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In-hospital clinical outcomes of transcatheter aortic valve replacement in patients with concomitant carotid artery stenosis: Insights from the national inpatient sample

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ABSTRACT

Background: Carotid artery stenosis (CAS) is a common occurrence in elderly patients undergoing transcatheter aortic valve replacement (TAVR). We conducted a retrospective study to identify the impact of CAS on in-hospital outcomes following TAVR.
Methods: We queried the National Inpatient Sample (NIS) for 2016–2017 and identified patients who underwent TAVR with concomitant CAS using the ICD-10 codes. The primary endpoint of our study was in-hospital mortality and acute ischemic stroke.
Results: We identified 80,740 TAVR-related hospitalizations. Of these, 6.9% (N = 5555) patients had concomitant CAS. The mean age for CAS patients was 80 ± 7.4 years. Females were represented equally in both groups. Traditional comorbidities like dyslipidemia [78.3% (N = 4350) vs. 68.2% (N = 51261); P < 0.001] and peripheral arterial disease [27.4% (N = 1525) vs. 12.7% (N = 9526); P < 0.001] were more frequently observed among CAS patients. Patients with CAS had higher rates of previous stroke [17.5% (N = 970) vs. 11.8% (N = 8902); P < 0.001] and CABG 23.8% (N = 1320) vs. 18.6% (N = 14022); P < 0.001]. Other cardiovascular risk factors were similar between the two groups. Moreover, no differences in in-hospital outcomes including mortality [odds ratio (OR): 1.35, CI: 0.48–3.83; P = 0.57] were observed in the propensity matched cohort.
Conclusions: Our study did not find any major differences in outcomes in the CAS group following TAVR; however, a more detailed randomized controlled study with long-term follow-up of these patients is needed.

1. Introduction

Transcatheter aortic valve replacement (TAVR) has emerged as a safe and effective therapeutic option in high, intermediate, and low surgical risk patients with symptomatic aortic stenosis [1]. Concomitant carotid artery stenosis (CAS) and aortic stenosis are frequent in elderly patients undergoing TAVR [2]. Ischemic stroke, a significant safety concern following TAVR, occurs in 2.3% of patients with a 0.4% transient ischemic attack, as reported in a

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recent study of the US registry population [3]. Plausible risk factors are atherosclerosis of the implantation site and aortic arch [4], valve deployment, and hemodynamic compromise following rapid ventricular pacing [5]. Extracranial carotid artery stenosis is associated with increased *peri*-procedural stroke risk following isolated aortic valve replacement (AVR) [6]. Current guidelines do not give a specific recommendation toward screening for CAS in patients undergoing TAVR [7]; hence we sought to determine the outcome of TAVR in patients with CAS using a large nationally representative database.

2. Methods

We used the 2016 and 2017 nationwide inpatient sample (NIS) for our cohort study. Relevant ICD-10 codes (Supplemental Table 1) were used to identify all patients who underwent TAVR (N = 80,740). Patients were divided into two groups, with (N = 5555) and without CAS (N = 75,185). The primary outcome of interest was all-cause in-hospital mortality. Secondary outcomes of interest were acute ischemic stroke, cardiogenic shock, cardiac arrest, acute kidney injury (AKI), length of stay (LOS), and cost of care. Categorical data were represented as frequency and percentage, and continuous data were represented as means with standard deviation and standard error. Pearson's Chi-square test was used to analyze categorical variables, whereas the Student's *t*-test was used to analyze continuous variables. Univariate and multivariate logistic regression were used to adjust for potential confounders. We also used propensity score matching to match patients with TAVR and concomitant CAS to those who had TAVR without CAS. A nonparsimonious multivariate logistic regression model was used to estimate the propensity score for CAS patients with the following variable: Age, month, weekend admission status, discharge weight, disposition of patients at discharge, admission status elective vs. non-elective, sex, length of stay, race, total charge, transfer status, median household income in patients zip code, hospital bed size, hospital location and teaching status, hospital region, total cost, anemia, atrial fibrillation, prior stroke prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass surgery, pulmonary hypertension, coronary artery disease equivalent, hypertension, obesity, dyslipidemia, peripheral vascular disease, chronic lung disease, diabetes mellitus, chronic kidney disease, charlson category, payer status (Fig. 1). The double robust method is then used to generate treatment weights, and the inverse probability of treatment weighing was used to match cases with controls using generalized linear model. STATA 15.10/MC (STATA CORP LLC) was used for statistical analysis. All analysis was done according to the recommended methods due to the complex survey design of the NIS dataset [8]. Institutional review board (IRB) approval was not required as it is a publicly available database containing de-identified patient's information.

