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Transcatheter Versus Surgical Aortic Valve Replacement

Propensity-Matched Comparison

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ABSTRACT

BACKGROUND Randomized trials support the use of transcatheter aortic valve replacement (TAVR) for the treatment of aortic stenosis in high- and intermediate-risk patients, but the generalizability of those results in clinical practice has been challenged.

OBJECTIVES The aim of this study was to determine the safety and effectiveness of TAVR versus surgical aortic valve replacement (SAVR), particularly in intermediate- and high-risk patients, in a nationally representative real-world cohort.

METHODS Using data from the Transcatheter Valve Therapy Registry and Society of Thoracic Surgeons National Database linked to Medicare administrative claims for follow-up, 9,464 propensity-matched intermediate- and high-risk (Society of Thoracic Surgeons Predicted Risk of Mortality score ≥3%) U.S. patients who underwent commercial TAVR or SAVR were examined. Death, stroke, and days alive and out of the hospital to 1 year were compared, as well as discharge home, with subgroup analyses by surgical risk, demographics, and comorbidities.

RESULTS In a propensity-matched cohort (median age 82 years, 48% women, median Society of Thoracic Surgeons Predicted Risk of Mortality score 5.6%), TAVR and SAVR patients experienced no difference in 1-year rates of death (17.3% vs. 17.9%; hazard ratio: 0.93; 95% confidence interval [CI]: 0.83 to 1.04) and stroke (4.2% vs. 3.3%; hazard ratio: 1.18; 95% CI: 0.95 to 1.47), and no difference was observed in the proportion of days alive and out of the hospital to 1 year (rate ratio: 1.00; 95% CI: 0.98 to 1.02). However, TAVR patients were more likely to be discharged home after treatment (69.9% vs. 41.2%; odds ratio: 3.19; 95% CI: 2.84 to 3.58). Results were consistent across most subgroups, including among intermediate- and high-risk patients.

CONCLUSIONS Among unselected intermediate- and high-risk patients, TAVR and SAVR resulted in similar rates of death, stroke, and DAOH to 1 year, but TAVR patients were more likely to be discharged home.
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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

DAOH = days alive and out of the hospital

IQR = interquartile range

PROM = Predicted Risk of Mortality

SAVR = surgical aortic valve replacement

STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

Aortic valve disease is the third most common cause of cardiovascular disease in the United States, affecting an estimated 2.5 million adults (5% of those affected are 65 years or older) (1,2). Severe untreated aortic valve stenosis substantially affects life expectancy and quality (3); however, patients with aortic valve disease are often older, with multiple comorbidities, making recovery from open surgical aortic valve replacement (SAVR) challenging (4). Over the past decade, transcatheter aortic valve replacement (TAVR) has emerged as a less invasive alternative to SAVR, thereby offering potential advantages for this older patient cohort (5). TAVR was approved by the U.S. Food and Drug Administration in 2011; since then, >80,000 commercial TAVR procedures have been performed in the United States in patients at intermediate, high, and prohibitive surgical risk (Matthew Brennan, February 4, 2017, personal communication).

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To date, 3 high-quality randomized controlled trials have supported the use of TAVR in intermediate- and high-risk patients (6–8), but these clinical trials excluded important groups of patients with higher risk comorbidities and were conducted at a select group of high-volume valve centers. Consequently, whether these results are applicable to clinical practice has been questioned (9), and concerns regarding the safety and effectiveness of TAVR have been raised (10,11). These concerns are of increasing relevance because TAVR is applied to low- and intermediate-risk patients, in whom the risk of SAVR is less, and its long-term outcomes are well-documented (12).

To address these lingering questions, we used observational data from 2 large U.S. procedural registries to examine the real-world comparative effectiveness of TAVR versus SAVR in a nationally representative real-world cohort of older patients who may have been considered eligible for either TAVR or SAVR.

TABLE 1 Baseline Characteristics of the Aortic Valve Replacement Cohort After Propensity Matching*

	SAVR (n = 4,732)	TAVR (n = 4,732)	Standardized Difference, TAVR vs. SAVR, %
Age, yrs	82 (77-85)	81 (77-85)	−1.01
Female	2,278 (48.1)	2,256 (47.7)	−0.93
Body surface area, m^2	1.9 (1.7-2.1)	1.9 (1.7-2.0)	0.04
Creatinine, mg/dl	1.1 (0.9-1.4)	1.1 (0.9-1.5)	−0.32
Dialysis	186 (3.9)	179 (3.8)	−0.77
LVEF, %	55.0 (45.0-55.0)	55.0 (45.0-55.0)	−1.10
Heart failure symptoms <2 weeks			4.28
None or Class I	447 (9.4)	335 (7.1)	
Class II	947 (20.0)	995 (21.0)	
Class III	2,499 (52.8)	2,509 (53.0)	
Class IV	839 (17.7)	893 (18.9)	
Chronic lung disease			1.62
None	2,793 (59.0)	2,784 (58.8)	
Mild	872 (18.4)	866 (18.3)	
Moderate	564 (11.9)	558 (11.8)	
Severe	503 (10.6)	524 (11.1)	
Home oxygen use	385 (8.1)	378 (8.0)	−0.54
Prior stroke	524 (11.1)	506 (10.7)	−1.22
Peripheral vascular disease	1,138 (24.0)	1,113 (23.5)	−1.24
Pre-operative atrial fibrillation/flutter	1,619 (34.2)	1,572 (33.2)	−2.10
Prior MI			2.21
Recent	161 (3.4)	173 (3.7)	
Old	954 (20.2)	924 (19.5)	
Prior PCI	1,278 (27.0)	1,233 (26.1)	−2.15
CAD: number of diseased vessels			0.95
None	2,292 (48.4)	2,326 (49.2)	
1	770 (16.3)	757 (16.0)	
2	520 (11.0)	512 (10.8)	
3	1,150 (24.3)	1,137 (24.0)	
Prior CV surgery	1,484 (31.4)	1,406 (29.7)	−3.58
Prior aortic valve replacement	219 (4.6)	214 (4.5)	−0.51
Aortic valve mean gradient, mm Hg	42.0 (35.0-52.0)	42.0 (36.0-52.0)	0.46
Aortic insufficiency (moderate/severe)	956 (20.2)	947 (20.0)	−0.47
Mitral insufficiency (moderate/severe)	1,166 (24.6)	1,125 (23.8)	−2.02
PA systolic pressure, mm Hg	41.0 (37.0-46.0)	41.0 (37.0-46.0)	1.09
Pre-operative IABP/inotropes	128 (2.7)	123 (2.6)	−0.66

