JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 10, 2019

PUBLISHED BY ELSEVIER

Hospital Resource Utilization Before and After Transcatheter Aortic Valve Replacement

The STS/ACC TVT Registry

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ABSTRACT

BACKGROUND Patients with severe aortic stenosis (AS) have repeat hospitalizations for multiple conditions.

OBJECTIVES The purpose of this study was to assess the effect of transcatheter aortic valve replacement (TAVR) on hospitalizations in severe AS.

METHODS Using data from the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) registry with linkage to Medicare claims, the authors examined rates of all-cause, cardiovascular, and noncardiovascular hospitalizations and hospital days, as well as inpatient costs in the year pre-TAVR and post-TAVR. Multivariable modeling was used to determine rate ratios of post-TAVR versus pre-TAVR hospitalizations and costs.

RESULTS Among 15,324 patients at 328 sites with Medicare linkage undergoing TAVR, the median age was 84 years, the median Society of Thoracic Surgeons Predicted Risk of Mortality score was 7.0, and 61.1% patients underwent TAVR via transfemoral access. Post-TAVR, heart failure hospitalization rates and hospitalized days were reduced compared with pre-TAVR (rate ratio: 0.87 and 0.95 respectively; $p < 0.01$ for all). However, all-cause, noncardiovascular, and bleeding hospitalization rates and hospitalized days were increased ($p < 0.01$ for all). Post-TAVR hospitalizations were reduced the most among those with left ventricular ejection fraction <30%. Mean post-TAVR costs were reduced among all TAVR patients and among 1-year survivors (rate ratio: 0.95, $p < 0.01$; and 0.90; $p < 0.01$, respectively).

CONCLUSIONS Patients had lower costs and fewer heart failure hospitalizations but more all-cause, noncardiovascular, and bleeding hospitalizations post-TAVR. Reduction in hospitalizations varied by specific patient subgroups, and thus, payors and providers seeking to reduce resource use may consider strategies designed to improve processes of care among patients with increased resource utilization post-TAVR as compared with pre-TAVR.
(J Am Coll Cardiol 2019;73:1135–46) © 2019 by the American College of Cardiology Foundation.

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Manuscript received January 8, 2018; revised manuscript received November 24, 2018, accepted December 16, 2018.

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2018.12.049

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

LVEF = left ventricular ejection fraction

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

Aortic stenosis is one of the most common valvular diseases in western countries and was responsible for $1.3 billion in hospitalization costs in 2001 alone. Overall, aortic valve disease hospitalizations increased 59% from 2000 to 2012, with a resultant increase in hospitalization costs from $1.3 billion to $2.1 billion in 2012 (1). In the setting of this growing clinical and economic burden, clinical trials have provided evidence supporting the superiority of transcatheter aortic valve replacement (TAVR) versus medical therapy in patients with prohibitive surgical risk (2). More recently, clinical trials have established the efficacy of TAVR in preventing all-cause death compared with surgical aortic valve replacement (SAVR) in high (3,4) and intermediate (5,6) surgical-risk patients, and ongoing trials will evaluate the comparative efficacy of TAVR versus SAVR in low-risk patients.

SEE PAGE 1147

Multiple secondary analyses have also established the cost-effectiveness of TAVR compared with SAVR and medical therapy based on clinical trial data (7–9). However, compared with the pivotal trial experience, patients treated with TAVR after regulatory approval in the United States include some patients previously excluded from the pivotal trials, patients treated at sites without trial experience, and patients treated by a broader group of less-experienced operators with less rigidly standardized treatment protocols. To date, no analyses have examined health care resource utilization pre-TAVR and post-TAVR in a real-world setting. Accordingly, the objective of this study is to describe the change in 1-year cardiovascular event rates, rate of hospitalizations, and hospitalization costs in patients undergoing TAVR in the United States.

METHODS

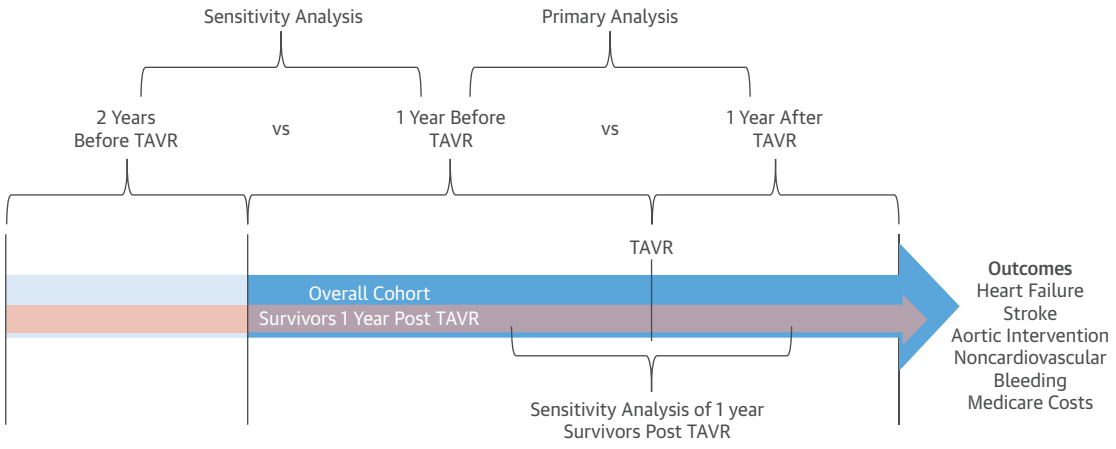
TVT REGISTRY. Participating centers use standardized definitions to collect information on consecutive TAVR cases. Data quality checks have been implemented at the National Cardiovascular Data Registry data warehouse and Duke Clinical Research Institute to optimize data completeness and accuracy. The TVT (Transcatheter Valve Therapy) Registry protocol has been granted a waiver of informed consent by the Chesapeake Research Review Incorporated institutional review board and the Duke University Institutional Review board.

