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Original Research

Association of Relative Left Ventricular Outflow Tract Area and Transcatheter Aortic Valve Replacement Related Paravalvular Leak

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ABSTRACT

Background: Post-transcatheter aortic valve replacement (TAVR), paravalvular leak (PVL) is a quality metric associated with worse clinical outcomes. Transcatheter heart valve (THV) sizing is based primarily on the systolic annular size without regard to the left ventricular outflow tract (LVOT), which also lies within the THV landing zone. We hypothesized that LVOT size relative to the annulus is associated with post-TAVR PVL.

Methods: Data from consecutive patients undergoing TAVR in a single high-volume center from January 2018 to March 2019 were used. Pre-TAVR data from multidetector computed tomography (MDCT) were collected. Relative LVOT area was defined as LVOT area/annular area during systole. Logistic regression analysis was used to evaluate association with post-TAVR mild or greater PVL by transthoracic echocardiography before discharge.

Results: Among 293 patients (median age, 81.1 years; female, 49.5%; White, 88.0%), 81.6% received SAPIEN 3 and 18.4% received CoreValve THV models. Aortic valve morphology was bicuspid in 10.9% of patients. Prevalence of mild or greater PVL was 23.5% (mild in 20.1%). Relative LVOT area had a significant inverse association such that the odds of mild or greater PVL decreased significantly with every 1% increase in relative LVOT area (adjusted odds ratio, 0.96; 95% CI, 0.93-0.98; $P = .002$). There was no interaction between the type of implanted valve and the relative LVOT area. Patients in the highest relative LVOT tertile had significantly lower odds of mild or greater PVL (adjusted odds ratio, 0.42; 95% CI, 0.21-0.87; $P = .018$ vs first tertile).

Conclusions: In patients undergoing TAVR with the newer generation of THV (SAPIEN 3 and CoreValve models), a relatively narrower LVOT area vs annular area was independently associated with increased odds of mild or greater PVL before discharge.

Introduction

The advent and widespread adoption of transcatheter aortic valve replacement (TAVR) has led to a seismic shift in the treatment of patients with severe aortic stenosis (AS).[1] Although TAVR is associated with comparable mortality as compared with surgical AVR, there is a lower risk of complications, such as atrial arrhythmia, bleeding, and prolonged hospital or intensive care unit stay.[1,2] TAVR, however, is associated with a higher incidence of paravalvular leak (PVL) that carries adverse long-term prognosis.[2–5] In the last decade, there has been an emphasis on reducing the incidence of PVL as relatively younger and lower risk patients with longer life expectancy are undergoing TAVR.[6]

This PVL is due to impaired sealing of the transcatheter heart valve (THV) within the device landing zone.[4] In patients being considered for TAVR, guidelines recommend that TAVR valve sizing is performed based on the systolic annulus as sized on preprocedural imaging by electrocardiogram gated multidetector computed tomography (MDCT).[7] Although the systolic annulus is the standard of care for valve sizing, the anatomic structures in the exact device landing zone may vary according to the design of the THV and patient-specific characteristics, such as the left ventricular outflow tract (LVOT).[8]

Previous studies suggest that LVOT dimension and calcification are associated with post-TAVR PVL.[7,9] In AS, LVOT undergoes conformational changes and calcification due to associated chronic

Abbreviations: AUC, area under the reciever operating characteristic curve; IQR, interquartile range; LVEF, left ventricular ejection fraction; LVOT, left ventricle outflow tract; MDCT, multidetector computed tomography; PVL, paravalvular leak; TAVR, transcatheter aortic valve replacement; THV, transcatheter heart valve; TTE, transthoracic echocardiogram.

Keywords: CoreValve; left ventricle outflow tract; paravalvular leak; SAPIEN 3; transcatheter aortic valve replacement; transcatheter heart valve.

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hemodynamic changes.[10] The area of LVOT, relative to the aortic annulus, thus reflects chronic remodeling of the device landing zone in severe AS.[11] We hypothesize that the LVOT has unique sizing and features compared with the aortic annulus which may be independently associated with post-TAVR PVL.

Materials and methods

The study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. The study was approved by the Henry Ford Health Institutional Review Board.

