ORIGINAL RESEARCH

Association of Smoking Status With Long-Term Mortality and Health Status After Transcatheter Aortic Valve Replacement: Insights From the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry

Mohammed Qintar, MD, MSc; Zhuokai Li, PhD; Sreekanth Vemulapalli, MD; Adnan K. Chhatriwalla, MD; Suzanne J. Baron, MD, MSc; Andrzej S. Kosinski, PhD; John T. Saxon, MD; John A. Spertus, MD, MPH; David J. Cohen, MD, MSc; Suzanne V. Arnold, MD, MHA

***Background*—**Smoking is a significant risk factor for aortic stenosis but its impact on clinical and health status outcomes after transcatheter aortic valve replacement (TAVR) has not been described.

***Methods and Results*—**Patients (n=72 165) undergoing TAVR at 457 US sites in the STS/ACC TVT (Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy) Registry between November 2011 and June 2016 were categorized at the time of TAVR as current/recent smokers versus prior/nonsmokers. A series of multivariable models examined the association between smoking status and outcomes, including 1-year mortality, rehospitalization, mean gradient, and health status (measured by the 12-item Kansas City Cardiomyopathy Questionnaire–Overall Summary Score [KCCQ-OS]) and in-hospital outcomes. A total of 4063 patients (5.6%) were smokers. Smokers presented for TAVR at a younger age (75 [68–81] years versus 83 [77–88] years) but with a greater burden of cardiovascular and lung disease. In adjusted models, smoking was associated with lower in-hospital mortality (relative risk, 0.74; 95% CI, 0.62–0.89 [*P*=0.001]) but not with in-hospital stroke/transient ischemic attack or myocardial infarction. Smoking status had no association with postdischarge mortality, stroke, myocardial infarction, or heart failure (HF) but was associated with slightly lower 1-year KCCQ-OS scores (2.4-point lower KCCQ-OS; 95% CI, −4.6 to −0.2 [*P*=0.031]) and higher mean aortic valve gradients (11.1 versus 10.2 mm Hg, *P*<0.001) in adjusted models.

***Conclusions*—**The current/recent smoking rate in US patients with TAVR is 5.6% and smokers present at a younger age for TAVR. Smoking was associated with lower in-hospital but similar long-term survival after TAVR, slightly worse long-term health status, and marginally higher mean aortic valve gradients. Further research is needed to understand the effect of smoking cessation on outcomes. **(*J Am Heart Assoc*. 2019;8:e011766. DOI: 10.1161/JAHA.118.011766.)**

Key Words: aortic stenosis • health status • mortality • smoking • transcatheter aortic valve replacement

While more intricately linked with atherosclerosis, cigarette smoking is a significant risk factor for a broad spectrum of cardiovascular diseases, including aortic stenosis (AS).[1–3] Two studies have linked current smoking to faster aortic valve degeneration in patients with established AS.[4,5] In fact, only smoking, initial valve area, and valve calcium levels were independent predictors of faster AS progression—not traditional risk factors of age, diabetes mellitus, and hypertension.[5] The role of current smoking on outcomes after valve replacement, however, is less clear, as the evidence among patients undergoing aortic valve surgery is both scarce and conflicting.[6–8]

Transcatheter aortic valve replacement (TAVR) is quickly emerging as an alternative option to valve surgery for patients at high and intermediate risk with at least equivalent outcomes to surgery,[9–11] but the long-term mortality rates continue to be high, because of the age and comorbidities of patients who undergo these procedures. Multiple studies have attempted to identify predictors of poor outcomes after TAVR —to aid in risk stratification and mitigation of these risks. While both severe lung disease and home oxygen[12,13] have been associated with increased mortality and worse health

From the Saint Luke's Mid America Heart Institute and University of Missouri-Kansas City, Kansas City, MO (M.Q., A.K.C., S.J.B., J.T.S., J.A.S., D.J.C., S.V.A.); Duke Clinical Research Institute and Division of Cardiology, Duke University Medical Center, Durham, NC (Z.L., S.V., A.S.K.).

Accompanying Tables S1 through S3 and Figure S1 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011766

Correspondence to: Mohammed Qintar, MD, MSc, Saint Luke's Mid America Heart Institute, 4401 Wornall Road, Kansas City, MO 64111. E-mail: qintarm@umkc.edu

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Clinical Perspective

What Is New?

- The current/recent smoking rate in US patients with transcatheter aortic valve replacement (TAVR) is 5.6% and its impact on clinical and health status outcomes after TAVR has not been described before.
- Smoking was associated with lower in-hospital mortality but similar long-term survival after TAVR, slightly worse long-term health status, and marginally higher mean aortic valve gradients.

What Are the Clinical Implications?

- This suggests that while the younger age allows smokers to survive the initial procedure, the associated comorbidities impact long-term recovery.
- Further studies are needed to understand the effect of smoking cessation on outcomes in patients undergoing TAVR, especially as TAVR is being offered to a wider and potentially younger population.

status after TAVR, the role of current smoking has not been explored. This may be attributable to a lower prevalence of current smokers in the very elderly (as compared with cohorts with myocardial infarction [MI] or peripheral artery disease). However, as with other conditions, it is possible that smoking could impact risk of stroke, MI, mortality, or health status after TAVR. This question is particularly relevant as smoking, unlike many of the known risk factors for poor outcomes after TAVR, is potentially modifiable. As such, we leveraged the STS/ACC TVT (Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy) Registry to examine the association of smoking with clinical and health status outcomes after TAVR.