Continued on the next page

METHODS

STUDY DESIGN AND DATA SOURCES. This was a multicenter, nonrandomized analysis of older patients with severe, symptomatic aortic valve stenosis at intermediate or high surgical risk who underwent treatment with TAVR or SAVR in the United States and may have been considered eligible for either treatment (on the basis of available data). Data for this analysis were drawn from 2 U.S. procedural registries: 1) SAVR data were drawn from the Society of Thoracic Surgeons (STS) National Database; and 2) TAVR data were drawn from the STS/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry. The development and application of these registries have been described previously (13,14). More than 90% of cardiac surgery programs in the United States participate in the STS National Database, and participation in the TVT Registry is necessary for Medicare reimbursement. Notably, the involvement of a heart team is also necessary for Medicare reimbursement in the United States. For each registry, participants are required to submit 100% of their case records to the registry for quality

assessment purposes. Missing data fields trigger critical warnings, and each registry has an independent data auditing program to ensure data accuracy. Records were linked to the Centers for Medicare and Medicaid Services fee-for-service administrative insurance claims files to create a longitudinal record including vital status and rehospitalization events, using validated techniques (15).

The most updated Medicare-linked files available were used from the TVT Registry and STS National Database. TVT Registry files are linked with Medicare claims by the Centers for Medicare and Medicaid Services twice each year, using updated files from the Centers for Medicare and Medicaid Services Chronic Conditions Data Warehouse. STS National Database files are linked with Medicare claims by the Duke Clinical Research Institute annually, using research-identifiable files from ResDAC (Minneapolis, Minnesota) (16). The availability of ResDAC files generally lags 12 to 18 months behind the date of service provision. Detailed clinical information and Medicare claims-based follow-up were available for 25,786 TAVR cases performed between January 1, 2014, and September 30, 2015, and 198,077 SAVR (or SAVR plus coronary artery bypass grafting) cases performed between July 1, 2011, and December 31, 2013.

Patients with characteristics that were thought to strongly favor 1 treatment or another were excluded (Online Figure 1). These characteristics included age <65 or >90 years, other major cardiac operations, history of endocarditis, emergency or salvage status, primary aortic insufficiency, hostile chest or porcelain aorta, moderate to severe mitral stenosis, and STS Predicted Risk of Mortality (PROM) score <3%. Subsequent aortic valve replacement procedures during the initial aortic valve replacement admission were excluded, and hospitals submitting <10 total SAVR or TAVR records during the study interval were also excluded. Following these exclusions, the population of interest included 17,910 TAVR and 22,618 SAVR patients who were available for propensity matching.

The Patient-Centered Outcomes Research Institute funded this study (grant CER-1306-04350), which the Institutional Review Board at the Duke University School of Medicine approved. The Duke Clinical Research Institute (Durham, North Carolina) was responsible for data management and statistical analysis, with oversight by a multidisciplinary research team that included patient and caregiver representatives, as well as statistical analysts and representatives from both the STS and American College of Cardiology.

TABLE 1 Continued

	SAVR (n = 4,732)	TAVR (n = 4,732)	Standardized Difference, TAVR vs. SAVR, %
Hematocrit, %	36.0 (32.3–39.5)	36.0 (32.1–39.6)	0.27
Pre-operative total albumin, g/dl	3.7 (3.5–4.0)	3.7 (3.5–4.0)	−0.50
Immunosuppression	363 (7.7)	344 (7.3)	−1.53
Status (elective, urgent)	3,871 (81.8)	3,813 (80.6)	−3.14
STS PROM score, %	5.8 (4.2–8.6)	5.5 (4.2–8.0)	7.23
3%–5%	1,850 (39.1)	1,953 (41.3)	
5%–8%	1,545 (32.7)	1,596 (33.7)	
≥8%	1,337 (28.3)	1,183 (25.0)	
Transfemoral access	—	3,612 (76.3)	
Concomitant CABG	1,565 (33.1)	—	
Medications at hospital discharge			
Aspirin	3,961 (83.7)	3,852 (81.4)	−6.07
$P2Y_{12}$ inhibitor	646 (13.7)	2,864 (60.5)	110.96
Anticoagulant agent†	1,871 (39.5)	1,132 (23.9)	−34.03

Values are median (interquartile range) or n (%), unless otherwise indicated. *A more complete listing of patient characteristics and standardized differences before and after propensity matching is included in the Online Appendix. †Anticoagulant agents include warfarin and novel oral anticoagulant agents.

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CV = cardiovascular; IABP = intra-aortic balloon pump; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PA = pulmonary artery; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement.

