

Outcomes of concomitant percutaneous coronary interventions and transcatheter aortic valve replacement

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Abstract

Introduction: Coronary artery disease is a common diagnosis among patients undergoing transcatheter aortic valve replacement (TAVR). The treatment and timing of percutaneous coronary intervention (PCI) remain controversial. We sought to compare in-hospital periprocedural outcomes of combined TAVR and PCI during the same index hospitalization versus the isolated TAVR procedure.

Material and methods: The study population was extracted from the 2016 Nationwide Readmissions Data (NRD) using International Classification of Diseases, tenth edition, clinical modifications/procedure coding system codes for TAVR, coronary PCI, and post-procedural complications. Study endpoints included in-hospital all-cause mortality, length of index hospital stay, cardiogenic shock, need for mechanical circulatory support (MCS) devices, mechanical complications of prosthetic valve, paravalvular leak (PVL), acute kidney injury (AKI), bleeding and total hospital charges. Propensity matching was used to adjust for baseline characteristics.

Results: There were 23,604 TAVRs in the 2016 NRD, of which 852 were combined with PCI during the same index hospitalization. Mean age was 80.5 years and 45.9% were female. In comparison to isolated TAVR, TAVR-PCI was associated with higher in-hospital all-cause mortality (4.5% vs. 1.7%, $p < 0.01$), longer length of stay (10.5 vs. 5.4 days, $p < 0.01$), and higher incidence of cardiogenic shock (9.4% vs. 2.1%, $p < 0.01$), use of MCS devices (6.8% vs. 0.7%, $p < 0.01$), mechanical complications of prosthetic valve (6.8% vs. 0.7%, $p < 0.01$), PVL (0.9% vs. 0.4%, $p = 0.01$), AKI (25.5% vs. 11.5%, $p < 0.01$), bleeding (25.2% vs. 18.1%, $p < 0.01$), and total hospital charges (\$354,725 vs. \$220,474, $p < 0.01$).

Conclusions: In comparison to isolated TAVR, combined TAVR-PCI was associated with a higher incidence of in-hospital morbidity and mortality. The association and mechanism of increased mortality warrant further study.

Key words: transcatheter aortic valve replacement, percutaneous coronary intervention, in-hospital endpoints.

Introduction

The use of transcatheter aortic valve replacement (TAVR) for management of severe aortic stenosis (AS) is progressively expanding given the

emerging data confirming its non-inferiority to surgical aortic valve replacement (SAVR) regardless of the surgical risk [1–3]. In the United States, there are more than 200,000 patients with severe symptomatic AS eligible for TAVR [4].

AS and coronary artery disease (CAD) frequently coexist due to their common pathogenesis and risk factors. It is estimated that more than 50% of TAVR patients have some degree of CAD [5–7]. Early reports did not recognize CAD as an independent risk factor in TAVR patients. However, more recent reports have shown that concomitant CAD is associated with higher rates of adverse outcomes [8]. There is no clear consensus in the literature for the optimal treatment strategy for concomitant CAD and timing of revascularization (i.e. before, during or after TAVR). While all of these approaches can be applied to patients on an individual basis, current common practice is to perform percutaneous coronary intervention (PCI), when indicated, before or at the time of TAVR, as performing it after TAVR involves potential technical difficulties accessing the coronary arteries through the prosthetic valve struts [9]. Certain clinical scenarios may favor performing PCI at the time of TAVR and treating both pathologies during the same session, such as clinical deterioration (i.e. advanced heart failure/cardiogenic shock) from severe aortic valve stenosis or rarely to treat coronary obstruction secondary to TAVR, which do not permit staging these procedures. We conducted this study to compare in-hospital peri-procedural outcomes of combined TAVR and PCI during the same index hospitalization versus the isolated TAVR procedure.

Material and methods

Data source

The Nationwide Readmissions Data (NRD) is a part of the Healthcare Cost and Utilization Project (HCUP) databases which include the largest collection of de-identified longitudinal hospital care data in the United States, with all-payer and encounter-level information. The NRD is a unique data subset designed to support various types of analyses with safeguards to protect the privacy of individual patients, physicians, and hospitals. It contains more than a hundred clinical and non-clinical variables for each hospital stay, including a verified patient linkage number for linking hospital visits for the same patient across hospitals, International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System (ICD-10-CM/PCS) for principal and secondary procedures and diagnoses (including comorbidities and complications), age, gender, length of stay (LOS), and others [10, 11].

