



ORIGINAL RESEARCH

Comorbidity Burden and Adverse Outcomes After Transcatheter Aortic Valve Replacement

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BACKGROUND: Transcatheter aortic valve replacement (TAVR) has become the preferred treatment for symptomatic patients with aortic stenosis and elevated procedural risk. Many deaths following TAVR are because of noncardiac causes and comorbid disease burden may be a major determinant of postprocedure outcomes. The prevalence of comorbid conditions and associations with outcomes after TAVR has not been studied.

METHODS AND RESULTS: This was a retrospective single-center study of patients treated with TAVR from January 2015 to October 2018. The association between 21 chronic conditions and short- and medium-term outcomes was assessed. A total of 341 patients underwent TAVR and had 1-year follow-up. The mean age was 81.4 (SD 8.0) years with a mean Society of Thoracic Surgeons predicted risk of mortality score of 6.7% (SD 4.8). Two hundred twenty (65%) patients had ≥ 4 chronic conditions present at the time of TAVR. There was modest correlation between Society of Thoracic Surgeons predicted risk of mortality and comorbid disease burden ($r=0.32$, $P<0.001$). After adjusting for Society of Thoracic Surgeons predicted risk of mortality, age, and vascular access, each additional comorbid condition was associated with increased rates of 30-day rehospitalizations (odds ratio, 1.21; 95% CI, 1.02–1.44), a composite of 30-day rehospitalization and 30-day mortality (odds ratio, 1.20; 95% CI, 1.02–1.42), and 1-year mortality (odds ratio, 1.29; 95% CI, 1.05–1.59).

CONCLUSIONS: Comorbid disease burden is associated with worse clinical outcomes in high-risk patients treated with TAVR. The risks associated with comorbid disease burden are not adequately captured by standard risk assessment. A systematic assessment of comorbid conditions may improve risk stratification efforts.

Key Words: cardiac disease ■ cardiovascular disease risk factors ■ clinical cardiology ■ transcatheter aortic valve implantation

Aortic stenosis (AS) is increasingly common with advancing age¹ and if left untreated has a mortality rate of 50% 2 years after the onset of symptoms.² In recent years, transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of AS for many patients with symptomatic disease.^{3,4} While TAVR improves quality of life and decreases mortality, for high-risk patients mortality is $\approx 24\%$ 1 year after treatment.⁵ Approximately half of deaths after TAVR are noncardiac in nature⁶, an observation that

highlights the importance of understanding chronic disease burden for patients considering treatment.

Patients with cardiovascular disease are commonly affected by comorbid conditions⁷ that impact quality of life, overall prognosis, treatment decisions, and increase healthcare costs.⁸ Chronic conditions may decrease the absolute benefit of disease-specific interventions by presenting competing risks. For patients with cardiovascular disease, the most common comorbid conditions are hypertension,

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CLINICAL PERSPECTIVE

What Is New?

- This retrospective cohort study assessed the significance of comorbid diseases in 358 high-risk patients treated with transcatheter aortic valve replacement.
- Increased comorbid disease burden present at the time of transcatheter aortic valve replacement was associated with worse outcomes following treatment.
- Risks associated with comorbid disease burden are not adequately captured by standard risk assessment and should be incorporated into decision making for high-risk patients with AS.

What Are the Clinical Implications?

- Multiple chronic conditions are common for high-risk patients treated with transcatheter aortic valve replacement, and risks associated with multiple chronic conditions should be incorporated into procedural decision making.

Nonstandard Abbreviations and Acronyms

AS	aortic stenosis
STS-PROM	Society of Thoracic Surgeons predicted risk of mortality
TAVR	transcatheter aortic valve replacement

dyslipidemia, and diabetes mellitus.⁹ Chronic conditions for older adults with advanced cardiac disease, in particular those seeking interventional treatments, have not been systematically studied. TAVR, which has seen rapid adoption over the past few years, provides an opportunity to study chronic conditions for high-risk patients with advanced cardiovascular disease.

There is no consensus on how to assess chronic disease burden, and it is likely that different conditions are relevant for distinct clinical settings. Recently, a score based on the presence or absence of 21 cardiac and noncardiac conditions was shown to be predictive of 1-year mortality for older adults.¹⁰ The clinical relevance of these conditions for patients with advanced cardiovascular disease remains unknown. Here, using detailed chart review, our aim is to determine the association between comorbid disease burden and short- and medium-term clinical outcomes after TAVR, and to determine whether

comorbid disease burden has added prognostic significance beyond standard approaches to risk stratification.