Methods

Study Design and Population

The STS/ACC TVT Registry was started in 2011 and serves as a platform for quality assurance, device safety monitoring, and clinical research initiatives.[14] The data supporting this study are available for request from the NCDR (National Cardiovascular Data Registry) TVT registry and the authors do not have a copy. Data are analyzed at an NCDR analytic center and the analytic files and methods are available upon request. Participation in the registry is mandated by the Centers for Medicare and Medicaid Services (CMS) in order to get reimbursed for the procedures, and so TVT collects data on nearly all commercial TAVR procedures performed in the United States. Participating sites collect detailed information on patient characteristics, medical history (including smoking status), procedural details, echocardiographic data, clinical outcomes, and patient-reported health status. Smoking status is collected at the time of TAVR procedures as current/recent smoker, with recent smoker defined as the use of any cigarettes within the past year. Furthermore, adjudication of in-hospital and follow-up stroke/transient ischemic attack (TIA) and any aortic valve reintervention is performed. Registry activities have been approved by a central institutional review board, and the Duke University School of Medicine's institutional review board granted a waiver of informed consent for this study. Data quality checks are performed annually and are implemented at the NCDR data warehouse, including reports on data quality feedback, data range, and consistency checks.

Study Outcomes

The primary outcome of this study was all-cause postdischarge mortality within 1 year after TAVR. Secondary outcomes included in-hospital mortality, stroke/TIA, and MI; 30-day health status, mean aortic gradient, and left ventricular ejection fraction (LVEF); postdischarge rehospitalization for stroke/TIA, MI, or HF within 1 year post-TAVR; and health status, mean aortic gradient, and LVEF at 1 year.

Rehospitalizations and survival after discharge were assessed through linkage to administrative claims from CMS (*International Classification of Diseases, Ninth Revision* [*ICD-9*]) codes that were performed using direct patient identifiers are available upon request. In-hospital clinical events and echocardiographic data (at all time points) were provided by the individual participating sites. Patient health status was assessed at baseline and follow-up by site personnel using the 12-item Kansas City Cardiomyopathy Questionnaire–Overall Summary Score (KCCQ-OS).[15] The KCCQ is a disease-specific, patient-centered health status tool that was developed to monitor and assess functional status and quality of life in patients with HF[16] and has been validated in patients with AS.[17] KCCQ-OS scores range from 0 to 100, with higher scores indicating fewer symptoms, less functional limitation caused by HF/valve disease, and better quality of life. A change of 5, 10, and 20 points corresponds to small, moderate, and large clinical improvements, respectively.[18]

Statistical Analysis

Demographic and clinical characteristics were compared between current/recent smokers versus prior/nonsmokers (recent smoker was defined by NCDR as the use of any cigarettes within the past year) using Wilcoxon rank sum tests for continuous variables and Pearson chi-square tests for categorical variables. The association between smoking and

in-hospital outcomes were assessed using modified Poisson regression models with robust sandwich estimates of standard errors to account for clustering of patients within sites and to correct variance estimation in Poisson model for binary data. The models also adjusted for covariates selected on the basis of a validated TAVR in-hospital mortality risk prediction model,[19] to account for factors that could confound the association between smoking status and outcomes. These variables included age, sex, race, sex-specific body surface area, procedure date, nonfemoral access, acuity of TAVR procedure, prior stroke/TIA, hypertension, diabetes mellitus, prior percutaneous coronary intervention, prior coronary artery bypass grafting, prior MI, peripheral arterial disease, severe chronic obstructive pulmonary disease, home oxygen, estimated glomerular filtration rate, dialysis, prior endocarditis, carotid stenosis, atrial fibrillation/flutter, hostile chest, porcelain aorta, permanent pacemaker, implantable cardiac defibrillator, prior cardiac operations, prior aortic valve intervention, prior nonaortic valve intervention, aortic valve etiology (degenerative versus other), aortic valve morphology (tricuspid versus other), mean aortic valve gradient, LVEF, left main stenosis ≥50%, proximal left anterior descending coronary artery ≥70%, moderate/severe aortic regurgitation, moderate/severe mitral regurgitation, moderate/severe tricuspid regurgitation, hemoglobin, platelet count, and baseline KCCQ-OS score. All covariates had a missing rate of <3% except that baseline KCCQ-OS score was missing in 17.2% of patients. Missing covariate data were handled using multiple imputation with 20 imputed data sets.

Unadjusted cumulative incidences of long-term outcomes (postdischarge mortality and rehospitalization for stroke, MI, and HF) were compared between current/recent smokers and prior/nonsmokers using Gray's test. Cox proportional hazards models were used to evaluate the association of smoking with mortality; Fine and Gray's proportional subdistribution hazards models were used to assess nonfatal outcomes with death being a competing risk. The models adjusted for the covariates as listed above and accounted for clustering of patients within sites by using the robust sandwich estimates of standard errors.

