Original Investigation

Clinical Outcomes at 1 Year Following Transcatheter Aortic Valve Replacement

David R. Holmes Jr, MD; J. Matthew Brennan, MD, MPH; John S. Rumsfeld, MD, PhD; David Dai, PhD; Sean M. O'Brien, PhD; Sreekanth Vemulapalli, MD; Fred H. Edwards, MD; John Carroll, MD; David Shahian, MD; Fred Grover, MD; E. Murat Tuzcu, MD; Eric D. Peterson, MD, MPH; Ralph G. Brindis, MD, MPH; Michael J. Mack, MD; for the STS/ACC TVT Registry

IMPORTANCE Introducing new medical devices into routine practice raises concerns because patients and outcomes may differ from those in randomized trials.

OBJECTIVE To update the previous report of 30-day outcomes and present 1-year outcomes following transcatheter aortic valve replacement (TAVR) in the United States.

DESIGN, SETTING, AND PARTICIPANTS Data from the Society of Thoracic Surgeons/American College of Cardiology (STS/ACC) Transcatheter Valve Therapies Registry were linked with patient-specific Centers for Medicare & Medicaid Services (CMS) administrative claims data. At 299 US hospitals, 12 182 patients linked with CMS data underwent TAVR procedures performed from November 2011 through June 30, 2013, and the end of the follow-up period was June 30, 2014.

EXPOSURE Transcatheter aortic valve replacement.

MAIN OUTCOMES AND MEASURES One-year outcomes including mortality, stroke, and rehospitalization were evaluated using multivariate modeling.

RESULTS The median age of patients was 84 years and 52% were women, with a median STS Predicted Risk of Operative Mortality (STS PROM) score of 7.1%. Following the TAVR procedure, 59.8% were discharged to home and the 30-day mortality was 7.0% (95% CI, 6.5%-7.4%) (n = 847 deaths). In the first year after TAVR, patients were alive and out of the hospital for a median of 353 days (interquartile range, 312-359 days); 24.4% (n = 2074) of survivors were rehospitalized once and 12.5% (n = 1525) were rehospitalized twice. By 1 year, the overall mortality rate was 23.7% (95% CI, 22.8%-24.5%) (n = 2450 deaths), the stroke rate was 4.1% (95% CI, 3.7%-4.5%) (n = 455 stroke events), and the rate of the composite outcome of mortality and stroke was 26.0% (25.1%-26.8%) (n = 2719 events). Characteristics significantly associated with 1-year mortality included advanced age (hazard ratio [HR] for ≥95 vs <75 years, 1.61 [95% CI, 1.24-2.09]; HR for 85-94 years vs <75 years, 1.35 [95% CI, 1.18-1.55]; and HR for 75-84 years vs <75 years, 1.23 [95% CI, 1.08-1.41]), male sex (HR, 1.21; 95% CI, 1.12-1.31), end-stage renal disease (HR, 1.66; 95% CI, 1.41-1.95), severe chronic obstructive pulmonary disease (HR, 1.39; 95% CI, 1.25-1.55), nontransfemoral access (HR, 1.37; 95% CI, 1.27-1.48), STS PROM score greater than 15% vs less than 8% (HR, 1.82; 95% CI, 1.60-2.06), and preoperative atrial fibrillation/flutter (HR, 1.37; 95% CI, 1.27-1.48). Compared with men, women had a higher risk of stroke (HR, 1.40; 95% CI, 1.15-1.71).

CONCLUSIONS AND RELEVANCE Among patients undergoing TAVR in US clinical practice, at 1-year follow-up, overall mortality was 23.7%, the stroke rate was 4.1%, and the rate of the composite outcome of death and stroke was 26.0%. These findings should be helpful in discussions with patients undergoing TAVR.

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Author Affiliations: Mayo Clinic, Rochester, Minnesota (Holmes); Duke Clinical Research Institute, Durham, North Carolina (Brennan, Dai, O'Brien, Vemulapalli); Denver VA Medical Center, Denver, Colorado (Rumsfeld); University of Florida, Jacksonville (Edwards); University of Colorado, Denver (Carroll, Grover); Massachusetts General Hospital, Boston (Shahian); Cleveland Clinic, Cleveland, Ohio (Tuzcu); Duke University Medical Center, Durham, North Carolina (Peterson); University of California, San Francisco (Brindis); Baylor Scott & White Health, Plano, Texas (Mack).

Group Information: A current list of STS/ACC TVT Registry participating hospitals can be found at https://www.ncdr.com/TVT/Private/Resources/ParticipantDirectory.aspx.

Corresponding Author: David R. Holmes Jr, MD, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (holmes.david@mayo.edu).

Following US Food and Drug Administration approval in 2011, transcatheter aortic valve replacement (TAVR) has been used with increasing frequency for the treatment of severe aortic stenosis in patients who have high or prohibitive risks with conventional surgical AVR.[1-12] Compared with the pivotal trial experience, patients treated after regulatory approval in the United States include some patients previously excluded from the pivotal trials, such as those with untreated clinically significant coronary artery disease requiring revascularization or hemodynamic instability requiring inotropic support or ileofemoral vessel characteristics that precluded safe placement of commercial devices then available for implantation. Additionally, these patients were often treated at sites without trial experience, with a broader group of less experienced operators, and with less rigidly standardized treatment protocols.

AVR *aortic valve replacement*

COPD *chronic obstructive pulmonary disease*

LVEF *left ventricular ejection fraction*

STS PROM *Society of Thoracic Surgeons Predicted Risk of Mortality*

TAVR *transcatheter aortic valve replacement*

In a previous study following the initial postapproval commercial experience with this device among 7710 patients in the Society of Thoracic Surgeons/American College of Cardiology (STS/ACC) Transcatheter Valve Therapies (TVT) Registry who underwent TAVR from November 2011 to May 2013, the overall in-hospital mortality rate was 5.5% and the stroke rate was 2.0%, and among patients with available follow-up at 30 days (n = 3133), the overall mortality rate was 7.6% and the stroke rate was 2.8%.[13] However, the longer-term outcomes for these patients remain unknown.

