malposition, embolization, dislodgement, fracture or malfunction; (3) VC included accidental puncture or injury of blood vessels or retroperitoneum, arteriovenous fistula formation, VC requiring surgery, and other VC; and (4) IE codes included bacterial, fungal and non-specified IE (Supplemental Table 2).

The 30-day readmission rate was calculated based on AHRQ and HCUP recommendations. We identified all-cause (including planned admission, injury, trauma, etc.) and all readmissions (including first and subsequent admissions) within the specified period (i.e., 30 days) to any hospital within the same state (as cross-state readmissions cannot be tracked by the NRD database). Transfers were not considered readmissions. We excluded patients who died during the index hospitalization (0% and 1.4% in PPVI and SPVI groups, respectively) or who had missing LOS from the readmission rate calculations. PVI procedures which were performed in the month of December were excluded from the readmission rate calculations because it cannot be calculated in 2 different years [16].

2.4. Statistical analysis

Statistical Analysis System (SAS) software 9.4 (TS1M4, SAS Institute Inc., Cary, North Carolina) was used for data management, extraction, and statistical analysis. Statistical analysis was performed on the actual number of discharges. Pearson Chi-Square test was used to compare the categorical variables. Mann-Whitney test and unpaired-sample t-test were used to compare the medians and the mean of the continuous variables, respectively. Multivariate logistic and linear regression models were used to identify the predictors of PPVI categorical and continuous dependent outcomes, respectively, by calculating adjusted odds ratios (OR) and 95% confidence intervals (95% CI) for baseline characteristics and common comorbidities (Supplemental Table 3) [17,18]. A p-value of <0.05 was used for statistical significance.

3. Results

In the 2014 NRD database, there were approximately 14.9 million unweighted (the actual number) which converts to 36 million discharges weighted (the national estimate which roughly equals 2.2 times actual number) based on the NRD variables provided to estimate the national rates. [8] The PPVI group included 176 unweighted (536 weighted) and SPVI group included 799 unweighted (2211 weighted) discharges (Fig. 1). Mean age was 25.7 years with 57.5% male. A total of 95% (167 cases) of the PPVI was performed via an endovascular approach and 5% (9 cases) was transapical. PPVI procedures were performed in 44 hospitals; 11 hospitals performed >5 procedures a year. The highest number of PPVI performed by a single hospital was 15. Transapical PPVIs were performed in 7 hospitals; most of these hospitals performed >5 endovascular PPVIs in the same year. Pulmonic valve disorder, anomaly, and tetralogy of Fallot represented the most common underlying causes of RVOT dysfunction, estimated at 40%, 26%, and 14%, respectively.

