Outcomes of transcatheter aortic valve replacement for patients with severe aortic stenosis and concomitant aortic insufficiency: Insights from the TVT Registry

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Aims Data regarding outcomes for patients with severe aortic stenosis (AS) with concomitant aortic insufficiency (AI), undergoing transcatheter aortic valve replacement (TAVR) are limited**.** This study aimed to analyze the prevalence of severe AS with concomitant AI among patients undergoing TAVR and outcomes of TAVR in this patient group.

Methods and results Using data from the STS/ACC-TVT Registry, we identified patients with severe AS with or without concomitant AI who underwent TAVR between 2011 and 2016. Patients were categorized based on the severity of pre-procedural AI. Multivariable proportional hazards regression models were used to examine all-cause mortality and heart failure (HF) hospitalization at 1-year. Among 54,535 patients undergoing TAVR, 42,568 (78.1%) had severe AS with concomitant AI. Device success was lower in patients with severe AS with concomitant AI as compared with isolated AS. The presence of baseline AI was associated with lower 1 year mortality (HR 0.94 per 1 grade increase in AI severity; 95% CI, 0.91-0.98, $P < .001$) and HF hospitalization (HR 0.87 per 1 grade increase in AI severity; 95% CI, 0.84-0.91, $P < .001$).

Conclusions Severe AS with concomitant AI is common among patients undergoing TAVR, and is associated with lower 1 year mortality and HF hospitalization. Future studies are warranted to better understand the mechanisms underlying this benefit.

Short Abstract In this nationally representative analysis from the United States, 78.1% of patients undergoing TAVR had severe AS with concomitant AI. Device success was lower in patients with severe AS with concomitant AI as compared with isolated AS. The presence of baseline AI was associated with lower 1 year mortality (HR 0.94 per 1 grade increase in AI severity; 95% CI, 0.91-0.98, $P < .001$) and HF hospitalization (HR 0.87 per 1 grade increase in AI severity; 95% CI, 0.84-0.91, $P < .001$). (Am Heart J 2020;228:57-64.)

In patients with severe symptomatic aortic stenosis (AS), transcatheter aortic valve replacement (TAVR) is beneficial across a range of patient populations.[1-4] Frequently, patients with severe AS have concomitant aortic insufficiency (AI).[5] Patients with severe AS with concomitant AI represent a unique challenge as hemodynamics and pathophysiology differ from both isolated AS and AI.[6-8] Only limited studies are available regarding the pathophysiology and non-surgical management of severe AS with concomitant AI despite its high prevalence.[9-13] Prior studies of surgical aortic valve replacement (SAVR) for severe AS with concomitant AI have shown variable outcomes.[6,7] Whether similar findings are seen with TAVR is less clear. To address this gap in knowledge, we used data from the National Cardiovascular Data Registry (NCDR) Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry to examine the prevalence of severe AS with concomitant AI among patients undergoing TAVR in contemporary practice and whether the presence of pre-procedural AI affects early and late outcomes.

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Methods

Data source

The STS/ACC TVT Registry is the largest data repository and reporting infrastructure for TAVR and has been operational since 2011. Participation in the Registry is a requirement for reimbursement by the Centers for Medicare and Medicaid Services (CMS) for all centers performing TAVR in the United States. The Registry collects data on patient demographics, procedural details, and in-hospital, 30-day and 1-year outcomes (including patient-reported health status).[14] The data elements reported by the Registry are regularly audited for completeness and accuracy including yearly independent auditing of a random 10% of sites.[15] Additionally, the Registry has been linked to CMS claims data to facilitate the reporting of long-term-outcomes.[15] The statistical support for the study was provided by STS/ACC TVT registry. The authors were solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

Study cohort

The study cohort consisted of all TAVR procedures performed between 1/1/2011 and 3/31/2016 for isolated severe AS or severe AS with concomitant AI. Patients with a bicuspid aortic valve, pure AI, prior SAVR, or prior TAVR were excluded from this analysis. Although in-hospital outcomes are reported for the entire study cohort, the 1-year outcomes analysis included only patients with CMS linked data.