METHODS

Cohort Description

This is a retrospective single-center cohort study that was performed at Tufts Medical Center (Boston, MA). The data that support the findings of this study are available from the corresponding author upon reasonable request. The study cohort included patients with symptomatic AS who underwent TAVR between January 2015 and October 2018. Severe AS was defined by standard echocardiographic criteria,¹¹ and all patients had symptoms at the time of treatment. All patients were deemed to be at elevated risk for conventional surgical aortic valve replacement. Patients were excluded from the study if they had a previous history of either a prior surgical or prior TAVR that was implanted before the study dates. This study was approved by the Tufts institutional review board and the informed consent requirement was waived.

Baseline Characteristics and Outcomes

The STS/ACC TVT Registry (Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry) was used to evaluate basic demographic data including the STS predicted risk of mortality (STS-PROM) score. Morbidity and mortality were assessed by investigating the 30-day rehospitalization rate, 30-day mortality (a composite of 30-day rehospitalization and 30-day mortality), and 1-year mortality from the studied patient population. The 1-year mortality outcome was determined through a combination of chart review and events identified in the Institutional STS/ACC TVT Registry report.

Comorbid Disease Burden

Comorbidity burden was assessed based on physician review of the electronic medical record. Consensus definitions of the 21 distinct conditions present in the Combined Comorbidity Score¹⁰ were created. The clinical definitions are shown in Table S1 and are consistent with the originally presented definitions.^{12,13} Presence or absence of a condition was defined based on whether or not the condition was present in the electronic medical record at any point in the year before TAVR. Two physician members of the study team (D.R.F. and M.D.R.) reviewed all records. Discrepancies and instances of diagnostic ambiguity were discussed by the study group to arrive at consensus.

Statistical Analysis

The overall prevalence of comorbid conditions was assessed. The 30-day follow-up was available for 346/358 (96.6%) patients and the 1-year follow-up was available for 341/358 (95%) patients. We present a complete case analysis of patients with 1-year follow-up. Event rates are presented across tertiles of comorbid diseases present at the time of TAVR. The association between comorbid disease burden and rates of 30-day rehospitalization, 30-day mortality, composite of 30-day rehospitalization and 30-day mortality, and 1-year mortality was assessed using logistic regression. Multivariable logistic regression was used to evaluate the association between comorbid disease burden with clinical outcomes after adjusting for age, STS-PROM, and vascular access site. Comorbid disease burden was plotted against STS-PROM at the time of TAVR. Correlation was assessed using the Pearson correlation coefficient.

RESULTS

The cohort consisted of 358 patients treated with TAVR during this timeframe. Our analysis focuses on the 341 patients (95%) with available 1 year follow-up. Baseline demographic, clinical, and echocardiographic parameters are shown in Table 1. The mean patient age was 81.4 years old (SD 8.0 years) and 51.9% of the patients were female. A transfemoral approach was performed with 86.8% of these patients. The average STS-PROM score was 6.7% (SD 4.8).

Outcomes

A total of 199 (58.4%) of patients had a long length of stay (defined as >4 days). The 30-day rehospitalization rate was 13.2%. The observed inpatient, 30-day, and 1-year mortality rates were 1.2% (4 patients), 2.9% (10 patients), and 9.1% (31 patients), respectively.

Comorbid Disease Burden

The average number of comorbid conditions present in the year leading up to TAVR was 4.4 (SD 1.9). A total of 325 (95%) of patients had ≥ 2 chronic conditions in the year before TAVR and 220 (65%) patients had ≥ 4 chronic conditions. The graphical representation of these comorbid conditions among the studied population is shown in Figure 1, while the full list of comorbid conditions is shown in Table 2. The most common noncardiac comorbid conditions seen in this patient population were anemias (132, 38.7%), chronic pulmonary disease (112, 32.8%), electrolyte disorders (73, 21.4%), and coagulopathy (71, 20.8%).

