Original Investigation

Outcomes Following Transcatheter Aortic Valve Replacement in the United States

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IMPORTANCE Transcatheter aortic valve replacement (TAVR) was approved by the US Food and Drug Administration for the treatment of severe, symptomatic aortic stenosis and inoperable status (in 2011) and high-risk but operable status (starting in 2012). A national registry (the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy [STS/ACC TVT] Registry) was initiated to meet a condition for Medicare coverage and also facilitates outcome assessment and comparison with other trials and international registries.

OBJECTIVE To report the initial US commercial experience with TAVR.

DESIGN, SETTING, AND PARTICIPANTS We obtained results from all eligible US TAVR cases (n=7710) from 224 participating registry hospitals following the Edwards Sapien device commercialization (November 2011–May 2013).

MAIN OUTCOMES AND MEASURES Primary outcomes included all-cause in-hospital mortality and stroke following TAVR. Secondary analyses included procedural complications and outcomes by clinical indication and access site. Device implantation success was defined as successful vascular access, deployment of a single device in the proper anatomic position, appropriate valve function without either moderate or severe AR, and successful retrieval of the delivery system. Thirty-day outcomes are presented for a representative 3133 cases (40.6%) at 114 centers with at least 80% complete follow-up reporting.

RESULTS The 7710 patients who underwent TAVR included 1559 (20%) cases that were inoperable and 6151 (80%) cases that were high-risk but operable. The median age was 84 years (interquartile range [IQR], 78-88 years); 3783 patients (49%) were women and the median STS predicted risk of mortality was 7% (IQR, 5%-11%). At baseline, 2176 patients (75%) were either not at all satisfied (1297 patients [45%]) or mostly dissatisfied (879 patients [30%]) with their symptom status; 2198 (72%) had a 5-m walk time longer than 6 seconds (slow gait speed). The most common vascular access approach was transfemoral (4972 patients [64%]), followed by transapical (2197 patients [29%]) and other alternative approaches (536 patients [7%]); successful device implantation occurred in 7069 patients (92%; 95% CI, 91%-92%). The observed incidence of in-hospital mortality was 5.5% (95% CI, 5.0%-6.1%). Other major complications included stroke (2.0%; 95% CI, 1.7%-2.4%), dialysis-dependent renal failure (1.9%; 95% CI, 1.6%-2.2%), and major vascular injury (6.4%; 95% CI, 5.8%-6.9%). Median hospital stay was 6 days (IQR, 4-10 days), with 4613 (63%) discharged home. Among patients with available follow-up at 30 days (n=3133), the incidence of mortality was 7.6% (95% CI, 6.7%-8.6%) (noncardiovascular cause, 52%); a stroke had occurred in 2.8% (95% CI, 2.3%-3.5%), new dialysis in 2.5% (95% CI, 2.0%-3.1%), and reintervention in 0.5% (95% CI, 0.3%-0.8%).

CONCLUSIONS AND RELEVANCE Among patients undergoing TAVR at US centers in the STS/ACC TVT Registry, device implantation success was achieved in 92% of cases, the overall in-hospital mortality rate was 5.5%, and the stroke rate was 2.0%. Although these postmarket US approval findings are comparable with prior published trial data and international experience, long-term follow-up is essential to assess continued efficacy and safety.

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In November 2011, the US Food and Drug Administration (FDA) approved use of a device for transcatheter aortic valve replacement (TAVR) using the transfemoral approach for the treatment of severe, symptomatic aortic stenosis in patients with inoperable status.[1] The label for the device was expanded in September 2012 to include patients with high-risk but operable status by either a transfemoral or transapical approach.[2] Since commercial approval, this first-to-US-market TAVR device has been introduced to nearly 250 US clinical sites. To meet Medicare insurance coverage requirements, facilities must comply with coverage criteria outlined by the Centers for Medicare & Medicaid Services (CMS) National Coverage Determination,[3] including participation in a national procedural registry designed to answer outstanding evidentiary questions. To satisfy this requirement, the Society of Thoracic Surgeons (STS) and the American College of Cardiology (ACC) developed the STS/ACC Transcatheter Valve Therapy (TVT) Registry.[4]

AVR *aortic valve replacement*

KCCQ-12 *12-item Kansas City Cardiomyopathy Questionnaire*

PROM *predicted risk of operative mortality*

TAVR *transcatheter aortic valve replacement*

TVT *transcatheter valve therapy*

Although the pivotal PARTNER trials demonstrated efficacy of TAVR within a select cohort of patients and hospital centers, there are no data on dissemination and utilization patterns of this technology in routine clinical practice in the United States.[5,6] Additionally, concerns persist regarding the safety and effectiveness of this novel technology as it moves beyond protocolized trial care and highly experienced centers and operators.

In this analysis, we describe the initial US TAVR experience, including patient selection, procedural details, and in-hospital and 30-day outcomes following TAVR among patients enrolled in the TVT Registry.