Definitions

Severity of AI was defined based on the greatest value within the 12 months prior to the procedure based on the American Heart Association/ACC practice guidelines for management of patients with valvular heart disease.[16] Details of the criteria used to define severity of AI are available in the TVT data coder dictionary and the online supplement.[17] All other registry based endpoints were reported using Valve Academic Research Consortium-2 (VARC-2) definitions.[18,19] Device success was defined as: absence of procedural mortality; correct positioning of a single prosthetic heart valve in the proper anatomical location; no prosthesis-patient mismatch; mean aortic valve gradient <20 mmHg or peak velocity <3 m/s; and no moderate or severe prosthetic valve insufficiency.[19] All site-reported events of stroke, transient ischemic attack, and repeat valve intervention were centrally adjudicated. One year mortality data were obtained using the Medicare Denominator file and 1-year heart failure hospitalizations were obtained from the inpatient Standard Analytic claims file by using the *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*) and *ICD-10* diagnosis codes (see Online Supplement for details).

End points

The co-primary end points of the study were 1-year all-cause mortality and heart failure (HF) hospitalization. Secondary end points included device success, residual AI, and in-hospital major vascular complications.

Statistical analysis

The study population was stratified into four groups based on the severity of AI at baseline: isolated severe AS, severe AS with trace or mild AI, severe AS with moderate AI, and severe AS with severe AI. Continuous variables are summarized using medians with 25^{th} and 75^{th} percentiles, and categorical variables are summarized as frequencies and percentages. Comparison across categories of AI was performed using Pearson χ^2 test or Fisher exact test for categorical variables and the Kruskal-Wallis test for continuous variables. Rates of mortality were estimated using the Kaplan-Meier method and compared across groups using the log-rank test. A Cox proportional hazards model with a robust sandwich covariance estimator was used to estimate the association between severe AS with concomitant AI category and mortality while accounting for the effect of clustering by hospital. For these analyses, severe AS with concomitant AI was modeled both as a categorical variable with isolated AS as the reference group and as an ordinal variable. The covariates included in these models were selected by expert opinion and are listed in Online Supplement Table I.[20,21] Multiple imputation was used to account for missing values for left ventricular internal diastolic dimensions, and single imputation was used for all other covariates. Results were combined across 20 imputed datasets.

For the endpoint of HF hospitalization, we plotted cumulative incidence curves for the 4 groups, accounting for the competing risk of death. Fine and Gray's sub-distribution hazards model was used to assess the association between HF hospitalization at 1-year and the severity of severe AS with concomitant AI , with death as a competing risk.[22] A robust sandwich covariance estimator was used to account for clustering of patients within sites. To test whether the effect of pre-procedure AI on outcomes was mediated by better tolerance of post-procedure AI, we repeated the multivariable analyses while also adjusting for the severity of post-procedural AI and by restricting the analysis to patients with trace or less post procedural AI. In addition, we also analyzed the interaction between year of procedure with 1-year outcomes. Because 1-year outcomes were available only in patients with CMS linked data, we compared the baseline characteristics and in-hospital outcomes in patients with and without long term data available. Because patients with CMS coverage are typically age 65 or older, we also compared the baseline characteristics and in-hospital outcomes in patients age 65 or older with and without long term follow-up.

We considered $P < .05$ to be significant for all analyses without adjustment for multiple comparisons. The analysis was performed using SAS version 9.4 (SAS