DATA DEFINITIONS AND OUTCOMES. By design, data definitions are identical for most patient characteristics and outcomes across the STS National Database and the TVT Registry and are available for review in Online Table 1 and online (17,18). Outcomes from the index hospitalization were drawn from registry records. A list of potential outcomes available through Medicare claims were reviewed by a broad stakeholder panel that included patients, caregivers, clinicians, health science researchers, and statisticians. Primary outcomes of interest were chosen by consensus and included death, stroke, days alive and out of an acute care hospital facility (i.e., days alive and out of the hospital [DAOH]) to 1 year, and discharge home. Stroke and mortality were evaluated to 30 days and 1 year over a median follow-up period of 169.5 days for TAVR and 328 days for SAVR. Stroke was identified during the index procedural hospitalization using registry data. Following hospital discharge, stroke was identified using Medicare rehospitalization claims with a primary position International Classification of Diseases, Ninth Revision, Clinical Modification code of 434.x1, 436, 433.x1, 997.02, 437.1, 437.9, 430, 431, or 432.x.

STATISTICAL ANALYSIS. An analytic sample was created using propensity score-based matching to correct for differences in characteristics of patients in the 2 registries. A propensity score, defined as the

probability of receiving TAVR given measured covariates, was calculated using logistic regression. Detailed methods, including an extensive list of covariates identified by clinical input regarding factors thought to be related to both procedure selection and outcomes, and common to the 2 registries, are provided in Online Table 2. Overlap in the covariate distribution and propensity scores between study groups was assessed. Because patients at the tails (<5% and >95%) of the propensity distribution were thought to represent subjects with an overwhelming likelihood of treatment with 1 or the other of the 2 treatments, these patients were excluded (Online Figure 2). Propensity score matching was conducted in a 1:1 ratio, by greedy matching, using a caliper of 0.20 SDs in the linear predictor. The adequacy of the propensity model was confirmed by checking covariate balance before and after matching (Online Figure 3). Furthermore, to assess the potential for unmeasured confounding, the 2 treatments were compared using 2 falsification endpoints: lower extremity fracture and urinary tract infection. No statistically significant difference was observed for these outcomes to 1 year in the propensity-matched cohort (Online Figure 4).

Baseline characteristics of patients undergoing SAVR and TAVR were described and compared overall and within pre-specified subgroups on the basis of standardized differences (Online Figure 5). Cox proportional hazard models were used to compare outcomes of TAVR versus SAVR by hazard ratios and 95% confidence intervals (CIs). DAOH was modeled as count data using generalized estimating equations with a log link and a fixed offset (adjusting for differential follow-up time) to obtain rate ratios and 95% CIs. Models for treatment on outcomes were fit to the matched sample using a robust empirical variance to account for within-hospital clustering. Associations were estimated in pre-specified subgroups, along with 95% CIs and tests of interaction. Statistical significance was defined as $p < 0.10$, and significant values were evaluated for biological plausibility. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

PATIENTS. The propensity-matched cohort included 4,732 SAVR and 4,732 TAVR patients, with a median age of 82 years (interquartile range [IQR]: 77 to 85 years), 47.9% women, and a median STS PROM score of 5.6% (IQR: 4.2% to 8.2%). Baseline characteristics were well balanced across the 2 treatment groups (Table 1). Among TAVR patients, transfemoral access was used in 76%, and the valve prosthesis used was the CoreValve (Medtronic, Dublin, Ireland) in 33% and the Sapien (Edwards Lifesciences, Irvine, California) in 67%.

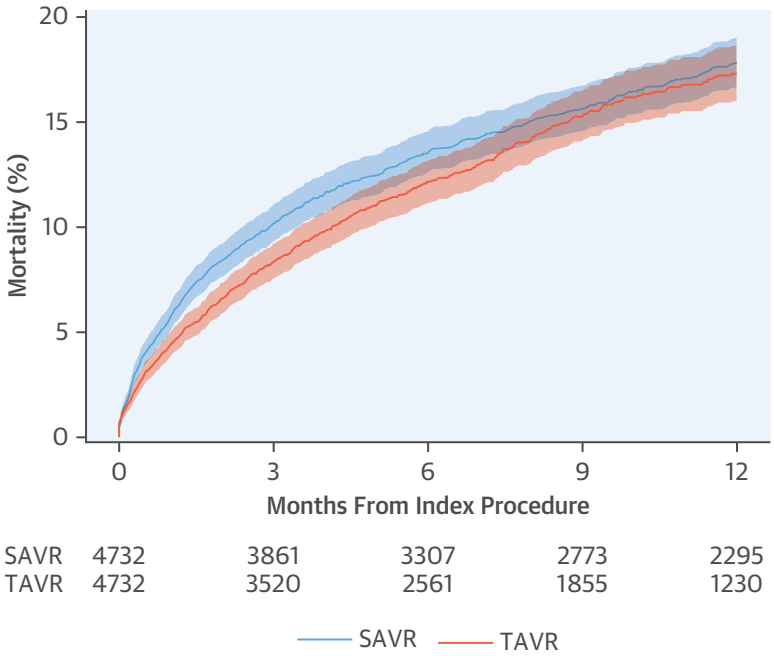
OUTCOMES. Procedure outcomes. On average, TAVR patients spent 31 h (IQR: 24 to 57 h) in the intensive care unit and a total of 4 days (IQR: 3 to 6 days) in the hospital during the index admission, whereas SAVR patients spent an average of 68 h (IQR: 37 to 119 h) in the intensive care unit and 8 days (IQR: 6 to 11 days) in the hospital during the index admission. In-hospital mortality was lower among TAVR patients than SAVR patients (3.0% vs. 5.0%; $p < 0.001$), while the incidence of stroke was no different (2.5% vs. 2.7%; $p = 0.40$). Compared with SAVR patients, TAVR patients experienced a higher incidence of new pacemaker or implantable cardioverter-defibrillator placement (12.8% vs. 6.3%; $p < 0.001$) and major vascular complications (4.2% vs. 0.4%; $p < 0.001$) but a lower incidence of blood transfusions (packed red blood cells: TAVR, 0 U [IQR: 0 to 0 U]; SAVR, 2 U [IQR: 0 to 4 U]; $p < 0.001$) and new requirement for hemodialysis (1.7% vs. 3.2%; $p < 0.001$) during the initial hospitalization.