Methods

The TVT Registry

The STS/ACC TVT Registry was launched in December 2011 following FDA approval of the Sapien Transcatheter Heart Valve.[7] The TVT Registry is a joint initiative of the STS and ACC including participation of more than 250 clinical sites (eTable 1 in the Supplement), with multistakeholder involvement on the steering and stakeholder advisory committees. The TVT Registry is responsive to the CMS National Coverage Determination (May 2012) requirement for national registry participation of all TAVR centers and is intended to serve as a platform for (1) device and procedural surveillance; (2) quality assurance and improvement initiatives; and (3) efficient conduct of device-labeling studies that will speed US access to new devices and support expansion of device labeling with evidence development. Registry activities have been approved by a central institutional review board, and the Duke University School of Medicine institutional review board granted a waiver of informed consent and authorization for this study.

Participating TVT Registry centers collect information on patient demographics, comorbidities, functional status, patient-reported quality of life, hemodynamics, procedural details, and postoperative, 30-day, and 1-year outcomes.[8] Data quality checks are implemented both at the National Cardiovascular Data Registry data warehouse and the Duke Clinical Research Institute Analysis Center, including data quality feedback reports and data range and consistency checks. Additionally, site training is conducted by the National Cardiovascular Data Registry through frequent informational webinars. In the case of missing data, sites have been contacted to encourage complete reporting.

Data Element Definitions

Data elements were collected using standardized definitions,[9] which have been harmonized with the STS National Database wherever possible. The following represent several definitions of interest. The clinical indication for TAVR (inoperable or high-risk status) was based on determination by 2 experienced local cardiac surgeons using risk calculations from the STS predicted risk of operative mortality (PROM) from isolated surgical aortic valve replacement (AVR)[10] and clinical judgment. The STS PROM estimates expected risk of operative mortality, with a range of 0% to 100% risk.

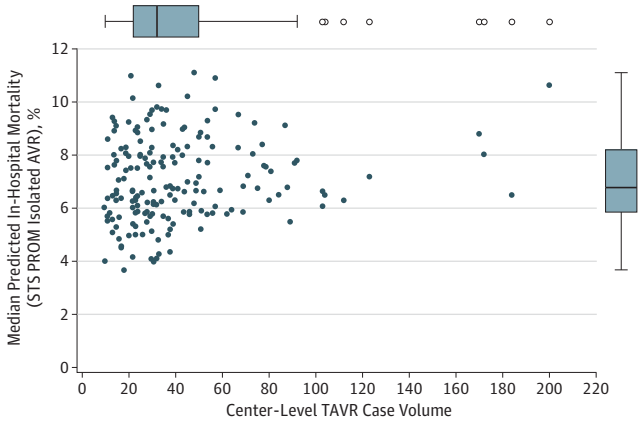
For the purposes of this analysis, patients were considered to have high-risk but operable status if the procedure was chosen based on extreme risk (due to comorbid conditions or technical reasons) or patient preference. A hybrid operating room was defined by the registry as a procedure room with standard fluoroscopic catheterization laboratory imaging situated in an operative suite. Porcelain aorta was defined as extensive circumferential calcification of the ascending aorta precluding safe surgical entry. "Hostile chest" included medical conditions that preclude open chest procedures, including abnormal chest wall anatomy (congenital or acquired), extensive mediastinal radiation, complete absence of sternal reconstructive options based on plastic surgery consultation, or other anatomical reasons to consider repeat sternotomy or right anterior thoracotomy prohibitively hazardous. Gait speed was defined as slow if the reported 5-m walk time was longer than 6 seconds.[11] The 12-question Kansas City Cardiomyopathy Questionnaire (KCCQ-12) has been validated[12] and is available online through the TVT Registry data coders dictionary.

Study End Points

Both in-hospital and 30-day outcomes were site-reported to the TVT Registry using standardized definitions, including harmonization with Valve Academic Research Consortium (VARC) and VARC-2 definitions for stroke, transient ischemic attack, aortic valve reintervention, major bleeding, and major vascular complications.[13,14] All site-reported stroke, transient ischemic attack, and valve reintervention events were adjudicated by a board-certified cardiologist using a combination of site-reported clinical information and targeted chart reviews.

Device implantation success was defined as successful vascular access, delivery and deployment of a single device in the proper anatomic location, appropriate performance of the prosthetic heart valve (aortic valve area >1.2 cm^2 and mean aortic

Figure. Center-Level Median STS PROM by Reported TAVR Case Volume (n=182 Centers)



STS indicates Society of Thoracic Surgeons; PROM, predicted risk of operative mortality; TAVR, transcatheter aortic valve replacement. In the box-and-whisker plots, the middle line is the median, the top and bottom of the box indicate the interquartile range, and the error bars are minimum and maximum values excluding outliers.

valve gradient <20 mm Hg or peak velocity <3 m/s, without moderate or severe prosthetic valve aortic regurgitation), and successful retrieval of the delivery system. Aborted procedures were defined as those that were cancelled or terminated after the patient entered the procedure room. Incident renal failure included a new post-TAVR requirement for hemodialysis or increase in serum creatinine level to 3.0 mg/dL or higher.