The PPVI group included higher patients with an underlying diagnosis of tetralogy of Fallot (22.7% versus 10.9%, $p < 0.01$) and truncus arteriosus (8.0 versus 2.3%, $p < 0.01$). The surgical group, on the other hand, had higher percentages of diabetes mellitus (5.7% versus 13.6%, $p < 0.01$), hypertension (11.4% versus 20.8%, $p < 0.01$), higher right atrium/ventricle to pulmonary artery conduit (0.6% versus 4.4%, $p = 0.02$), mean number of diagnoses (7.2% versus 10.7, $p < 0.01$) and number of chronic conditions (3.3% versus 4.5%, $p < 0.01$) in the discharge
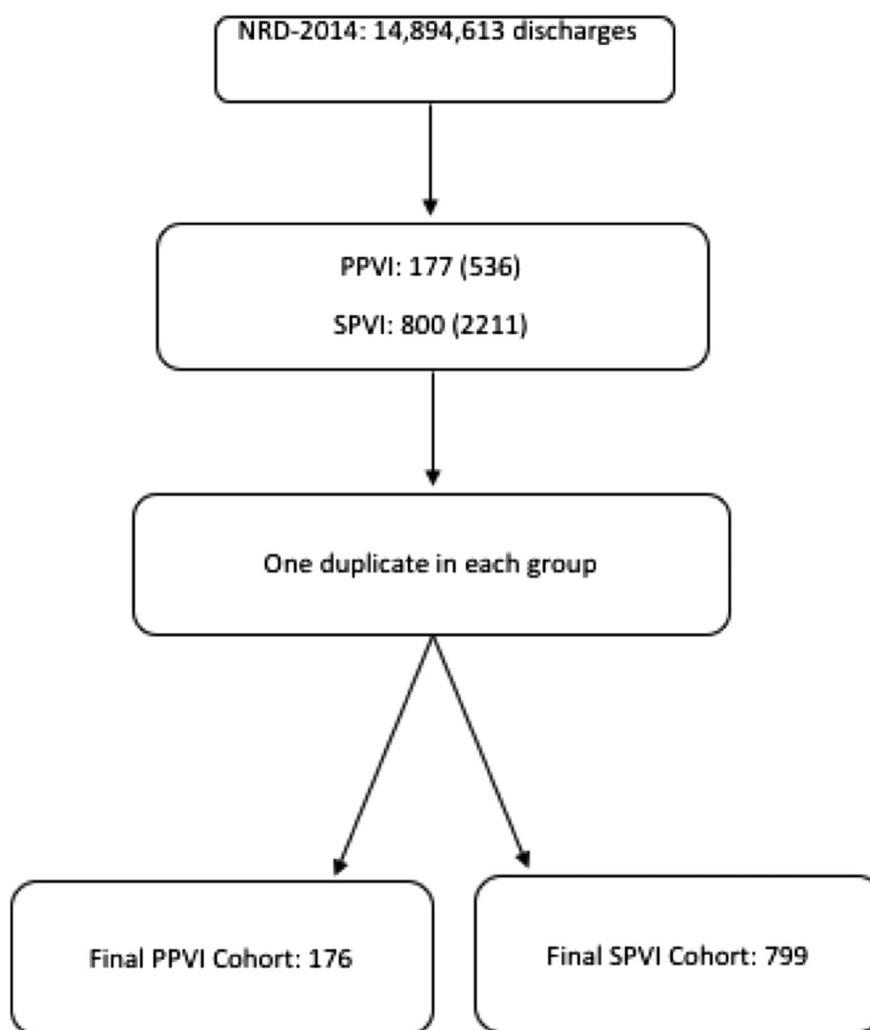
Fig. 1. Data extraction flowchart showing the unweighted (and the weighted) number of discharges.

charts. Otherwise, both groups were comparable in terms of basic demographics, baseline characteristics, anticoagulation status and other comorbidities, such as diabetes mellitus, atrial fibrillation, heart failure, cor pulmonale, pulmonic valve disorders and anomalies, and other congenital anomalies. There was no history of bioprosthetic pulmonic valve replacement in the PPVI group (Table 1).

PPVI was associated with significantly shorter median LOS (25th–75th percentiles) (1 day (1–2) versus 5 days (4–8), the mean LOS was 3.6 versus 8.5 days, respectively, all $p < 0.01$), lower risk of bleeding (4.6% versus 26.4%, $p < 0.01$), lower total ($169,551.7 versus $210,681.8, $p = 0.02$), and actual hospitalization charges ($52,802.6 versus $63,245.2, $p = 0.03$). There was no significant difference between both groups in terms of all-cause in-hospital mortality (0% versus 1.4%, $p = 0.12$), mechanical complications of heart valve prosthesis (1.7% versus 2.0%, $p = 0.78$), VC (2.3% versus 2.0%, $p = 0.82$), IE (1.7% versus 3.1%, $p = 0.31$), and 30-day readmission rates (4.4% versus 7.6%, $p = 0.16$). There were no coronary occlusion events documented in either group (Table 2 and Fig. 2A–C).

Multivariate regression models for PPVI group showed that hypertension, pulmonary hypertension (with/without cor pulmonale), heart failure, and the number of diagnoses were all associated with longer LOS (all $p < 0.05$). Age (OR = 1.03, 95% CI 1.02–1.05), diabetes (OR = 1.82, 95% CI 1.14–2.90), and number of diagnoses (OR = 1.22, 95% CI 1.16–1.28) were associated with increased bleeding (all $p < 0.05$). Truncus arteriosus (OR = 9.69, 95% CI 2.33–40.27), history of infundibular stenosis or resection (OR = 20.69, 95% CI 1.56–274.67), and the number of diagnoses (OR = 1.19, 95% CI 1.08–1.32) were associated with higher mechanical complications of heart valve prosthesis (all $p < 0.05$). Only the number of diagnoses was associated with increased VC (OR = 1.15, 95% CI 1.05–1.27, $p < 0.05$). Both the age (OR = 1.04, 95% CI 1.01–1.07) and the number of diagnoses (OR = 1.28, 95% CI 1.17–1.41) were associated with increased risk of IE (all $p < 0.05$).