Discharge home was more common among TAVR patients than SAVR patients (69.9% vs. 41.2%), overall and within each subgroup that was studied (Online Figure 6). Discharge to an extended care facility, transitional care unit, or rehabilitation unit was more common among SAVR patients (41.2% vs. 20.5%; $p < 0.01$).

Death and stroke. No difference in death at 1 year was observed with TAVR versus SAVR (17.3% vs. 17.9%; $p = 0.40$), although a lower early risk for mortality was observed with TAVR (**Central Illustration**). A similar 1-year risk for death was observed across most subgroups of interest (**Figure 1A**); however, those with prior cardiac surgery experienced a lower 1-year risk for mortality when treated with TAVR versus SAVR (p for interaction = 0.09).

The risk for stroke was highest in the first 30 days following treatment and was identical between TAVR and SAVR (2.8% vs. 2.8%; $p = 0.13$) patients. An increase in the incidence of stroke was observed among TAVR (vs. SAVR) patients between 30 days and 1 year, with a progressive divergence of the stroke event curves. Nevertheless, the overall risk for stroke remained low during this interval (0.5% vs. 1.4%) (**Figure 2**), and the overall difference in risk for stroke was not significant to 1 year (TAVR vs. SAVR hazard ratio: 1.18; 95% CI: 0.95 to 1.47). Patients with

CENTRAL ILLUSTRATION **Transcatheter Aortic Valve Replacement and Surgical Aortic Valve Replacement: Rate of Mortality**



Brennan, J.M. et al. J Am Coll Cardiol. 2017;70(4):439-50.

Among unselected intermediate- and high-risk patients, transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR) resulted in similar rates of death (shown here), stroke, and days alive and out of the hospital to 1 year, but TAVR patients were more likely to be discharged home. Results were consistent across most subgroups, including among intermediate- and high-risk patients.

home oxygen experienced a lower risk for stroke to 1 month with TAVR versus SAVR (p for interaction = 0.06) (**Figure 1B**), but by 1 year, neither treatment was favored in these patients (Online Figure 8).

Days alive and out of hospital. In the first year following hospital discharge, ≥80% of patients were alive and out of an acute care hospital for at least 11 of 12 months (**Figure 3**). The proportion of DAOH was similar between TAVR and SAVR patients (rate ratio: 1.0; 95% CI: 0.98 to 1.02), a result that was consistent across all subgroups (**Figure 1C**).

INFLUENCE OF PRE-OPERATIVE SURGICAL RISK. After verifying covariate balance across 3 risk levels of STS PROM (3% to 5%, 5% to 8%, and ≥8%), a stratified analysis was performed. Increasing pre-operative surgical risk was associated with a lower likelihood of discharge home, fewer DAOH, a higher risk for stroke, and a higher risk for death to 1 year; however, the relative treatment effect (TAVR vs. SAVR) was consistent for each outcome of interest across the spectrum of intermediate to high baseline surgical risk (STS PROM) (**Table 2**).

DISCUSSION

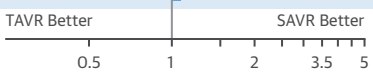
In a broad cohort of older U.S. patients with severe aortic stenosis who were eligible for treatment with either TAVR or SAVR, no significant difference was observed in death, stroke, or DAOH to 1 year. TAVR patients were more often discharged directly home, reflecting a less demanding post-operative recovery. Results were consistent across most patient subgroups and across the spectrum of intermediate to high pre-operative surgical risk. These findings are largely consistent with those observed in pivotal randomized clinical trials and support the safety and effectiveness of TAVR in real-world intermediate- and high-risk patients.

In 3 previous randomized clinical trials among patients with severe aortic stenosis and intermediate or high surgical risk, TAVR has demonstrated similar (or superior) outcomes to 1 year when compared