Statistical Analysis

Thirty-day outcomes are reported among patients with a known 30-day status among the hospitals with 80% or higher 30-day follow-up for each of the primary and secondary outcomes of interest (death, stroke, incident dialysis-dependent renal failure, and aortic valve reintervention), beginning with prospective TVT Registry data collection on May 1, 2012. Thirty-day follow-up status was considered to be known for cases that involved in-hospital death, death within 30 days of the index procedure, or no death within 30 days of the index procedure but affirmation that the patient was alive (with or without an adverse event) within the 30-day follow-up window (25-75 days following the index procedure). Baseline characteristics and in-hospital outcomes for patients with vs without 30-day follow-up are presented in eTable 2 in the Supplement.

Patient- and case-specific results were summarized and reported as medians and interquartile ranges (IQRs). Confidence intervals were calculated using exact 95% binomial confidence limits for key in-hospital and 30-day outcomes. Descriptive statistics are stratified by risk status (inoperable/high risk) and access site; however, statistical comparisons were not performed because of a lack of adequate comparator groups.

The median STS PROM was calculated for each hospital center using the STS isolated surgical AVR risk algorithm and variables reported to the TVT Registry and shown as a function of center-level TAVR volume (**Figure**) evaluating the relationship between observed center-level variation in patient selection and procedural volume, with the hypothesis that a larger proportion of low-volume centers would select lower-risk TAVR cases. In the Figure, each dot represents an individual center and the median PROM is the median predicted risk for patients at each center. Although the STS PROM for surgical isolated AVR may not be an accurate predictor of TAVR risk, it does provide a uniform summary statistic for assessing baseline case complexity.

SAS statistical software version 9.1 (SAS Institute Inc) was used for all calculations, and analyses were performed at the TVT Registry Analysis Center at the Duke Clinical Research Institute.

Results

Patient Cohort

There were 8075 TAVR cases entered into the TVT Registry between November 1, 2011, and May 31, 2013, allowing 60 days for data entry. Among these patients, 292 cases had missing data for in-hospital events, discharge status, or valve sheath access site; in addition, in 73 cases the operator assessment of procedural risk (either inoperable or high risk) was unknown. The baseline characteristics and in-hospital outcomes of these 365 patients are documented in eTable 3 in the Supplement. These patients were excluded from the primary analysis, leaving 7710 TAVR procedures from 224 hospitals. There were 2911 patients in whom KCCQ-12 data were available and 3065 for whom 5-m walk times were available. These patients were included in a secondary analysis. Characteristics of patients with vs without complete data for the KCCQ-12 and 5-m walk test are also presented in eTable 3.

Among the 7710 patients undergoing TAVR, the median age was 84 years (IQR, 78-88 years) and 51% % were male (**Table 1**). The median calculated STS PROM was 7% (IQR, 5%-11%), with considerable site-level variation (median site-level PROM ranged from 1.2% to 17.4%, including all centers; the Figure shows results for centers with 10 or more cases).

Documentation of preoperative evaluation of a patient's suitability for surgical AVR by at least 2 cardiac surgeons was reported in 91% of cases (n = 7020). A total of 1559 patients (20%) were considered to have an inoperable status and 6151 patients (80%) were considered at high operative risk (multiple comorbidities, 59%; severe deconditioning/debilitation, 17%; other, 4%). Markers of increased risk with surgical AVR were common: 7% with a left ventricular ejection frac-

Table 1. Patient Characteristics[a]