In this study, we extended the follow-up for this cohort of patients in the STS/ACC TVT Registry who underwent TAVR to evaluate 1-year outcomes linked with Centers for Medicare & Medicaid Services (CMS) administrative claims data to address the following questions: (1) What is the 1-year incidence of death and stroke among US patients undergoing TAVR? (2) What associations, if any, exist between baseline patient characteristics and 1-year clinical outcomes that could be used to guide clinical decision making for future candidates? and (3) What are the rate of rehospitalization and the average time alive and out of the hospital during the first 6 months following TAVR?

Methods

Design, Setting, and Participants

TVT Registry

The TVT Registry[3] is a collaborative clinical registry program developed by the STS and the ACC in response to the CMS National Coverage Determination (May 2012) requirement for national registry participation of all US TAVR centers.[3] Participating centers use standardized definitions[3,9,14] to collect clinical information on consecutive TAVR cases including patient demographics, comorbidities, functional status, quality-of-life indexes, and procedural details and outcomes (eAppendixes 1 and 2 in the Supplement). Race and ethnicity data are captured by each hospital and based on US Census Bureau data standards. Data quality checks have been implemented at the National Cardiovascular Data Registry data warehouse and Duke Clinical Research Institute to optimize data completeness and accuracy.

The ACC and STS understand the importance of protecting human research participants and have signed a Federal-Wide Assurance with the Department of Health and Human Services that requires all human subjects research to be conducted in compliance with the Common Rule (45 CFR §46). The ACC and STS have designated Chesapeake Research Review Incorporated as its institutional review board of record. Each registry has submitted a protocol to the institutional review board, which governs all human subjects research conducted by the registry. The TVT Registry protocol on file has been granted a waiver of informed consent.

Study Cohort

TVT Registry clinical records for procedures performed from November 2011, through June 2013, were linked to Medicare administrative claims using direct patient identifiers (name and social security number) by the CMS (eFigure 1 in the Supplement). Claims filed through the end of June 2013 were included in the analysis set. Per the CMS National Coverage Determination, all patients had echocardiographic documentation of severe aortic stenosis and an assessment by 2 cardiothoracic surgeons who independently deemed the patients as at high or prohibitive surgical risk of mortality from AVR. Of the Medicare-linked TVT records, 3610 records were excluded from this study cohort because of patient nonparticipation in the Medicare Parts A and B fee-for-service program at the time of the index procedure or an inability to link the index admission to a Medicare inpatient claim. For calculation of both rehospitalization and number of days alive and out of the hospital in the first year after TAVR, procedures performed on or before June 30, 2013, were included, allowing for a minimum of 1 year of follow-up for all patients in this cohort.

Study Outcomes

Primary outcomes included death, stroke, and combined death and stroke at 30 days and 1 year and days alive and out of the hospital at 1 year. In-hospital outcomes were collected from the TVT Registry, and both stroke and reoperation outcomes were adjudicated by a board-certified cardiologist at the Duke Clinical Research Institute Analysis Center using Valve Academic Research Consortium definitions.[9,14] This process involved review of specific site queries and deidentified source records as needed. Following hospital discharge, death was identified using the Medicare Denominator file. Patient follow-up was considered to be censored at the end of the follow-up period (June 30, 2014).

Medicare in-hospital administrative claims files were used for detection of rehospitalization events during the study interval using the following *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes: for stroke, 433.x1, 434.x1, 997.02, 436, 437.1, 437.9, 430, 431, and 432.x; for heart failure, 398.x, 402.x1, 404.x1, 404.x3, and 428.x; and for aortic valve reintervention, 35.11, 35.21, 35.22,

35.01, 35.05, 35.06, and 35.09. For rehospitalization, follow-up was censored at the time of death, end of fee-for-service coverage, loss of Part A or B coverage, or end of the follow-up period, whichever occurred first. As an outcome of particular interest to patients, days alive and out of the hospital were calculated during the first 365 days after TAVR by counting the number of days alive during that period and subtracting the sum of the number of days of index hospitalization plus those of all hospital admissions following index hospital discharge. The days alive and out of the hospital are reported for a total of 1 year of eligible days after TAVR.

Statistical Analysis

Baseline patient characteristics were summarized as percentages or medians and interquartile ranges as appropriate and compared across subgroups using χ^2, Wilcoxon, or Kruskal-Wallis 2-sided tests. For analyses of mortality, including an exploratory analysis in a small group of potentially very high-risk patients, the Kaplan-Meier method was used for unadjusted event rates to 1 year overall and within subgroups based on the following patient preprocedural covariates: age, sex, renal function, left ventricular ejection fraction (LVEF), access site, chronic obstructive pulmonary disease (COPD), and the STS Predicted Risk of Operative Mortality (PROM) score. The STS PROM score has been validated for predicting mortality from surgical AVR; it uses an algorithm of 24 variables from a total of more than 50 risk factors.[15]

Differences in mortality risk across covariate subgroups were assessed using Cox proportional hazards models. For unadjusted analyses, we fit a separate univariate Cox model for each covariate and included a set of binary subgroup indicators for modeling subgroups. Patients with missing data for the covariate of interest were excluded. For adjusted analyses, all subgroup indicator variables were included as covariates in a single multivariate Cox model. For these analyses, missing data were imputed to the most common category. Multiple imputations were not used for this analysis because of the low rate of missing data and because multiple imputation has had negligible statistical effect on previous analyses of other STS and ACC registries.[16]

Unadjusted and adjusted hazard ratios (HRs) comparing mortality risks across subgroups were estimated along with 95% approximate confidence intervals and Wald-type *P* values. For all analyses, a 2-sided $P<.05$ was considered statistically significant, and all analyses were performed at the Duke Clinical Research Institute using SAS software, version 9.3 (SAS Institute Inc).