Study design setting and participants

In this single-center retrospective study, we assessed data from preprocedural MDCT data of consecutive patients who underwent TAVR from January 2018 to March 2019. Patients with previous aortic valve interventions were excluded. All patients underwent annular sizing using MDCT. The study was performed at a high-volume quaternary care regional valve referral center.[12] Patients received either SAPIEN 3 (Edwards Lifesciences) or CoreValve Evolut (Medtronic) THV models. Valve size selection was based on the manufacturer's recommendations (systolic annular area for SAPIEN 3 valve and systolic annular perimeter for CoreValve) (Supplemental Table S1).

Imaging protocol

The area of the aortic annulus and LVOT were measured by planimetry at 10% intervals throughout the cardiac cycle. The systolic and diastolic phases with the largest interpretable images were selected for analysis. Annular measurements were obtained inferior to the coronary cusp insertion points with the inclusion of 10% of annular or subannular calcifications in the region of interest. LVOT measurements were recorded approximately 5 mm inferior to the aortic annulus in a double oblique orientation. All patients underwent transthoracic echocardiography (TTE) before discharge. TTE data were abstracted from studies that were clinically interpreted by cardiologists board-certified in echocardiography.

Data collection and variables

Aortic valve calcium was classified into 2 categories: mild to moderate or moderate to severe based on visual assessment. Annular ellipticity was defined as 1 – (minimum annular diameter / maximum annular diameter) during systole.[7,13] Annular distensibility was defined as 1 – (annular diameter in diastole / annular diameter in systole). Cover index was defined as 1 – (maximum annular diameter / THV diameter). Data on demographic factors, preprocedural transthoracic echocardiogram-derived left ventricular ejection fraction (LVEF), baseline rhythm abnormalities, and valve characteristics were collected. The relative LVOT area was calculated by dividing the systolic LVOT area by the systolic annular area determined by MDCT. PVL was graded on post-TAVR TTE as none/trace/trivial, mild, moderate, or severe using valvular academic research consortium-2 criteria.[14]

Study outcome

The study outcome was to estimate the incidence and independent association of relative LVOT area with post-TAVR mild or greater PVL determined by TTE before discharge.

Statistical analysis

Continuous variables were represented as medians with interquartile ranges (IQR) and categorical variables were represented as counts with proportions. The Wilcoxon rank-sum test and χ^2 tests were used to identify the differences in baseline characteristics in continuous and categorical variables, respectively.

We assessed the independent association of relative LVOT area with mild or greater post-TAVR PVL in an a priori multivariable logistical model consisting of the type of valve (SAPIEN 3 or CoreValve Evolut models), aortic valve calcium (mild-moderate or moderate-severe), systolic annular size, annular ellipticity, cover index, and relative LVOT area. These variables were selected because they have been previously shown to have an association with PVL.[3,4,13,15,16] We did not impute any missing variables. If the relative LVOT was not normally distributed, we did sensitivity analysis by doing a logarithmic transformation. We did not include the TAVR approach because >95% of patients had a transfemoral approach.[15]

We compared the diagnostic accuracy of the multivariate model before and after the addition of the relative LVOT area category using the area under the curve. Furthermore, we ranked the predictive value of the components in the logistic model to predict post-TAVR mild or greater PVL. These factors were ranked using the likelihood χ^2 statistics, area under the reciever operating characteristic curve (AUC), and standardized domination statistic for the logistic regression analyses.[17] We then divided the relative LVOT area into tertiles and tested the same association. All statistical analyses were performed in Stata/SE version 17.0 (StataCorp). All P values were 2-sided with <.05 considered statistically significant.

Results

Baseline characteristics

Among 293 patients with severe AS eligible for this study, the median age was 81.1 (IQR, 74.9-86.6) years; 49.5% were women and 88.0% were self-reported as white. The proportion of patients with hypertension, diabetes mellitus, and chronic lung disease was 89.4%, 45.7%, and 25.3%, respectively. The median Society of Thoracic Surgeons (STS) risk score was 3.9% (IQR, 2.5-5.8). There were 50.9% of patients in the low-risk category (STS score 0%-3%) and 36.2% of patients in the intermediate-risk category (STS score 4%-8%). Aortic valve morphology was bicuspid in 10.9% of patients. Other baseline characteristics are given in Table 1.