STUDY COHORT. TVT Registry clinical records for procedures performed from November 2011 through September 2015 were linked to Medicare administrative claims using direct patient identifiers (name and social security number). To ensure that all patients in the present study were followed for 1 year after their TAVR, TAVR procedures from 2011 through September 2014 were included in the present study. Because we planned to compare cardiovascular events in the year before and after TAVR, we required that all patients in the study cohort have available fee-for-service Medicare linkage for the year prior to TAVR and 1 year of follow-up (or death if sooner) as well. Patients were censored at death or at the end of 1 year of follow-up, whichever came first. To reflect the trend over time of increasing transfemoral access for TAVR, we repeated all outlined analyses for the transfemoral subgroup.

STUDY OUTCOMES. Medicare administrative claims files linked to the TVT Registry by the Centers for Medicare and Medicaid Services were used for detection of inpatient events in the year before and after TAVR using International Classification of Diseases-Ninth Revision-Clinical Modification codes (Online Appendix 1). Outcomes of interest included the rates of hospitalization for: stroke, aortic valve intervention, heart failure (HF), HF plus aortic valve disease, all causes, and the number of hospitalized days. The "pre" period end date was defined as the day before the index TAVR procedure admission date, whereas the "post" period start date was defined as the day following the index TAVR discharge date. For each patient, we enumerated both the number of events and the number of hospitalized days for each outcome type during the pre-TAVR and post-TAVR periods. Hospital admissions resulting in death were classified by the primary reason for hospitalization. Hospitalizations in the year pre-TAVR and post-TAVR were graphically displayed using a 3-month moving average technique. The moving average was calculated by counting the number of patients who had an event divided by the total number of eligible patients in a daily, moving 90-day time period.

MEDICARE COSTS ANALYSIS. Medicare costs in the pre-TAVR and post-TAVR periods were defined as the amount paid by the Medicare program for care received while in the hospital, as recorded in the inpatient claims. Costs for the initial TAVR hospitalization and any associated rehab stay were excluded. Costs were adjusted to 2010 U.S. dollars based on the Medical Care component of the Consumer Price Index reported for December of each year. To prevent extreme outliers from affecting the results, costs were Winsorized at 99% for each period.

FIGURE 1 Study Design



TAVR = transcatheter aortic valve replacement.

STATISTICAL ANALYSIS. Events. Baseline patient characteristics are summarized as percentages or medians and interquartile ranges as appropriate. We summarized both the number of events and the number of days hospitalized for each outcome type for all patients in each period. To account for mortality during the post-TAVR period, we also standardized the observed event counts as rates per 1,000 person-years using the person-time contributed by each patient during the pre-TAVR and post-TAVR periods.

Differences in event rates between the pre-TAVR and post-TAVR period were estimated as incidence rate ratios with 95% confidence intervals using log-Poisson multilevel models with random intercepts for each patient and an offset of the person-years contributed by each patient within each period. We also performed several sensitivity analyses: 1) because the use of an offset to account for censored data assumes a constant event rate over the follow-up period, we also modeled the incidence rate ratios restricted to patients who survived the full post-TAVR period; and 2) to assess whether changes in event rates pre-TAVR versus post-TAVR may be due to the passage of time, we also compared event rates 2 years prior to TAVR against those 1 year prior to TAVR (Figure 1).

Differences in event rate ratios (post-TAVR event rate/pre-TAVR event rate) for all-cause hospitalizations were assessed using a log-Poisson multi-level model with random intercepts for each hospital and an offset of the person-years contributed by each patient within each period. All subgroup indicator variables were included as covariates in a single multivariable model. For these analyses, missing data were imputed to the most common category.

Medicare costs. Post-TAVR versus pre-TAVR cost comparisons were estimated as cost ratios using a multilevel log-gamma regression model with a random intercept for each patient and a single covariate for time period (post- and pre-TAVR).

Because patients in our cohort were required to be alive and in Fee-For-Service Medicare in the year prior to TAVR but may have died in the subsequent year after TAVR (and therefore had no further Medicare costs), this approach may result in lower overall post-TAVR health care costs due to death. As a sensitivity analysis, we calculated Medicare expenditures after excluding those patients who died in the year after TAVR.

In the above analyses, we specifically excluded costs from the index TAVR hospitalization to understand the impact of TAVR on inpatient costs after the "up-front cost" of the initial TAVR hospitalization. As a second sensitivity analysis, we also calculated pre-TAVR and post-TAVR cost ratios as described above after including index TAVR hospitalization costs within the post-TAVR time-period.

Statistical significance was defined as $p < 0.05$. All analyses were performed by the NCDR data analysis center at the Duke Clinical Research Institute using SAS software versions 9.3 and 9.4 (Cary, North Carolina).

TABLE 1 Baseline Characteristics at the Time of TAVR and In-Hospital Outcomes After TAVR (N = 15,324)