Days alive and out of the hospital were summarized by simple descriptive statistics and compared across subgroups using Wilcoxon or Kruskal-Wallis 2-sided tests. For analyses of stroke, heart failure, and aortic valve reintervention, analysis focused on estimating the cumulative incidence function (CIF), the cumulative probability of an end point occurring over time in a patient's lifetime. The CIF is the appropriate parameter for describing nonfatal events from a patient perspective in a setting of high competing mortality risk. Unlike standard time-to-event methods, which describe the probability of a nonfatal end point occurring in a hypothetical death-free environment, the CIF models the probability that an end point will actually occur, given that death may preclude an event from occurring. For each subgroup of interest, the CIF for stroke was estimated nonparametrically using the Fine and Gray method.[17-20]

Differences in unadjusted and adjusted stroke incidence across subgroups were assessed using the Fine and Gray proportional subdistributions hazards model.[17-20] Covariates for this model were identical to the mortality Cox model. Hazard ratios from this model describe the relative risk of experiencing a stroke in a setting in which stroke events may be precluded by early deaths in some patients. All analyses were performed using SAS version 9.3. The clinically selected variables to evaluate association with both death and stroke included age, sex, race, COPD, renal function, dialysis therapy, LVEF, procedural access site (transfemoral vs alternative access), and STS PROM score.

Results

Study Cohort

After including only the first TVT Registry admission for each patient, 12 182 TVT Registry records linked to CMS administrative claims data from 299 sites were identified and included in the final study cohort (eFigure 1 in the Supplement); 51.9% were women. These 12 182 patients were similar to the excluded patients in baseline characteristics and in-hospital mortality and stroke (eAppendixes 3 and 4 in the Supplement). The median age was 84 years (interquartile range, 79-88 years) and 258 patients (2.1%) were aged 95 years or older, 95.3% were white, 2.8% were black, and 1.8% were Hispanic or other single or combined nationality group (**Table 1**).

Baseline functional status was poor, with New York Heart Association class III/IV in 82.5%. Among the study cohort, the median STS PROM score was 7.1% (interquartile range, 4.8%-10.9%), including 30.8% of patients (n = 3748) with an 8% to 15% risk and 11.9% (n = 1444) with greater than 15% risk. The 5-m walk time considered to be a slow gait indicative of patient frailty was longer than 6 seconds and was found in 39.6% of patients. Comorbidities were common, including reduced LVEF (<45%) in 25.5%, prior stroke (12.2%), moderate or severe lung disease (27.8% overall, with 14.1% oxygen dependent), renal failure (15.9% overall, with 3.9% undergoing dialysis), peripheral vascular disease (32.4%), and atrial fibrillation (41.9%). The prevalence of prior open heart surgery was 34.0%; a calcified aorta was present in 6.8%, and surgeons described anatomical conditions that precluded safe sternal reentry for open cardiac procedures ("hostile chest") in 8.2%. A transfemoral approach for TAVR was used in the majority, but alternative modes of access were used in 43.6% of patients.

Procedural Outcomes

As shown in Table 1, in-hospital death occurred in 633 cases (5.2%), stroke in 231 (1.9%), and transient ischemic attack in 34 (0.3%). A "valve-related complication" occurred in 236

Table 1. Patient Characteristics

Characteristics	No. (%) of Study Cohort (N = 12 182)[a]
Age, y	
Median (IQR)	84 (79-88)
<75	1546 (12.7)
75-84	4652 (38.2)
85-94	5726 (47.0)
>95	258 (2.1)
Female	6316 (51.9)
Race	
White	11 615 (95.3)
Black	346 (2.8)
Asian	108 (0.9)
Other	113 (0.9)
STS PROM score, %	
Median (IQR)	7.1 (4.8-10.8)
<8	6988 (57.4)
8-15	3748 (30.8)
>15	1444 (11.9)
NYHA class III/IV heart failure	9879 (82.5)
Coronary artery disease	7504 (62.8)
Prior open heart surgery	4145 (34.0)
No. of prior cardiac surgeries	
0	8016 (67.9)
1	3247 (27.5)
≥2	548 (4.6)
Previous stroke	1489 (12.2)
Peripheral arterial disease	3935 (32.4)
Chronic obstructive pulmonary disease[b]	
None/mild	8694 (72.2)
Moderate	1709 (14.2)
Severe	1640 (13.6)
Oxygen-dependent lung disease	1704 (14.1)
Renal failure	
Dialysis dependent	474 (3.9)
Creatinine level ≥2.0 mg/dL without dialysis	798 (6.6)
Creatinine <2.0 mg/dL	10 861 (89.5)
5-m walk time >6 s	4775 (39.6)
Atrial fibrillation	5086 (41.9)
Permanent pacemaker/ICD	2394 (19.7)
Hostile chest[c]	993 (8.2)
Porcelain aorta	817 (6.8)
Left ventricular ejection fraction, %	
<30	836 (7.1)
30-45	2177 (18.4)
>45	8803 (74.5)
Pre-TAVR mitral insufficiency	
None/trivial/mild	6562 (63.4)
Moderate	3222 (31.1)
Severe	568 (5.5)
Access site	
Transfemoral	6807 (56.4)
Other	5256 (43.6)

(continued)

Table 1. Patient Characteristics (continued)

Characteristics	No. (%) of Study Cohort (N = 12 182)[a]
In-hospital events	
Death	633 (5.2)
Any stroke	231 (1.9)
Transient ischemic attack	34 (0.3)
Any valve complication	236 (1.9)
Conversion to open heart surgery	169 (1.4)
Discharge location	
Home	6907 (59.8)
Extended-care/transitional-care unit or rehabilitation facility	3733 (32.3)
Other acute care hospital	75 (0.6)
Nursing home	722 (6.3)
Hospice	64 (0.6)
Other	40 (0.3)

Abbreviations: ICD, implantable cardioverter-defibrillator; IQR, interquartile range; NYHA, New York Heart Association; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR, transcatheter aortic valve replacement.

[a] Data are expressed as No. (%) of patients unless otherwise indicated.

[b] Chronic obstructive pulmonary disease categories are defined as follows: none, no documented chronic lung disease; mild, forced expiratory volume in the first second (FEV_1) 60% to 75% of predicted and/or long-term inhaled or oral bronchodilator therapy; moderate, FEV_1 50% to 59% of predicted and/or long-term steroid therapy aimed at lung disease; severe, FEV_1 <50% predicted and/or room air Po_2 <60 mm Hg or room air Pco_2 >50 mm Hg.

[c] Hostile chest is a medical condition that precludes an open chest procedure and that is documented in the medical record.