Short- and long-term echocardiographic measures and KCCQ-OS scores were compared between current/recent smokers and prior/nonsmokers using ANCOVA, adjusting for the baseline value of the respective measure. The association of smoking with 1-year health status was explored using a multivariable linear regression model with Generalized Estimating Equations–based robust sandwich estimates of standard errors. The 1-year KCCQ was missing in 46.9% of patients who were eligible for 1-year follow-up assessment and had baseline KCCQ data. To account for the high degree of missing 1-year KCCQ data, we first excluded sites with <50% completion rates for KCCQ among surviving patients. Next, among included sites, we used inverse probability weighting to make the analytic sample more representative of patients who survived 1 year after TAVR. To accomplish this, a multivariable logistic regression model was constructed to predict the probability of having 1-year KCCQ data among surviving patients, which included demographic and clinical variables along with in-hospital complications. Patients with 1-year KCCQ data were then weighted by the inverse of their probability of having follow-up KCCQ data in order to make the analytic sample more representative of the overall cohort of surviving patients.[20] All analyses were performed with SAS software (version 9.4; SAS Institute Inc), and statistical significance was defined as a 2-sided $P<0.05$.

Results

Study Cohorts

Between November 2011 and June 2016, 72 249 patients underwent TAVR at 457 US sites, of whom smoking status was documented in 72 165; this comprised the in-hospital cohort. For postdischarge clinical outcomes, we excluded 3058 patients younger than 65 years and an additional 24 887 patients who could not be linked to CMS (characteristics of patients with versus without CMS linkage are found in Table S1; patients without CMS linkage more likely to have higher smoking and diabetes mellitus rates but otherwise comparable characteristics) and 1526 patients who died before discharge. Thus, our 1-year clinical cohort consisted of 42 694 patients for whom we could assess postdischarge mortality and rehospitalization for stroke, MI, and HF. Aortic valve gradient and LVEF data were available for 38 596 and 39 534 patients at 30 days, respectively, and 14 255 and 14 623 patients at 1 year, respectively. The 30-day and 1-year KCCQ cohorts consisted of 37 144 and 12 790 patients, respectively (Figure S1).

Patient Characteristics

The median age of patients in the in-hospital cohort was 83 years, 48% were women, median Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) score was 6.4%, and median KCCQ-OS score was 40 (roughly equivalent to New York Heart Association functional class IV). There were 4063 patients (5.6%) who reported being current/recent smokers at the time of their TAVR, and many of the demographic and clinical factors differed between current/recent smokers and prior/nonsmokers (Table 1). Current/recent smokers (versus prior/nonsmokers) were more likely to be younger (75 versus 83 years), men (60% versus 52%), and have a greater burden of atherosclerosis (prior MI, carotid disease, peripheral arterial disease, and porcelain aorta) and

Table 1. Demographic and Clinical Characteristics of Patients Undergoing TAVR Stratified by Smoking Status

	Current/Recent Smoker N=4063	Prior/Nonsmoker N=68 102	*P* Value
Age, y	75.0 (68.0–81.0)	83.0 (77.0–88.0)	<0.001
Women, n (%)	1632 (40.2)	32 843 (48.2)	<0.001
White race, n (%)	3784 (93.1)	63 951 (93.9)	0.047
Body surface area, m^2	1.9 (1.7–2.0)	1.8 (1.7–2.0)	<0.001
Hypertension, n (%)	3613 (89.0)	61 122 (89.8)	0.110
Diabetes mellitus, n (%)	1523 (37.5)	25 487 (37.5)	0.926
Prior MI, n (%)	1232 (30.4)	16 691 (24.6)	<0.001
Prior coronary stenting, n (%)	1441 (35.5)	23 763 (35.0)	0.457
Prior CABG, n (%)	1057 (26.1)	19 075 (28.0)	0.006
Prior stroke/TIA, n (%)	806 (19.9)	12 709 (18.7)	0.061
Carotid stenosis, n (%)	1156 (33.5)	13 162 (23.4)	<0.001
Peripheral arterial disease, n (%)	1945 (47.9)	20 027 (29.4)	<0.001
Porcelain aorta, n (%)	403 (9.9)	3741 (5.5)	<0.001
Atrial fibrillation/flutter, n (%)	1326 (32.7)	27 978 (41.1)	<0.001
Permanent pacemaker/ICD, n (%)	578 (14.3)	12 565 (18.5)	<0.001
Renal disease (creatinine ≥2 mg/dL), n (%)	408 (10.1)	6603 (9.7)	0.470
Moderate/severe chronic lung disease, n (%)	2071 (51.1)	17 426 (25.8)	<0.001
Home oxygen use, n (%)	871 (21.5)	7709 (11.3)	<0.001
Hemoglobin, g/dL	12.0 (10.5–13.4)	11.8 (10.5–13.0)	<0.001
Platelet count, K/μL	199.0 (156.0–249.0)	192.0 (153.0–238.0)	<0.001
STS PROM score, %	5.6 (3.5–8.9)	6.4 (4.2–10.0)	<0.001
5-Meter Walk Test, s	7.3 (6.0–9.7)	8.0 (6.0–10.3)	<0.001
KCCQ-OS score	36.5 (20.3–55.6)	39.6 (22.9–59.4)	<0.001
LVEF, %	55.0 (43.0–63.0)	58.0 (45.0–63.0)	<0.001
Aortic valve mean gradient, mm Hg	43.0 (35.0–51.0)	42.0 (35.0–51.0)	0.032
Moderate/severe aortic insufficiency, n (%)	1115 (27.6)	13 599 (20.1)	<0.001
Moderate/severe mitral insufficiency, n (%)	981 (24.3)	19 880 (29.4)	<0.001
Transfemoral access, n (%)	2525 (62.3)	54 091 (79.9)	<0.001

CABG indicates coronary artery bypass grafting; ICD, implantable cardioverter-defibrillator; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire–Overall Summary Score; LVEF, left ventricular ejection fraction; MI, myocardial infarction; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR, transcatheter aortic valve replacement; TIA, transient ischemic attack.

lung disease (51% versus 26%), with 21.5% of current/recent smokers on home oxygen versus 11.3% of prior/nonsmokers. Current/recent smokers had lower median STS PROM scores (5.6% versus 6.4%) and were less likely to be treated with transfemoral access (62% versus 80%; all $P<0.001$). Current/recent smokers had a slightly lower new pacemaker implantation but higher rates of atrial fibrillation postprocedure (Table S2).