3. Results

Among subjects undergoing TAVR (N = 80,740), 6.9% (N = 5555) patients had concomitant CAS. Patients were divided into two groups—with and without CAS. The mean age for patients without CAS was 80 ± 8.46 years, while for those with CAS was 80 ± 7.4 y ears. Females were represented equally in both groups (Table 1A). Patients with CAS had higher rates of previous stroke [17.5% (N = 970) vs. 11.8% (N = 8902); P < 0.001] and CABG [23.8% (N = 1320) vs. 18.6% (N = 14022); P < 0.001]. Risk factors for vascular events like dyslipidemia [78.3% (N = 4350) vs. 68.2% (N = 51261); P < 0.001] and peripheral arterial disease (PAD) [27.4% (N = 1525) vs. 12.7% (N = 9526); P < 0.001] were more prevalent in CAS cohort. Prevalence of diabetes mellitus (DM), hypertension, and heart failure (HF) were equally distributed between the two groups (Table 1B). There was no statistically significant difference in length of stay (LOS) and resource utilization (Table 2). On multivariate and propensity matched analysis, there was no significant difference in all-cause in-hospital mortality [odds ratio (OR): 0.82, CI: 0.48–1.41; P = 0.47], propensity matched

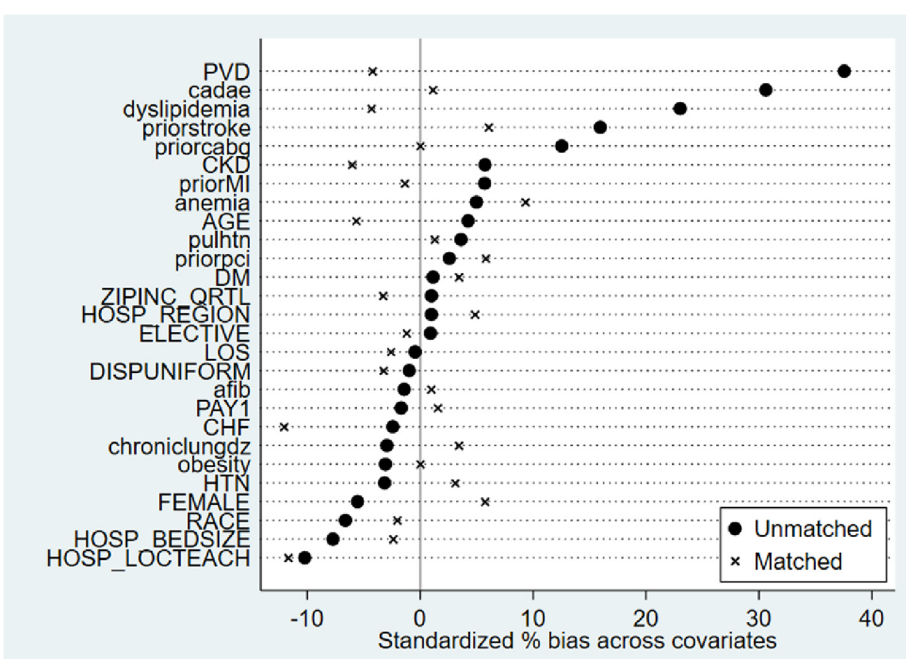

Fig. 1. Propensity match representing balancing of covariates.

Table 1A
Baseline demographics of patients undergoing Transcatheter aortic valve replacement (TAVR) with and without concomitant carotid artery stenosis (CAS).

Variable	TAVR without CAS, N (%)	TAVR with CAS, N (%)	P value
Annual hospitalization	75,185	5555	
Age	80 ± 8.46	80 ± 7.40	0.16
Female	34,555 (46)	2,400 (43.2)	0.07
Race			
Caucasian	65,208 (86.7)	5,014 (90.3)	
African American	3,361 (4.5)	142 (2.5)	
Hispanic	3,519 (4.7)	184 (3.3)	
Asian	970 (1.3)	84 (1.5)	
Native American	195 (0.3)	5 (0.1)	
Others	1,932 (2.5)	126 (2.3)	
Charlson comorbidity Index			
0	18,232 (24.3)	295 (5.3)	
1	15,503 (20.6)	860 (15.5)	
2 and above	41,450 (55.1)	4,400 (79.2)	
Insurance			
Medicare	68,900 (91.6)	5,109 (92.0)	
Medicaid	902 (1.2)	61 (1.1)	
Private	5,060 (6.7)	375 (6.7)	
Uninsured	323 (0.4)	10 (0.2)	
Disposition			0.80
Routine	45,622 (60.68)	3,370(60.7)	
Transfer to short-term Hospital	368 (0.49)	15(0.3)	
Skilled nursing facility	10,654 (14.2)	785 (14.1)	
Home health care	17,262 (23.0)	1,310 (23.6)	
Against medical advice	53 (0.1)	0 (0.0)	
Died	1,226 (1.6)	75 (1.3)	

Table 1B
Baseline comorbidities of patients undergoing TAVR with and without CAS. TAVR: Transcatheter aortic valve replacement, CAS: carotid artery stenosis, PCI: percutaneous coronary intervention, CABG: coronary artery bypass surgery, MI: myocardial infarction, HTN: hypertension.