Study cohort

The ICD-10-CM/PCS codes were used to search discharges in the 2016 NRD who had TAVR during the index hospitalization; baseline characteristics, comorbidities, patients who also had concomitant PCI (defined as one or more balloon angioplasty, bare-metal stent, and/or drug-eluting stent placement in one or more vessel) during the same hospitalization, in-hospital post-procedural complications, and endpoints of interest were subsequently extracted. The 2016 NRD is the latest NRD dataset that has been released to date. To differentiate post-procedural complications from chronic conditions, the 2016 NRD has a present-on-admission indicator for chronic conditions that present on admission. We also utilized the ICD-10-CM codes used in the Elixhauser comorbidity index to identify comorbid conditions and utilized ICD-10-CM codes that are specific for post-procedural complications (Supplementary Table S1) [11]. The NRD excludes discharges with missing age, missing or questionable linkage numbers or from hospitals with more than 50% of their discharges excluded because of these criteria, as patients treated in these hospitals may not be reliably tracked over time [10]. All HCUP recommendations and best practices to use the HCUP datasets highlighted by Khera *et al.* were followed [12].

Study endpoints

Study endpoints included were in-hospital all-cause mortality, length of index hospital stay (LOS), cardiogenic shock, need for mechanical circulatory support (MCS) devices, mechanical complications of prosthetic valve, paravalvular leak (PVL), acute kidney injury (AKI), bleeding, and total hospital charges. The 2016 NRD reports in-hospital all-cause deaths, means LOS, and mean total charges. The other endpoints were assessed during the index hospitalization using specific ICD-10 codes for post-procedural complications (Supplementary Table S1). Cardiogenic shock included post-procedural cardiogenic shock. Mechanical circulatory support devices included intermittent or continuous intra-aortic balloon pump, Impella, extracorporeal membrane oxygenation, ventricular assist devices, and/or other devices that assist cardiac output. Mechanical complications of prosthetic valve were defined as TAVR valve embolization, displacement, breakdown, or other mechanical complications (excluding fibrosis, infection, stenosis, and thrombosis). PVL was defined as any leakage of TAVR valve regardless of the mechanism, location, and severity. AKI included any new post-procedural acute worsening of kidney function. Bleeding included any circulatory or central nervous system bleeding during or after the procedure, or post-procedure hemorrhage/anemia.

Statistical analysis

Statistical Analysis System (SAS) software 9.4 (TS1M4, SAS Institute Inc, Cary, North Carolina) was used for data extraction, propensity score matching and statistical analysis which was performed on unweighted (i.e. the actual number) discharges. Pearson's χ^2 test of independence and the unpaired-sample *t*-test were used to compare the endpoints of interest between TAVR-PCI and no PCI. Logistic regression was used to create a propensity score, based on the basic demographics and baseline characteristics for a one-to-one parallel, balanced propensity score matching

model using a caliper of 0.001. The McNemar test was used to compare paired categorical variables of the baseline characteristics and endpoints of interest, while the paired-samples *t*-test was used to compare continuous variables. A two-tailed *p*-value of < 0.05 was used for statistical significance [13, 14].

Results

The 2016 NRD database includes approximately 17.2 million discharges. There were 23,604 discharges after TAVR; 852 (3.6%) patients had a concomitant PCI during the index hospitaliza-

Table I. Demographics, baseline characteristics and comorbidities of overall transcatheter aortic valve replacement (TAVR) group, and TAVR-percutaneous coronary interventions (TAVR-PCI) and matched (TAVR-M) groups after propensity matching with *p*-values for each variable