Table 1. Baseline Characteristics of Study Population

	Patients (N=341)
Age (y)	81.4 \pm 8.0
Race	
White	324 (95.0)
Black	3 (0.9)
Asian	10 (2.9)
Other*	4 (1.2)
Women	177 (51.9)
Previous PCI	78 (22.9)
Previous CABG	66 (19.4)
Previous stroke	46 (13.5)
Previous myocardial infarction	74 (21.7)
Current/recent smoker	14 (4.1)
Diabetes mellitus	115 (33.7)
Heart failure within 2 wks	312 (91.5)
NYHA Class	
I	13 (3.8)
II	49 (14.4)
III	223 (65.4)
IV	55 (16.1)
STS-PROM score, %	6.7 \pm 4.8
Echocardiographic parameters	
Left ventricular ejection fraction, %	54 \pm 13
Aortic-valve area, cm ²	0.8 \pm 0.2
Transaortic velocity, m/s	4.0 \pm 0.7
Mean pressure gradient of AV, mm Hg	40 \pm 15
Aortic valve annulus size, mm	25 \pm 3
Procedure status	
Elective	278 (81.5)
Urgent	63 (18.5)
Access site	
Transfemoral	296 (86.8)
Other	45 (13.2)

Data provided as mean \pm SD or n (%). AV indicates aortic valve; CABG indicates coronary artery bypass graft; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; and STS-PROM, Society of Thoracic Surgeons predicted risk of mortality.

*Other includes American Indian/Alaskan Native or Native Hawaiian/Pacific Islander.

Dementia was documented in 25 (7.3%) patients. Among these patients, 20 (5.9%) had a history of alcohol abuse and 19 (5.6%) had a history of renal dysfunction.

The association between burden of comorbid conditions and STS-PROM is shown in Figure 2. One hundred sixty-six (49%) patients had a STS-PROM score $\geq 4.0\%$ and high comorbid disease burden that was defined as ≥ 4 comorbid conditions (Q1, concordant risk markers). Sixty-five (19%) patients had a

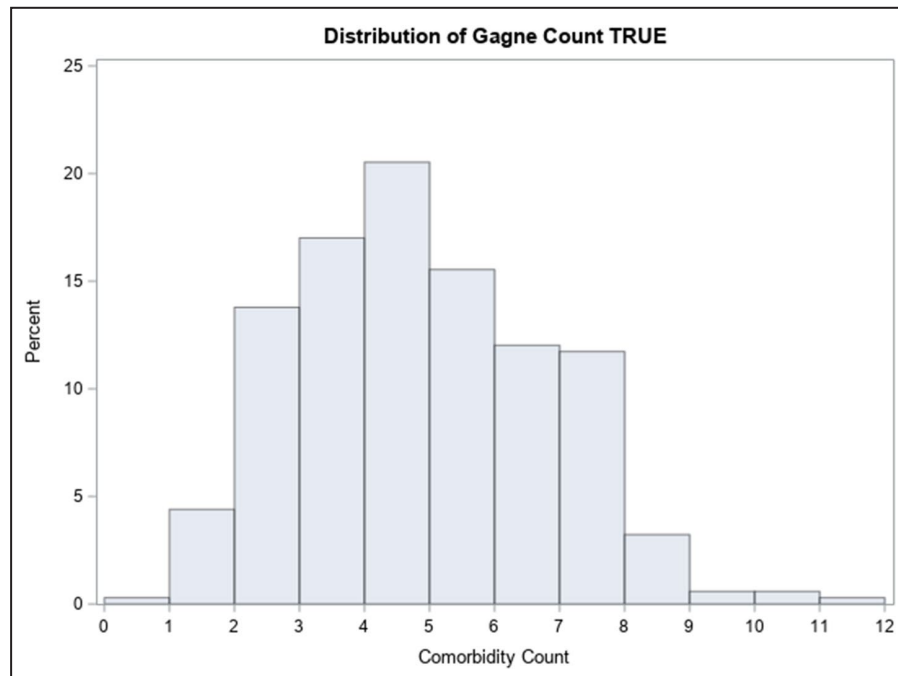


Figure 1. Distribution of comorbid disease count: a graphic representation of comorbid disease among the studied population.

The average number of comorbid conditions present in the year leading up to TAVR was 4.4 (SD 1.9). TAVR indicates transcatheter aortic valve replacement.

STS-PROM score $\geq 4.0\%$ and low comorbid disease burden defined as <4 comorbidity conditions (Q2, discordant risk markers). Fifty-six (16%) patients had a STS-PROM score $<4.0\%$ and low comorbid disease burden (Q3, concordant risk markers) and 54 patients (16%) had a STS-PROM score $<4.0\%$ with high comorbid disease burden at the time of TAVR (Q4, discordant risk markers). Twenty-five percent of patients with high comorbid disease burden present at the time of TAVR (Q1 + Q4) had a STS-PROM score $<4.0\%$. There was modest correlation between STS-PROM and comorbid disease burden ($r=0.32$, $P<0.001$).