Anatomic characteristics

Median systolic and diastolic aortic annulus areas were 452 (392-527) and 411 (358-482) mm^2, respectively, Median systolic and diastolic LVOT areas were 437 (379-520) and 406 (339-484) mm^2, respectively. There was higher dynamism in the annulus dimensions as compared to LVOT dimensions (dynamism defined as systolic–diastolic areas). Other anatomical characteristics are given in Table 1.

There was an almost linear association between the systolic LVOT area and the systolic annual area (r = 1.03; $P < .001$, Figure 1A). The annular area was larger than the LVOT area in 60.4% of patients. The median relative LVOT area (defined as systolic LVOT/systolic annular area) was 97.4 (IQR, 89.3-104.1). The distribution of the relative LVOT area is given in Figure 1B.

Procedural characteristics

The median time interval from preprocedural CT to TAVR was 47 days (IQR, 32-72). Indication of TAVR was severe AS in 88% of patients

Table 1. Baseline characteristics of the study population and stratified by tertiles of relative LVOT area.

Factor	Overall population (N = 293)	Lowest tertile (n = 95)	Middle tertile (n = 100)	Highest tertile (n = 98)	*P* value
Demographic characteristics					
Age, y	81.1 (74.9-86.6)	80.7 (72.9-85.9)	81.4 (75.7-87.4)	81.3 (73.1-85.5)	.390
Female	145 (49.5%)	56 (58.9%)	37 (37.0%)	52 (53.1%)	.006
Race (self-reported)					.590
White	257 (88.0%)	81 (85.3%)	90 (90.0%)	86 (88.7%)	
Black	32 (11.0%)	12 (12.6%)	9 (9.0%)	11 (11.3%)	
Asian	3 (1.0%)	2 (2.1%)	1 (1.0%)	0 (0.0%)	
Comorbidities					
STS PROM score	3.9 (2.5-5.8)	3.5 (2.3-5.5)	4.1 (2.6-6.6)	3.7 (2.7-5.5)	.370
Hypertension	262 (89.4%)	86 (90.5%)	90 (90.0%)	86 (87.8%)	.800
Diabetes mellitus	134 (45.7%)	39 (41.1%)	52 (52.0%)	43 (43.9%)	.280
Prior myocardial infarction	77 (26.3%)	20 (21.1%)	27 (27.0%)	30 (30.6%)	.310
Current dialysis	13 (4.4%)	2 (2.1%)	7 (7.0%)	4 (4.1%)	.250
Coronary artery disease	130 (44.4%)	36 (37.9%)	53 (53.0%)	41 (41.8%)	.870
Prior stroke	28 (9.6%)	8 (8%)	10 (10%)	10 (10%)	.890
Smoker	17 (5.8%)	5 (5.3%)	6 (6.0%)	6 (6.1%)	.960
Body mass index, kg/m^2	28.3 (24.7-33.4)	27.6 (24.3-33.9)	28.6 (25.2-33.4)	28.5 (24.3-33.0)	.780
NYHA III/IV in prior 2 wk	220 (75.1%)	67 (70.5%)	66 (66.0%)	77 (78.6%)	.120
Atrial fibrillation or flutter	108 (36.9%)	29 (30.5%)	35 (35.0%)	44 (44.9%)	.110
Prior PAD	51 (17.4%)	13 (13.7%)	22 (22.0%)	16 (16.3%)	.290
Moderate or severe chronic lung disease	24 (8.2%)	9 (9.4%)	7 (7.0%)	8 (8.2%)	.310
TTE					
LV ejection fraction, %	61.0 (54.0-66.0)	65.0 (61.0-69.0)	60.0 (53.0-65.0)	57 (40.0-64.0)	<.001
LV internal diameter-systole, cm	3.0 (2.5-3.7)	2.6 (2.3-3.2)	3.0 (2.6-3.6)	3.3 (2.8-4.2)	<.001
LV internal diameter-diastole, cm	4.5 (3.9-5.0)	4.1 (3.6-4.6)	4.6 (4.2-5.0)	4.8 (4.1-5.3)	<.001
Anatomical characteristics					