(1.9%), prompting conversion to open heart surgery in 169 (1.4%). The majority of patients were discharged to home (n = 6907 [59.8%]), an extended-care/transitional-care unit or rehabilitation facility (n = 3733 [32.3%]), or a nursing facility (n = 722 [6.3%]), while a small minority were discharged to an acute care facility (n = 75 [0.6%]) or hospice (n = 64 [0.6%]).

Outcomes to 1 Year

At 30 days, 7.0% of patients had died, and stroke had occurred in 2.5%. Mortality increased at 6 months to 16.7% and was 23.7% at 1 year (**Table 2** and **Figure 1**A). The incidence of stroke was 4.1% at 1 year. The 1-year composite outcome of incidence of death or stroke was 26.0%.

Among the study population (n = 12 182), 2074 patients (24.4%) were rehospitalized only once within 1 year, 1525 (12.5%) were hospitalized twice, and 1415 (11.6%) had 3 or more hospitalizations. The specific cause of readmission during the first year using *ICD-9-CM* codes (Table 2) included heart failure in 14.3%, repeat aortic valve intervention in 1.4%, and a composite of stroke/heart failure or repeat aortic valve intervention in 18.6% (Figure 1B). The cumulative composite incidence of mortality and valve-related hospitalization is shown in Figure 1C. Among patients with a full 12 months of available follow-up data (n = 6314), the patients were alive and out of the hospital for a median of 353 days (interquartile range, 312-359 days). Of the characteristics examined, several were associated with less time alive and out of the hospital during this interval,

Table 2. Postprocedure Outcomes

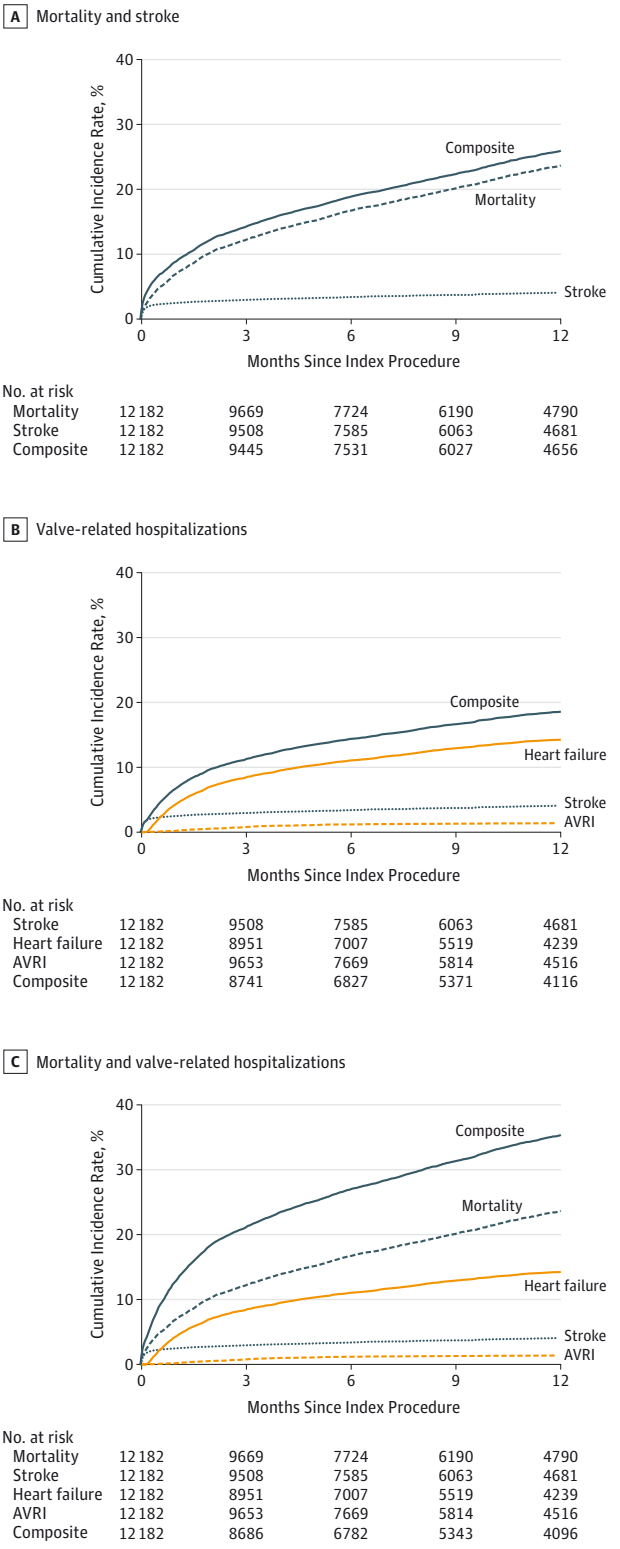
Events by Time From Index Procedure to Event	No. of Events	Rate, % (95% CI)
Mortality		
30 d	847	7.0 (6.5-7.4)
6 mo	1911	16.7 (16.1-17.4)
1 y	2450	23.7 (22.8-24.5)
Stroke		
30 d	298	2.5 (2.2-2.7)
6 mo	402	3.4 (3.1-3.7)
1 y	455	4.1 (3.7-4.5)
Heart failure		
30 d	525	4.3 (4.0-4.7)
6 mo	1272	11.1 (10.5-11.7)
1 y	1525	14.3 (13.6-15.0)
Aortic valve reintervention		
30 d	26	0.2 (0.1-0.3)
6 mo	134	1.2 (1.0-1.4)
1 y	150	1.4 (1.2-1.6)
Any-cause readmission		
30 d	2106	17.4 (16.7-18.1)
6 mo	4821	42.1 (41.2-43.0)
1 y	5689	53.2 (52.2-54.2)
Mortality or stroke		
30 d	1078	8.9 (8.4-9.4)
6 mo	2120	18.9 (18.2-19.6)
1 y	2719	26.0 (25.1-26.8)
Stroke, heart failure, or aortic valve reintervention		
30 d	818	6.7 (6.3-7.2)
6 mo	1664	14.4 (13.8-15.1)
1 y	1993	18.6 (17.8-19.3)
Mortality, stroke, heart failure, or aortic valve reintervention		
30 d	1563	12.9 (12.3-13.5)
6 mo	3123	27.1 (26.3-27.9)
1 y	3775	35.4 (34.4-36.3)

including female sex, moderate or severe lung disease, renal failure, low LVEF, increased STS PROM score, and a need for alternative TAVR access (**Table 3**).