Association with Clinical Outcomes

As the burden of comorbid disease present at the time of TAVR increases, rates of 30-day rehospitalization, 30-day rehospitalization or death, and 1-year mortality increase (Table 3). Average length of stay also increased as comorbid disease burden increased ($P=0.0017$). There was no association between comorbid disease burden and inpatient mortality or 30-day mortality, though rates of these events were low (4 total inpatient deaths, 10 total deaths by 30 days). The association between comorbid disease burden and outcomes is shown in Table 4. Each additional comorbid condition present at the time of TAVR was associated with increased 30-day rehospitalization rate (odds ratio [OR], 1.28;

95% CI, 1.09–1.51), 30-day mortality (OR, 1.37; 95% CI, 1.00–1.87), composite of 30-day rehospitalizations and mortality (OR, 1.27; 95% CI, 1.09–1.49), and 1-year mortality (OR, 1.39; 95% CI, 1.14–1.68). After adjusting for age, STS-PROM, and access site, each additional comorbid condition present at the time of TAVR remained independently associated with 30-day rehospitalizations (OR, 1.21; 95% CI, 1.02–1.44), a composite of 30-day rehospitalization and 30-day mortality (OR, 1.20; 95% CI, 1.02–1.42), and 1-year mortality (OR, 1.29; 95% CI, 1.05–1.59).

DISCUSSION

These data demonstrate that comorbid conditions are common for patients with elevated procedural risk and symptomatic AS who are treated with TAVR and that chronic disease burden present at the time of TAVR is associated with worse outcomes and increased resource utilization after the procedure. Two thirds of high-risk patients have ≥ 4 chronic conditions present at the time of treatment and of those, 25% have STS-PROM $<4.0\%$. Taken together, these observations suggest that for patients considered for treatment with TAVR, there are clinically relevant short- and medium-term risks associated with comorbid illness that are not adequately captured by standard risk assessment.

Table 2. Comorbidity Count

Hypertension	284 (83.3)
Cardiac arrhythmia	231 (67.7)
Congestive heart failure	223 (65.4)
Deficiency anemia	132 (38.7)
Peripheral vascular disease	114 (33.4)
Chronic pulmonary disease	112 (32.8)
Fluid and electrolyte disorders	73 (21.4)
Coagulopathy	71 (20.8)
Cerebrovascular disease	62 (18.2)
Active tumor	34 (10.0)
Complicated diabetes mellitus	30 (8.8)
Dementia	25 (7.3)
Pulmonary circulation disorders	24 (7.0)
Alcohol abuse	20 (5.9)
Renal failure	19 (5.6)
Liver disease	12 (3.5)
Hemiplegia	10 (2.9)
Weight loss	10 (2.9)
Metastatic cancer	4 (1.2)
Psychosis	1 (0.3)
HIV/AIDS	0 (0.0)

Full list of comorbid conditions for our studied population. Data provided as n (%). The most common conditions were hypertension (284, 83.3%), cardiac arrhythmias (231, 67.7%), and congestive heart failure (223, 65.4%). The most common noncardiac comorbid conditions seen in this patient population were anemias (132, 38.7%), chronic pulmonary disease (112, 32.8%), electrolyte disorders (73, 21.4%), and coagulopathy (71, 20.8%).

The STS-PROM was used for inclusion in early TAVR clinical trials and is a prediction tool that continues to play a role in preprocedure risk stratification. This was the primary motivation for including this variable in our analysis. There are known limitations to these predictive models applied to TAVR. These regression models were originally created to predict 30-day outcomes for patients undergoing surgical aortic valve replacement with or without coronary artery bypass grafting¹⁴ and as a result, tend to perform poorly when used to predict in-hospital and 30-day mortality after TAVR.¹⁵ This poor performance may be because important risk predictors are not included in these models—in the effort to achieve a parsimonious (and usable) model. Newer models^{16,17} exclude many of the chronic conditions studied here and thus are unlikely to fully capture the risks associated with comorbid disease burden present at the time of treatment. A more comprehensive approach to risk stratification should include conceptions of procedural risk and also consideration of the competing risks that may be present from comorbid conditions.