Short-Term Outcomes

In unadjusted analyses, current/recent smokers had a trend toward lower in-hospital mortality compared with prior/nonsmokers (3.0% versus 3.5%, $P=0.097$) but no differences in the rates of stroke/TIA (2.3% versus 2.2%, $P=0.898$) or MI (0.3% versus 0.4%, $P=0.468$). After adjusting for patient characteristics, current/recent smoking was associated with a lower rate of in-hospital mortality (relative risk [RR], 0.74; 95% CI, 0.62–0.89 [$P=0.001$]) but still no association with in-hospital stroke/TIA (RR, 1.01; 95% CI, 0.81–1.26 [$P=0.931$]) or MI (RR, 0.65; 95% CI, 0.38–1.13 [$P=0.131$]). At 30 days post-TAVR, smoking was associated with significantly higher mean aortic valve gradient compared with prior/nonsmoking (10.6 versus 9.8 mm Hg, $P<0.001$), but LVEF and KCCQ-OS scores were not significantly different between groups (Table 2).

Table 2. Unadjusted Health Status Outcomes and Echocardiographic Measures After TAVR

	Current/Recent Smokers			Prior/Nonsmokers			
	N	Baseline, Mean±SD	Follow-Up, Mean±SD	N	Baseline, Mean±SD	Follow-Up, Mean±SD	*P* Value*
30-d							
KCCQ-OS score	1996	40.6±23.9	69.2±24.4	35 148	42.8±23.8	70.4±23.6	0.340
Mean gradient, mm Hg	2095	44.8±14.2	10.6±5.8	36 501	44.0±14.6	9.8±5.3	<0.001
LVEF, %	2163	52.3±14.5	54.5±12.4	37 371	54.2±13.7	55.8±12.0	0.307
1 y							
KCCQ-OS score	626	41.4±23.1	72.1±23.6	12 164	43.6±23.5	75.6±21.9	0.004
Mean gradient, mm Hg	719	45.6±14.1	11.1±6.7	13 536	44.8±14.5	10.2±5.4	<0.001
LVEF, %	737	53.0±13.9	55.0±12.4	13 886	54.2±13.5	56.2±11.4	0.182

KCCQ-OS indicates Kansas City Cardiomyopathy Questionnaire–Overall Summary Score; LVEF, left ventricular ejection fraction; TAVR, transcatheter aortic valve replacement.
*Refers to the comparison of follow-up measures (adjusted for baseline) between current/recent smokers and prior/nonsmokers.

Long-Term Outcomes

In unadjusted analyses, current/recent smokers had higher 1-year postdischarge mortality compared with prior/nonsmokers (18.6% versus 16.6%, *P*=0.039 [Figure, Panel A]), but there were no differences in the rates of rehospitalization for stroke (2.0% versus 2.3%, *P*=0.362; Figure, Panel B), MI (2.0% versus 1.8%, *P*=0.461 [Figure, Panel C]), or HF (14.7% versus 13.9%, *P*=0.320 [Figure, Panel D]). After adjusting for patient characteristics, however, there was no significant association of smoking with any of the long-term outcomes (mortality: HR, 1.06; 95% CI, 0.93–1.20 [*P*=0.384]; stroke: HR, 0.93; 95% CI, 0.65–1.33 [*P*=0.682]; MI: HR, 0.92; 95% CI, 0.67–1.26 [*P*=0.604]; HF: HR, 1.09; 95% CI, 0.98–1.23 [*P*=0.120]) (Table 3).

Current/recent smokers who survived to 1 year had lower unadjusted KCCQ-OS scores compared with prior/nonsmokers (72.1±23.6 versus 75.6±21.9, *P*=0.004 [Table 2]). After weighting the observed KCCQ scores for lack of follow-up and adjusting for patient characteristics and baseline KCCQ-OS scores, current/recent smoking remained associated with a small but significantly lower KCCQ-OS score at 1 year after TAVR (2.4 points lower KCCQ-OS; 95% CI, −4.6 to −0.2 [*P*=0.031]). Mean aortic valve gradients remained slightly higher in current/recent smokers compared with prior/nonsmokers (11.1 versus 10.2 mm Hg, *P*<0.001), but LVEF was similar between groups (Table 2).

Discussion

Identifying patient-specific factors associated with outcomes of TAVR is important in evaluating the risks and benefits of treatment for individual patients. In this study, we found that the current/recent smoking rate in patients undergoing TAVR in the United States was low at 5.6%. Moreover, smokers appeared to present for treatment at a younger age and with a greater burden of atherosclerosis and lung disease. Current/recent smokers had lower in-hospital mortality but higher postdischarge mortality, although this association went away after adjusting for demographics and comorbidities. In addition, current/recent smokers who survived to 1 year had slightly worse HF-related symptoms, function, and quality of life. The finding of worse unadjusted long-term outcomes, despite younger age, with similar outcomes after adjustment indicates that the smoking itself is not associated with strikingly different outcomes, but that the comorbidities associated with the smoking, eg, home oxygen use and peripheral artery disease (requiring alternative access for TAVR), likely make put these patients at higher risk.