Median age, yrs	84 (79, 88)
<75	1,891 (12.3)
75–84	5,998 (39.1)
85–94	7,120 (46.5)
≥95	315 (2.1)
Female	7,686 (50.2)
Race	
White	14,639 (95.5)
Black	431 (2.8)
Asian	137 (0.9)
Other	117 (0.8)
Median STS PROM score	7.0 (4.7, 10.7)
<8%	8,910 (58.1)
8%–15%	4,674 (30.5)
>15%	1,739 (11.3)
NYHA functional class III/IV heart failure	12,433 (82.0)
Coronary artery disease	9,552 (63.1)
Prior open heart surgery	5,162 (33.7)
Prior cardiac surgeries	
0	10,318 (68.3)
1	4,137 (27.4)
≥2	641 (4.2)
Prior aortic valve intervention	2,375 (15.5)
Balloon aortic valvuloplasty	2,101 (88.5)
Surgical AVR	256 (1.7)
TAVR	10 (0.4)
Previous stroke	1,855 (12.1)
Peripheral arterial disease	4,823 (31.5)
COPD	
None/mild	11,004 (72.3)
Moderate	2,184 (14.4)
Severe	2,030 (13.3)
Oxygen-dependent lung disease	2,076 (13.6)
Renal failure	
Dialysis dependent	600 (3.9)
Serum creatinine ≥2.0 without dialysis	996 (6.5)
Serum creatinine <2.0	13,693 (89.6)
5-min walk time >6 s	6,450 (42.2)
Atrial fibrillation	6,457 (42.2)
Permanent pacemaker/ICD	3,021 (19.7)
Hostile chest	1,220 (8.0)
Porcelain aorta	961 (6.3)
LV ejection fraction	
<30%	1,043 (7.0)
30%–45%	2,796 (18.6)
>45%	11,155 (74.4)
Aortic valve morphology	
Bicuspid	227 (1.5)
Tricuspid	13,947 (91.0)
Other/unknown	1,150 (7.5)
Pre-TAVR mitral insufficiency	
None/trivial/mild	8,745 (68.6)
Moderate	3,916 (30.7)
Severe	93 (0.7)
Access site	
Transfemoral	9,306 (61.1)
Other	5,916 (38.9)
Discharge antithrombotic	
Warfarin	3,708 (24.6)
Aspirin	12,618 (83.9)
$P2Y_{12}$ inhibitor	8,948 (59.6)
Dabigatran	223 (1.5)
Factor Xa inhibitor	349 (2.3)
In-hospital outcomes	
In-hospital death	773 (5.0)
Any in-hospital stroke	329 (2.2)
In-hospital TIA	42 (0.3)
Any in-hospital valve complication	258 (1.7)
Conversion to open heart surgery	215 (1.4)
Discharge location	
Home	8,990 (61.8)
Extended care/TCU/rehab	4,503 (31.0)
Other acute care hospital	91 (0.6)
Nursing home	843 (5.8)
Hospice	76 (0.5)
Other	7 (0.0)

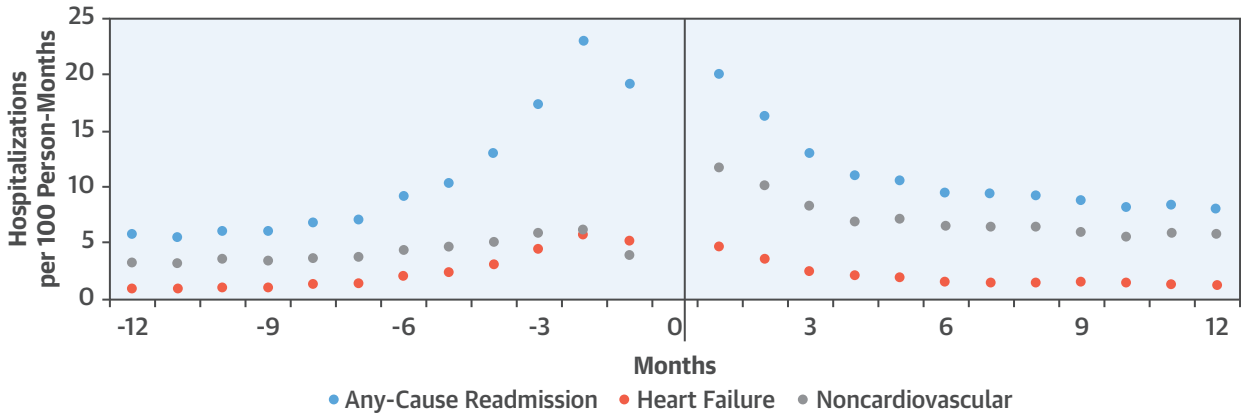
Values are median (25th, 75th percentile) or n (%).

AVR = aortic valve replacement; COPD = chronic obstructive pulmonary disease; ICD = implantable cardioverter-defibrillator; LV = left ventricular; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement; TCU = transitional care unit; TIA = transient ischemic attack.

RESULTS

STUDY COHORT. After including only the first TVT Registry TAVR procedure for each patient, 15,324 TVT Registry records linked to Centers for Medicare & Medicaid Services (CMS) administrative claims data from 328 sites were identified and included in the final study cohort (Online Figure 1). The 15,324 patients in the study cohort are clinically similar to patients without CMS linkage in baseline characteristics (Online Table 1) and in-hospital outcomes (Online Table 2). The median age was 84 years (interquartile range: 79 to 88 years) and 50.2% were female. A total of 96% of patients were white, and the median Society of Thoracic Surgeons Predicted Risk of Mortality was 7.0 (interquartile range: 4.5 to 10.4). Comorbidities were common, including left ventricular ejection fraction (LVEF) <30% (7.0%), New York Heart Association (NYHA) functional class III/IV HF (82.0%), prior stroke (12.1%), oxygen-dependent lung disease (13.6%), peripheral arterial disease (31.5%), dialysis dependence (3.9%), and atrial fibrillation (42.2%). A transfemoral approach for TAVR was used in most patients (61.1%) (Table 1).

CENTRAL ILLUSTRATION 3-Month Moving Average and Hospitalization Cause-Specific Event Rates in the Year Pre-Transcatheter Aortic Valve Replacement and Post-Transcatheter Aortic Valve Replacement



Vemulapalli, S. et al. J Am Coll Cardiol. 2019;73(10):1135–46.

Among patients undergoing transcatheter aortic valve replacement (TAVR) in the United States, the rate of heart failure hospitalizations decreased in the year after TAVR as compared to the year before. However, noncardiovascular hospitalizations, including bleeding, increased in the year after TAVR as compared to the year before. Moving averages were calculated using 3-month intervals.

Demographics of the transfemoral subpopulation were clinically similar to those of the overall cohort, with a median age of 85 years (interquartile range: 79 to 88 years), 45.5% female, 95% white, and a Society of Thoracic Surgeons Predicted Risk of Mortality of 6.7 (interquartile range: 4.5 to 10.2). Comorbidities were common and similar to those in the overall population with the exception of peripheral artery disease, which was less common at 23.4%.