4. Discussion

This study reports 176 discharges who had PPVI from the NRD 2014 database, with a national estimate of 536 PPVI and approximately 2200 SPVI which is on par with what the Society of Thoracic Surgeons databases had reported, approximately 10,000 SPVI between 2007 and 2013 [19]. There is no accurate estimate on frequency of transapical PPVIs, however, it is an uncommon procedure which is used when the conventional endovascular PPVI fails secondary to complex anatomy. The transapical PPVI experience has been limited to case reports only [1,20]. Although the transapical approach might appear over-presented in this study (i.e. 5%), the absolute number was relatively low and was performed in a limited number of higher-volume hospitals.

Pulmonic valve disorders and anomalies represented 66% of the underlying causes of RVOT dysfunction in this cohort and tetralogy of Fallot represented 14.2%, which is in accordance with the Pediatric Health Systems Database report [21]. However, it is unclear why the presence of right atrium/ventricle to pulmonary artery conduits was

Table 1

Demographics and baseline characteristics of PPVI and SPVI groups. A p-value <0.05 indicates a statistically significant difference between both groups.

Baseline characteristic	PPVI	SPVI	p-Value
Number	176	799	–
Male %	55.7	59.3	0.37
Age (SD) in years	25.0 (14.3)	26.4 (18.6)	0.30
Transapical PPVI %	5.0	–	–
Endovascular PPVI %	95.0	–	–
Diabetes mellitus %	5.7	13.6	<0.01
Hypertension %	11.4	20.8	<0.01
Chronic kidney disease %	2.3	3.4	0.45
Atrial fibrillation %	6.3	10.3	0.10
Atrial flutter %	3.4	5.8	0.21
Long-term anticoagulation %	4.0	3.3	0.63
Heart failure %	15.3	19.4	0.21
Pulmonic valve disorder %	39.8	42.4	0.52
Pulmonic valve anomaly %	26.7	26.5	0.96
Pulmonic artery anomaly %	16.5	12.4	0.15
Cor pulmonale/pulmonary hypertension %	7.4	9.3	0.43
Tetralogy of Fallot %	22.7	10.9	<0.01
Truncus arteriosus %	8.0	2.3	<0.01
Transposition of great vessels %	0.0	0.0	–
Infundibular stenosis with/without infundibulectomy %	0.6	0.4	0.72
Right atrium/ventricle to pulmonary artery conduit	0.6	4.4	0.02
The number of chronic conditions in the chart	7.2	10.7	<0.01
The number of diagnoses in the chart	3.3	4.5	<0.01

%: percentage; SD: standard deviation, PPVI: percutaneous pulmonic valve implantation, SPVI: surgical pulmonic valve implantation.

under-presented, it could indicate that PPVI has been performed more frequently for other indications such as unoperated RVOT dysfunction.

By comparing PPVI with SPVI, this study shows that PPVI was associated with four days shorter median LOS and lower bleeding rates which could be secondary to the less invasive nature of PPVI. The reported mean LOS post-PPVI and SPVI in the Pediatric Health Systems Database and in case-series varies from 1.0–5.3 days and 4.0–10.1 days, respectively [21–23]. Expectedly, a higher number of diagnoses during the index hospitalization, heart failure, cor pulmonale, and pulmonary hypertension were predictors of longer LOS and bleeding. Although previous data suggested that PPVI was associated with a small increase in long-term (i.e., over 25 years follow up) cost [24], this study shows PPVI was associated with lower total and actual cost during the index hospitalization, possibly because of the significantly shorter LOS and avoidance/delaying the surgery. The mean actual PPVI cost in the NRD dataset was $52,802.6 which is comparable to what has been previously reported [21].

There was no significant difference between PPVI and SPVI in regards to VC. VC (including conduit rupture, access site complications, and pulmonary artery injury) has been reported in 9% of the PPVIs in a recent meta-analysis [25]. Conduit rupture has been reported in <1% up to 4.1% [7,25]. This study reports total VC at 2.3%, it is not clear if conduit

rupture was included as it has no specific ICD-9-CM code and the presence of conduit was under-represented. Furthermore, ultrasound-guided access has become a standard and shown to be associated with lower VC in comparison to using anatomical landmarks which could have contributed to the lower VC reported in this study [26,27].