Chronic comorbidities, N (%)	TAVR without CAS, N (%)	TAVR with CAS, N (%)	P value
Anemia	2,887 (3.8)	270 (4.9)	0.09
Prior stroke	8,902 (11.8)	970 (17.5)	<0.001
Prior MI	9,812 (13.2)	835(15.0)	0.06
Prior PCI	1,917 (2.5)	165 (3.0)	0.35
Prior CABG	14,022 (18.6)	1,320 (23.8)	<0.001
Pulmonary HTN	11,917 (15.8)	955 (17.2)	0.22
HTN	23,563 (31.3)	1,660 (29.9)	0.35
Obesity	13,187 (17.5)	910 (16.4)	0.30
Dyslipidemia	51,261 (68.2)	4,350 (78.3)	<0.001
Peripheral vascular disease	9,526 (12.7)	1,525 (27.4)	<0.001
Chronic lung disease	6,639 (8.8)	445 (8.0)	0.34
Diabetes	28,209 (37.5)	2,115 (38.1)	0.72
Congestive heart failure	44,682 (59.4)	3,235 (58.2)	0.48
Chronic Kidney disease	24,285(32.30)	1,945(35.01)	0.07

[odds ratio (OR): 1.35, CI: 0.48–3.83; P = 0.57] (Table 2.) between the two groups. Other in-hospital outcomes also did not differ significantly between the two groups in multivariate and propensity matched models (Table 2).

4. Discussion

In our retrospective analysis, 6.9% of patients undergoing TAVR had pre-existing CAS. Patients with CAS were found to have a higher incidence of previous stroke, previous CABG, and more vascular risk factors. There was no difference in all-cause in-hospital mortality, acute ischemic stroke, and other in-hospital complications after adjusting for potential confounders.

CAS prevalence reported in our study is much less than reported in other studies. A recently published prospective study and STS/TVT (Society of Thoracic Surgeons and Transcatheter Valve Therapy) registry have reported 22–31% prevalence of CAS; among them, severe CAS (carotid artery stenosis between 70 and 99%) was reported in 3.2–6.4% patients [9,10]. The discrepancy in this finding with that in the published literature is likely due to coding errors and selective bias toward coding only severe cases of CAS. Trials reporting post-TAVR stroke recorded it in 3.3% patients in the retrospective analysis of (PARTNER) trial [11]. Early phase (0–10 days; 4.1% of strokes) and late phase (11–365 days; 4.3% of strokes) of (FRANCE-2) registry reported stroke rates around 4% [(0–10 days; 4.1% of strokes) and (11–365 days; 4.3% of strokes) respectively] [12], whereas, 2.6% stroke rate was reported in the carotid disease group of STS/TVT registry [9].

The acute ischemic stroke rate reported in our study might be related to procedural embolization caused by catheter manipulation within the aorta and prosthesis, or catheter and wire manipulation across the diseased native aortic valve. Lower rates of strokes in CAS patients undergoing TAVR in our study likely representing coding errors and lack of documentation of minor strokes and transient ischemic attack. Formal neurologic evaluation post TAVR is not part of standard evaluation protocol and multiple subclinical and image proven strokes which are asymptomatic will be missed. Stroke rates beyond the index hospitalization were also not available in the dataset. Hence our study does not allow up to study this endpoint effectively. The complex and multifactorial pathogenesis and variable presentation of neurological injury early and late after these procedures warrants continued attention to additional factors that could modulate the known embolic risk and its clinical consequences. No difference in mortality was found between the two groups, which is supported by a cohort study [10] and reported data from the SOURCE registry [13].