FIGURE 1 Subgroup Analyses

A

Subgroup	No. of Patients	SAVR	TAVR	P Value for Interaction
		One Year Mortality		
Age				0.97
65-79	3,607	19.3 (17.3-21.4)	19.5 (17.2-21.9)	
80+	5,857	17.0 (15.6-18.5)	16.1 (14.5-17.7)	
Home oxygen				0.15
Yes	763	30.3 (25.5-35.3)	23.7 (18.9-28.8)	
No	8,701	16.7 (15.5-17.9)	16.7 (15.4-18.1)	
Prior cardiac surgery				0.09
Yes	2,890	18.2 (16.1-20.4)	15.6 (13.3-18.0)	
No	6,574	17.7 (16.3-19.1)	18.0 (16.5-19.7)	
Chronic Lung Dz				0.94
None	5,577	14.8 (13.5-16.3)	14.8 (13.2-16.5)	
Mild	1,738	17.8 (15.1-20.7)	15.8 (13.0-18.9)	
Moderate	1,122	23.7 (19.9-27.6)	22.8 (18.6-27.4)	
Severe	1,027	28.2 (24.1-32.6)	26.8 (22.2-31.6)	
Creatinine<2 and no dialysis				0.77
Yes	8,515	16.3 (15.1-17.5)	15.8 (14.5-17.1)	
No	949	31.8 (27.3-36.3)	30.7 (25.6-36.0)	
Left ventricular ejection fraction				0.37
<35	1,136	22.8 (19.1-26.7)	24.9 (20.8-29.2)	
35-49	1,519	21.5 (18.4-24.6)	18.1 (14.8-21.8)	
50+	6,809	16.2 (14.9-17.6)	15.7 (14.2-17.2)	
Sex				0.52
Male	4,930	19.7 (18.0-21.5)	19.2 (17.3-21.2)	
Female	4,534	15.9 (14.3-17.6)	15.2 (13.5-17.0)	
CAD extent				0.36
None	4,618	17.2 (15.5-18.9)	16.8 (15.0-18.7)	
1	1,527	15.6 (12.9-18.5)	17.6 (14.3-21.2)	
2	1,032	18.8 (15.4-22.6)	15.8 (12.1-19.8)	
3	2,287	20.3 (17.9-22.9)	18.7 (16.0-21.5)	
Peripheral vascular disease				0.89
Yes	7,213	16.6 (15.3-17.9)	16.0 (14.6-17.5)	
No	2,251	21.9 (19.3-24.5)	21.3 (18.4-24.4)	
Immunosuppression				0.60
Yes	707	25.3 (20.6-30.2)	23.4 (18.0-29.3)	
No	8,757	17.2 (16.0-18.5)	16.8 (15.5-18.2)	
Prior stroke				0.88
Yes	1,030	19.2 (15.7-22.9)	18.9 (14.7-23.4)	
No	8,434	17.7 (16.5-19.0)	17.1 (15.7-18.5)	
Mitral insufficiency				0.31
Moderate/severe	2,291	20.0 (17.6-22.5)	21.7 (18.7-24.8)	
Other	7,173	17.2 (15.8-18.5)	16.0 (14.5-17.5)	
PA systolic pressure				0.72
≤40	2,959	14.7 (12.8-16.7)	13.4 (11.4-15.6)	
41-55	5,258	17.6 (16.1-19.2)	18.0 (16.2-19.8)	
56+	1,247	26.2 (22.5-30.1)	23.6 (19.7-27.7)	
Mean aortic valve gradient				0.69
<40	3,248	20.9 (18.7-23.0)	19.8 (17.4-22.2)	
40-59	4,792	16.2 (14.6-17.9)	15.9 (14.1-17.7)	
60+	1,424	16.4 (13.7-19.4)	16.5 (13.4-19.9)	



Subgroup analyses are shown comparing TAVR versus SAVR for **(A)** death to 1 year (hazard ratio [95% confidence interval (CI)]), **(B)** stroke to 30 days (hazard ratio [95% CI]), and **(C)** days alive and out of an acute care hospital (DAOH) to 1 yr (RR [risk ratio] [95% CI]). For DAOH, the proportion of DAOH in the first year following initial hospital discharge was calculated for each patient (Online Figure 7). Subgroup results for stroke to 1 year are presented separately because of nonproportional hazards (Online Figure 8). A balance of covariates within each subgroup was forced with inclusion of interaction terms in the propensity score. The p value for interaction represents the likelihood of interaction between the variable and the relative treatment effect. Comparative treatment effects were similar across most subgroups, with few significant interactions noted. CAD = coronary artery disease; Dz = disease; PA = pulmonary artery; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

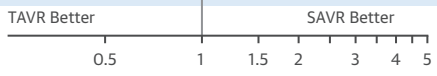
Continued on the next page

FIGURE 1 Continued

B

One Month Stroke

Subgroup	No. of Patients	SAVR	TAVR	P Value for Interaction
Age				0.15
65-79	3,607	2.4 (1.8-3.2)	3.0 (2.3-4.0)	
80+	5,857	3.1 (2.5-3.8)	2.7 (2.1-3.4)	
Home oxygen				0.06
Yes	763	3.7 (2.1-6.0)	1.4 (0.5-3.1)	
No	8,701	2.8 (2.3-3.3)	3.0 (2.5-3.5)	
Prior cardiac surgery				0.42
Yes	2,890	2.9 (2.1-3.9)	2.5 (1.7-3.5)	
No	6,574	2.8 (2.3-3.4)	3.0 (2.4-3.6)	
Chronic Lung Dz				0.28
None	5,577	3.0 (2.4-3.6)	2.8 (2.2-3.5)	
Mild	1,738	2.6 (1.7-3.9)	2.2 (1.3-3.4)	
Moderate	1,122	3.5 (2.2-5.2)	3.3 (2.0-5.1)	
Severe	1,027	1.8 (0.9-3.3)	3.5 (2.1-5.5)	
Creatinine<2 and no dialysis				0.80
Yes	8,515	2.8 (2.4-3.4)	2.9 (2.4-3.4)	
No	949	2.9 (1.6-4.8)	2.6 (1.4-4.4)	
Left ventricular ejection fraction				0.83
<35	1,136	3.1 (1.9-4.9)	2.8 (1.6-4.4)	
35-49	1,519	2.3 (1.4-3.6)	2.8 (1.7-4.3)	
50+	6,809	2.9 (2.4-3.5)	2.9 (2.3-3.5)	
Sex				0.23
Male	4,930	2.7 (2.1-3.4)	3.1 (2.5-3.9)	
Female	4,534	3.0 (2.3-3.7)	2.5 (1.9-3.2)	
CAD extent				0.62
None	4,618	2.5 (2.0-3.3)	2.7 (2.1-3.4)	
1	1,527	2.5 (1.6-3.9)	2.5 (1.5-3.8)	
2	1,032	2.7 (1.6-4.4)	3.9 (2.4-6.0)	
3	2,287	3.6 (2.7-4.9)	2.9 (2.0-4.1)	
Peripheral vascular disease				0.22
Yes	7,213	2.9 (2.4-3.5)	2.6 (2.1-3.2)	
No	2,251	2.7 (1.9-3.8)	3.5 (2.5-4.8)	
Immunosuppression				0.29
Yes	707	2.2 (1.1-4.2)	3.5 (1.9-6.1)	
No	8,757	2.9 (2.4-3.4)	2.8 (2.3-3.3)	
Prior stroke				0.33
Yes	1,030	3.1 (1.8-4.9)	4.2 (2.6-6.3)	
No	8,434	2.8 (2.3-3.3)	2.7 (2.2-3.2)	
Mitral insufficiency				0.99
Moderate/severe	2,291	2.6 (1.8-3.7)	2.6 (1.8-3.7)	
Other	7,173	2.9 (2.4-3.5)	2.9 (2.4-3.5)	
PA systolic pressure				0.02
≤40	2,959	2.0 (1.4-2.8)	3.2 (2.3-4.2)	
41-55	5,258	3.4 (2.7-4.1)	2.5 (1.9-3.2)	
56+	1,247	2.5 (1.4-3.9)	3.5 (2.2-5.3)	
Mean aortic valve gradient				0.41
<40	3,248	3.1 (2.4-4.1)	2.5 (1.8-3.4)	
40-59	4,792	2.5 (1.9-3.2)	2.8 (2.2-3.6)	
60+	1,424	3.3 (2.1-4.8)	3.7 (2.5-5.4)	