Aortic annulus					
SMAAD, mm	24.0 (22.2-25.8)	23.1 (21.8-25.1)	24.5 (23.0-26.5)	24.1 (22.0-25.6)	.004
Systolic area, mm^2	452.0 (392.0-527.0)	430.0 (369.0-492.0)	472.5 (422.0-552.5)	451.5 (377.0-523.0)	.001
Diastolic area, mm^2	411.0 (358.0-482.0)	382.0 (332.0-439.0)	436.0 (389.0-505.5)	410.5 (358.0-494.0)	<.001
Dynamism	35.0 (23.0-51.0)	41.0 (26.0-61.0)	38.0 (25.0-51.5)	29.5 (21.0-45.0)	.002
Systolic perimeter, mm	77.0 (71.0-83.0)	74.0 (70.0-79.0)	79.0 (74.0-84.0)	77.0 (71.0-83.0)	<.001
Diastolic perimeter, mm	74.0 (69.0-80.0)	70.0 (67.0-77.0)	75.5 (71.0-81.0)	73.0 (69.0-80.0)	<.0001
Systolic diameter min, mm	21.6 (19.9-23.1)	20.7 (19.3-22.2)	21.8 (20.3-23.8)	21.7 (20.1-23.1)	.001
Systolic diameter max, mm	26.6 (24.6-28.7)	25.8 (23.9-28.1)	27.5 (25.3-29.3)	26.2 (24.0-28.6)	.002
Diastolic diameter min, mm	19.6 (18.2-21.8)	18.9 (17.3-20.5)	20.5 (18.5-22.3)	19.7 (18.5-21.8)	<.001
Diastolic diameter max, mm	26.3 (24.1-28.6)	25.2 (23.5-27.3)	27.0 (25.2-29.3)	26.4 (24.2-28.8)	<.001
LVOT					
Relative area, %	97.4 (89.3-104.1)	86.2 (81.4-88.9)	97.4 (95.2-99.2)	106.6 (104.1-113.3)	<.001
Systolic area, mm^2	437.0 (379.0-520.0)	370.0 (317.0-411.0)	461.0 (405.0-530.5)	500.0 (413.0-563.0)	<.001
Diastolic area, mm^2	406.0 (338.5-484.0)	333.0 (291.0-400.0)	435.0 (358.0-509.0)	451.5 (387.0-542.0)	<.001
Dynamism	26.5 (1.0-57.5)	22.0 (-12.0-53.0)	25.0 (1.0-59.0)	31.0 (12.0-61.0)	.160
Systolic perimeter, mm	77.0 (72.0-83.0)	70.0 (66.0-75.0)	79.0 (73.0-84.0)	81.0 (76.0-86.0)	<.001
Diastolic perimeter, mm	76.0 (71.0-83.0)	70.0 (67.0-75.0)	79.0 (74.0-86.0)	80.0 (74.0-88.0)	<.001
Systolic diameter min, mm	20.4 (18.4-22.6)	18.0 (16.7-20.0)	21.0 (19.7-23.0)	22.0 (20.1-23.8)	<.001
Systolic diameter max, mm	28.0 (25.7-30.0)	26.5 (24.5-28.1)	28.7 (26.7-30.5)	28.4 (26.8-30.7)	<.001
Diastolic diameter min, mm	18.0 (16.1-20.3)	16.2 (14.4-18.0)	19.0 (16.8-21.0)	19.3 (17.5-21.6)	<.001
Diastolic diameter max, mm	28.2 (26.0-30.7)	26.2 (24.7-28.4)	29.0 (27.2-30.8)	28.7 (26.9-32.1)	<.001
Procedural characteristics					
Bicuspid aortic valve	32 (10.9%)	15 (15.8%)	10 (10.0%)	7 (7.1%)	.150
Moderate-severe AV calcium	229 (78.2%)	78 (82.1%)	74 (74.0%)	77 (78.6%)	.390
Type of valve					.230
CoreValve	54 (18.4%)	20 (21.1%)	13 (13.0%)	21 (21.4%)	
SAPIEN 3	239 (81.6%)	75 (78.9%)	87 (87.0%)	77 (78.6%)	
Access					.500
Transfemoral	281 (95.9%)	92 (96.8%)	94 (94.0%)	95 (96.9%)	
Alternative	12 (4.1%)	3 (3.2%)	6 (6.0%)	3 (3.1%)	
SAPIEN valve size					.250
20 mm	13 (5.4%)	7 (9%)	2 (2.0%)	4 (5%)	
23 mm	81 (33.9%)	32 (43%)	22 (25%)	27 (35%)	
26 mm	94 (39.3%)	27 (36%)	37 (43%)	30 (39%)	
29 mm	51 (21.3%)	9 (12%)	26 (30%)	16 (21%)	
CoreValve valve size					.470
23 mm	1 (2%)	0 (0%)	1 (8%)	0 (0%)	
26 mm	16 (30%)	8 (40%)	2 (15%)	6 (29%)	
29 mm	31 (57%)	10 (50%)	9 (69%)	12 (57%)	
34 mm	6 (11%)	2 (10%)	1 (8%)	3 (14%)	