It is increasingly recognized that information about comorbid diseases should be considered when making treatment decisions for older adults

with advanced cardiac disease. This issue is especially important in the context of treatment decisions for patients with structural heart disease since older adults with increased procedural risk are regularly treated with these advanced procedures. Comorbid disease burden has historically been difficult to define and quantify¹⁸ and as a result there is no consensus method of assessment. The Combined Comorbidity Score¹⁰ was recently proposed as a way to combine existing models to predict 1-year mortality. In a claims-based environment, this score demonstrated better performance (discrimination and calibration) than preexisting models for predicting long-term mortality for older adults. Given the strengths of this score (it captures both cardiac and noncardiac conditions) and the potential applicability to large databases, we studied electronic medical record–based definitions of the chronic conditions contained in this index. We demonstrate that worse outcomes are seen as the number of chronic conditions present at the time of TAVR increases. The associations seen with these conditions stand to be replicated in larger (multicenter) databases since the comorbidity index used here is compatible with claims-based data resources.

Many of the comorbid conditions studied here, when evaluated in isolation, have been shown to be associated with worse outcomes after TAVR. For example, patients with end-stage renal disease¹⁹ and chronic pulmonary disease²⁰ are documented to have worse outcomes after TAVR. Unfortunately, analyses of lone chronic conditions do not adequately capture the complexity of older adults encountered in real-world practice who often have more than 1 condition and who would have been excluded from pivotal clinical trials (eg, an 88-year-old who has symptomatic AS, peptic ulcer disease, thrombocytopenia, and end-stage renal disease and who is referred for treatment). Multiple conditions (and multiple treatments) that may interact with each other can increase the risk of adverse outcomes over time and present competing risks that often persist after AS is treated. Ultimately, understanding the comorbid disease burden and specific interactions between conditions and treatments and planned procedures as well as patient-centered goals can enhance shared decision-making for these high-risk older adults.

Limitations

There are several limitations to this analysis. Because this is a single-center retrospective study, the relevance to other electronic medical records and other health systems needs to be further explored. The limited sample size and rare outcomes do not allow us to create a usable predictive model and that is

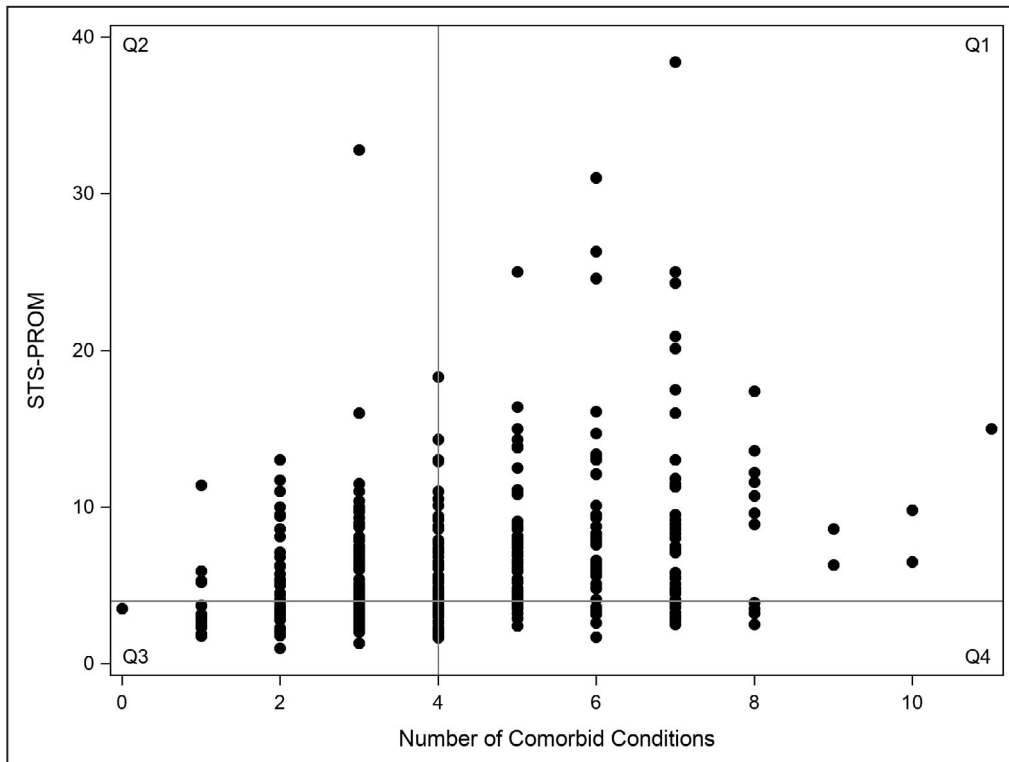


Figure 2. STS-PROM vs comorbidity count: a graphic representation of STS-PROM plotted against comorbid disease burden.