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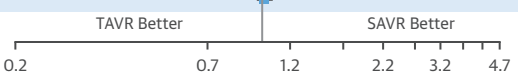
with SAVR. In high-risk patients, Cohort A of the randomized PARTNER (Placement of Aortic Transcatheter Valves) trial (n = 699, 25 U.S. centers) demonstrated similar rates of death to 1 year with a first-generation balloon-expandable TAVR prosthesis versus SAVR (24.2% vs. 26.8; p = 0.44) but with an increased risk for stroke or transient ischemic attack (8.3% vs. 4.3%; p = 0.04) (6). In a lower risk cohort, the U.S. CoreValve trial (n = 795, 45 U.S. centers) demonstrated lower rates of death to 1 year with a self-expanding TAVR prosthesis (14.2% vs. 19.1%; p = 0.04 for superiority), without an increased risk for stroke (8.8% vs. 12.6%; p = 0.10) (8). These results were consistent across most subgroups of patients. Among intermediate-risk patients in the PARTNER 2A trial (n = 2,032, 57 centers), patients randomized to a balloon-expandable second-generation TAVR prosthesis (vs. SAVR) experienced similar rates of

FIGURE 1 Continued

C

Days Alive and Out of Hospital

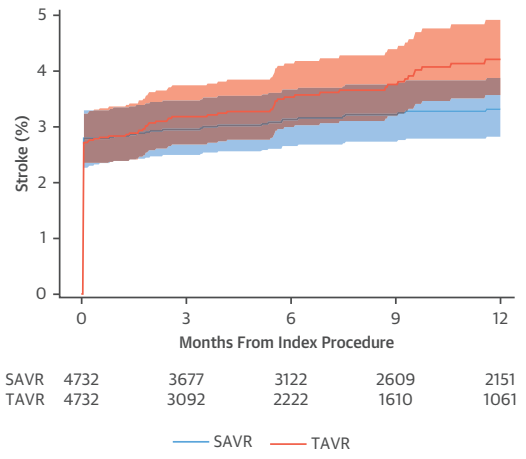
Subgroup	No. of Patients	SAVR	TAVR	P Value for Interaction
Age				0.43
65-79	3,323	85.6	87.8	
80+	5,446	86.7	89.1	
Home oxygen				0.20
Yes	718	76.2	83.0	
No	8,051	87.2	89.1	
Prior cardiac surgery				0.21
Yes	2,669	86.2	89.8	
No	6,100	86.3	88.0	
Chronic Lung Dz				0.95
None	5,177	88.1	90.2	
Mild	1,602	87.0	89.3	
Moderate	1,043	84.0	85.9	
Severe	947	77.5	81.6	
Creatinine<2 and no dialysis				0.97
Yes	7,885	87.6	89.6	
No	884	74.4	79.9	
Left ventricular ejection fraction				0.78
<35	1,032	82.2	84.7	
35-49	1,395	84.6	87.9	
50+	6,342	87.3	89.4	
Sex				0.56
Male	4,555	85.6	88.2	
Female	4,214	87.0	88.9	
CAD extent				0.39
None	4,293	86.8	88.7	
1	1,415	88.0	88.7	
2	953	85.6	89.2	
3	2,108	84.4	87.8	
Peripheral vascular disease				0.82
Yes	6,687	87.1	89.2	
No	2,082	83.8	86.6	
Immunosuppression				0.50
Yes	657	80.4	86.0	
No	8,112	86.8	88.8	
Prior stroke				0.79
Yes	953	84.4	87.5	
No	7,816	86.5	88.7	
Mitral insufficiency				0.38
Moderate/severe	2,129	84.2	86.1	
Other	6,640	87.0	89.3	
PA systolic pressure				0.72
≤40	2,760	88.8	90.9	
41-55	4,855	86.2	88.3	
56+	1,154	80.6	84.2	
Mean aortic valve gradient				0.85
<40	3,006	84.6	87.0	
40-59	4,446	87.4	89.7	
60+	1,317	86.6	88.2	



death (12.3% vs. 12.9%; p = 0.69) or stroke (8.0% vs. 8.1%; p = 0.88) at 1 year (7). Again, no significant subgroup interactions were observed.