Characteristics	Overall (n = 7710)	High Risk (n = 6151)		Inoperable (n = 1559)	
		Transfemoral (n = 3833)	Nontransfemoral (n = 2318)	Transfemoral (n = 1139)	Nontransfemoral (n = 420)
Age, median (IQR), y	84 (78-88)	85 (79-89)	83 (78-88)	83 (77-88)	82 (77-87)
Male	3862 (50)	2053 (54)	992 (43)	616 (54)	201 (48)
STS PROM score, median (IQR), %	7 (5-11)	7 (5-11)	8 (5-12)	7 (4-10)	7 (4-11)
NYHA class III/IV heart failure	6272 (81)	3104 (81)	1884 (81)	962 (84)	322 (77)
Coronary artery disease	5316 (69)	2506 (66)	1706 (74)	793 (70)	311 (74)
No. of prior cardiac surgeries					
1	2045 (27)	905 (24)	700 (30)	309 (27)	133 (32)
≥2	400 (5)	164 (5)	140 (6)	71 (6)	25 (6)
Prior aortic valve intervention					
Balloon aortic valvuloplasty	1197 (16)	516 (13)	432 (19)	177 (16)	72 (17)
Surgical AVR	123 (2)	58 (2)	32 (1)	25 (2)	8 (2)
TAVR	14 (0.2)	7 (0.2)	4 (0.2)	2 (0.2)	1 (0.2)
Previous stroke	1004 (13)	503 (13)	321 (14)	130 (11)	50 (12)
Peripheral arterial disease	2416 (31)	898 (23)	1067 (46)	274 (24)	177 (42)
COPD					
Moderate	1081 (14)	511 (13)	358 (15)	154 (14)	58 (14)
Severe	1064 (14)	536 (14)	336 (15)	138 (12)	54 (13)
Oxygen-dependent lung disease	1135 (15)	569 (15)	347 (15)	161 (14)	58 (14)
Renal failure					
Dialysis-dependent	350 (5)	190 (5)	95 (4)	47 (4)	18 (4)
Serum creatinine level ≥3.0 mg/dL	361 (5)	194 (5)	103 (4)	47 (4)	17 (4)
5-m walk time >6 s	2198 (72)	1008 (73)	784 (73)	304 (70)	102 (57)
Atrial fibrillation	3148 (41)	1627 (42)	919 (40)	445 (39)	157 (37)
Permanent pacemaker/ICD	1500 (19)	774 (20)	433 (19)	215 (19)	78 (19)
Hostile chest	742 (10)	272 (7)	167 (7)	222 (19)	81 (19)
Porcelain aorta	587 (8)	174 (5)	215 (9)	113 (10)	85 (20)
Left ventricular ejection fraction <30%	540 (7)	276 (7)	141(6)	87 (8)	36 (9)
Bicuspid aortic valve	122 (2)	66 (2)	35 (2)	16 (1)	5 (1)
Pre-TAVR mitral insufficiency					
Moderate	2037 (26)	1028 (27)	619 (27)	290 (25)	100 (24)
Severe	347 (5)	179 (5)	104 (4)	49 (4)	15 (4)

Abbreviations: AVR, aortic valve replacement; COPD, chronic obstructive pulmonary disease; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; NYHA, New York Heart Association; PROM, predicted risk of operative mortality; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement.

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

tion of 30% or less (n = 540), 13% with a previous stroke (n = 1004), 5% with dialysis-dependent renal failure (n = 350), 28% with moderate/severe chronic obstructive pulmonary disease (n = 2145), and 15% with oxygen-dependent lung disease (n = 1135) (Table 1). "Hostile chest" was reported in 10% (n = 742), 1 or more prior cardiac surgeries in 32% (n = 2445), and a porcelain aorta in 8% (n = 587).

Patients in this cohort had a high burden of advanced heart failure, with severe functional limitations. Prior to the TAVR procedure, more than 81.3% had New York Heart Association class III/IV heart failure symptoms (n = 6272). Among the 3065 patients for whom a 5-m walk test results was reported, a slow gait speed was present in 2198 patients (72%) (median time, 8 seconds; IQR, 6-11 seconds). Among the 2911 patients for whom KCCQ-12 results were available at baseline, 763 (26%) were "quite a bit" or "extremely" limited in their ability to shower or bathe, 1524 (52%) had similar limitations with walking on level ground, and 2042 (70%) had similar limitations with hurried activities. A majority said that they would be mostly dissatisfied (1297 patients [30%]) or not at all satisfied (879 patients [45%]) if their remaining life were spent with a similar degree of symptoms.

Transcatheter AVR was performed for degenerative aortic stenosis in 7090 patients (92%), with a median aortic valve area of 0.6 cm^2 (IQR, 0.5-0.8 cm^2). Among those with reported pre-TAVR mitral valve function data (n=6528), mitral valve insufficiency was none/trace in 1015 (16%), mild in 3129 (48%), moderate in 2037 (31%), and severe in 347 (5%).

Procedural Characteristics

A total of 4391 procedures (57%) were performed in hybrid operating rooms, 2165 (28%) in hybrid catheterization laboratories, and 1050 (14%) in standard catheterization laboratories; general anesthesia was used in 7565 cases (98%) (**Table 2**). The most common approach was transfemoral (4972 cases [64%]), followed by transapical (2197 cases [29%]) and other ap-

Table 2. Operative Characteristics[a]

Characteristics	Overall (n = 7710)	High Risk (n = 6151)		Inoperable (n = 1559)	
		Transfemoral (n = 3833)	Nontransfemoral (n = 2318)	Transfemoral (n = 1139)	Nontransfemoral (n = 420)
Procedure location					
Hybrid operating room	4391 (57)	2099 (55)	1515 (65)	545 (48)	232 (55)
Hybrid catheterization laboratory	2165 (28)	1124 (29)	516 (22)	410 (36)	115 (27)
Catheterization laboratory	1050 (14)	549 (14)	272 (12)	162 (14)	67 (16)
Procedure status					
Elective	6873 (89)	3401 (89)	2052 (89)	1039 (91)	391 (91)
Urgent/emergent	832 (11)	430 (11)	265 (11)	98 (9)	39 (9)
Reason for procedure					
Procedure aborted	200 (3)	147 (4)	13 (0.6)	35 (3)	5 (1)
Cardiopulmonary bypass used	315 (4)	73 (2)	183 (8)	38 (3)	21 (5)
Type of anesthesia					
General anesthesia	7565 (98)	3730 (97)	2304 (99)	1113 (98)	418 (100)
Moderate sedation	126 (2)	95 (2)	5 (0.2)	25 (2)	1 (0.2)
Access site					
Transfemoral	4972 (64)	3833 (100)		1139 (100)	
Transapical	2197 (29)		1929 (83)		268 (64)
Transaortic	293 (4)		248 (11)		45 (11)
Axillary/subclavian	9 (0.1)		6 (0.3)		3 (0.7)
Access method for transfemoral procedures					
Cut-down	3132 (63)	2319 (61)		813 (71)	
Percutaneous	1792 (36)	1480(39)		312 (27)	
Conversion to open-heart surgery	94 (1)	31 (0.8)	41 (2)	16 (1)	6 (1)