Baseline Factors Associated With Increased 1-Year Mortality and Stroke

Several patient characteristics were associated with post-TAVR 1-year mortality. These included advancing age, male sex, severe lung disease, renal failure (dialysis dependent and non-dialysis dependent), nontransfemoral access, and increasing baseline STS PROM score (**Figure 2** and eFigures 2-9 in the Supplement). There was a graded increase in mortality as age increased. The youngest patients (<75 years) had a mortality of 18.9% (95% CI, 16.8%-21.2%) compared with those aged 95 years or older, in whom mortality was 31.4% (95% CI, 25.3%-37.7%) (≥95 vs <75 years: HR, 1.61; 95% CI, 1.24-2.09). Men had significantly greater mortality than women (25.8% [95% CI, 24.6%-27.1%] vs 21.7% [95% CI,

Figure 1. Cumulative Incidence of Outcomes Over Time



AVRI indicates aortic valve reintervention. A, Composite is the combination of mortality and stroke outcomes. B, Composite is the combination of stroke, heart failure, and AVRI outcomes. C, Composite is the combination of mortality, stroke, heart failure, and AVRI outcomes.

Table 3. Days Alive and Out of the Hospital at 12 Months

Characteristics	No. of Patients	No. of Days Alive and Out of the Hospital		*P* Value
		Mean	Median (IQR)	
Overall	6314	290.99	353 (312-359)	
Age, y				
<75	772	298.58	353 (312-360)	.18
75-84	2386	292.94	353 (314-360)	
85-94	3009	288.00	353 (312-359)	
>95	147	280.59	353 (274-359)	
Sex				
Male	3126	288.78	354 (298-360)	.002
Female	3178	293.00	352 (318-359)	
Missing data	10	342.10	356 (329-360)	
Chronic obstructive pulmonary disease[a]				
None/mild	4572	297.13	354 (327-360)	<.001
Moderate	886	280.58	351 (273-359)	
Severe	856	268.97	347 (206-358)	
Renal function				
Dialysis	261	237.69	325 (87-355)	<.001
Creatinine ≥2 mg/dL without dialysis	440	256.08	345 (118-357)	
Creatinine <2 mg/dL without dialysis	5588	296.15	354 (323-360)	
Missing data	25	309.12	353 (333-361)	
Left ventricular ejection fraction, %				
<30	438	270.21	349 (183-359)	<.001
30-45	1170	284.30	352 (291-359)	
>45	4526	294.59	353 (321-359)	
Missing data	180	294.58	352 (313-359)	
Access site				
Transfemoral	3999	300.31	355 (326-360)	<.001
Other	2315	274.90	349 (256-358)	
STS PROM score, %				
<8	3593	306.98	356 (335-360)	<.001
8-15	1955	280.08	350 (274-359)	
>15	766	243.81	339 (84-356)	

Abbreviations: IQR, interquartile range; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality.

[a] Chronic obstructive pulmonary disease categories are defined as follows: none, no documented chronic lung disease; mild, forced expiratory volume in the first second (FEV_1) 60% to 75% of predicted and/or long-term inhaled or oral bronchodilator therapy; moderate, FEV_1 50% to 59% of predicted and/or long-term steroid therapy aimed at lung disease; severe, FEV_1 <50% predicted and/or room air Po_2 <60 mm Hg or room air Pco_2 >50 mm Hg.

20.6%-22.8%], respectively; HR, 1.21; 95% CI, 1.12-1.31). Patients with a history of atrial fibrillation or flutter also had increased mortality (HR, 1.37; 95% CI, 1.27-1.48). As renal function worsened, so did mortality; however, the strongest association was observed among patients receiving dialysis. Patients receiving dialysis compared with those with a baseline creatinine level less than 2.0 mg/dL had a mortality of 41.0% (95% CI, 35.9%-46.0%) vs 22.3% (95% CI, 21.4%-23.2%) (HR, 1.66; 95% CI 1.41-1.95). Another difference in outcomes was observed among the 11.9% of patients with an STS PROM score higher than 15%, in whom 1-year mortality was 39.5% (95% CI, 36.7%-42.2%) compared with those with STS PROM scores of less than 8%, in whom mortality was 18.6% (95% CI, 17.5%-19.6%) (HR, 1.82; 95% CI, 1.60-2.06).

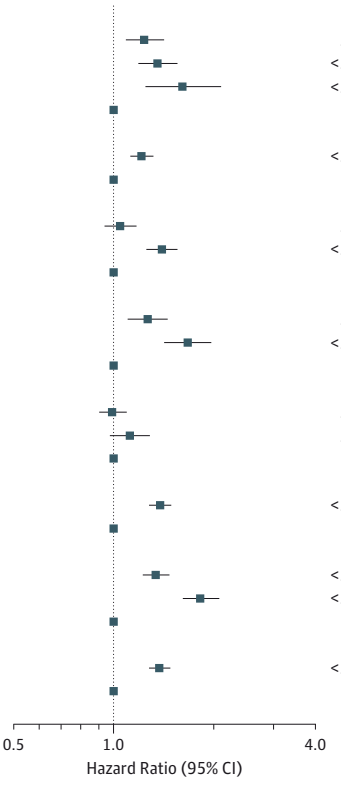
An exploratory analysis was performed in a small, potentially very high-risk group of patients with severe composite comorbidities including combinations of age, dialysis, and increased STS PROM score. In this analysis, of 77 patients (0.63% of 12 182) who were aged 85 to 94 years, undergoing dialysis, and had an STS PROM score higher than 15%, in-hospital mortality was 10.39% (n = 8) and 1-year mortality was 53.51% (n = 35). In a somewhat larger group of 198 patients aged 75 years or older, undergoing dialysis and with an STS PROM score higher than 15% (1.63% of the total of 12 182), in-hospital mortality was 11.62% (n = 23) and 1-year mortality was 48.75% (n = 84).