The mechanical complications of heart valve prosthesis (including valve dislodgement, embolization, and significant stent fracture) were reported at 3.8–6.9% depending on type and severity of stent fracture [25], however, this study reports mechanical complications in 1.7%. This lower rate was probably secondary to the fact that this cohort captured post-procedural complications during the index hospitalization but not long-term complications. Furthermore, pre-stenting status was unknown, as pre-stenting prior to valve deployment decreases the risk of valve fracture [28]. ICD-9-CM codes for mechanical complications of the heart valve prosthesis are not specific for one complication, therefore limiting the ability to specify which complication was more prevalent. History of truncus arteriosus, infundibular stenosis or resection were all predictors of mechanical complications probably because of the more complex anatomy.

IE complicates 1–5.8% of PPVI and it is considered the most important cause of late mortality. A total of 35% of IE occurs in the first year post-PPVI; early IE has been reported in 0.5–3.5% of PPVIs. It is reported more frequently after PPVI than SPVI which may be secondary to a higher likelihood of valve damage during expansion and ballooning of the percutaneous valve [1,7,25,29,30]. Our study reported early IE in 1.7% of the PPVI group, however, it also showed that IE was not statistically different between PPVI and SPVI groups. Access site, type of valve (more with Melody than Sapien), the timing of documentation (IE is a late complication) and other factors, such as sex, periprocedural antibiotic prophylaxis, and dental hygiene, are all risk factors that might have affected the incidence of IE in our study [1]. Furthermore, improved valve technology over time and improved operators' skills all might have decreased the need for post-implantation valve dilation and ballooning and subsequently decreased the degree of valve damage and the reported incidence of IE. It was noted in a recent study, that despite longer follow-up (55 versus 32 months), the historical bare metal stents in RVOT was associated with 100% freedom of IE as compared to 64% of Melody valve PPVI. Therefore, it was suggested that patients with multiple IE risk factors should be considered for SPVI or deferral melody PPVI, if possible, until more data is available [31].

All-cause in-hospital mortality and 30-day readmission rates were relatively low and were comparable in both groups in this cohort. All-cause mortality post-PPVI has been reported in literature at 0.6%. Coronary occlusion, which complicate 0–1% of PPVI, is one of the serious complications of PPVI valve implantation that occurs because of coronary artery compression by balloon inflation during valve implantation [7,25]. This cohort didn't report any coronary occlusions probably because of the increasing utilization of balloon testing (which tests for evidence of coronary compression by balloon inflation without the deployment of the valve) prior to the valve implantation [32].

Table 2

The study results. A p-value <0.05 indicates a statistically significant outcome.

Endpoint	PPVI %	SPVI %	Odds ratio	95% CI	p-Value
In-hospital all-cause mortality	0.0	1.4	0.19	0.01–3.31	0.12
Median LOS (25th–75th percentiles) in days	1 (1–2)	5 (4–8)	–	–	
Mean LOS (range) in days	3.6 (1–82)	8.5 (0–124)	–	–	<0.01
Mechanical complications of heart valve prosthesis	1.7	2.0	0.85	0.24–2.94	0.78
Bleeding	4.6	26.4	0.13	0.06–0.27	<0.01
IE	1.7	3.1	0.54	0.16–1.80	0.31
VC	2.3	2.0	1.14	0.38–3.45	0.82
Coronary occlusion	0.0	0.0	–	–	–
Total hospitalization charges	$169,551.7	$210,681.8	–	–	0.02
Readmission	4.4	7.6	0.57	0.27–1.21	016