[a] Data are expressed as No. (%) of procedures.

proaches (536 cases [7%]); percutaneous access was used in 1792 transfemoral cases (36%). In patients with inoperable status, 420 (27%) procedures were performed by a "nontransfemoral" approach, an off-label use of the TAVR device.

Device implantation success for the transcatheter valve was achieved in 7069 cases (92%; 95% CI, 91%-92%); among those without a prior transcatheter or surgical AVR, 2 or more valves were used in 2.9%. Intraprocedural death was uncommon (0.8%); however, conversion to open-heart surgery (94 cases [1% of total]) was associated with a 49% incidence of in-hospital mortality (46 deaths). The most common causes of open-heart conversion included dislodged valve (22 cases), ruptured annulus (13 cases), ruptured ventricle (11 cases), and aortic dissection (12 cases).

In-Hospital Outcomes

Overall, 94.5% of patients (n=7283) survived to hospital discharge (in-hospital mortality, 5.5%; 95% CI, 5.0%-6.1%) (**Table 3**). Major in-hospital complications included stroke (2.0%; 95% CI, 1.7%-2.4%), major vascular injury (6.4%; 95% CI, 5.8%-6.9%), acute renal insufficiency (5.5%; 95% CI, 5.0%-6.0%), and major bleeding (3.5%; 95% CI, 3.1%-3.9%). New-onset atrial fibrillation was observed in 6.0% (95% CI, 5.5%-6.5%) and need for new pacemaker or implantable cardioverter-defibrillator in 6.6% (95% CI, 6.1%-7.2%). Patients with inoperable status or who had a nontransfemoral procedure experienced a higher incidence of most adverse events compared with those with operable status and transfemoral procedures. Median intensive care unit stay was 46 hours (IQR, 25-77 hours), and median hospital stay was 6 days (IQR, 4-10 days). The majority of patients were discharged either to home (n=4613 [63%]) or to a rehabilitation facility (n=2134 [29%]).

Among the 5979 patients with an immediate pre-hospital discharge echocardiogram, moderate or severe aortic insufficiency was observed in 508 patients (8.5%); moderate in 481 (8%), and severe in 27 (0.5%). Among patients with available baseline and post-TAVR echocardiogram results (n = 4918), the degree of mitral regurgitation was reduced in 2402 (49%), unchanged in 1962 (40%), and worsened in 554 (11%).

30-Day Outcomes

Thirty-day outcomes data are reported from 114 hospitals (51% of the 224 hospitals in the registry) with 80% or higher 30-day follow-up for each of the primary and secondary outcomes of interest (death, stroke, incident dialysis-dependent renal failure, and aortic valve reintervention). These 114 hospitals enrolled 3528 patients, and follow-up data were not available for 395 patients (eTable 2 in the Supplement). Among the 3133 patients for whom 30-day outcome data were available, the incidence of death was 7.6% (95% CI, 6.7%-8.6%), including 52% with a noncardiovascular cause (**Table 4**). Stroke occurred in 2.8% (95% CI, 2.3%-3.5%), incident hemodialysis in 2.5% (95% CI, 2.0%-3.1%), and aortic valve reintervention in 0.5% (95% CI, 0.3%-0.8%). Among patients with available follow-up, the incidence of class III/IV heart failure during follow-up was 12% (compared with 81% at baseline). Overall,

Table 3. In-Hospital Clinical Outcomes[a]