By 30 days and 1 year after TAVR, stroke occurred in 2.5% (95% CI, 2.2%-2.7%) and 4.1% (95% CI, 3.7%-4.5%) of patients, respectively. Several preoperative covariates were not associated with increased 1-year stroke rates, including increasing age, COPD, LVEF, access site, STS PROM score, and atrial fibrillation/flutter. Only 1 baseline variable, female sex, was associated with increased stroke (**Figure 3**A). Among women, stroke was reported in 4.8% (95% CI, 4.3%-5.4%) at 1 year vs 3.3% (95% CI, 2.8%-3.8%) in men (HR, 1.40; 95% CI, 1.15-1.71).

Multiple variables were associated with subsequent heart failure (Figure 3B), mainly preprocedural baseline comorbidities, including more severe COPD, LVEF, STS PROM score, and preoperative atrial flutter. Neither age nor sex had a significant association.

Figure 2. Multivariate Risk-Adjusted Outcome of Mortality

	Mortality		Hazard Ratio (95% CI)	P Value
	No./Total	% (95% CI)		
Age, y				
75-84	934/4652	23.8 (22.4-25.2)	1.23 (1.08-1.41)	.002
85-94	1203/5726	24.5 (23.2-25.7)	1.35 (1.18-1.55)	<.001
≥95	72/258	31.4 (25.3-37.7)	1.61 (1.24-2.09)	<.001
<75	241/1546	18.9 (16.8-21.2)	1 [Reference]	
Sex				
Male	1273/5848	25.8 (24.6-27.1)	1.21 (1.12-1.31)	<.001
Female	1176/6316	21.7 (20.6-22.8)	1 [Reference]	
COPD				
Moderate	376/1709	25.9 (23.6-28.3)	1.04 (0.94-1.17)	.43
Severe	457/1640	33.1 (30.5-35.7)	1.39 (1.25-1.55)	<.001
None/mild	1597/8694	21.6 (20.6-22.5)	1 [Reference]	
Renal function				
Creatinine ≥2 mg/dL without dialysis	221/798	31.5 (28.0-35.1)	1.26 (1.10-1.44)	.001
Dialysis	163/474	41.0 (35.9-46.0)	1.66 (1.41-1.95)	<.001
Creatinine <2 mg/dL without dialysis	2056/10861	22.3 (21.4-23.2)	1 [Reference]	
LVEF, %				
30-45	476/2177	25.7 (23.7-27.8)	0.99 (0.90-1.09)	.83
<30	215/836	30.4 (26.9-34.0)	1.11 (0.97-1.28)	.12
>45	1689/8803	22.6 (21.6-23.6)	1 [Reference]	
Access site				
Other	1200/5256	26.6 (25.2-27.9)	1.37 (1.27-1.48)	<.001
Transfemoral	1211/6807	21.2 (20.1-22.3)	1 [Reference]	
STS PROM score, %				
8-15	868/3748	27.1 (25.5-28.7)	1.33 (1.21-1.46)	<.001
>15	503/1444	39.5 (36.7-42.2)	1.82 (1.60-2.06)	<.001
<8	1078/6988	18.6 (17.5-19.6)	1 [Reference]	
Preoperative atrial fibrillation				
Yes	1252/5086	29.0 (27.6-30.4)	1.37 (1.27-1.48)	<.001
No	1193/7058	19.9 (18.9-21.0)	1 [Reference]	



COPD indicates chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality.

Discussion

This study merged data from the STS/ACC TVT Registry with CMS administrative claims data using direct patient identifiers to determine 1-year outcomes in 12 182 patients from 299 sites in the TVT Registry. The major findings were that (1) after approval of the device and widespread commercialization, patient outcomes in the broader community included 1-year rates of 23.7% for mortality, 4.1% for stroke, and 26.0% for the composite outcome of death and stroke; (2) at 12 months of follow-up, 46.8% of patients who remained alive had not been rehospitalized and 24.4% had required only 1 additional hospitalization; (3) readmission for a composite of stroke, heart failure, or repeat aortic valve intervention occurred in 18.6%; (4) specific baseline characteristics were found to be independently associated with 1-year mortality, including male sex, severe COPD, end-stage renal disease requiring dialysis, increased STS PROM score, advancing age, and history of atrial fibrillation/flutter; in addition, nontransfemoral access was associated with increased mortality; and (5) in contrast to factors associated with increased 1-year mortality, only female sex was associated with increased stroke.

Although 3 randomized trials and multiple single-center and multicenter registry studies have been published,[4,6,10,11,21-26] the profile and longer-term outcomes of US TAVR cases in routine clinical practice remains limited.[13] The STS/ACC TVT Registry was developed in response to a CMS mandate to capture all patients in the United States undergoing commercial TAVR procedures to have an accurate assessment of enrollment in and outcomes of this approach in the broadest possible population.[3]

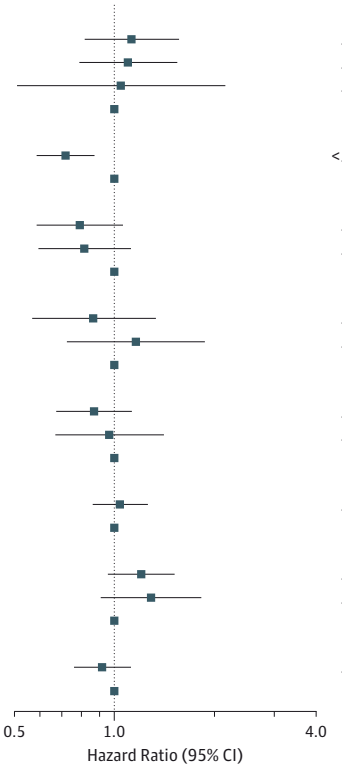
In the current study of 12 182 patients, the patients treated were elderly and had multiple comorbidities, similar to prior TAVR studies. An important consideration in this cohort is the median STS PROM score of 7.1%, with STS PROM scores higher than 15% in 11.9% of patients and between 8% and 15% in 30.8% of patients. The median STS PROM score in the current study is lower than in the PARTNER A[11] and B trials,[10] in which the mean STS PROM scores were 11.8% (SD, 3.3%) and 11.2% (SD, 5.8%), respectively. It is, however, similar to the mean STS PROM score observed in the recent randomized CoreValve study (7.3% [SD, 3.0%]).[4] Whether the lower STS PROM score in the TVT Registry represents a broadening in selection criteria to include lower-risk patients or whether that specific score may actually underestimate surgical risk as determined by experienced cardiovascular surgeons is unknown. Although several risk prediction scores have been developed, the results of cross comparisons of these have been quite variable.[27-31]