Baseline/group	TAVR-no PCI	TAVR-PCI	<i>P</i> -value	TAVR-no PCI	TAVR-PCI	<i>P</i> -value
	Pre-propensity matching			Post-propensity matching		
Number of patients	22,752	852	–	812	812	–
Mean age (SD) [years]	80.5 (8.3)	79.4 (8.8)	0.01	79.0 (8.8)	79.7 (8.8)	0.03
Female	46.0%	44.7%	0.47	45.4%	45.2%	0.92
Transapical TAVR	3.4%	4.3%	0.14	4.8%	4.4%	0.71
Endovascular TAVR	96.6%	95.7%	0.13	95.2%	95.6%	0.71
Hypertension	86.7%	86.2%	0.63	86.5%	85.8%	0.72
Diabetes mellitus	35.9%	39.1%	0.06	40.2%	39.2%	0.69
Hyperlipidemia	69.0%	68.0%	0.51	66.8%	67.9%	0.62
Chronic kidney disease	34.1%	40.6%	< 0.01	39.4%	40.6%	0.60
Congestive heart failure	71.5%	75.6%	0.01	74.6%	75.3%	0.77
Systolic heart failure	23.6%	34.9%	< 0.01	34.1%	33.5%	0.76
Coronary artery disease	69.8%	88.7%	< 0.01	88.7%	88.7%	1.00
Presented with acute myocardial infarction	0.4%	6.2%	< 0.01	2.0%	2.0%	1.00
Atrial fibrillation	40.3%	36.5%	0.03	38.1%	37.2%	0.72
Atrial flutter	4.0%	6.1%	< 0.01	7.4%	5.9%	0.21
Long-term anticoagulation	18.8%	14.9%	< 0.01	17.4%	15.3%	0.24
Aspirin	28.0%	25.4%	0.10	24.4%	25.4%	0.63
Abnormal coagulation profile	0.3%	0.6%	0.23	0.4%	0.5%	0.71
Peripheral vascular disease	25.6%	29.8%	< 0.01	30.3%	28.8%	0.52
Chronic pulmonary disease	30.0%	28.9%	0.47	29.8%	28.7%	0.63
Chronic liver disease	3.0%	3.2%	0.72	2.7%	3.2%	0.56
Smoking	37.8%	35.5%	0.16	39.7%	35.6%	0.07
Obesity	17.1%	16.0%	0.39	16.4%	16.1%	0.90

SD – standard deviation.

tion (81.1% had PCI to one vessel, 15.8% had PCI to two vessels, and 3.1% had PCI to three or more vessels). The mean age of the overall TAVR cohort was 80.5 ±8.3 years and 45.9% were women. PCI was a principal procedure in 66.3% of the TAVR-PCI group, which indicates that PCI was performed before TAVR; the vast majority of PCIs were performed within the first day of admission. The TAVR-PCI group had 46.8% elective admissions versus 79.1% of the control group ($p < 0.01$).

History of CAD, hypertension, hyperlipidemia, congestive heart failure, and diabetes were the most common comorbidities. More than 96% of TAVR procedures were performed using the endovascular approach. The TAVR-PCI group had a higher prevalence of coronary and peripheral vascular disease, chronic kidney disease and congestive (including systolic) heart failure. After propensity matching, each group had 812 patients who were comparable in terms of baseline characteristics (Table I).

In comparison to isolated TAVR, TAVR-PCI was associated with higher in-hospital all-cause mortality (4.5% vs. 1.7%, $p < 0.01$), longer length of stay (10.5 vs. 5.4 days, $p < 0.01$), and higher incidence of cardiogenic shock (9.4% vs. 2.1%, $p < 0.01$), the use of MCS devices (6.8% vs. 0.7%, $p < 0.01$), mechanical complications of prosthetic valve (6.8% vs. 0.7%, $p < 0.01$), PVL (0.9% vs. 0.4%, $p = 0.01$), AKI (25.5% vs. 11.5%, $p < 0.01$), bleeding (25.2% vs. 18.1%, $p < 0.01$), and total hospital charges (\$354,725 vs. \$220,474, $p < 0.01$).

The results remained unchanged after adjustment to baseline characteristics (listed in Table I) using propensity matching. Sensitivity analysis was first performed after excluding patients who presented with acute myocardial infarction or acute decompensated heart failure/cardiogenic shock (6.2% and 2.9% of TAVR-PCI, respectively)

as a principal diagnosis; the results remained the same. The analysis was also performed on TAVR patients with a history of CAD who received PCI versus who did not and the results remained unchanged compared to the original analysis. The results also remained unchanged even after excluding TAVR-PCI patients who had unspecified intra/postprocedural circulatory complications (which include coronary ostial occlusion).

When we looked at the outcomes of TAVR-PCI patients who were admitted electively versus non-electively, they had comparable in-hospital mortality, but the elective group had lower post-procedural AMI, AKI, bleeding, CS and higher MCS device use. The number of vessels (single versus multiple) treated with PCI was associated significantly with higher use of MCS devices, complications, and longer LOS (Table II).

Discussion

The current study represents one of the largest observational analyses showing that combined TAVR and PCI during the same index hospitalization was associated with higher in-hospital mortality, periprocedural complications and total hospitalization charges. Such observation remained unchanged after adjustment for common baseline characteristics using propensity matching and in multiple sensitivity analyses.