Table I. Baseline characteristics

	Isolated AS N = 11,967	AS–Mild AI N = 32,153	AS–Moderate AI N = 8933	AS–Severe AI N = 1482	*P*
Age in years	83.0 (77.0-87.0)	84.0 (78.0-88.0)	83.0 (77.0-87.0)	82.0 (76.0-87.0)	<.001
Sex					
Male	6014 (50.3%)	16,705 (52.0%)	4481 (50.2%)	757 (51.1%)	.001
Female	5952 (49.7%)	15,438 (48.0%)	4449 (49.8%)	725 (48.9%)	
Race					
White	11,394 (95.8%)	30,343 (95.0%)	8225 (92.8%)	1355 (92.4%)	<.001
Black	395 (3.3%)	1102 (3.5%)	435 (4.9%)	73 (5.0%)	
Other	103 (0.9%)	494 (1.5%)	205 (2.3%)	38 (2.6%)	
BMI§	28.0 (24.3-33.0)	26.9 (23.7-31.2)	26.0 (22.9-30.1)	26.1 (23.0-30.5)	<.001
Prior MI‖	2870 (24.0%)	8081 (25.2%)	2415 (27.1%)	365 (24.7%)	<.001
Prior CABG#	3232 (27.0%)	9083 (28.3%)	2476 (27.7%)	402 (27.1%)	.067
Prior stroke	1395 (11.7%)	3924 (12.2%)	1117 (12.5%)	192 (13.0%)	.194
Mitral valve disease	9227 (77.2%)	27,222 (84.8%)	7899 (88.6%)	1269 (86.0%)	<.001
Current/recent smoker	549 (4.6%)	1540 (4.8%)	622 (7.0%)	118 (8.0%)	<.001
Hypertension	10,765 (90.0%)	28,979 (90.2%)	8054 (90.2%)	1301 (87.8%)	.034
Diabetes mellitus	5230 (43.7%)	12,001 (37.3%)	2933 (32.9%)	467 (31.6%)	<.001
Prior PAD **	3649 (30.5%)	10,091 (31.4%)	2919 (32.7%)	447 (30.2%)	.006
GFR†† and dialysis					
On dialysis	543 (4.5%)	1282 (4.0%)	397 (4.5%)	83 (5.6%)	<.001
GFR <60 milliliters per minute	5282 (44.2%)	14,810 (46.1%)	4205 (47.2%)	704 (47.7%)	
GFR >=60 milliliters per minute	6115 (51.2%)	16,004 (49.9%)	4311 (48.4%)	688 (46.6%)	
Porcelain aorta	619 (5.2%)	1799 (5.6%)	737 (8.3%)	120 (8.1%)	<.001
Aortic annular calcification	9548 (80.8%)	25,905 (81.8%)	7154 (81.2%)	1224 (84.6%)	.001
Patient predicted mortality (%)	6.4 (4.2-9.8)	6.5 (4.3-10.1)	6.7 (4.4-10.3)	6.6 (4.3-10.1)	<.001
AV§§ gradient (mmHg)	42.0 (34.0-50.0)	43.0 (35.0-51.0)	43.0 (36.0-52.0)	42.0 (32.0-51.0)	<.001
AV area (cm^2)	0.7 (0.6-0.8)	0.7 (0.5-0.8)	0.7 (0.5-0.8)	0.7 (0.6-0.8)	<.001
LVEF‖‖ (%)	58.0 (50.0-65.0)	58.0 (45.0-64.0)	55.0 (45.0-63.0)	55.0 (41.0-60.0)	<.001
Left vent internal systolic dim (cm)	3.1 (2.6-3.8)	3.1 (2.6-3.8)	3.3 (2.7-3.9)	3.3 (2.7-4.1)	<.001
Left vent internal diastolic dim (cm)	4.6 (4.0-5.1)	4.6 (4.0-5.1)	4.7 (4.2-5.2)	4.7 (4.1-5.3)	<.001
AV peak velocity (m/s)	4.1 (3.7-4.5)	4.2 (3.8-4.6)	4.2 (3.8-4.6)	4.1 (3.6-4.5)	<.001
Valve access site (femoral)	9176 (76.7%)	24,426 (76.0%)	6643 (74.4%)	1108 (74.8%)	.004
Valve size, mm					
≤23	3372 (28.6%)	9298 (29.4%)	2792 (31.8%)	464 (31.9%)	<.001
25–27	4943 (42.0%)	13,423 (42.4%)	3623 (41.2%)	622 (42.7%)	
≥29	3460 (29.4%)	8939 (28.2%)	2373 (27.0%)	370 (25.4%)	
Valve type	2752 (23.4%)	7242 (22.9%)	2002 (22.8%)	302 (20.7%)	.197
Self-Expanding valve					
Balloon Expandable Valve	9020 (76.6%)	24,422 (77.1%)	6785 (77.2%)	1153 (79.2%)	
Valve sheath access site					
Femoral	9176 (77.1%)	24,426 (76.4%)	6643 (74.9%)	1108 (75.1%)	.002
Axillary	39 (0.3%)	83 (0.3%)	26 (0.3%)	3 (0.2%)	
Transapical	1799 (15.1%)	5055 (15.8%)	1457 (16.4%)	236 (16.0%)	
Subclavian	171 (1.4%)	438 (1.4%)	129 (1.5%)	31 (2.1%)	
Transcarotid	32 (0.3%)	53 (0.2%)	12 (0.1%)	0 (0.0%)	
Other	692 (5.8%)	1937 (6.1%)	607 (6.8%)	98 (6.6%)	

All values are presented as n (%) or median (25th–75th percentile)
Abbreviations: †Aortic stenosis, ‡aortic insufficiency, §body mass index, ‖myocardial infarction, #coronary artery bypass grafting, **peripheral arterial disease, ††glomerular filtration rate, §§aortic valve, ‖‖left ventricular ejection fraction.