%: percentage; PPVI: percutaneous pulmonic valve implantation, SPVI: surgical pulmonic valve implantation, LOS: length of stay; IE: infective endocarditis; VC: vascular complications; 95% CI: 95% confidence interval.
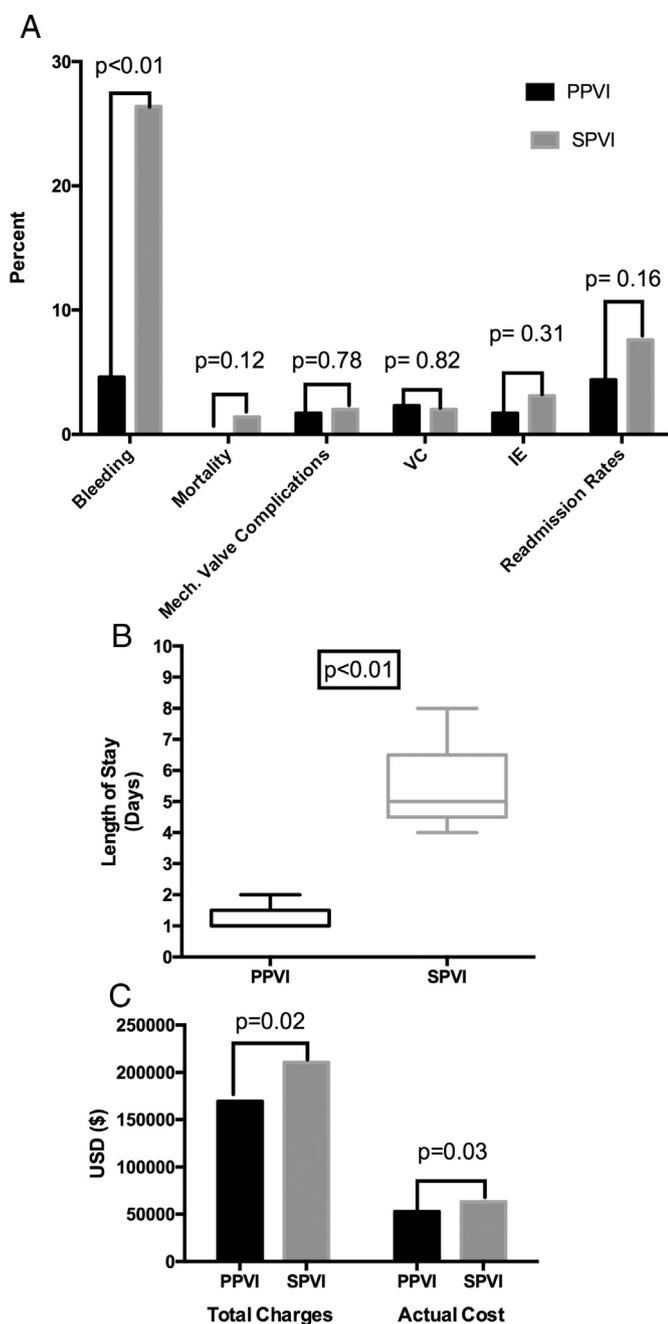
Fig. 2. The study outcomes and results. A) In-hospital all-cause mortality, bleeding, the mechanical complication of heart valve prosthesis, vascular complications (VC), infective endocarditis (IE), and 30-day readmission rates. B) Median length of stay (LOS). C) Total and actual hospitalization charges.

To our knowledge, this is the largest study to directly compare outcomes of PPVI to SPVI. It supports the safety of PPVI as an alternative option to SPVI for RVOT dysfunction with lower hospitalization costs. It also implies that PPVI can be the first line of treatment when the anatomy is suitable, with comparable periprocedural outcomes.

4.1. Limitations

This is a retrospective study, however, PPVI is performed in a limited number of centers in the country. Therefore, using large national databases, such as the NRD, is a judicious way to explore the real-world outcomes. The type of valve used, pre-stenting prior to PPVI, vascular access site, type, and severity of RVOT dysfunction, associated anomalies, and severity of illness of an individual patient were not specified in detail in the database which might have influenced the selection of treatment strategy and outcomes; it is possible that patients who were sicker (as indicated by the higher number of active diagnoses and chronic conditions) and/or had more complex anatomy were more likely to be treated surgically. Finally, the longer-term complications and outcomes, such as valve fracture, IE, and associated cost, could not be assessed.

5. Conclusion

PPVI appears to be a safe treatment option for RVOT dysfunction compared to SPVI with shorter LOS, lower hospitalization cost, and comparable peri-procedural complications. Certainly, additional studies are still needed to help address the remaining unanswered questions including: the long-term mortality, cost-effectiveness, and the outcomes of the newer valve technology (i.e. self-expanding) on the outcomes in general and on the incidence of the IE in particular.

Appendix A. Supplementary data

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