CARDIOVASCULAR AND NONCARDIOVASCULAR OUTCOMES IN THE YEAR PRE-TAVR AND POST-TAVR. All-cause hospitalizations (Central Illustration) and hospitalized days (Table 2) increased in the year after TAVR compared with the year prior to TAVR. The single most common cause of hospitalization was HF hospitalization, which occurred in 15.9% of patients in the year prior to TAVR and 14.2% in the year after TAVR (Table 3). Accordingly, HF hospitalization rates and hospitalized days decreased in the year after TAVR compared with the year prior to TAVR (Central Illustration, Table 2). When aortic valve disorders are included as causes of HF hospitalization, HF hospitalization rates and hospitalized days decreased further. Conversely, rates of hospitalization for stroke and hospital days due to stroke increased significantly from the year before TAVR to the year after TAVR. Only 57 of 334 (17.1%) of hospitalizations for stroke in the year after TAVR occurred in the first 30 days.

Noncardiovascular hospitalizations and hospitalized days increased in the year after TAVR compared with the year prior to TAVR (Central Illustration,

TABLE 2 Rates of Days Alive and Out of the Hospital in the Year Before Versus the Year After TAVR

Event	Observed Rates		Difference in Hospitalized Days (Rates)	Rate Ratio (95% CI)	p Value
	Pre-TAVR Hospitalized Days (Hospitalized Days per 1,000 Patient-Yrs)	Post-TAVR Hospitalized Days (Hospitalized Days per 1,000 Patient-Yrs)			
Any readmission	123,712 (8,073.09)	119,357 (9,107.25)	−4,355 (1,034.16)	1.134 (1.125-1.143)	<0.001
Heart failure	23,923 (1,561.15)	19,400 (1,480.27)	−4,523 (−80.88)	0.953 (0.935-0.972)	<0.001
Heart failure and AoV disease	50,485 (3,294.51)	20,787 (1,586.10)	−29,698 (−1,798.41)	0.483 (0.475-0.491)	<0.001
Stroke	972 (63.43)	1,956 (149.25)	984 (85.82)	2.357 (2.182-2.545)	<0.001
AVI	8,089 (527.86)	1,890 (144.21)	−6,199 (−383.65)	0.271 (0.258-0.285)	<0.001
Noncardiovascular	48,509 (3,165.56)	84,689 (6,461.99)	36,180 (3,296.43)	2.056 (2.034-2.079)	<0.001
Bleeding	5,690 (371.31)	6,652 (507.57)	962 (136.26)	1.374 (1.326-1.424)	<0.001

AoV = aortic valve; AVI = aortic valve intervention; CI = confidence interval; TAVR = transcatheter aortic valve replacement.

TABLE 3 Most Frequent Causes of 1-Year Pre-TAVR and 1-Year Post-TAVR Hospitalizations

1-Yr Pre-TAVR		1-Yr Post-TAVR	
Percentage of All Hospitalizations (Hospitalizations per 1,000 Patient-Yrs)	Diagnosis	Diagnosis	Percentage of All Hospitalizations (Hospitalizations per 1,000 Patient-Yrs)
17.9 (179)	Aortic valve disorders	Heart failure	14.2 (142)
15.9 (159)	Heart failure	Septicemia	4.2 (42)
4.6 (46)	MI	Rehab	3.7 (37)
3.7 (37)	CAD	Pneumonia	3.6 (36)
2.9 (29)	Pneumonia	Acute kidney injury	2.5 (25)
2.8 (28)	Atrial fibrillation	Atrial fibrillation	2.1 (21)
2.6 (26)	Mitral regurgitation and aortic stenosis	Urinary tract infection	1.8 (18)
2.2 (22)	Rehab	GI bleeding	1.7 (17)
1.7 (17)	COPD	COPD	1.5 (15)
1.6 (16)	GI bleeding	MI	1.4 (14)
1.50 (15)	Septicemia	Post-operative infection	1.3 (13)
1.42 (14)	Acute kidney injury	Respiratory failure	1.2 (12)

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; GI = gastrointestinal; MI = myocardial infarction; TAVR = transcatheter aortic valve replacement.

Table 2). The top causes for noncardiovascular hospitalizations in the year after TAVR were septicemia, pneumonia, inpatient rehabilitation, acute kidney injury, urinary tract infections, gastrointestinal bleeding, chronic obstructive pulmonary disease, and respiratory failure (Table 3). Similar patterns were seen in the TF subgroup (Online Table 2TF). Additionally, hospitalizations and hospitalized days due to all-cause bleeding increased after the procedure compared with before the procedure. Only 221 of 1,295 (17.1%) of bleeding hospitalizations in the year after TAVR occurred in the first 30 days post-TAVR. Notably, post-TAVR discharge rates of warfarin (30.8% vs. 24.1%; $p < 0.001$), aspirin (89.5% vs. 84.5%; $p < 0.001$), and $P2Y_{12}$ inhibitor (63.9% vs. 59.3%; $p = 0.003$) were higher among those experiencing a bleeding hospitalization post-TAVR than those who did not. Among those who survived for a full year after TAVR, all event rates changed in a similar fashion to the full cohort, except for all-cause readmissions, which decreased (Online Table 3).

Unlike in the overall cohort, in the TF subgroup, all-cause hospitalizations did not change significantly in the year after TAVR compared with the year prior to TAVR. Aortic valve disease was the single most common cause of hospitalization in the year prior to TAVR, and HF hospitalization was the most common cause of hospitalization after TAVR. As in the overall analysis, HF hospitalizations and hospitalized days decreased in the year after TAVR and decreased dramatically when aortic valve disorders were included as causes of HF hospitalizations (Online Figures 2TF and 3TF). Stroke, bleeding, and noncardiovascular hospitalizations and hospitalized days all increased significantly in the year after compared with the year before—just as in the overall analysis.

CHANGE IN HOSPITALIZATION RATES 2 YEARS PRIOR TO TAVR THROUGH 1 YEAR AFTER TAVR. To understand whether the changes in hospitalization rates were due to aging, we performed a sensitivity analysis comparing the hospitalization rate 2 years prior to TAVR versus the rate 1 year prior to TAVR among patients with at least 2 years of Medicare data available prior to TAVR. All-cause hospitalization rate increased from 574.3 per 1,000 patient-years 2 years prior to TAVR to 1,287.2 per 1,000 patient-years 1 year prior to TAVR (rate ratio: 2.24; $p < 0.001$). HF (rate ratio: 3.86; $p < 0.001$), HF plus aortic valve disease (rate ratio: 5.31; $p < 0.001$), stroke (rate ratio: 1.26; $p = 0.034$), noncardiovascular (rate ratio: 1.43; $p < 0.001$), and bleeding hospitalizations (rate ratio: 1.78; $p < 0.001$) all increased in the year prior to TAVR compared with 2 years prior to TAVR (Table 4).