Prior Studies

Prior data on the association of smoking with outcomes after aortic valve replacement are limited to patients undergoing surgical treatment and have shown conflicting results.[6–8] In a large retrospective analysis of 2790 Australian patients who underwent isolated surgical aortic valve replacement, no association of smoking with long-term mortality was observed.[6] However, this analysis grouped former and current smokers, and the mean age of current/former smokers was 55 years. A more recent retrospective analysis of UK patients undergoing surgical aortic valve replacement with or without coronary artery bypass grafting found that current (but not former) smoking was an independent predictor of long-term mortality.[21] Our study is the first that we are aware of to investigate the association of smoking and outcomes after TAVR; to examine potential explanatory outcomes such as MI, stroke, and aortic valve gradient; and to explore the association of smoking with health status outcomes.

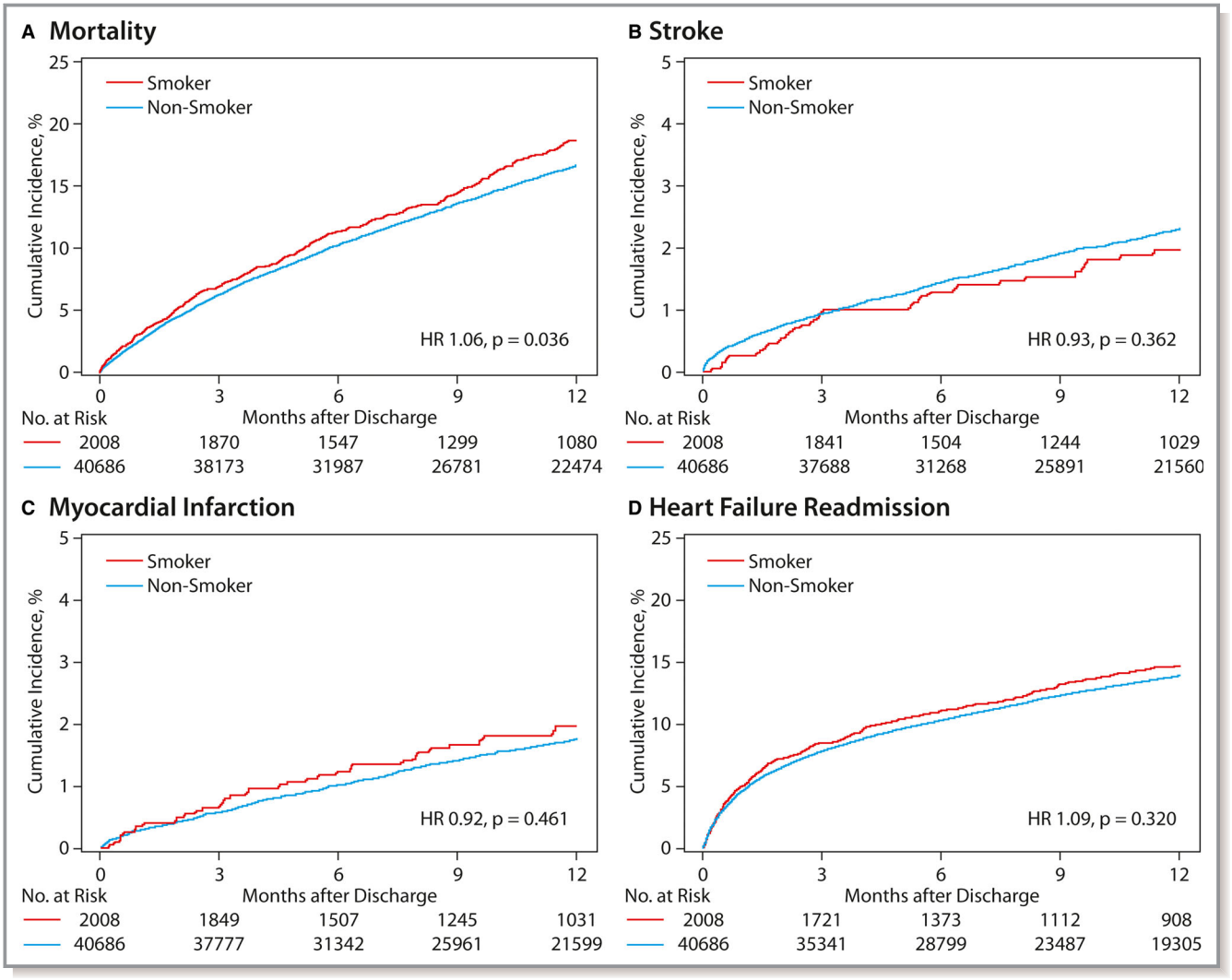

Figure. Cumulative incidence of postdischarge mortality (**A**), stroke (**B**), myocardial infarction (**C**), and heart failure (**D**) by smoking status.

Clinical Implications

Although the smoking rate among patients undergoing TAVR in the United States is relatively low, current/recent smokers were generally much younger but with more comorbidities. This indicates that despite being younger, the higher rate of comorbidities in this group is associated with slightly higher risk of poor recovery. As TAVR is being offered to a wider and younger patient population, the percentage of smokers undergoing TAVR will likely increase, and thus the impact of smoking on TAVR outcomes may become more relevant. This issue is particularly important given the concern of differences in valve longevity in smokers versus nonsmokers (which may have been evident to a small degree in the difference in aortic gradients at 1 year), which are of greater concern when treating younger patients. Importantly, it will be interesting to study the effects of smoking cessation on outcomes after TAVR and whether this may ameliorate some of the long-term adverse effects of smoking. Prior studies have shown that smoking cessation can improve outcomes after MI—an effect that was greater when patients quit for a longer time before the MI,[22] but smoking cessation has not yet been a focus of treatment before TAVR. We believe that our study suggests that there may be a benefit in studying this, despite the advanced age of the patients and the duration of smoking before TAVR.