The initial in-hospital and 30-day outcome data from the TVT Registry have now been published and are reported to be within the range of multiple other published experiences.[13] Similarly,

Figure 3. Multivariate Risk-Adjusted Outcomes of Stroke and Heart Failure

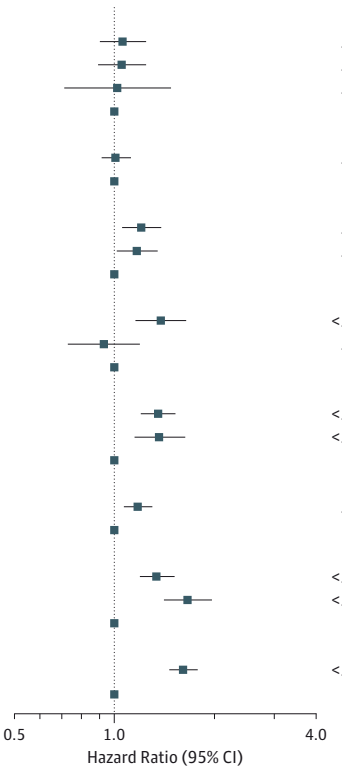
A Stroke

	Stroke		Hazard Ratio (95% CI)	*P* Value
	No./Total	% (95% CI)		
Age, y				
75-84	171/4652	4.1 (3.5-4.8)	1.12 (0.81-1.56)	.49
85-94	224/5726	4.2 (3.7-4.8)	1.09 (0.78-1.53)	.60
≥95	14/258	5.8 (3.3-9.3)	1.04 (0.51-2.14)	.91
<75	46/1546	3.3 (2.4-4.3)	1 [Reference]	
Sex				
Male	175/5848	3.3 (2.8-3.8)	0.71 (0.58-0.87)	<.001
Female	280/6316	4.8 (4.3-5.4)	1 [Reference]	
COPD				
Moderate	56/1709	3.5 (2.7-4.5)	0.79 (0.58-1.06)	.11
Severe	50/1640	3.2 (2.4-4.2)	0.81 (0.59-1.12)	.20
None/mild	344/8694	4.4 (3.9-4.8)	1 [Reference]	
Renal function				
Creatinine ≥2 mg/dL without dialysis	28/798	3.9 (2.7-5.5)	0.86 (0.56-1.32)	.50
Dialysis	19/474	4.4 (2.7-6.6)	1.16 (0.72-1.86)	.55
Creatinine <2 mg/dL without dialysis	407/10861	4.1 (3.7-4.5)	1 [Reference]	
LVEF, %				
30-45	69/2177	3.5 (2.7-4.4)	0.87 (0.67-1.12)	.28
<30	31/836	4.2 (2.9-5.8)	0.96 (0.66-1.40)	.84
>45	342/8803	4.2 (3.8-4.7)	1 [Reference]	
Access site				
Other	201/5256	4.1 (3.6-4.7)	1.04 (0.86-1.26)	.69
Transfemoral	252/6807	4.1 (3.6-4.6)	1 [Reference]	
STS PROM score, %				
8-15	157/3748	4.5 (3.9-5.3)	1.20 (0.95-1.51)	.12
>15	59/1444	4.3 (3.3-5.5)	1.29 (0.91-1.82)	.16
<8	239/6988	3.8 (3.3-4.3)	1 [Reference]	
Preoperative atrial fibrillation				
Yes	186/5086	4.0 (3.4-4.6)	0.92 (0.76-1.12)	.41
No	267/7058	4.2 (3.7-4.7)	1 [Reference]	



B Heart failure

	Heart Failure		Hazard Ratio (95% CI)	*P* Value
	No./Total	% (95% CI)		
Age, y				
75-84	586/4652	14.2 (13.2-15.3)	1.06 (0.90-1.24)	.50
85-94	729/5726	14.6 (13.6-15.6)	1.05 (0.89-1.24)	.56
≥95	35/258	14.6 (10.4-19.4)	1.02 (0.70-1.48)	.92
<75	175/1546	13.2 (11.4-15.2)	1 [Reference]	
Sex				
Male	753/5848	14.6 (13.6-15.6)	1.01 (0.91-1.12)	.88
Female	769/6316	14.0 (13.0-14.9)	1 [Reference]	
COPD				
Moderate	272/1709	18.0 (16.1-20.1)	1.20 (1.05-1.38)	.007
Severe	244/1640	17.0 (15.1-19.0)	1.16 (1.01-1.34)	.03
None/mild	995/8694	13.1 (12.3-13.8)	1 [Reference]	
Renal function				
Creatinine ≥2 mg/dL without dialysis	153/798	21.5 (18.5-24.6)	1.37 (1.15-1.63)	<.001
Dialysis	70/474	17.2 (13.6-21.1)	0.93 (0.72-1.19)	.55
Creatinine <2 mg/dL without dialysis	1296/10861	13.6 (12.9-14.3)	1 [Reference]	
LVEF, %				
30-45	351/2177	18.3 (16.6-20.1)	1.35 (1.20-1.52)	<.001
<30	145/836	19.8 (16.9-22.8)	1.36 (1.14-1.62)	<.001
>45	986/8803	12.8 (12.1-13.6)	1 [Reference]	
Access site				
Other	744/5256	16.1 (15.0-17.2)	1.17 (1.07-1.29)	.001
Transfemoral	770/6807	12.9 (12.1-13.8)	1 [Reference]	
STS PROM score, %				
8-15	561/3748	17.0 (15.7-18.4)	1.34 (1.19-1.51)	<.001
>15	287/1444	22.2 (19.9-24.6)	1.65 (1.40-1.95)	<.001
<8	676/6988	11.1 (10.3-12.0)	1 [Reference]	
Preoperative atrial fibrillation				
Yes	834/5086	18.7 (17.5-19.9)	1.60 (1.45-1.77)	<.001
No	687/7058	11.1 (10.3-11.9)	1 [Reference]	



COPD indicates chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality.

the rate of 1-year mortality reported within the TVT Registry is similar to that in other comprehensive reports.[21,22,32-34] Although this study includes only patients considered to have high risks with AVR, the majority of this mortality does not represent periprocedural complications, as 30-day mortality was only 7.0%. As such, this makes it imperative to focus on better prediction of the overall risks and benefits of the procedure, particularly given the existing comorbidities of the group of patients being considered for TAVR.