Outcomes	Overall (n = 7710)	High Risk (n = 6151)		Inoperable (n = 1559)	
		Transfemoral (n = 3833)	Nontransfemoral (n = 2318)	Transfemoral (n = 1139)	Nontransfemoral (n = 420)
Death					
From any cause	427 (5.5)	146 (3.8)	190 (8.2)	61 (5.4)	30 (7.1)
In laboratory/operating room	65 (0.8)	17 (0.4)	30 (1.3)	12 (1.1)	6 (1.4)
Cardiac arrest	447 (5.8)	152 (4.0)	199 (8.6)	66 (5.8)	30 (7.1)
Transient ischemic attack	28 (0.4)	14 (0.4)	11 (0.5)	2 (0.2)	1 (0.2)
Stroke	156 (2.0)	84 (2.2)	36 (1.6)	2 (1.9)	14 (3.3)
Death or stroke	556 (7.2)	219 (5.7)	219 (9.4)	75 (6.6)	43 (10.2)
Myocardial infarction	56 (0.7)	19 (0.5)	26 (1.1)	9 (0.8)	2 (0.5)
New-onset atrial fibrillation	460 (6.0)	118 (3.1)	274 (11.8)	29 (2.6)	39 (9.3)
Transapical access site complications	61 (0.8)		55 (2.4)		6 (1.4)
Renal failure					
Dialysis-dependent	145 (1.9)	48 (1.3)	68 (2.9)	19 (1.7)	10 (2.4)
Postoperative serum creatinine level ≥3 mg/dL[b]	276 (3.8)	111 (3.1)	115 (5.3)	34 (3.2)	16 (3.1)
Valve Academic Research Consortium major bleeding	267 (3.5)	121 (3.2)	83 (3.6)	41 (3.6)	22 (5.2)
Multiple transcatheter valves used[c]	221 (2.9)	96 (2.6)	76 (3.3)	38 (3.4)	11 (2.7)
New permanent pacemaker	509 (6.6)	222 (5.8)	181 (7.8)	79 (6.9)	27 (6.4)
Intensive care unit duration, median (IQR), h	46 (25-77)	34 (24-64)	54 (29-115)	37 (24-71)	55 (28-102)
Hospital duration, median (IQR), d[d]	6 (4-10)	5 (4-9)	8 (6-12)	5 (4-9)	8 (6-11)
Discharge location[d]					
Home	4613 (63)	2472 (67)	1164 (55)	753 (70)	224 (57)
Extended care/transitional care unit/rehabilitation center	2134 (29)	981 (27)	767 (36)	258 (24)	128 (33)
Nursing home	405 (6)	170 (5)	150 (7)	50 (5)	35 (9)
Other	125 (2)	60 (2)	46 (2)	16 (1)	3 (1)

Abbreviation: IQR, interquartile range.

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

[b] Among cases who did not have dialysis-dependent renal failure and did not develop in-hospital dialysis-dependent renal failure.

[c] Among cases without a prior transcatheter or surgical aortic valve replacement.

[d] Among patients discharged alive.

there were no major differences between patient characteristics and mortality outcome for patients enrolled at the 114 hospitals with 80% or higher follow-up and patients enrolled at the 110 hospitals with lower than 80% complete 30-day follow-up (eTable 2 in the Supplement).

Discussion

This analysis represents the first public report from the US national STS/ACC TVT Registry and documents 2 major findings. First, postapproval commercial introduction of this new technology with an early-generation device has yielded success rates and complication patterns that are similar to those documented in carefully performed randomized trials. Second, the outcomes of procedures even with this early-generation approved device are similar to the global experience of TAVR, which now is based on second- and third-generation improved devices. These findings help address a lingering question of clinical outcomes with the first-generation TAVR device after controlled US dissemination to a relatively narrow group of treatment centers. As a part of the FDA Strategic Initiative,[15] the TVT Registry has helped to address critiques of the adequacy of postmarket surveillance of high-risk medical device performance and safety.[16-18]

Whether outcomes of postapproval medical device use are comparable with those obtained in regulatory approval trials has been a long-standing point of concern. The commercial introduction of TAVR was unique in that the CMS and several professional societies collaborated to define requirements for certification of clinical sites and operators through the CMS National Coverage Determination, with an unprecedented level of site training and case supervision by the industry sponsor. This initial report provides early evidence that similar results from clinical trials can be achieved for complex medical devices in the postapproval experience when a controlled rollout is followed. Patients with inoperable status in the PARTNER trial had 30-day death and stroke rates of 5% and 6.7%, respectively.[5] Although the in-hospital mortality and stroke rates of 5.8% and 2.3%, respectively, reported in TVT Registry for inoperable cases are less than the 30-day outcome rates (7.7% and 2.5%, respectively), they are consistent with the trial outcomes on which device approval was based. Likewise, the in-hospital mortality and stroke rates of 5.5% and 2.0% and 30-day rates of 6.6% and 2.5%, respectively, in the high-risk operable patient cohort of the TVT Registry are in a similar range as the 3.4% and 4.7% 30-day mortality and stroke rates in PARTNER "cohort A".[6]

In-hospital transfemoral mortality rates were 5.4% and 3.8% in the inoperable and high-risk groups (30-day rates, 6.7%

Table 4. 30-Day Clinical Outcomes[a]