Continuous variables are expressed as median (interquartile range) and categorical variables are expressed as n (%). Dynamism is defined as the difference in systolic and diastolic areas.
AV, aortic valve; LV, left ventricle; LVOT, left ventricle outflow tract; NYHA, New York Heart Association; PAD, peripheral arterial disease; SMAAD, systolic mean aortic annulus diameter; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TTE, transthoracic echocardiogram.

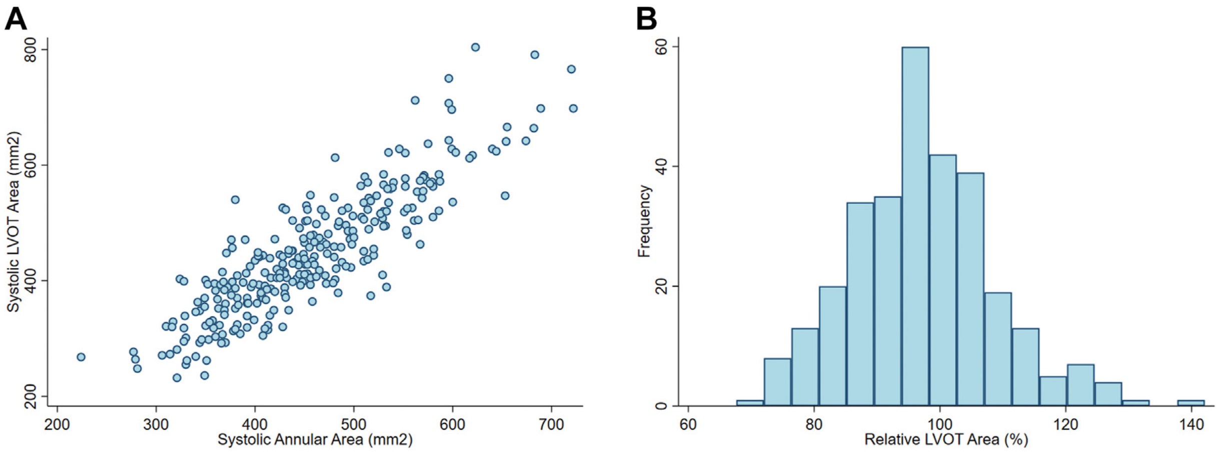


Figure 1.
Scatter plot showing linear association of systolic annular area (x-axis) and systolic left ventricle outflow tract (LVOT) area (y-axis) (A). Frequency distribution histogram for the relative LVOT area (**B**).

and both AS and aortic insufficiency in 11.3%. Two patients had primary aortic insufficiency. SAPIEN 3 and CoreValve Evolut models were implanted in 81.6% and 18.4% of patients, respectively. Transfemoral access was used in >95% of patients. For SAPIEN valves, utilizing manufacturer-recommended sizing by area, oversizing was found in 3 (1.3%) patients and undersizing in 4 (1.7%) patients. All CoreValve models fell within manufacture sizing recommendations by perimeter. The distribution of THV size implanted is given in Supplemental Table S2 for the SAPIEN valve and Supplemental Table S3 for CoreValve.