Q1 identifies a STS-PROM score $\geq 4.0\%$ and high comorbidity burden (≥ 4 comorbid conditions), which represents 166 patients (49%) from the studied population. Q2 represents a STS-PROM score $\geq 4.0\%$ and low comorbidity burden (< 4 comorbid conditions), which represents 65 patients (19%) from the studied population. Q3 represents a STS-PROM score $< 4.0\%$ and low comorbidity burden (< 4 comorbid conditions), which represents 56 patients (16%) from the studied population. Q4 highlights a STS-PROM score $< 4.0\%$ and high comorbidity burden (> 4 comorbid conditions), which represents 54 patients (16%) from the studied population. STS-PROM indicates Society of Thoracic Surgeons predicted risk of mortality.

not our intent, because there are numerous predictive models available for TAVR. While we assessed comorbid diseases based on detailed chart review, the reproducibility of these results should be explored using claims data so that these observations

can be assessed in larger data sets. The comorbidity index that was used here was originally derived using claims data. Additionally, the outcomes that were evaluated here were hard clinical outcomes that are relatively easily measured (rehospitalizations and

Table 3. Clinical Outcomes by Comorbidity Count Tertile

Comorbid Condition Tertile	1	2	3	P Value
Comorbid condition range	0–3	4–5	6–11	
N	121	123	97	
Age, mean (SD)	81.0 (8.5)	83.2 (7.4)	79.7 (7.6)	0.2687
STS-PROM, mean (SD)	5.4 (3.8)	6.4 (3.7)	9.1 (6.5)	< 0.0001
Length of stay, mean (SD)	5.6 (4.3)	7.2 (4.8)	7.9 (6.6)	0.0017
Inpatient mortality, n (%)	2 (1.7)	0 (0.0)	2 (2.1)	0.8589
30-d rehospitalization, n (%)	8 (6.6)	17 (13.8)	20 (20.6)	0.0023
30-d death/rehosp, n (%)	10 (8.3)	17 (13.8)	22 (22.7)	0.0027
30-d mortality, n (%)	3 (2.5)	1 (0.8)	6 (6.2)	0.1386
1-y mortality, n (%)	4 (3.3)	12 (9.8)	15 (15.5)	0.0018

Outcomes according to comorbid disease burden. Presented as tertile of cumulative conditions present at the time of TAVR. P value represents P for trend across tertiles. STS-PROM indicates Society of Thoracic Surgeons Predicted Risk of Mortality; and TAVR, transcatheter aortic valve replacement.

Table 4. Comorbid Disease Burden Associations

Unadjusted			
Panel A	OR	95% CI	P Value
30-d rehospitalization	1.28	1.09–1.51	0.0025
30-d mortality	1.37	1.00–1.87	0.0470
30-d rehospitalization and mortality composite	1.27	1.09–1.49	0.0024
1-y mortality	1.39	1.14–1.68	0.0008
Adjusted for Age, STS-PROM Score, and Access Site			
Panel B	OR	95% CI	P Value
30-d rehospitalization	1.21	1.02–1.44	0.0337
30-d mortality	1.33	0.91–1.95	0.1385
30-d rehospitalization and mortality composite	1.20	1.02–1.42	0.0322
1-y mortality	1.29	1.05–1.59	0.0169

OR are presented as single condition increase in cumulative comorbid disease count present at the time of TAVR. Unadjusted associations with outcomes are presented in panel A. OR adjusted for age, STS-PROM, and access site are shown in panel B. OR indicates odds ratio; ST-PROM, Society of Thoracic Surgeons predicted risk of mortality; and TAVR, transcatheter aortic valve replacement.

mortality). There are also (perhaps more important) patient-centered outcomes that are likely more relevant for this patient population (for example, home time or symptomatic improvement).

CONCLUSIONS

This analysis demonstrates the importance of systematically assessing comorbid disease burden when considering treatment of complex older adults with symptomatic AS. High-risk patients considering TAVR have a significant burden of comorbid conditions present at the time of treatment and these risks are not adequately captured by standard risk assessment tools. These conditions are associated with worse outcomes and higher resource utilization after the procedure. A better understanding of the comorbid disease burden present at the time of treatment may lead to improved risk stratification tools and better help us improve our understanding of who is more (or less) likely to do well following treatment.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Table S1

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Supplemental Material

Table S1. Definitions of Comorbid Conditions.