Outcomes	Overall (n = 3528)	High Risk (n = 2834)		Inoperable (n = 694)	
		Transfemoral (n = 1687)	Nontransfemoral (n = 1147)	Transfemoral (n = 489)	Nontransfemoral (n = 205)
Death	243 (7.6)	77 (5.0)	112 (10.8)	30 (6.7)	24 (12.6)
Primary cause of death					
Cardiac	108 (44.8)	24 (31.6)	55 (49.1)	18 (62.1)	11 (45.8)
Valvular	7 (2.9)	3 (4.0)	1 (0.9)	1 (3.5)	2 (8.3)
Neurologic	13 (5.4)	7 (9.2)	3 (2.7)	2 (6.9)	1 (4.2)
Pulmonary	26 (10.8)	8 (10.5)	16 (14.3)	0	2 (8.3)
Renal	7 (2.9)	2 (2.6)	4 (3.6)	1 (3.5)	0
Vascular	18 (7.5)	9 (11.8)	5 (4.5)	2 (6.9)	2 (8.3)
Infection	12 (5.0)	5 (6.6)	7 (6.3)	0	0
Other	28 (11.6)	12 (15.8)	10 (8.9)	3 (10.3)	3 (12.5)
New York Heart Association classification					
I	1243 (50.2)	671 (54.8)	377 (47.5)	139 (42.6)	56 (43.1)
II	933 (37.7)	420 (34.3)	305 (38.5)	153 (46.9)	55 (42.3)
III	257 (10.4)	110 (9.0)	99 (12.5)	30 (9.2)	18 (13.9)
IV	41 (1.7)	24 (2.0)	12 (1.5)	4 (1.2)	1 (0.77)
Stroke	90 (2.8)	49 (3.2)	23 (2.2)	7 (1.6)	11 (5.9)
Death or stroke	319 (10.1)	120 (7.9)	131 (12.8)	34 (7.8)	34 (17.8)
New dialysis-dependent renal failure	78 (2.5)	23 (1.5)	42 (4.1)	7 (1.6)	6 (3.2)
Aortic valve reintervention	16 (0.5)	8 (0.5)	4 (0.4)	2 (0.5)	2 (1.1)

[a] Data are expressed as No. (%) of patients treated at centers with follow-up data available on 80% or more of transcatheter aortic valve replacement cases performed following the Centers for Medicare & Medicaid Services National Coverage Determination (May 1, 2012) through May 31, 2013 (n = 114 centers).

Table 5. In-Hospital and 30-Day Mortality in the STS/ACC TVT Registry Compared With Previous Studies

	Mortality, No./Total (%)											
	STS/ACC TVT Registry			PARTNER Trial[5,6]				SOURCE[20]		GARY[21]		
	Inoperable	High-Risk		Inoperable	High-Risk							
	TF	TF	TA	TF	TF	TA	FRANCE 2[19]	TF	TA	TF	TA	UK SATIRE[22]
In-hospital	61/139 (5.4)	146/3833 (3.8)	190/2318 (8.2)	NR	NR	NR	NR	NR	NR	138/2694 (5.1)	62/870 (7.1)	NR
30-Day	30/489 (6.1)	77/1687 (4.6)	112/1147 (9.8)	9/179 (5.0)	9/244 (3.7)	9/104 (8.7)	293/3195 (9.2)	29/463 (6.3)	59/575 (10.3)	NA	NA	91/1181 (7.1)

Abbreviations: NR, data not reported; STS/ACC TVT, Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy; TA, transapical; TF, transfemoral.

and 5.0%), comparable with PARTNER trial as-treated 30-day mortality rates of 5% and 3.7% in the same cohorts, respectively. The observed in-hospital mortality rates in the nontransfemoral cohort of 7.1% and 8.2% (30-day rates, 12.6% and 10.8%) for inoperable and high-risk status were slightly higher than the mortality rate of 8.7% in the PARTNER Trial, which was studied only in the high-risk, operable population.

These US registry results also suggest comparability with those reported in international registries (**Table 5**). The FRANCE 2 Registry, which included not only the device evaluated in our study but also a later generation of the device as well as other TAVR devices, reported outcomes of 3195 patients treated in 34 French centers between January 2010 and October 2011.[19] The 30-day mortality rate was 9.7%. The Sapien Aortic Bioprosthesis European Outcome (SOURCE) Registry, an industry-sponsored postapproval European study, reported a 30-day mortality of 6.3% after transfemoral and 10.3% after transapical procedures.[20] The German Aortic Valve Registry (GARY) has reported results in 3866 patients undergoing TAVR in 2011.[21] Two-thirds underwent the procedure by a transfemoral approach, with an in-hospital mortality of 5.1%, and the remaining one-third by a transapical approach, with a mortality of 7.7%, which approximate the results reported herein. Similar results are reported from the UK SATIRE Registry in the United Kingdom, in which 30-day mortality was 7.1% in 870 patients undergoing the procedure through 2010.[22]

Vascular and bleeding complications were relatively uncommon despite this early experience and the availability of only early-generation, larger-sheath-size delivery systems in this country. Based on experience outside of the United States, vascular and bleeding complications appear to decrease with smaller-caliber, next-generation delivery system availability.

