

Impact of smoking in patients undergoing transcatheter aortic valve replacement

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Background: The paradox that smokers have better clinical outcomes in cardiovascular diseases remains controversial. No literature exists studying impact of smoking on outcomes following transcatheter aortic valve replacement (TAVR).

Methods: We performed an electronic search of the 2011–2012 National Inpatient Sample (NIS) database to identify all TAVR hospitalizations. Outcomes were measured comparing smokers to non-smokers.

Results: A total of 8,345 TAVR hospitalizations were identified with 24% being smokers. Compared to non-smokers, smokers were younger (80.4±8.8 *vs.* 81.4±9.2 years, $P<0.001$), were more often men (63.6% *vs.* 47.8%, $P<0.001$), and had a higher disease burden. Despite a higher disease burden, smokers had lower post procedure stroke (2.8% *vs.* 3.1%), hemorrhage events (28.2% *vs.* 32.0%, $P<0.05$) and lower all cause in-hospital mortality (1.2% *vs.* 5.7%, adjusted odds ratio 0.21, 95% CI: 0.13–0.32, $P<0.001$) compared to non-smokers.

Conclusions: Despite having a higher cardiovascular disease burden, smokers had better outcomes compared to non-smokers. Therefore the smoker's paradox is applicable in the TAVR cohort.

Keywords: Smoker's paradox; transcatheter aortic valve replacement (TAVR); aortic stenosis; National Inpatient Sample database

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Introduction

Transcatheter aortic valve replacement (TAVR) has become a standard of care for severe aortic stenosis patients, with intermediate, high or prohibitive risk for surgical aortic valve replacement (1). Smoking is an established risk factor for the development of cardiovascular diseases and has been shown to accelerate the progression of aortic stenosis (2). Interestingly, data exists supporting better survival outcomes in smokers compared to no-smokers with cardiovascular

diseases and after cardiovascular interventions (3,4). This thought-provoking observation has been termed as the "Smoker's paradox." While smoking related diseases such as chronic obstructive pulmonary disease has been associated with adverse clinical outcomes in patients undergoing TAVR, to the best of our knowledge there is no existing literature on the impact of smoking on in-hospital mortality in patients undergoing TAVR. Therefore, we analyzed the Nationwide Inpatient Sample (NIS) database from 2011–2012 to determine the association of smoking status

with in-hospital clinical outcomes in TAVR patients.

Methods

All TAVR admissions between January 1, 2011 and December 31, 2012 were identified in the NIS database using the International Classification of Diseases, ninth edition, and Clinical Modification (ICD-9-CM) codes (35.05, 35.06). The study protocol was exempted from review by the Institutional Review Board of the University of Tennessee Health Science Center, Memphis. Baseline patient demographic characteristics (age, sex, and race), and comorbidities (as listed in *Table 1*) were extracted from the NIS database. Our outcome measures included all-cause in-hospital mortality, defined as “died” during the index hospitalization in the database, acute cerebrovascular accidents (CVAs) (CCS-109) and post-procedure hemorrhage (identified using ICD-9 CM codes-998.11, 998.12, 285.1, 568.81). Baseline patient demographics and comorbidities were compared using Pearson’s Chi-square test for categorical variables and Student’s t-test for continuous variables. In addition to patient demographics and comorbidities, smoking was used as an independent variable in a multivariable unconditional regression model to examine predictors of primary and secondary outcomes. Statistical analysis was performed using SPSS 23.0 (IBM corp., Armonk, NY, USA). We used a 2-sided P value of <0.05 to identify statistical significance.

Results

Among the 8,345 patients who underwent the TAVR procedure, 24% were smokers (n=2,004) and 76% were non-smokers (n=6,341). The mean age of the overall study population was 81.1±9.1 years, with 51.6% being male and 83.6% being Caucasian. Patient demographics and comorbidities are listed in *Table 1*. Smokers were more likely to be male, younger and had higher prevalence of hypertension, dyslipidemia, obesity, coronary artery disease, peripheral arterial disease and chronic pulmonary disease than non-smokers. The prevalence of hypertension, hyperlipidemia, obesity, peripheral arterial disease, carotid artery disease, coronary artery disease, cerebrovascular disease and chronic obstructive pulmonary disease, was higher in smokers than non-smokers (all P<0.001). Smokers were less likely to have congestive heart failure and renal failure (all P<0.001). Despite having a higher prior medical

history of CVA, smokers compared to non-smokers were less likely to have acute CVA (2.8% vs. 3.1%), post procedure hemorrhage (28.2% vs. 32.0%) or in-hospital death (1.2% vs. 5.7%, adjusted OR 0.21, 95% CI, 0.13–0.32) (*Table 2*).

Discussion

We observed that smokers had lower in-hospital mortality and adverse clinical outcomes compared to non-smokers. This observation was valid even after multivariate adjustment for patient demographics and comorbidities. Hence, we concluded that smoker’s paradox does exist in TAVR patients.