The increased in-hospital all-cause mortality and longer hospitalization may be explained by the higher rate of complications observed, including post-procedural cardiogenic shock, AKI, bleeding, and paravalvular leak, all of which have been associated with adverse outcomes and increased mortality following the TAVR procedure [15, 16]. The PCI procedure itself has its own complications and some of them overlap with TAVR complica-

Table II. Results of the study endpoints based on the number of vessels (single versus multiple) treated with percutaneous coronary intervention (PCI)

Endpoint	Single vessel PCI	Multiple vessels PCI	P-value
Percentage	81.1%	18.9%	–
All-cause mortality	4.3%	5.0%	0.73
Cardiogenic shock	8.3%	14.3%	0.02
Mechanical circulatory support devices	5.5%	12.4%	< 0.01
Acute kidney injury	23.9%	32.3%	0.03
Bleeding	23.9%	31.1%	0.06
Paravalvular leak	0.9%	1.2%	0.66
Mechanical complication of prosthetic valve	1.3%	2.5%	0.27
Length of stay (± SD*)	9.8 (9.4) days	13.5 (11.3) days	< 0.01

*Standard deviation.

tions; therefore, combining the two procedures might have additional risk. Furthermore, performing PCI concomitantly with TAVR can be associated with increased procedure time, contrast use, and the use of anticoagulation and antiplatelet therapy, which might lead to acute left ventricular volume overload and a negative effect on myocardial function, and subsequently increased peri-procedural complications such as cardiogenic shock, AKI, and bleeding [17].

The fact that two thirds of the PCIs were performed prior to TAVR and within the first day of admission and the consistency of our results in patients with/without history of CAD, after excluding the patients who presented with AMI, decompensated heart failure/cardiogenic shock, and after excluding postprocedural circulatory complications (which include coronary ostial occlusion), and regardless of the type of admission – elective vs. non-elective – support the above-mentioned explanation of added risk of combined TAVR-PCI rather than just increased risk from the severity of clinical presentation and selection bias.

This explanation is also supported by several observations including the higher morbidity seen in patients who received multivessel, compared to single vessel, PCI in this analysis; taking into consideration that both AS and PCI are independently associated with coronary microvascular dysfunction, which is linked to adverse outcomes in both AS and PCI (including elective PCI for stable angina) patients [18].

Studies evaluating outcomes of patients undergoing TAVR along with PCI for significant CAD have shown conflicting results. Historically, it was believed that PCI carries a higher risk of procedural complications in patients with AS undergoing TAVR [19]; however, multiple small observational studies proved the safety and feasibility of the concomitant procedure with no significant difference in all-cause mortality at variable follow up intervals [20–24]. A recent meta-analysis also reported a lack of significant differences in mortality and complication rates between TAVR alone and the TAVR-PCI group; however, the studies included had smaller patient population size, and most of them showed non-significantly higher mortality and complication rates in the TAVR-PCI group [25].

It is also important to mention the economic aspect of our study. The lower cost associated with TAVR, compared to TAVR-PCI, could be attributed not only to the cost of equipment, but also the avoidance of complications that would be costly for the hospital and patients [26].

The current study supports the occurrence of higher complication rates in patients undergoing concomitant TAVR and PCI compared to those with TAVR alone. It involves a large sample size derived from a large national registry that is rep-

resentative of real-world outcomes in the United States.

This is a retrospective observational study, and heterogeneity and confounders are still a concern despite the statistical adjustment to multiple clinical baseline characteristics; the TAVR-PCI group might have represented sicker patients with an increased burden of comorbidities and more advanced and complex CAD that prompted the concomitant PCI. The severity, distribution, and complexity of the involved vessels were not recorded by the registry. The procedural details such as the coronary height, sinuses size, type of stent, procedure duration, type of medical therapy, procedural anticoagulation and contrast volume could not be captured among either group. Furthermore, the reasons for performing PCI and TAVR as a single or staged procedure during the same hospitalization could not be determined. Finally, long-term outcomes could not be evaluated.

In conclusion, in this retrospective analysis, combining TAVR and PCI procedures in the same index hospitalization was associated with higher in-hospital mortality and morbidities in comparison to the isolated TAVR procedure. With the expanding indications and variable patient populations undergoing TAVR, CAD will be among the most frequent comorbidities encountered. Future randomized trials are essential to confirm these results and to determine the optimal time of revascularization in TAVR patients with concomitant CAD.

Conflict of interest

The authors declare no conflict of interest.

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