Limitations

Our study findings should be interpreted in light of the following potential limitations. First, the TVT registry collects smoking status as current/recent versus none and therefore we could not differentiate between current and recent smokers. In addition, data regarding smoking cessation during the follow-up period are unavailable. Second, although the TVT registry has intensified efforts to assure complete

Table 3. Association of Smoking With Postdischarge Clinical Outcomes After TAVR

1-Year Outcomes	Unadjusted		Adjusted for Baseline Factors	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Mortality	1.12 (1.00–1.27)	0.055	1.06 (0.93–1.20)	0.384
Rehospitalization*				
Stroke	0.85 (0.60–1.21)	0.372	0.93 (0.65–1.33)	0.682
MI	1.14 (0.84–1.54)	0.412	0.92 (0.67–1.26)	0.604
HF	1.06 (0.95–1.19)	0.282	1.09 (0.98–1.23)	0.120

HF indicates heart failure; HR, hazard ratio; MI, myocardial infarction; TAVR, transcatheter aortic valve replacement.
*Death considered as a competing risk.

follow-up data assessment, follow-up KCCQ and echocardiographic data were missing in a large proportion of patients (Table S3). We limited our analysis to sites with at least 50% KCCQ completion and used inverse probability weighting to minimize the biases from missing data; however, it is possible that there is some residual bias. Third, we were unable to examine outcomes beyond 1 year. Given the association of smoking with follow-up aortic valve gradients and previously established roles of smoking in the progression of AS, the impact of smoking on valve degeneration is interesting but would require extended follow-up. Finally, the differences in long-term health status and aortic valve gradients between smoking groups were statistically significant but small in magnitude. As such, it is unclear whether these represent clinically meaningful changes between groups.

Conclusions

Although only 5.6% of patients undergoing TAVR in the United States are current or recent smokers, these patients are generally younger with a greater burden of comorbidities, at least in part secondary to their smoking status. Smoking was associated with better in-hospital but similar postdischarge survival after TAVR and slightly worse long-term health status. This suggests that while the younger age allows smokers to survive the initial procedure, the associated comorbidities impact long-term recovery. Further studies are needed to understand the effect of smoking cessation on outcomes in patients undergoing TAVR, especially as TAVR is being offered to a wider and potentially younger population.

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Supplemental Material

Table S1. Baseline characteristics of patients 65 years or older with and without CMS linkage.

	Overall N=69017	With CMS Linkage N=44220	Without CMS Linkage N=24797
Current/Recent Smoker	3,431 (5.0%)	2,069 (4.7%)	1,362 (5.5%)
Age, years	83.0 (78.0-88.0)	84.0 (78.0-88.0)	83.0 (77.0-87.0)
Female	33,115 (48.0%)	21,379 (48.4%)	11,736 (47.4%)
White	64,989 (94.2%)	42,155 (95.3%)	22,834 (92.1%)
Body Surface Area, m2	1.8 (1.7-2.0)	1.8 (1.7-2.0)	1.9 (1.7-2.0)
STS PROM score, %	6.5 (4.3-10.0)	6.6 (4.4-10.2)	6.3 (4.2-9.7)
STS PROM score > 10%	17,300 (25.1%)	11,492 (26.0%)	5,808 (23.4%)
NYHA Class III/IV within 2 Weeks	55,962 (81.9%)	35,791 (81.6%)	20,171 (82.2%)
Five Meter Walk Test, seconds	8.0 (6.0-10.3)	8.0 (6.0-10.3)	8.0 (6.0-10.3)
KCCQ-12 Overall Summary Score	39.6 (23.4-59.4)	39.6 (23.4-59.4)	39.6 (22.9-58.9)
Hypertension	62,188 (90.2%)	39,846 (90.2%)	22,342 (90.1%)
Diabetes Mellitus	25,562 (37.1%)	15,870 (35.9%)	9,692 (39.1%)
Prior MI	17,126 (24.9%)	10,802 (24.5%)	6,324 (25.6%)
Prior PCI	24,249 (35.2%)	15,588 (35.3%)	8,661 (35.0%)
Prior CABG	19,372 (28.1%)	12,341 (27.9%)	7,031 (28.4%)
Prior Stroke/TIA	13,017 (18.9%)	8,311 (18.8%)	4,706 (19.0%)
Carotid Stenosis	13,916 (24.3%)	8,854 (24.1%)	5,062 (24.7%)
Peripheral Arterial Disease	21,132 (30.6%)	13,625 (30.8%)	7,507 (30.3%)
Porcelain Aorta	3,805 (5.5%)	2,350 (5.3%)	1,455 (5.9%)
Atrial Fibrillation/Flutter	28,549 (41.4%)	18,655 (42.2%)	9,894 (40.0%)
Permanent Pacemaker/ICD	12,741 (18.5%)	8,489 (19.2%)	4,252 (17.2%)
Renal Disease (creatinine ≥ 2 mg/dL)	6,367 (9.2%)	4,204 (9.5%)	2,163 (8.7%)
Moderate/Severe Chronic Lung Disease	18,272 (26.6%)	11,800 (26.9%)	6,472 (26.3%)
Home Oxygen	8,074 (11.7%)	5,346 (12.1%)	2,728 (11.0%)
Hemoglobin, g/dL	11.8 (10.5-13.0)	11.8 (10.5-13.0)	11.8 (10.6-13.0)
Platelet Count, K/µL	192.0 (154.0-238.0)	192.0 (154.0-238.0)	192.0 (154.0-238.0)
LVEF, %	58.0 (45.0-63.0)	58.0 (46.0-63.0)	57.0 (45.0-63.0)
Aortic Valve Mean Gradient, mmHg	42.0 (35.0-51.0)	42.0 (35.0-51.0)	42.0 (35.0-51.0)
Moderate/Severe Aortic Insufficiency	13,650 (19.9%)	8,700 (19.8%)	4,950 (20.2%)
Moderate/Severe Mitral Insufficiency	20,122 (29.3%)	13,296 (30.2%)	6,826 (27.7%)
Transfemoral Access	54,083 (78.8%)	34,498 (78.4%)	19,585 (79.4%)