Active tumor (includes lymphoma, leukemia)	Any tumor, lymphoma, or leukemia that was active or underwent treatment for within the 12 months prior to TAVR
Alcohol abuse	Alcohol dependence, history of alcohol withdrawal, or end-organ effects of chronic alcohol use such as amnesia, dementia, or psychosis, within the prior 12 months
Cardiac arrhythmia	Previous diagnosis of any supraventricular tachycardia (including atrial fibrillation, atrial flutter, atrial tachycardia, multifocal atrial tachycardia, AVNRT, AVRT), VT, VF, and/or Torsades de pointes. Also includes a previous diagnosis of recurrent or persistent sinus tachycardia, junctional tachycardia, or sick sinus syndrome. In addition, was considered positive if the patient had a bundle branch block, 1 st , 2 nd , or 3 rd degree AV block within the last 12 months or ever requiring pacemaker
Cerebrovascular Disease	Previous history of TIA, Ischemic Stroke (includes lacunar stroke) or hemorrhagic stroke ever in the patient's life as based on history or imaging
Chronic Pulmonary disease	Chronic obstructive or restrictive disease including but not limited to chronic bronchitis, emphysema, bronchiectasis, asthma, allergic alveolitis, pneumoconiosis, fibrotic lung disease
Coagulopathy	Factor deficiency, thrombocytopenia (defined as platelets \leq 120), qualitative platelet defect, or any unspecified coagulation defect in the last 12 months. Also includes a history of iatrogenic or pathogenic coagulopathy causing clinically significant hemorrhage ever in the patient's history
Complicated diabetes	Diabetes complicated by renal, ophthalmic, circulatory, and other complications. Includes patients with unknown complications with HbA1c \geq 8% within last 12 months
Congestive Heart Failure	Diastolic or systolic heart failure, cardiomyopathy, or heart transplant. Diastolic HF is defined by requirement of fluid removal by dialysis or a diuretic, and/or signs of diastolic HF on echocardiogram
Deficiency anemia	Anemia defined as (Male Hgb $<$ 13.5 AND Hct 37.0. Female Hgb $<$ 11.0 AND Hct $<$ 32.0 measured as such within the last 12 months) due to what is most likely nutritional deficiency such as iron, B12, folate or EPO deficiency in CKD
Dementia	Any dementia such as Alzheimer's, vascular, frontotemporal, lewy body, parkinsonian, or otherwise unspecified. For patients that had a designated MOCA conducted, a score of less than 22 was considered positive
Fluid and electrolyte disorders	Any derangement in Na, K, Mg, Ca (corrected for Alb or iCa), Phos, bicarbonate, or acidosis/ alkalosis seen on repeat measurements at least 72 consecutive hours apart immediately prior to TAVR
Hemiplegia	Spastic or flaccid hemiplegia or hemiparesis, mono-, di-, and paraplegia, and/or other unspecified paralytic syndromes
HIV/AIDS	Previous diagnosis of HIV

Hypertension	Diagnosis of hypertension ever in the patient's history
Liver disease	Active cirrhosis or history of previous liver transplant
Metastatic cancer	Active solid tumor with known metastatic disease within the 12 months prior to TAVR or requiring chemotherapy within that time period
Peripheral vascular disease	Previously diagnosed with peripheral vascular disease, including aortic aneurysm (at least moderate grade), intestinal ischemia (at least moderate stenosis), arterial dissection and stricture, and/or at least moderate peripheral arterial stenosis. Includes severe or heavy atherosclerosis/calcification of the peripheral vessels on imaging
Pulmonary circulation disorders	Pulmonary hypertension (excluding what is believed to be Group II, secondary to left heart disease). Includes active pulmonary embolism within last 12 months
Psychosis	History of schizophrenia, delusions, psychosis not otherwise specified ever
Renal Failure	CKD stage 5 (or eGFR < 15 prior to TAVR), dialysis dependence, or history of renal transplant
Weight loss	BMI < 20 or loss of >20% of weight over the previous 12-month period

Clinical definitions for comorbid conditions used in this study. The presence or absence of any of these conditions were based on whether or not the condition was present in the EMR at any point in the year prior to TAVR.