It may be possible to identify patients who may not benefit from this procedure and who should be counseled accordingly. For instance, in this study, small, very high-risk subsets of patients such as those aged 85 to 94 years, undergoing dialysis, and having an STS PROM score higher than 15% can be identified. In this small group (n=77 patients), 1-year mortality of 53.51% was documented. This must be taken into consideration in patient selection criteria and in counseling patients and their families. However, even though mortality at 1 year is high in this group, quality of life and the potential to decrease rehospitalizations for congestive heart failure are important additional issues to be considered. The low event numbers in this exploratory analysis mandate that caution should be used in applying these data to decisions regarding patient selection.

This database of the large majority of patients being treated in the United States during this time using a commercially available device identified different risk factors associated with death, stroke, and time alive and out of the hospital. The factors associated with 1-year mortality included specifically end-stage renal disease requiring dialysis, severe COPD, increasing age, male sex, and 1 procedural factor—alternative access, which may be a surrogate for more advanced disease such as peripheral arterial disease or the inability to tolerate a more invasive procedure.

In contrast, when the same risk factors were evaluated for the risk of stroke at 1 year, only female sex was statistically significant. Whether this relates to other unmeasured comorbidities in women, such as the presence and distribution of ascending aortic atheroma or the use of large delivery sheaths, is unknown but may be important for patient and family counseling. The increased risk of mortality but lower risk of stroke among men vs the benefit of improved relative survival at the risk of increased stroke in women must be taken into consideration and further studied.

An important consideration for these elderly patients with severe comorbidities is the need for repeat hospitalizations, which are not only very costly but also are indicative of an unacceptable quality-of-life outcome. Factors associated with reduced time alive and out of the hospital included mainly baseline comorbidities: female sex, moderate or severe lung disease, renal failure, increased STS PROM score, and the need for nontransfemoral access.

This analysis that links both clinical and administrative data sets has several important limitations. First, at present, STS PROM scores are calculated on-site using the STS scoring system. The data quality checks were limited to submitted data. These data did not include post-TAVR paravalvular leak or mitral regurgitation, which require core laboratory assessment and are beyond the scope of this registry. Second, there are no data on center/physician outcome nor specific data in the administrative database on cause of death, only on cause of rehospitalization, which from the medical care resource utilization perspective is of great importance. Third, there are also no data on a comparable group of patients who received surgical AVR. Only Medicare fee-for-service patients were included, although current criteria were used that likely capture the majority of patients being considered for TAVR. Fourth, only commercially approved devices were evaluated. As the number of newer investigational devices increases, data on the denominator of all US TAVR patients will not be available, although most newer devices will not have 1-year follow-up data and will not be used in a broad group of centers as seen in this experience. Fifth, administrative claims data have advantages and disadvantages, the latter of which relate to the sensitivity and specificity of events that may be different than the careful adjudication required in US Food and Drug Administration trials in highly selected centers. However, administrative claims data may better reflect TAVR use and outcomes in clinical practice and may be more useful for comparative effectiveness research because they reflect the presence of an event either during follow-up or necessitating a subsequent hospitalization. Finally, some unidentified but potentially prominent characteristics associated with end points dealing with frailty may not have been recognized or fully evaluated.

Conclusions

Patients undergoing TAVR in US clinical practice had a 1-year overall mortality of 23.7%, a stroke rate of 4.1%, and a rate of the composite outcome of death and stroke of 26.0%. These findings should be helpful in discussions with patients undergoing TAVR.

ARTICLE INFORMATION

Author Contributions: Dr Holmes had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy for the data analysis.
Study concept and design: Holmes, Brennan, Carroll, Shahian, Grover, Brindis, Mack.
Acquisition, analysis, and interpretation of data: Holmes, Brennan, Rumsfeld, Dai, O'Brien, Vemulapalli, Edwards, Carroll, Shahian, Tuzcu, Peterson, Mack.
Drafting of the manuscript: Holmes, Brennan, Dai, O'Brien, Edwards, Carroll, Shahian, Mack.
Critical revision of the manuscript for important intellectual content: Holmes, Brennan, Rumsfeld, Vemulapalli, Carroll, Shahian, Grover, Tuzcu, Peterson, Brindis, Mack.
Statistical analysis: Holmes, Dai, O'Brien, Vemulapalli, Tuzcu, Peterson.
Administrative, technical, or material support: Holmes, Brennan, Rumsfeld, Edwards, Shahian, Grover, Peterson.
Study supervision: Holmes, Brennan, O'Brien, Vemulapalli, Shahian, Tuzcu.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Rumsfeld reports that he is chief science officer for the National Cardiovascular Data Registry. Dr Vemulapalli reports receipt of a grant from Boston Scientific relating to Medicare analysis of resistant hypertension. Dr Carroll reports that he is a local site investigator on the PARTNER 2 trial sponsored by Edwards Lifesciences, a medical device company producing Sapien TAVR valves. Dr Grover reports that he is vice chair of the STS/ACC TVT Registry Steering Committee. Dr Peterson

reports receipt of grants and personal fees from Janssen and Eli Lilly and personal fees from Boehringer Ingelheim, Bayer, and AstraZeneca. Dr Brindis reports that he is senior medical officer for the National Cardiovascular Data Registry. Dr Mack reports that he is a member of the executive committee of the PARTNER trial sponsored by Edwards Lifesciences. No other disclosures were reported.

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