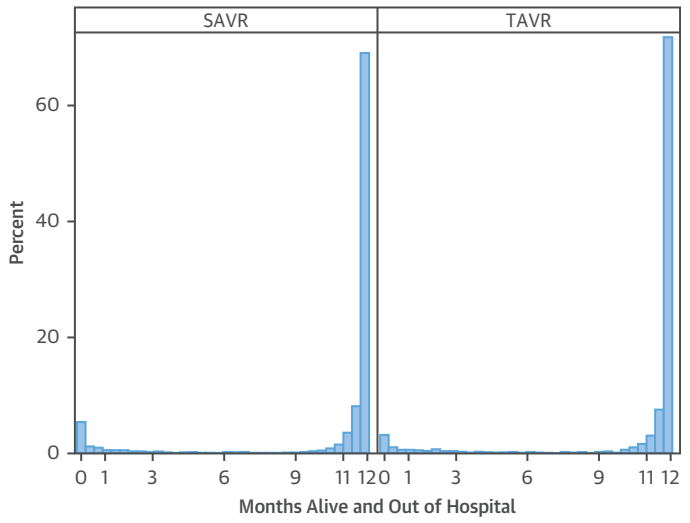
Despite favorable results in carefully controlled randomized trials, the generalizability of trial results to real-world patients has been questioned by some, because of systematic exclusion from clinical trials of patients with certain high-risk comorbidities (e.g., hemodialysis, recent stroke [<6 months prior], very low left ventricular ejection fraction [<20%]) (9). Responding to these concerns, nonrandomized evaluations of TAVR versus SAVR have been performed (19,20) with mixed results, particularly among intermediate-risk patients. A propensity-adjusted comparison of intermediate-risk TAVR patients from the SAPIEN 3 registry cohort (n = 963) versus SAVR patients from the PARTNER 2A trial (n = 747) demonstrated lower 1-year risks for mortality (7.4% vs. 13.0%) and stroke (4.6% vs. 8.2%) with TAVR using the third-generation Sapien 3 balloon-expandable

FIGURE 2 Time-to-Event Curves for Death and Stroke



The rate of rehospitalization for stroke are similar to 1 year among patients treated with transcatheter aortic valve replacement (TAVR) versus surgical aortic valve replacement (SAVR).

FIGURE 3 Days Alive and Out of the Hospital to 1 Year



For DAOH, the proportion of days alive and out of an acute care hospital in the first year following initial hospital discharge was calculated for each patient and displayed by treatment group. For ease of interpretation, proportion of DAOH is displayed across a 12-month interval. Patients with 0 DAOH died prior to discharge from the index hospitalization. Not all patients had a full year of follow-up post-TAVR. For those without a full year of follow-up, statistical methods adjusted for differential patient follow-up. Abbreviations as in Figures 1 and 2.

prosthesis versus SAVR (21). By contrast, in a propensity-matched analysis of 5,997 intermediate-risk patients undergoing TAVR versus SAVR as part of GARY (German Aortic Valve Registry), patients treated with TAVR had a substantially higher 1-year risk for mortality versus SAVR (15.5% vs. 10.9%; $p = 0.002$) (11).

The results of our analyses are largely consistent with those of the pivotal randomized clinical trials. In a broad cohort of both intermediate- and high-risk older patients, the 1-year incidences of mortality and stroke are similar to those previously published for both intermediate- and high-risk patients. Consistent with the PARTNER and PARTNER 2A trial results, we observed a similar comparative risk for mortality for TAVR and SAVR among both intermediate- and high-risk patients. In contrast to results from GARY, we did not observe an increased risk for mortality among intermediate-risk patients. In our study, we used detailed phenotypic information from both the STS National Database and the TVT Registry to both exclude patients who would not have been considered for both procedures and closely match the remaining eligible patients; many of these variables were not available in other observational datasets. The availability of these additional data elements may account for differences between our study outcomes and both the GARY and SAPIEN 3 results, allowing a more accurate approximation of the existing randomized trial results.

Notably, the rates of stroke reported to 1 year in this cohort are roughly 50% lower than those reported to 1 year in each of the reported clinical trials, including the intermediate-risk PARTNER 2A clinical trial. The reduced strokes rates observed here are consistent with those reported by others, including the nonrandomized SAPIEN 3 intermediate-risk analysis (21); the reason for this finding is unclear. This observation may represent an underascertainment or underreporting of stroke events, because dedicated post-operative neurology evaluations that were available in pivotal trials were likely to reveal a higher incidence of both clinically significant and insignificant strokes. Similar to results from the PARTNER trial, we observed a nonsignificant but progressive increase in the 1-year risk for stroke among TAVR patients in our cohort. The cause (and clinical importance) of this observation is unknown. No such increase in stroke risk was observed in either the U.S. CoreValve High Risk trial or the PARTNER 2A trial. However, this finding warrants further investigation. To evaluate alternative strategies to address the excess risk for stroke following TAVR, both the ATLANTIS (Anti-Thrombotic Strategy After Trans-Aortic Valve Implantation

TABLE 2 Clinical Outcomes to 1 Yr, Stratified by Surgical Risk (STS PROM)

Outcome	Overall (n = 9,464)			STS PROM Score ≥3% and <5% (n = 3,803)		
	SAVR (n = 4,732)	TAVR (n = 4,732)	HR (95% CI)	SAVR (n = 1,850)	TAVR (n = 1,953)	HR (95% CI)
Death	17.9	17.3	0.93 (0.83–1.04)	11.2	12.6	1.06 (0.86–1.31)
Stroke	3.3	4.2	1.18 (0.95–1.47)	3.3	3.8	1.06 (0.73–1.54)
Discharge home	41.2	69.9	3.19 (2.84–3.58)†	49.5	77.5	3.33 (2.83–3.92)†
% DAOH, median	100	100	1.00 (0.98–1.02)*	100	100	0.99 (0.97–1.01)*