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Results

Baseline characteristics

The final study population consisted of 54,535 patients who underwent TAVR at 442 sites. Of these, 11,967 (21.9%) had isolated AS, 32,153 (59.0%) had AS with mild AI, 8,933 (16.4%) had AS with moderate AI, and 1,482 (2.7%) had AS with severe AI (Table I).

Patients with moderate or severe AI at baseline had higher STS risk scores, greater left ventricular internal diastolic dimensions, higher right ventricular systolic pressures, more aortic annular calcification, and lower ejection fractions as compared with patients with AS and no or mild AI. Baseline echocardiographic variables including aortic valve area, peak aortic jet velocity, and

Table II. In-hospital outcomes

	Isolated AS N = 11,967	AS–Mild AI N = 32,153	AS–Moderate AI N = 8933	AS–Severe AI N = 1482	*P*
Device success	11,196 (94.7%)	29,982 (94.6%)	8246 (93.9%)	1352 (92.1%)	<0.001
In-hospital bleeding at access site	202 (1.7%)	575 (1.8%)	176 (2.0%)	22 (1.5%)	0.369
In-hospital hematoma at access site	193 (1.6%)	558 (1.7%)	137 (1.5%)	31 (2.1%)	0.310
Major vascular access site complication	133 (1.1%)	395 (1.2%)	90 (1.0%)	11 (0.7%)	0.131
In hospital RBC § transfusion	3475 (29.1%)	9356 (29.2%)	2661 (29.8%)	423 (28.7%)	0.591
Residual aortic insufficiency					
None	4702 (47.1%)	10,765 (40.5%)	2834 (38.2%)	469 (42.1%)	<0.001
Trace/trivial	2616 (26.2%)	7572 (28.5%)	2022 (27.3%)	270 (24.3%)	
1+/Mild	2316 (23.2%)	6960 (26.2%)	2048 (27.6%)	283 (25.4%)	
2+/Moderate	330 (3.3%)	1252 (4.7%)	476 (6.4%)	82 (7.4%)	
3-4+/Severe	11 (0.1%)	63 (0.2%)	35 (0.5%)	9 (0.8%)	
Post-procedure aortic valve mean gradient (mmHg)	9.0 (6.0-12.0)	9.0 (6.0-12.0)	9.0 (7.0-12.0)	10.0 (7.0-13.0)	<0.001
Conversion to surgery	120 (1%)	343 (1%)	82 (0.9%)	14 (0.9%)	0.326
AKI ‖					
No AKI	8806 (78.1%)	24,038 (78.8%)	6781 (80.3%)	1078 (78.3%)	0.005
Stage 1 AKI	2115 (18.8%)	5617 (18.4%)	1442 (17.1%)	272 (19.8%)	
Stage 2 AKI	46 (0.4%)	96 (0.3%)	28 (0.3%)	2 (0.1%)	
Stage 3 AKI	307 (2.7%)	745 (2.4%)	192 (2.3%)	25 (1.8%)	
Myocardial infarction	51 (0.4%)	123 (0.4%)	34 (0.4%)	7 (0.5%)	0.875
New pacemaker requirement	1118 (11.1%)	2890 (10.7%)	793 (10.5%)	126 (9.9%)	0.508
Stroke	265 (2.2%)	668 (2.1%)	175 (2.0%)	32 (2.2%)	0.635

All values are presented as n (%) or median (25th-75th percentile)
Abbreviations: †Aortic stenosis, ‡aortic insufficiency, §red blood cells, ‖acute kidney injury.

mean aortic valve gradients were generally comparable across the 4 groups.

Procedural and in-hospital outcomes

Procedural and in-hospital outcomes are summarized in Table II. Residual aortic valve gradient was higher among patients with severe baseline AI. In addition, patients with severe AS with concomitant AI were more likely to have residual AI than patients with isolated AS at baseline (Figure 1).

As a result, device success was lower among patients with more severe baseline AI (94.7% in isolated AS, 94.6% in AS with mild AI, 93.9% in AS with moderate AI, 92.1% in AS with severe AI; $P < .001$). In-hospital complications including acute kidney injury, major vascular complications, MI, new pacemaker requirement and stroke were comparable across the 4 groups (Table II).