Beyond the procedure, stroke is predominantly spontaneous and is related to established risk factors, such as age, comorbidities, arterial disease, and atrial fibrillation. Our study found that many patients (78.3%) had associated dyslipidemia and higher baseline vascular disease (27.4%), which could indicate that CAS is a marker of diffuse vascular disease. In our study, (17.5%) patients in the CAS group had previous strokes and 24% patients had prior CABG, explaining the higher risk of stroke in CAS patients with a prior history of stroke undergoing TAVR. Following surgical aortic valve replacement, patient's risk factors are associated with cerebrovascular events rather than prosthesis itself [6]. Based on findings from our analysis and previously reported literature, there is no evidence of an increased risk of post-procedural stroke in patients who had TAVR with CAS. Driven by the data available to date, the decision to undergo pre-operative screening for CAS or revascularization before TAVR does not seem beneficial as supported by current guidelines [14,15]. Randomized controlled trials are needed to determine whether the presence of CAS (especially severe stenosis) will be considered toward patient selection for TAVR after studies reporting adverse outcomes following surgical aortic valve replacement with concomitant CAS [6]. It is unsure whether knowledge of pre-existing CAS will result in better blood pressure control post-procedure, less rapid pacing, and improved pharmacologic management, which can translate to a better outcome, particularly in patients with severe stenosis.

Being a retrospective coding-based study, it is subjected to coding errors. Data regarding the fine granularity of procedure, valve type, imaging, labs, and severity of carotid stenosis is not available in the database. We do not have data regarding out of hospital cerebrovascular events or use of anticoagulation on discharge. Patients with anatomically severe but subclinical disease may

Table 2
In-hospital outcome and procedural outcome of patients undergoing Transcatheter aortic valve replacement (TAVR) with and without carotid artery stenosis (CAS). LOS: Length of stay.

	Non-Propensity Match					Propensity Matched	
Variable	TAVR with CAS	TAVR without CAS	P-Value	Odds Ratio	P-Value	Odds Ratio	P-Value
In-patient Mortality	75 (1.3)	1226 (1.6)	0.46	0.82 (0.48–1.41)	0.47	1.35 (0.48–3.83)	0.57
Acute Myocardial infarction	115 (2.1)	1293 (1.7)	0.37	0.83 (0.52–1.34)	0.45	–	–
Acute Kidney Injury	600 (10.8)	8330 (11.1)	0.78	0.91 (0.72–1.15)	0.42	1.21 (0.96–1.70)	0.27
Pacemaker insertion	65 (1.2)	729 (1.0)	0.51	1.30 (0.74–2.28)	0.36	–	–
Major bleeding requiring blood transfusion	480 (8.6)	5970 (7.9)	0.41	1.02 (0.80–1.28)	0.89	1.02 (0.72–1.44)	0.92
Acute ischemic stroke	50 (0.9)	368 (0.5)	0.05	1.41 (0.73–2.74)	0.31	–	–
Shock	120 (2.2)	1827 (2.4)	0.56	0.75 (0.48–1.15)	0.18	–	–
Respiratory failure	160 (2.9)	2068 (2.7)	0.81	1.01 (0.66–1.52)	0.99	–	–
Deep Vein Thrombosis/Pulmonary embolism	30 (0.5)	263 (0.3)	0.31	1.36 (0.54–3.45)	0.51	–	–
Pressor support requirement	125 (2.2)	1271 (1.7)	0.21	1.40 (0.86–2.29)	0.17	–	–
Mechanical ventilation	90 (1.6)	1571 (2.1)	0.27	0.78 (0.47–1.29)	0.33	–	–
Vascular complication	20 (0.4)	293 (0.4)	0.86	0.75 (0.28–2.05)	0.57	–	–
Complete heart block	625 (11.2)	7255 (9.6)	0.07	1.14 (0.94–1.40)	0.18	–	–
Mean LOS (Days)	4.60 ± 4.84	4.62 ± 5.72	0.434				
Median LOS (Interquartile range)	3 (2–5)	3 (2–5)					
Mean Total Cost ($)	54,145	49,316	0.938				

not be coded in the dataset. Moreover, 30-day and 1- year stroke rate is not available in the dataset. The use of embolic protection devices was also not captured in the dataset.

5. Conclusion

Although CAS is a risk factor for stroke and is prevalent in TAVR populations, this study suggests that patients with CAS undergoing TAVR have comparable outcomes compared with patients without CAS. Further investigation is needed to identify the impact of CAS based on severity and symptoms on TAVR outcomes, including the risk of stroke on longer follow-up.

CRediT authorship contribution statement

Sandipan Chakraborty: Conceptualization, Methodology, Supervision. **Md Faisaluddin:** Writing - original draft. **Kumar Ashish:** Methodology, Writing - original draft. **Birendra Amgai:** Data curation, Formal analysis. **Dhrubajyoti Bandyopadhyay:** Conceptualization, **Supervision Neelkumar Patel:** Data curation, Formal analysis, Methodology. **Adrija Hajra:** Writing - review & editing. **Gaurav Aggarwal:** Writing - review & editing. **Raktim K.Ghosh:** Supervision. **Ankur Kalra:** Supervision.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100621.

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