CMS: Center for Medicare and Medicaid Services, CABG: coronary artery bypass grafting, TIA: transient ischemic attack, ICD: implantable cardiac defibrillator, STS PROM: Society of Thoracic Surgeons Predicted Risk Of Mortality, KCCQ-OS: Kansas City Cardiomyopathy Questionnaire-overall summary score and LVEF: left ventricular ejection fraction.

Table S2. In-hospital outcomes by smoking status.

	Overall N=72165	Current/Recent Smoker N=4063	Prior/Non-Smoker N=68102	p-value
Mortality	2,482 (3.4%)	121 (3.0%)	2,361 (3.5%)	0.097
Stroke/TIA	1,613 (2.2%)	92 (2.3%)	1,521 (2.2%)	0.898
Myocardial Infarction	261 (0.4%)	12 (0.3%)	249 (0.4%)	0.468
Cardiac Arrest	2,646 (3.7%)	148 (3.6%)	2,498 (3.7%)	0.932
New Requirement for Dialysis	873 (1.2%)	45 (1.1%)	828 (1.2%)	0.539
Renal Insufficiency (new post-procedural creatinine ≥ 3 mg/dL)	5,361 (7.5%)	322 (8.0%)	5,039 (7.5%)	0.247
VARC Major/Life Threatening Bleeding	5,568 (7.8%)	326 (8.1%)	5,242 (7.8%)	0.509
Significant Vascular Complication	4,861 (6.7%)	255 (6.3%)	4,606 (6.8%)	0.229
Device Related Complication	1,085 (1.5%)	54 (1.3%)	1,031 (1.5%)	0.346
New Pacemaker/ICD	7,477 (10.4%)	367 (9.0%)	7,110 (10.5%)	0.004
Atrial Fibrillation	3,325 (4.6%)	247 (6.1%)	3,078 (4.5%)	<.001

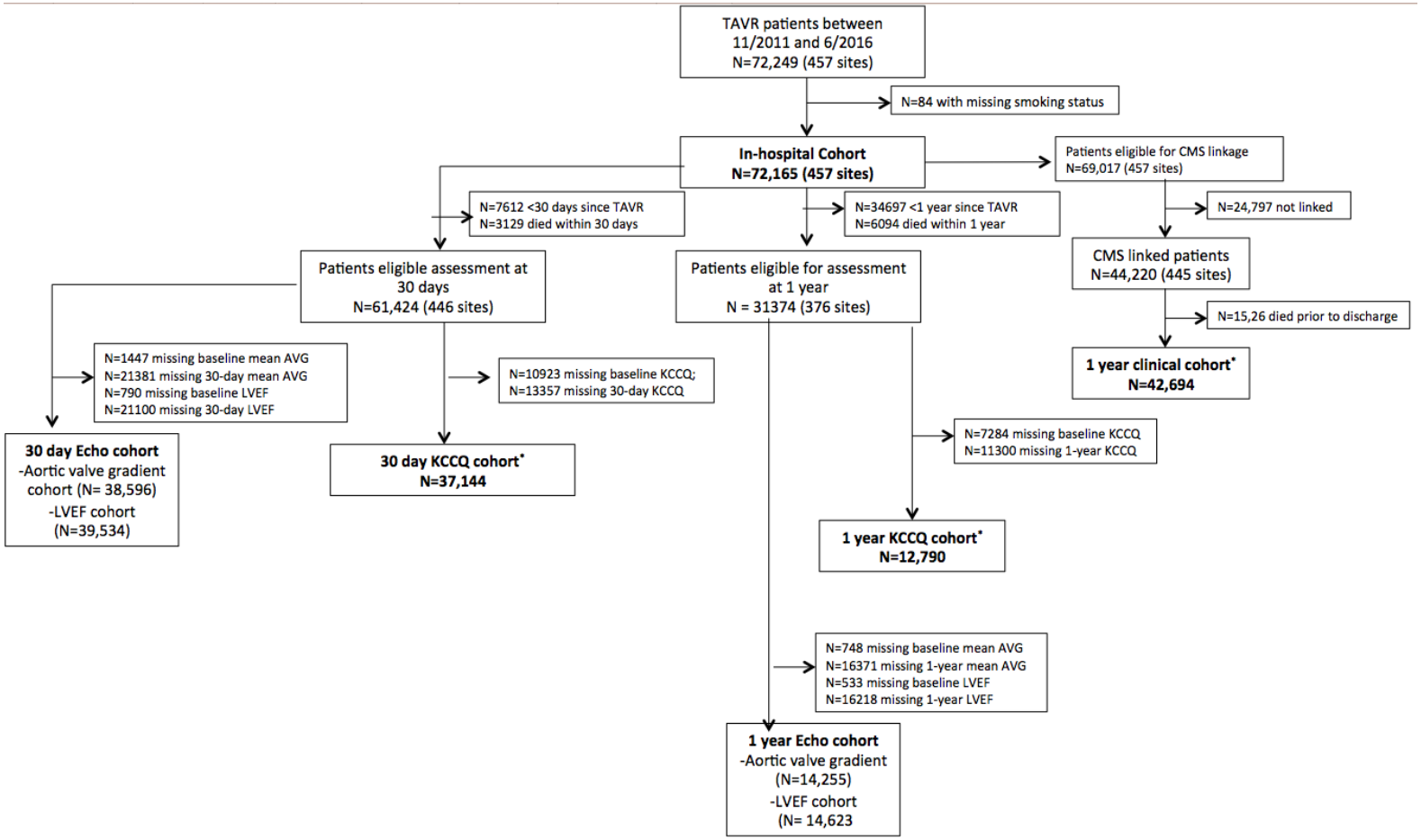
TIA: transient ischemic attack, VARC: Valve Academic Research Consortium, ICD: implantable cardiac defibrillator