Thus, compared with the change in hospitalizations from 2 years before TAVR to 1 year before TAVR,

TABLE 4 Hospitalizations and Hospitalization Rates the Year Prior to TAVR Versus 2 Years Prior to TAVR

Event	Observed Rates		Difference in Hospitalizations (Difference in Hospitalizations per 1,000 Patient-Yrs)	Rate Ratio (95% CI)	p Value
	2 Yrs Pre-TAVR (Hospitalizations per 1,000 Patient-Yrs)	1-Yr Pre-TAVR (Hospitalizations per 1,000 Patient-Yrs)			
Any readmission	8,606 (574.35)	19,287 (1,287.17)	10,681 (712.82)	2.241 (2.185–2.299)	<0.001
Heart failure	1,113 (74.28)	4,298 (286.84)	3,185 (212.65)	3.862 (3.615–4.125)	<0.001
Heart failure and AoV disease	1,444 (96.37)	7,665 (511.55)	62,221 (415.18)	5.308 (5.018–5.615)	<0.001
Stroke	157 (10.48)	197 (13.15)	40 (2.67)	1.255 (1.017–1.548)	0.034
AVI	10 (0.67)	70 (4.67)	60 (4.0)	7.000 (3.609–13.579)	<0.001
Noncardiovascular	5,237 (349.51)	7,512 (501.33)	2,275 (151.82)	1.434 (1.385–1.486)	<0.001
Bleeding	627 (41.84)	1,117 (74.55)	490 (32.71)	1.781 (1.616–1.965)	<0.001

Abbreviations as in Table 2.

in the year after TAVR there was a smaller increase in all-cause readmission (rate ratio: 1.045 vs. 2.241), and bleeding (rate ratio: 1.318 vs. 1.781) HF readmissions decreased in the year after TAVR versus the year before TAVR (rate ratio: 0.866), whereas they increased in the year prior to TAVR versus 2 years prior to TAVR (rate ratio: 3.86). Similar trends and findings were present in the TF subgroup (Online Table 3TF).

SUBGROUPS ASSOCIATED WITH DECREASED HOSPITALIZATIONS AFTER TAVR AMONG 1-YEAR SURVIVORS. To avoid the possibility that death in the year after TAVR would artificially decrease the number of hospitalizations post-TAVR, we identified factors associated with decreased hospitalizations in the year after TAVR among 1-year survivors (**Figure 2**). In general, higher-risk patients (age >95 years, prior myocardial infarction, prior stroke, home oxygen, NYHA functional class IV, moderate/severe aortic insufficiency, moderate/severe mitral insufficiency, and LVEF <30%) had the greatest reduction in post-TAVR hospitalizations compared with pre-TAVR. Similar findings were present in the TF subgroup (Online Figure 4TF).

INPATIENT MEDICARE COSTS. After exclusion of the index TAVR hospitalization, mean Medicare inpatient costs in the year prior to TAVR were $21,519 with a median of $13,652 compared with $20,425 and $10,174, respectively, in the year after TAVR (ratio: 0.95; 95% confidence interval: 0.92 to 0.98; $p < 0.01$) (**Table 5**). A cost ratio of 0.95 reflects a cost difference of ~–$1,090 for patients with mean ($21,519) pre-TAVR costs. A cost ratio of 0.95 reflects a cost difference of ~–$680 for patients with median ($13,652) pre-TAVR costs. This translated to mean pre-TAVR and post-TAVR costs per hospitalized day that were similar at ~$3,700 (Online Table 4). After excluding patients who died within 1 year after TAVR as a sensitivity analysis, costs remained slightly lower post-TAVR compared with pre-TAVR. After including index TAVR hospitalization costs as part of the post-TAVR costs, however, inpatient costs increased post-TAVR compared with pre-TAVR among the overall cohort and those that survived 1-year post-TAVR (**Table 5**). Similar findings were present in the TF subgroup (Online Table 4TF).

DISCUSSION

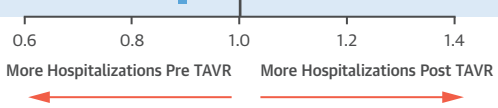
There are 4 major findings from this analysis of commercial TAVR in the United States:

1. Following TAVR, the most common reason for repeat hospitalization was HF.
2. In the year post-TAVR, the rate of HF hospitalizations and hospital days decreased significantly compared with the pre-TAVR period.
3. In the year post-TAVR, the rate of all-cause and noncardiovascular hospitalizations increased; however, the increase in all-cause hospitalization was less than the increases from 2 years prior to TAVR compared with 1 year prior to TAVR.
4. Inpatient Medicare costs were lower in the year after TAVR compared with the year pre-TAVR.

The PARTNER (Placement of Aortic Transcatheter Valves) B trial (2) compared TAVR versus medical therapy among those at prohibitive surgical risk, and a subsequent cost-effectiveness analysis evaluated health care resource utilization in the context of this clinical trial (8). Due to the lack of a large, multicenter, matched medical control group, however, there have been no large, multicenter, "real world" comparisons of health care resource utilization in TAVR versus medical therapy. To address the effect of TAVR on "real world" inpatient health care resource utilization, we compared cardiovascular event rates and costs pre-TAVR and post-TAVR, using pre-TAVR health care utilization as a "control period" approximating medical therapy assuming that pre-TAVR resource utilization would have continued had TAVR not been performed. Under this assumption, our study is the first to address the effect of TAVR on "real world" inpatient health care resource utilization. Additionally, using the TVT Registry, which captures all commercial TAVR implantations in the United States, we have presented the first study of the *change* in nonfatal major cardiovascular and noncardiovascular outcomes and hospital days after TAVR. We have shown that the rate of HF hospitalizations decreases in the year post-TAVR (rate ratio: 0.87), despite being on the rise in the 2 years prior to TAVR (rate ratio: 3.86); the rate of all-cause hospitalization increases less post-TAVR (rate ratio: 1.04) compared with 2 years prior to TAVR (rate ratio: 2.24); and noncardiovascular hospitalization increases more post-TAVR (rate ratio: 1.75) than 2 years pre-TAVR (rate ratio: 1.43). These findings stand in contrast to the result in PARTNER B, where TAVR was associated with a reduction in all-cause hospitalizations compared with patients treated with medical therapy, and there was no significant difference in noncardiovascular hospitalizations between TAVR and medical therapy (8). These discrepancies may be due to a decreasing 1-year mortality rate in "real world" TAVR (23.7% in the TVT Registry [10] vs. 50.7% in PARTNER B medical therapy [2]) as patients with aortic stenosis receive TAVR in lower-risk