A number of factors are related to the overall US outcomes reported in this analysis. First, there was already a broad experience with the device and procedure outside of the United States, which has been readily shared with US centers. Ex-

ploiting this global experience through international collaboration and common learning may well have shortened the US "learning curve." Second, at least 35 centers had significant experience with the procedure from participation in the PARTNER trial, which benefitted not only those centers but contributed to the shared learning that may have helped all centers. Third, the device manufacturer had an education program in place with mandated training in all aspects of patient selection, procedure performance, and postprocedure care. Company-employed clinical specialists were present during all procedures. Fourth, the presence of a national registry, with explicitly planned reporting of outcomes, may have resulted in a Hawthorne or observational effect, as has been seen with other registry experiences. Fifth, compared with immediate and broad introduction of medical devices on regulatory approval, the "rational dispersion" of this new technology may have been a factor in the outcomes achieved. Sixth, the risk profile of patients reported here is generally lower (inoperable, median, 7% [IQR, 4%-10%]; high-risk but operable, median, 7% [IQR, 5%-11%]) than that seen in randomized trials and in the reports from outside the United States. Patients with inoperable status in the PARTNER trial had a mean STS PROM of 11.2% (SD, 5.8%) and those with high-risk but operable status had a mean of 11.8% (SD, 3.3%). Although this may represent incomplete entry of variables into the risk calculator by US clinical sites, it could indicate "risk creep," meaning patients with lower surgical risk are being treated in the United States, leading to better outcomes with TAVR.

Several important and unexpected observations can be made from this initial report. There was wide variability based on center volume and selection of patients (Figure). This requires a future study examining the relationship of center volume to outcome, which could affect the CMS coverage criteria, which were based on a presumed relationship between volume and procedural outcome. In addition, 27% of patients with inoperable status received TAVR via an alternative access route, probably because of inability to use the FDA-approved and CMS-reimbursed femoral access route until after the recent FDA label expansion.[23]

However, several potential limitations should be considered in the interpretation of the results of this analysis. First, although there was an attempt to capture all TAVR procedures in the United States, not all cases have yet been entered into the TVT Registry since the issuance of the National Coverage Determination. By comparison with the Edwards Lifesciences record of procedures, it is estimated that this report represents approximately 88% of the procedures performed between the issuance of the National Coverage Determination (May 2012) and the end of the study interval (May 2013). It is likely that the early rolling enrollment of centers in the TVT Registry and an incomplete retrospective case capture has led to this discrepancy; however, it is unclear whether this underreporting is more prevalent among cases with poor outcomes. This could potentially limit generalizability of the results, although the vast majority of US TAVR cases are included in the current report, and other comparisons of missing vs complete case risk profiles and in-hospital outcomes do not suggest selective reporting of results (eTable 3 in the Supplement).

Second, the 30-day outcomes presented here are limited to a subset of centers and patients (eTable 2 in the Supplement). As analysis of missing vs complete cases does not suggest biased case reporting, similar outcomes were observed in those with and without 30-day data available, indicating that these outcomes most likely are generalizable. Subsequent reports from the TVT Registry will address more complete long-term (30-day and 1-year) outcomes, including survival and patient health status, to have a more comprehensive assessment of the outcomes of patients undergoing TAVR in the United States.

Third, there has been limited capture of patient health status and functional status follow-up data in the TVT Registry to date. As this became apparent during the early stages of the registry rollout, a robust site education program addressed the collection of this data at both baseline and follow-up. Subsequent reports will focus on health status and quality-of-life outcomes.

Conclusion

Among the 7710 patients undergoing TAVR at 224 sites in the STS/ACC TVT Registry, device success was achieved in 92% of cases, with a 5.5% incidence of in-hospital mortality and a 2% incidence of stroke. Although procedural complication rates were relatively low, within the first 30 days most deaths remained noncardiovascular in nature. These findings are comparable with prior published randomized trial and international registry experience. Longer-term follow-up is essential to assess continued safety and efficacy as well as patient health status.

ARTICLE INFORMATION

Author Contributions: Dr Brennan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Mack, Brindis, Carroll, Edwards, Grover, Shahian, Tuzcu, Rumsfeld, Hewitt, Michaels, Christensen, Holmes.
Acquisition of data: Carroll, Edwards, Hewitt, Shewan, Michaels, Christensen, Holmes.
Analysis and interpretation of data: Brennan, Brindis, Carroll, Edwards, Grover, Shahian, Tuzcu, Peterson, Rumsfeld, Hewitt, Shewan, Christian, O'Brien, Holmes.
Drafting of the manuscript: Mack, Brennan, Brindis, Carroll, Edwards, Holmes.
Critical revision of the manuscript for important intellectual content: Mack, Brindis, Carroll, Grover, Shahian, Tuzcu, Peterson, Rumsfeld, Hewitt, Shewan, Michaels, Christensen, Christian, O'Brien, Holmes.
Statistical analysis: Carroll, Edwards, Peterson, Christian, O'Brien, Holmes.
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Study supervision: Mack, Grover, Shahian, Hewitt, Christensen, Holmes.

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Correction: This article was corrected on November 19, 2013, to correct the name of the device in the abstract and an incorrectly indented row stub in Table 3.

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