Table S3. Baseline characteristics of patients eligible for 1-year KCCQ assessment according to availability of KCCQ data.

	Non-missing KCCQ N=10140	Missing KCCQ N=1823	p-value
Current/Recent Smoker	516 (5.1%)	96 (5.3%)	0.752
Age, years	83.0 (77.0-88.0)	84.0 (78.0-88.0)	0.561
Female	4,984 (49.2%)	916 (50.2%)	0.391
White	9,603 (94.7%)	1,729 (94.8%)	0.806
Body Surface Area, m2	1.8 (1.7-2.0)	1.8 (1.7-2.0)	0.155
STS PROM score, %	6.1 (4.1-9.2)	6.5 (4.3-10.0)	<.001
STS PROM score > 10%	2,089 (20.6%)	454 (24.9%)	<.001
NYHA Class III/IV within 2 Weeks	7,955 (78.9%)	1,433 (79.3%)	0.638
Five Meter Walk Test, seconds	7.7 (6.0-10.0)	8.0 (6.0-10.3)	0.005
KCCQ-12 Overall Summary Score	41.7 (25.5-60.9)	39.6 (23.6-56.8)	<.001
Hypertension	9,083 (89.6%)	1,623 (89.0%)	0.434
Diabetes Mellitus	3,680 (36.3%)	711 (39.0%)	0.028
Prior MI	2,558 (25.3%)	447 (24.5%)	0.515
Prior PCI	3,632 (35.8%)	606 (33.3%)	0.039
Prior CABG	3,139 (31.0%)	544 (29.9%)	0.345
Prior Stroke/TIA	1,861 (18.4%)	358 (19.7%)	0.196
Carotid Stenosis	2,029 (22.5%)	382 (24.0%)	0.208
Peripheral Arterial Disease	3,046 (30.1%)	538 (29.5%)	0.643
Porcelain Aorta	654 (6.5%)	117 (6.4%)	0.951
Atrial Fibrillation/Flutter	3,997 (39.5%)	746 (40.9%)	0.232
Permanent Pacemaker/ICD	1,812 (17.9%)	325 (17.8%)	0.971
Renal Disease (creatinine ≥ 2 mg/dL)	741 (7.3%)	159 (8.7%)	0.036
Moderate/Severe Chronic Lung Disease	2,483 (24.6%)	510 (28.1%)	0.002
Home Oxygen	1,075 (10.6%)	231 (12.7%)	0.009
Hemoglobin, g/dL	12.0 (10.8-13.1)	11.8 (10.6-13.1)	0.002
Platelet Count, K/µL	191.0 (154.0-235.0)	195.0 (154.0-241.0)	0.100
LVEF, %	58.0 (47.0-63.0)	58.0 (48.0-65.0)	0.358
Aortic Valve Mean Gradient, mmHg	43.0 (36.0-52.0)	43.0 (37.0-52.0)	0.080
Moderate/Severe Aortic Insufficiency	1,939 (19.2%)	352 (19.4%)	0.841
Moderate/Severe Mitral Insufficiency	2,933 (29.0%)	576 (31.8%)	0.018
Transfemoral Access	7,032 (69.5%)	1,271 (70.4%)	0.445

CMS: Center for Medicare and Medicaid Services, CABG: coronary artery bypass grafting, TIA: transient ischemic attack, ICD: implantable cardiac defibrillator, STS PROM: Society of Thoracic Surgeons Predicted Risk Of Mortality, KCCQ-OS: Kansas City Cardiomyopathy Questionnaire-overall summary score and LVEF: left ventricular ejection fraction.

Figure S1. Patient population.



*Clinical outcomes were assessed as post-discharge outcomes. Patients had to be alive at follow up to be eligible for the KCCQ cohorts.

TAVR: Transcatheter Aortic Valve Replacement, CMS: Center for Medicare and Medicaid Services, KCCQ-OS: Kansas City Cardiomyopathy Questionnaire-overall summary score and LVEF: left ventricular ejection fraction, AVG: aortic valve gradient.