Currently there is no data on the interaction between smoking and TAVR. In patients undergoing surgical aortic valve replacement, Saxena *et al.*, reported no worse perioperative clinical outcomes in smokers when compared to non-smokers in a study based on Australian and New Zealand Society of Cardiac and Thoracic Surgeons (SCTS) Cardiac Surgery Database Program (5). Similarly, another single center study reported no effect of smoking status on post-operative risk in patients undergoing valve (6). Other studies analyzing the impact of smoking on survival after cardiovascular events such as myocardial infarction, stroke, percutaneous coronary intervention and thrombolysis have previously reported findings supporting the smoker’s paradox (3,4). Generally, better survival in smokers has been related to factors such as younger age and lesser comorbidities (3). Nevertheless, we found a strong residual survival benefit in smokers even after multivariate adjustment for multiple factors including age and comorbidities. Hence, lower mortality in smokers in our study may be due to unmeasured confounding, or possibly a protective association.

It is critically important to emphasize that this paradoxical association of smoking with favorable survival in TAVR should not be seen as encouragement for smoking. These results suggest a strong association between smoking and in-hospital adverse clinical outcomes in TAVR, but these results do not assume causation. Also, extensive literature supports that smoking is an established risk factor for the epidemiology of CV diseases, as well as its morbidity and mortality. However the existence of smoker’s paradox deserves attention and needs further research to better explain the mechanism(s) behind this interesting observation.

Table 1 Comparison of TAVR patient's demographics and comorbidities based on smoking status

Characteristic	Overall (n=8,345)	Smokers (n=2,004)	Non-smokers (n=6,341)	P value [†]
Age, mean ± SD (years)	81.1±9.1	80.4±8.8	81.4±9.2	<0.001
Female (%)	48.4	36.4	52.2	<0.001
Race/ethnicity (%)				<0.001
White	83.6	82.7	83.9	
Black	3.7	2.5	4.1	
Hispanic	4.3	3.0	4.8	
Other	8.4	11.8	7.2	
Comorbidities* (%)				
Hypertension	79.8	84.7	78.2	<0.001
Diabetes mellitus	32.9	30.4	33.6	0.007
Dyslipidemia	60.1	68.4	57.5	<0.001
Obesity	12.7	15.9	11.7	<0.001
Congestive heart failure	1.5	0.5	1.9	<0.001
Atrial fibrillation	44.5	43.9	44.7	0.52
Peripheral arterial disease	29.6	32.6	28.7	0.001
Carotid artery disease	5.9	8.4	5.1	<0.001
Chronic pulmonary disease	34.4	48.1	30.0	<0.001
Cerebrovascular disease history	12.2	13.7	11.8	0.02
Renal failure	36.3	32.5	37.5	<0.001
Weight loss	4.5	3.2	4.9	0.002
Coronary artery disease	12.2	13.7	11.8	0.02
History of MI (%)	11.9	12.6	11.7	0.28
History of PCI (%)	17.3	23.6	15.4	<0.001
History of CABG (%)	22.2	28.4	20.3	<0.001
TAVR approach (%)				
Transfemoral	83.2	81.4	83.8	0.011
Transapical	17.0	19.1	16.3	0.004

*, co-morbidities were extracted from the database using International Classification of Diseases, Ninth Edition, Clinical Modification Diagnosis or Clinical Classification Software codes; †, P value representing difference between smokers and non-smokers. MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; SD, standard deviation; TAVR, transcatheter aortic valve implantation.

Table 2 In-hospital outcomes in non-smokers and smokers undergoing transcatheter aortic valve replacement

Outcome	Smokers (n=2,004) (%)	Non-smokers (n=6,341) (%)	Odds ratio (95% CI)		P value
			Unadjusted	Adjusted*	
In-hospital mortality	1.2	5.7	0.21 (0.14–0.32)	0.21 (0.13–0.32)	<0.001
Post-procedure hemorrhage	28.2	32.0	0.83 (0.75–0.93)	0.88 (0.78–0.98)	<0.05
Acute cerebrovascular events	2.8	3.1	0.79 (0.58–1.09)	0.96 (0.69–1.34)	0.81

*, adjusted for patient demographics, comorbidities and TAVR approach. CI, confidence interval; TAVI, transcatheter aortic valve implantation.

Study limitations

The main strength of our study is a large nationalized unselected sample size. However, lack of clinical information because of the administrative nature of the database along with the possibility of coding errors should be noted. In addition, we did not have any information regarding smoking status (former or current), number of pack years, and medications patient were using at the time of admission, procedure, and discharge. Finally, NIS is limited to in-hospital events and consequently, no information relating to long-term effects is available.

Conclusions

In our large nationalized observational study, smoking was independently associated with better clinical outcomes, supporting the smoker's paradox in patients undergoing TAVR.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study protocol was exempted from

review by the Institutional Review Board of the University of Tennessee Health Science Center, Memphis.

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