FIGURE 2 Hospitalization Rate Post-TAVR Versus Pre-TAVR Among 1-Year Survivors By Subgroups

Subgroups	Pre-TAVR	Post-TAVR	Ratio (95% CI)	P Value
Age				
<75	2,062 (1,352.13)	1,723 (1,129.84)	0.84 (0.78, 0.89)	<0.01
75-84	5,584 (1,202.93)	5,005 (1,078.20)	0.90 (0.86, 0.93)	<0.01
85-94	6,042 (1,118.27)	5,302 (981.31)	0.88 (0.85, 0.91)	<0.01
95+	255 (1,159.09)	198 (900.00)	0.78 (0.64, 0.94)	<0.01
Sex				
Male	6,615 (1,149.64)	5,783 (1,005.04)	0.87 (0.84, 0.91)	<0.01
Female	7,328 (1,214.05)	6,445 (1,067.76)	0.88 (0.85, 0.91)	<0.01
Race				
Non-Hispanic white	12,811 (1,165.48)	11,286 (1,026.75)	0.88 (0.86, 0.90)	<0.01
Other	1,132 (1,418.55)	942 (1,180.45)	0.83 (0.76, 0.91)	<0.01
BSA				
<2 m^2	10,782 (1,198.93)	9,256 (1,029.24)	0.86 (0.83, 0.88)	<0.01
≥2 m^2	3,161 (1,130.14)	2,972 (1,062.57)	0.94 (0.89, 0.99)	0.02
Prior MI				
Yes	3,971 (1,385.07)	3,079 (1,073.94)	0.78 (0.74, 0.81)	<0.01
No	9,972 (1,117.56)	9,149 (1,025.33)	0.92 (0.89, 0.94)	<0.01
Prior stroke or TIA				
Yes	2,931 (1,345.11)	2,405 (1,103.72)	0.82 (0.78, 0.87)	<0.01
No	11,012 (1,145.77)	9,823 (1,022.06)	0.89 (0.87, 0.92)	<0.01
Prior PAD				
Yes	4,524 (1,271.50)	4,073 (1,144.74)	0.90 (0.86, 0.94)	<0.01
No	9,419 (1,144.19)	8,155 (990.65)	0.87 (0.84, 0.89)	<0.01
COPD				
None/mild	9,609 (1,100.56)	8,358 (957.28)	0.87 (0.84, 0.90)	<0.01
Moderate	2,171 (1,366.27)	2,014 (1,267.46)	0.93 (0.87, 0.99)	0.02
Severe	2,070 (1,489.21)	1,776 (1,277.70)	0.86 (0.81, 0.91)	<0.01
GFR				
<15 or dialysis	823 (2,094.15)	747 (1,900.76)	0.91 (0.82, 1.00)	0.06
15-29	885 (1,603.26)	777 (1,407.61)	0.88 (0.80, 0.97)	<0.01
30-59	6,039 (1,232.45)	5,254 (1,072.24)	0.87 (0.84, 0.90)	<0.01
60-89	4,701 (1,034.32)	4,128 (908.25)	0.88 (0.84, 0.92)	<0.01
90+	1,495 (1,067.86)	1,322 (944.29)	0.88 (0.82, 0.95)	<0.01
Home oxygen				
Yes	2,345 (1,676.20)	1,888 (1,349.54)	0.81 (0.76, 0.86)	<0.01
No	11,598 (1,116.16)	10,340 (995.09)	0.89 (0.87, 0.92)	<0.01
Current/recent smoker				
Yes	673 (1,306.80)	548 (1,064.08)	0.81 (0.73, 0.91)	<0.01
No	13,270 (1,176.94)	11,680 (1,035.92)	0.88 (0.86, 0.90)	<0.01
Diabetes				
Yes	5,300 (1,298.07)	4,730 (1,158.46)	0.89 (0.86, 0.93)	<0.01
No	8,643 (1,121.45)	7,498 (972.88)	0.87 (0.84, 0.89)	<0.01
NYHA class				
IV	3,233 (1,451.73)	2,560 (1,149.53)	0.79 (0.75, 0.83)	<0.01
Other	10,710 (1,119.94)	9,668 (1,010.98)	0.90 (0.88, 0.93)	<0.01
Afib/flutter				
Yes	6,378 (1,374.27)	5,481 (1,181.00)	0.86 (0.83, 0.89)	<0.01
No	7,565 (1,058.19)	6,747 (943.77)	0.89 (0.86, 0.92)	<0.01



BSA = body surface area; CI = confidence interval; COPD = chronic obstructive pulmonary disease; GFR = glomerular filtration rate; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PAD = peripheral artery disease; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement; TIA = transient ischemic attack.