One-year outcomes

CMS linked data were available for 34,678 patients (63.6%). Unadjusted one-year clinical outcomes are summarized in Figure 2A and B and Supplementary Table II.

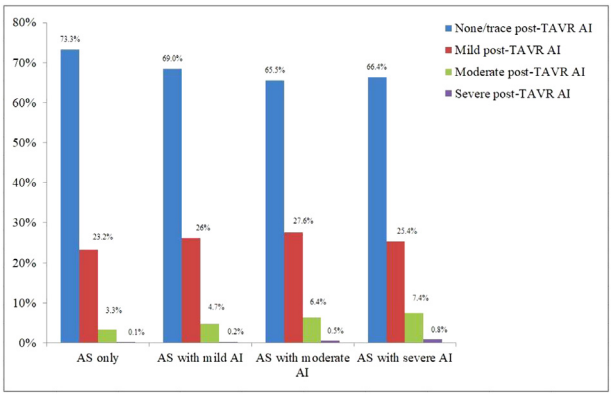
After risk-adjustment, the risk of both mortality and HF hospitalization decreased with increasing severity of pre-procedure AI (Table III).

As compared with patients with isolated AS, risk-adjusted mortality decreased by 6% for every one grade increase in pre-procedure AI (adjusted hazard ratio [HR] 0.94 per 1-grade increase in AI severity, 95% CI, 0.91-0.98; $P < .001$). For HF hospitalization, each 1 grade increase in pre-procedure AI was associated with a 13% relative decrease in HF hospitalization (adjusted HR 0.87 per 1-grade increase in AI severity; 95% CI, 0.84-0.91, $P < .001$).

In sensitivity analyses, addition of post-procedure AI severity to the adjusted model had little impact on the adjusted hazard ratios (Table III). Similarly, when the analysis was restricted to patients with ≤ trace post-procedure AI, the association between pre-procedure AI and heart failure remained significant, whereas the adjusted HR for mortality was numerically similar and not statistically significant. Finally, there was no interaction between year of procedure and either 1-year mortality or heart failure hospitalization, regardless of whether severe AS with concomitant AI group was analyzed as a categorical variable (P for interaction = .179 and .244, respectively) or as an ordinal variable (P for interaction = .140 and .097, respectively).

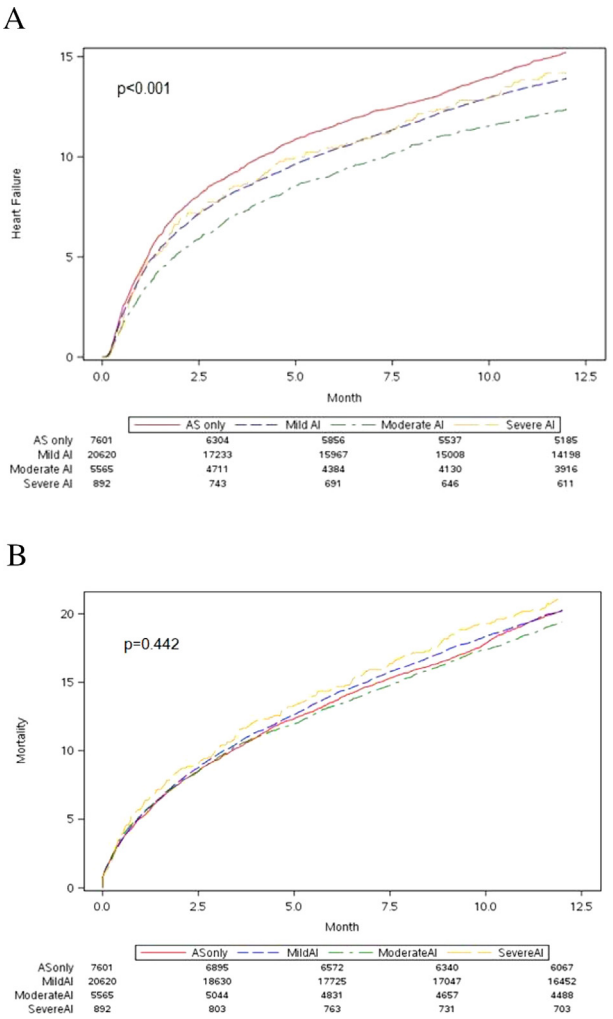
To assess for bias related to the use of CMS-linked data to establish 1-year outcomes of mortality and HF hospitalization, baseline characteristics and in-hospital outcomes were compared in patients with or without long-term data available. There were small, statistically significant differences in the baseline and echocardiographic characteristics among the patient groups with or without long term follow up (Supplementary Table IIIA, B). Small but statistically significant differences in in-hospital outcomes were also present among the patients with or without long term follow up (Supplementary Table IVA and B).