TABLE 2 Continued

Outcome	STS PROM Score ≥5% and <8% (n = 3,141)			STS PROM Score ≥8% (n = 2,520)			p for Interaction
	SAVR (n = 1,545)	TAVR (n = 1,596)	HR (95% CI)	SAVR (n = 1,337)	TAVR (n = 1,183)	HR (95% CI)	
Death	16.2	15.3	0.92 (0.75–1.13)	28.7	27.4	0.91 (0.78–1.08)	0.50
Stroke	3.5	4.5	1.22 (0.83–1.79)	3.1	4.4	1.33 (0.87–2.03)	0.73
Discharge home	41.9	70.4	2.37 (2.00–2.80)†	29.0	56.8	1.32 (1.13–1.55)†	0.89
% DAOH, median	98.9	99.3	0.99 (0.95–1.04)*	95.6	96.9	0.93 (0.83–1.05)*	0.598

*A rate ratio was calculated to compare treatment effects for the proportion (%) of DAOH to 1 yr. †An odds ratio was calculated to compare treatment effects for the probability of discharge home.
CI = confidence interval; DAOH = days alive and out of the hospital; HR = hazard ratio (TAVR vs. SAVR); other abbreviations as in Table 1.

for Aortic Stenosis) and the GALILEO (Global Study Comparing a Rivaroxaban-Based Antithrombotic Strategy to an Antiplatelet-Based Strategy after Transcatheter Aortic Valve Replacement to Optimize Clinical Outcomes) trials are randomizing patients post-TAVR to various post-TAVR anticoagulation strategies (22). Finally, we observed a significantly lower risk for stroke at 1 month among patients with home oxygen. We hypothesize that this finding is related to an increase in underlying aortic calcification (from tobacco exposure) among patients with home oxygen use. In these patients, avoiding direct manipulation of the ascending aorta with TAVR (vs. SAVR) may lead to a lower stroke incidence.

Importantly, we did not see significant differences in treatment effects across most patient subgroups, including within the intermediate- and high-risk strata. These results are generally consistent with available randomized data (23); however, our analysis does suggest that patients with significant lung disease and prior cardiac surgery may derive additional benefit from TAVR (vs. SAVR) for selected outcomes.

STUDY LIMITATIONS. First, this was not a randomized treatment comparison, and bias (particularly through imbalances in patient frailty) may have influenced our results.

Second, we found that nearly one-half of the patients in the United States had a very high likelihood of receiving treatment with either SAVR (31.5%) or TAVR (14.8%), making it unlikely that the alternative treatment was considered a reasonable option in nearly one-half of patients. Consequently, the results reported here are intended to evaluate treatment effects among those generally considered eligible for either procedure, excluding patients with extremely high or low propensities for TAVR.

Third, although results of our subgroup analyses have demonstrated general parity of treatment effects across patient subgroups, it is likely that certain comorbidity combinations may favor 1 treatment over another. The importance of developing decision assistance tools to help optimize individualized patient care cannot be overstated.

Fourth, because of differences in the mechanisms of Medicare linkage from the STS National Database and TVT Registry, there was an offset in the interval of inclusion for SAVR (July 1, 2011, to December 31, 2013) and TAVR (January 1, 2014, to September 30, 2015). Consequently, the results reported here may underestimate the safety and effectiveness of SAVR if surgical outcomes significantly improved during the offset interval.

Fifth, the outcomes presented here were selected from a list of available outcomes by a broad stakeholder panel that included patients and caregivers; however, there was general agreement that quality of life is an important metric for consideration when choosing between these 2 procedures. Quality-of-life data, physical functioning, and New York Heart Association functional class at follow-up were not available for SAVR patients and therefore could not be presented in our study. Likewise, several important surrogate outcomes were not available, such as degree of aortic valve

insufficiency and left ventricular remodeling. Also, expectations regarding long-term valve durability are key to treatment decisions, especially among younger patients and those at lower pre-operative surgical risk. An evaluation of the need for valve reintervention will be important as this cohort matures over time.

Sixth, cause of death was thought to be an important consideration that could not be addressed in our study because of a lack of necessary data.

Finally, it is important to recognize that the treatment of aortic valve disease is a rapidly developing field, with frequent modifications in device technology for both minimally invasive SAVR and TAVR. The data reported here are the most contemporary available in the United States and reflect outcomes of patients treated following the interval of early adoption of TAVR technology in the United States; however, recent TAVR device modifications have lowered device delivery profiles, improved prosthesis-annular apposition, and improved device repositioning capabilities. These modifications have lowered the incidence of procedural complications, including periprocedural stroke, acute vascular complications, device malposition, and perivalvular aortic insufficiency. As TAVR and SAVR devices continue to evolve, the relative risks and benefits of these 2 procedures may change. Diligent monitoring of outcomes will continue to help direct future device innovation in this field.

CONCLUSIONS

We used propensity score methods to compare 1-year outcomes of TAVR versus SAVR in a large, real-world cohort of older U.S. patients with aortic valve stenosis who were at intermediate or high surgical risk. Importantly, our results confirm and extend the observations of existing randomized studies in this field. Compared with SAVR, TAVR patients experienced a lower incidence of in-hospital mortality and were more often discharged directly to home. At 1-year follow-up, death, stroke, and DAOH were similar for the 2 treatments in the overall cohort and across most patient subgroups, including those within the spectrum of intermediate to high surgical risk.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Among unselected patients at intermediate or high surgical risk, TAVR and SAVR were associated with similar rates of stroke, DAOH, and death at 1 year, but those undergoing TAVR were more often discharged home, reflecting easier post-operative recovery.

TRANSLATIONAL OUTLOOK: Continued evolution of TAVR and SAVR technologies may change the relative risks and benefits of these procedures and influence clinical decision making.

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KEY WORDS outcomes, safety and effectiveness, surgical aortic valve replacement, transcatheter aortic valve replacement

APPENDIX For a supplemental Methods section as well as supplemental figures and tables, please see the online version of this article.