Continued on the next page

FIGURE 2 Continued

Subgroups	Pre-TAVR	Post-TAVR	Ratio (95% CI)	P Value
Aortic insufficiency				
Moderate/severe	2,790 (1,205.18)	2,199 (949.89)	0.79 (0.75, 0.83)	<0.01
Other	11,153 (1,177.10)	10,029 (1,058.47)	0.90 (0.88, 0.92)	<0.01
Mitral insufficiency				
Moderate/severe	4,463 (1,310.33)	3,690 (1,083.38)	0.83 (0.79, 0.86)	<0.01
Other	9,480 (1,130.73)	8,538 (1,018.37)	0.90 (0.87, 0.93)	<0.01
Tricuspid insufficiency				
Moderate/severe	3,372 (1,252.14)	3,045 (1,130.71)	0.90 (0.86, 0.95)	<0.01
Access site				
Transfemoral	8,476 (1,146.65)	7,249 (980.65)	0.86 (0.83, 0.88)	<0.01
Other	5,467 (1,243.07)	4,979 (1,132.11)	0.91 (0.88, 0.95)	<0.01
Procedure year				
2011-2012	3,003 (1,368.73)	2,419 (1,102.55)	0.81 (0.76, 0.85)	<0.01
2013	5,146 (1,179.19)	4,420 (1,012.83)	0.86 (0.83,0.89)	<0.01
2014	5,794 (1,107.42)	5,389 (1,03.01)	0.93 (0.90, 0.97)	<0.01
LVEF				
<30	1,141 (1,537.74)	726 (978.44)	0.64 (0.58, 0.70)	<0.01
30-45	2,932 (1,418.48)	2,208 (1,068.21)	0.75 (0.71, 0.80)	<0.01
>45	9,870 (1,098.99)	9,294 (1,034.85)	0.94 (0.92, 0.97)	<0.01
Baseline KCCQ				
<25	3,016 (1,420.63)	2,542 (1,197.36)	0.84 (0.80, 0.89)	<0.01
25-49	7,886 (1,208.21)	6,988 (1,070.63)	0.89 (0.86, 0.92)	<0.01
50-74	2,163 (991.29)	1,927 (883.13)	0.89 (0.84, 0.95)	<0.01
≥75	878 (916.49)	771 (804.80)	0.88 (0.80, 0.97)	<0.01
Five meter walk				
Not performed	5,353 (1,276.96)	4,451 (1,061.78)	0.83 (0.80, 0.87)	<0.01
Unable to walk	1.353 (1,433.26)	1,175 (1,244.70)	0.87 (0.80, 0.94)	<0.01
>10 s	2.275 (1,278.09)	2,086 (1,171.91)	0.92 (0.86, 0.97)	<0.01
7-10 s	3,530 (1,113.21)	3,129 (986.75)	0.89 (0.84, 0.93)	<0.01
≤6 s	1,432 (840.87)	1,387 (814.45)	0.97 (0.90, 1.04)	0.40
STS PROM				
<8%	7,430 (1,013.09)	6,783 (924.87)	0.91 (0.88, 0.94)	<0.01
8-15%	4,705 (1,378.15)	3,893 (1,140.30)	0.83 (0.79, 0.86)	<0.01
>15%	1,808 (1,736.79)	1,552 (1,490.87)	0.86 (0.80, 0.92)	<0.01

groups and at earlier stages in the natural history of severe AS in light of expanding indications. Decreased mortality due to AS may allow for greater longevity and, thus, more opportunity for noncardiovascular hospitalizations.

NONCARDIOVASCULAR HOSPITALIZATIONS. The post-TAVR increase we observed in noncardiovascular hospitalizations appears to be driven by sepsis, pneumonia, chronic obstructive pulmonary disease, respiratory failure, and bleeding. Previous studies of TAVR populations have identified noncardiovascular causes as being important in both 30-day readmission (11) as well as cause of death (12,13). These studies specifically identified sepsis/infection and bleeding as significant causes of death and 30-day readmission; however, ours is the first study to implicate them as: 1) the major drivers of noncardiovascular hospitalizations through 1 year after TAVR; and 2) a major cause for increased hospitalizations and hospital days in the year after TAVR compared with the year before.

Previous data regarding bleeding post-TAVR suggests that the 7.5% of patients with in-hospital major bleeding had hospital costs $43,374 higher and length of stay 7.7 days longer than patients without bleeding complications. As a result, bleeding was a major driver of initial hospitalization costs and length of stay (14). In the present study, we specifically excluded bleeding occurring during the index hospitalization and have documented the importance of bleeding as a driver of hospitalizations and Medicare after the initial TAVR hospitalization. Similarly,

TABLE 5 Medicare Costs

	Costs Within 1 Yr Before and After TAVR			
	Pre-TAVR	Post-TAVR	Cost Ratio (95% CI)	p Value
Without including index (TAVR) hospitalization				
Total cohort				
Mean cost	$21,519 ± $23,701	$20,425 ± $28,151	0.95 (0.92-0.98)	<0.01
Median cost	$13,652 ($4,315-$30,121)	$10,174 ($1,403-$27,299)		
1-yr survivors				
Mean cost	$19,722 ± $22,370	$17,882 ± $25,153	0.90 (0.88-0.93)	<0.01
Median cost	$12,195 ($3,744-$27,360)	$8,484 ($1,644-$23,378)		
Including index TAVR hospitalization*				
Total cohort				
Mean cost	$21,519 ± $23,701	$75,585 ± $41,135	3.56 (3.49-3.63)	<0.01
Median cost	$13,652 ($4,315-$30,121)	$65,660 ($48,592-$90,020)		
1-yr survivors				
Mean cost	$19,722 ± $22,370	$69,346 ± $35,735	3.57 (3.49-3.65)	<0.01
Median cost	$12,195 ($3,744-$27,360)	$61,119 ($46,294-$82,647)		

Values are mean ± SD or median (interquartile range), unless otherwise indicated. *Index hospitalization costs were included in post-TAVR hospital costs.
Abbreviations as in Table 2.

previous studies of hospitalizations (15) and deaths (12) after TAVR have highlighted the fact that noncardiovascular causes, including bleeding (16), accounted for the majority of hospitalizations and death in the year after TAVR. Unfortunately, we did not have access to pre-TAVR antithrombotic use, and therefore, we could not assess whether a change in antithrombotic agents was the cause of changes in bleeding hospitalizations pre-TAVR versus post-TAVR.