Figure 1



This figure shows overall incidence of post TAVR AI in the different groups of patients undergoing TAVR. The Y-axis represents the percentage of post TAVR AI and X axis shows the division of groups based on the severity of pre procedural AI. Abbreviations: TAVR, Transcatheter aortic valve replacement; AS, aortic stenosis; AI, aortic insufficiency.

Figure 2



A, Kaplan Meier curve for 1 year heart failure related hospitalization. This figure illustrates a cumulative incidence of 1-year heart failure (HF)–related hospitalizations for patients with severe AS or severe AS with concomitant AI who underwent TAVR. X-axis illustrates time in months whereas y-axis represents cumulative incidence (%) of HF hospitalization. The 4 groups are: AS with no AI (in red), AS with mild AI (in blue), and AS with moderate AI (in green) and AS with severe AI (in yellow). Abbreviations: TAVR: Transcatheter aortic valve replacement; AS: aortic stenosis; AI: aortic insufficiency. B: Cumulative incidence for 1 year all-cause mortality. This figure represents 1 year all-cause mortality for patients with severe AS or Severe AS with concomitant AI who underwent TAVR. X-axis shows time in months whereas the Y-axis represents cumulative incidence (%) of mortality. The 4 groups are AS with no AI (in red), AS with mild AI (in blue), AS with moderate or severe AI (in green), AS with severe AI (in yellow). Abbreviations: TAVR, Transcatheter aortic valve replacement; AS, aortic stenosis; AI, aortic insufficiency.

Discussion

In this real-world study, we found that severe AS with concomitant AI is common among patients undergoing TAVR in the United States and is associated with a lower rate of device success compared with patients with isolated AS—driven by higher rates of paravalvular aortic insufficiency. Nonetheless, in adjusted analyses, patients with severe AS with concomitant AI had lower rates of 1-year mortality and HF hospitalization than patients with isolated AS—differences that do not appear to be related to better tolerance of post-procedure AI.

Previous studies have demonstrated that severe AS with concomitant AI is common among patients undergoing aortic valve replacement.[5,23] In recent studies from both Sweden and the US, 18-19% of patients undergoing SAVR for AS had concomitant AI based on local assessment,[23,5]. However, in the Placement of Aortic Transcatheter Valve Trial (PARTNER) cohort A trial, which used an angiographic core laboratory, 89% of patients had some degree of concomitant AI.[24] Similarly in our study, the vast majority (78.1%) of patients had some degree of concomitant AI, including 19% who had moderate or severe AI prior to TAVR. The wide variation in the reported incidence of severe AS with concomitant AI in prior studies is likely related to differences in definitions and classification of AI with AS.

There is paucity of data regarding the pathophysiology of severe AS with concomitant AI. Vianello et al[8] compared echocardiographic, imaging, and biomarker features of patients with AS, AI, and severe AS with concomitant AI undergoing SAVR. Histologically, patients with severe AS with concomitant AI had more valve fibrosis whereas in patients with AS, there was 'calcium replacement' of the valve fibrous tissue.[8] Popescu et al[25] studied 79 patients with severe AS with

Table III. Risk adjusted hazard ratios for 1 year all-cause mortality and heart failure hospitalizations

Outcome	Adjusted HR*			Overall HR (per 1 level increase in baseline AR	*P* for trend
	Mild AI†	Moderate AI	Severe AI		
HR after adjustment for all variables					
Death	0.96 (0.90-1.02)	0.86 (0.79-0.94)	0.90 (0.78-1.04)	0.94 (0.91-0.98)	<.001
HF‡ Hospitalization	0.87 (0.82-0.93)	0.72 (0.66-0.79)	0.81 (0.64-1.02)	0.87 (0.84-0.91)	<.001
With adjustment for post procedure AI					
Death	0.95 (0.89-1.01)	0.85 (0.78-0.92)	0.86 (0.74-1.00)	0.93 (0.90-0.97)	<.001
HF Hospitalization	0.86 (0.81-0.92)	0.70 (0.64-0.77)	0.80 (0.63-1.01)	0.87 (0.83-0.90)	<.001
Among patients with none or trace post-TAVR AI					
Death	0.95 (0.88-1.04)	0.88 (0.78-1.00)	0.95 (0.76-1.17)	0.95 (0.90-1.00)	.072
HF Hospitalization	0.84 (0.76-0.92)	0.68 (0.60-0.77)	0.79 (0.61-1.03)	0.85 (0.80-0.90)	<.001

Abbreviations: *Hazard ratio, †aortic insufficiency, ‡heart failure.

concomitant AI and found that despite being younger, patients with severe AS with concomitant AI had worse New York Heart Association (NYHA) functional class and higher intracardiac pressures than patients with isolated severe AS. Some of the prior studies focused on SAVR in patients with a combination of moderate AS and moderate AI, reported outcomes comparable to severe AS.[26-28]

Prior data regarding outcomes of TAVR in patients with severe AS with concomitant AI are mostly limited to single center series or small multicenter registries.[9-13] Among previous studies regarding the long-term outcomes of TAVR in severe AS with concomitant AI patients Chieffo et al[11] reported worse 1-year and 2-year outcomes compared with patients with isolated AS, whereas Seeger et al[13] and Abdelghani et al[9] reported comparable 1 year outcomes. In a recent single-center study of 1,133 patients, Chahine et al[10] found that patients with severe AS with concomitant AI had better 1-year survival compared with patients with isolated AS. Our study confirms and extends these findings by demonstrating improved short and long-term outcomes for patients with severe AS with concomitant AI as compared with isolated AS undergoing TAVR in a much larger cohort, and performing a series of analyses to investigate the interaction between baseline and post-procedure AI and clinical outcomes following TAVR.

The mechanism for association between severe AS with concomitant AI and improved 1-year outcomes after TAVR is not fully understood. Although post-TAVR AI has been consistently associated with worse survival and increased risk of HF hospitalization after TAVR,[29] previous studies have suggested that post-procedure AI may be better tolerated in patients with pre-procedure AI.[9-11] Based on the results of our study, however, it does not appear that better tolerance of residual AI accounts for our findings, since inclusion of the severity of post-procedure AI in our multivariable analyses or restricting analysis patients with no more than trace AI did not change our findings.

Alternatively, differences in LV preconditioning and in LV mass may play a role in our findings.[9,30,31] Egbe et al have shown that an LV mass index to LVEDD ratio >3.1 and relative wall thickness >0.46 are predictors of early and late LV dysfunction after SAVR, suggesting that higher LV mass and concentric LVH can lead to LV dysfunction even 5 years after SAVR.[31] Since patients with severe AS with concomitant AI may become symptomatic at an earlier stage of disease than patients with isolated AS—at which point they have eccentric LVH and lower LV mass—these patients might be relatively protected from LV dysfunction following TAVR, resulting in a better long-term outcomes.

Our study should be considered in the light of several important limitations. First, this is a retrospective analysis of site-reported registry data. As such, our findings with respect to long-term outcomes may be subject to confounding, despite statistical adjustment. In addition, echocardiographic assessment and quantification of insufficient and stenotic valve lesions are prone to errors, and these data were not adjudicated. Third, health status outcomes were not assessed in this study, mainly because of high rates of missing data at 1 year. Fourth, data regarding LV mass and LV diastolic function both at baseline and after TAVR are not available in the TVT Registry, thus precluding our ability to examine some proposed mechanisms for the protective effect of pre-procedure AI in its entirety. Fifth, there were some small differences in baseline characteristics and in-hospital outcomes among the patients with or without long term follow up; however, such small differences are unlikely to influence the results of this analysis. And finally, although our study was intended to focus on patients with trileaflet aortic valves, the assessment of valve morphology in the setting of highly calcified valves can also be prone to error.

Conclusion

In this large, multicenter study of real world practice in the United States, a large proportion of the patients who

underwent TAVR for severe AS had concomitant AI. Although pre-procedure AI was associated with reduced procedural success, we found that compared with patients with isolated AS, patients with severe AS with concomitant AI have lower rates of risk-adjusted 1-year mortality and heart failure hospitalization. Further studies with detailed baseline and follow-up echocardiographic data are needed to better understand the mechanism of the protective benefit of baseline AI in patients with severe AS with concomitant AI undergoing TAVR.

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Declaration of competing interest

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Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2020.07.010.

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