We have shown that noncardiovascular hospitalizations increase to a greater extent from the year before TAVR to the year after TAVR than from 2 years prior to TAVR to 1 year prior to TAVR. However, we acknowledge that many disease states show nonlinear increases in hospitalizations with age (17). Thus, the increase in noncardiovascular hospitalizations may be due to: 1) nonlinear "background" increases in noncardiovascular hospitalizations that can be ascribed to "aging" or frailty; or 2) an aging/frailty effect potentiated by TAVR. Previous studies have shown that the prevalence of frailty among patients undergoing TAVR is between 50% and 70% (18). Because frailty is defined as a geriatric syndrome characterized by impaired homeostasis and decreased physiological reserve, we suspect that even after a successful TAVR, the high prevalence of frailty puts patients at increased risk for both procedure- and nonprocedure-related future events. Further studies of interventions that can affect frailty after TAVR (rehabilitation) will be needed to understand the exact mechanism for increased noncardiovascular hospitalizations after TAVR.

CARDIOVASCULAR HOSPITALIZATIONS. We examined change in HF hospitalizations and found a reduction in the rate post-TAVR compared with pre-TAVR (rate ratio: 0.82; $p < 0.001$). Although patients with aortic stenosis may have multiple etiologies for HF, including aortic valve disease, independent left ventricular dysfunction, coronary disease, and HF with preserved ejection fraction, correction of the aortic gradient would be expected to reduce myocardial demand and left ventricular end-diastolic pressure—thereby improving symptoms. Because HF hospitalizations remain the single greatest driver of Medicare costs and valvular disease is one of the strongest predictors of costs among inpatients hospitalized for HF (19), a reduction in the rate of HF hospitalizations among those with severe AS undergoing TAVR might be expected to lead to an overall reduction in inpatient Medicare costs.

MEDICARE COSTS AND IMPLICATIONS FOR PAYORS AND PROVIDERS. When we examined Medicare claims in the year before and after TAVR (exclusive of the index TAVR admission), we found a reduction in cost ratios for inpatient Medicare costs among the overall cohort. Given significant Medicare expenditures in the last 6 months of life (17) and the ~20% 1-year mortality in patients undergoing TAVR in the United States (10), we examined changes in Medicare costs among those surviving 1 full year after TAVR and found a larger reduction in Medicare costs in this subgroup as well—findings similar to those observed in the PARTNER B randomized trial (8). Thus, despite the increase in stroke, bleeding, and noncardiovascular hospitalizations, TAVR and the

subsequent reduction in HF hospitalizations were associated with a decline in inpatient Medicare costs. This suggests that HF is the major driver of Medicare costs in the year pre-TAVR and post-TAVR. Of note, however, when costs for the TAVR procedure (and associated hospitalization) were also included in our analysis, post-TAVR inpatient costs were significantly higher than pre-TAVR. These results are similar to those observed in the PARTNER B randomized trial as well (8). As a result, further work will be needed to identify ways to reduce index TAVR resource utilization, presumably in part by reducing complications such as bleeding and stroke (14,20).

As payers and providers explore bundled payment approaches in TAVR to incentivize efficiency of care, identification of patient subgroups associated with increased or decreased resource utilization may provide opportunities to improve processes of care. In the present study, higher-risk patients (age >95 years, prior myocardial infarction, prior stroke, home oxygen, NYHA functional class IV, moderate/severe aortic insufficiency, moderate/severe mitral insufficiency, and LVEF <30%) had the greatest reduction in post-TAVR hospitalizations compared with pre-TAVR. Although previous reports have identified atrial fibrillation and peripheral artery disease as comorbidities associated with late hospitalizations after TAVR (15), we found no significant difference in the ratio of hospitalizations after TAVR compared with pre-TAVR in patients with and without these comorbidities. Compared with previous studies that investigated post-TAVR hospitalizations among subgroups, the present study normalizes post-TAVR hospitalization rates by considering pre-TAVR hospitalization rates. By using the pre-TAVR period as a control, our experimental design helps isolate the effect of TAVR subgroup by considering a patient's baseline hospitalization rate.

STUDY LIMITATIONS. This is a retrospective analysis of a prospective registry, and therefore, it cannot assess causation. Specifically, although we assessed bleeding 1-year pre-TAVR and post-TAVR, we did not have access to pre-TAVR antithrombotic regimens and, therefore, could not link changes in these medications with changes in bleeding events. The population used in this analysis was limited to those with successful linkage to fee-for-service CMS claims data and may therefore not be fully representative of all patients undergoing TAVR in the United States, although there were few clinically significant differences in baseline characteristics between those with and without fee-for-service CMS linkage. Additionally, the present analysis of Medicare costs is limited to inpatient costs only and does not account for costs associated with outpatient services or patient out-of-pocket costs. We focused on inpatient costs because most Medicare costs are for hospital services (11), and direct costs to Medicare (rather than out-of-pocket patient costs) are the most relevant measure of public health care resource expenditure for the creation of government health care policy. Last, the present analysis of health care resource use and Medicare costs in the year pre-TAVR and post-TAVR is likely to change as delivery of TAVR care matures, TAVR enters intermediate and potentially low-risk populations, and processes of care improve with dissemination of best practices.

CONCLUSIONS

Patients undergoing TAVR in U.S. clinical practice had an increase in all-cause, noncardiovascular, bleeding, and stroke hospitalization rates, but a decrease in HF hospitalization rates post-TAVR compared with pre-TAVR. These changes in resource utilization were associated with a modest reduction in Medicare costs in the year post-TAVR compared with the year pre-TAVR (not including the cost of the TAVR hospitalization itself). Among all patients undergoing TAVR, only those with LVEF <30% have a reduction in overall hospitalizations post-TAVR compared with pre-TAVR. Payers and providers seeking to streamline resource use may consider targeting strategies designed to improved processes of care among patients with increased resource utilization post-TAVR compared with pre-TAVR.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: Compared with the year before, hospitalizations for HF decrease in the year following TAVR, whereas noncardiovascular hospitalizations increase.

TRANSLATIONAL OUTLOOK: Strategies that improve processes of care for patients prone to high post-procedural resource utilization could improve the health economic value of TAVR.

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KEY WORDS bleeding, costs, heart failure, hospitalizations, Medicare, transcatheter aortic valve replacement

APPENDIX For supplemental tables and figures, please see the online version of this paper.