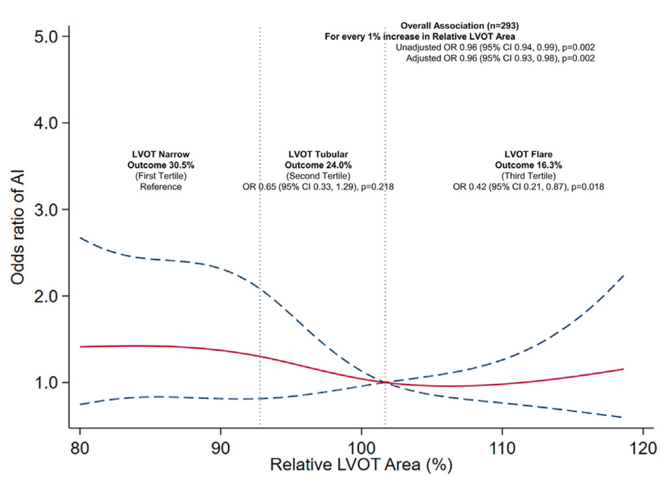
Around 97% of patients had TTE performed within 2 days of TAVR. Prevalence of mild or greater PVL was 23.5% (mild in 20.1% and moderate in 1.0%). Prevalence of mild or greater PVL with SAPIEN 3 compared with CoreValve Evolut models were 21.8% and 31.5%, respectively.

The absolute annular area and LVOT area were not associated with post-TAVR mild or greater PVL. Relative LVOT area had a significant inverse association such that the odds of mild or greater PVL decreased significantly with every 1% increase in relative LVOT area. This association remained significant in the multivariate model (odds ratio, 0.96; 95% CI, 0.93-0.98; P = .002, Central Illustration). The univariate and multivariate association of variables of interest with mild or greater PVL is given in Supplemental Table S4. Relative LVOT area was not normally distributed, and the above association remained robust after logarithmic transformation ($P = .002$). Cover index was the only other variable that was significantly associated with mild or greater PVL (adjusted odds ratio, 0.95; 95% CI, 0.90-0.99; $P = .024$). There was no interaction between the type of implanted valve and the relative LVOT area (P interaction > .05).

There was incremental improvement in the diagnostic accuracy of the model by stepwise addition of the variables of interest, with maximum AUC after the addition of relative LVOT area (model 6). However, this improvement was not statistically significant (Supplemental Figure S1). Relative LVOT area had the best predictive value for mild or greater PVL among all variables of interest (Figure 2).

The median relative LVOT area in the first, second, and third tertile of relative LVOT area was 86.2%, 97.4%, and 106.6%, respectively, $P <$ .001 (Table 1). The prevalence of mild or greater PVL in these tertiles was 30.5%, 24.0%, and 16.3%, respectively. In the adjusted analysis, patients in the highest tertile had significantly lower odds of mild or greater PVL (OR, 0.42; 95% CI, 0.21-0.87; $P = .018$ with first tertile as reference). There was no difference between the first and the second tertile (Central Illustration).

Patients in the lowest tertile of relative LVOT area had significantly higher LVEF (65% vs 60% vs 57%, P trend < .001), higher dynamism in the annulus (41.0 vs 38.0 vs 29.5, $P = .002$), and trend toward lower dynamism of the LVOT across the 3 tertiles (22.0 vs 25.0 vs 31.0, $P = .160$). Other baseline characteristics in these 3 tertiles are given in Table 1.



Central Illustration.
Relationship of post-TAVR aortic insufficiency (AI) with relative left ventricle outflow tract (LVOT) area. Restricted cubic spline logistic regression model estimates (solid red) which are presented with 95% CI (dashed blue). Odds ratio (OR) for tertiles in the multivariable model adjusted for the type of valve implanted, aortic valve calcium burden, systolic annular area, and annular ellipticity. TAVR, transcatheter aortic valve replacement.

Discussion

In this single-center cohort study of 294 consecutive patients undergoing TAVR, we found that the MDCT-derived LVOT area relative to the annular area had a significant inverse association with mild or greater PVL detected by TTE immediately after TAVR. LVOT area and annular area alone had no association with mild or greater PVL. Among the variables of interest, the relative LVOT area had the highest predictive value.

According to valvular academic research consortium-2 guidelines, PVL after TAVR is classified as none, mild, moderate, or severe.[14] There is convincing evidence that increasing the severity of PVL is associated with worse long-term outcomes.[3,18,19] This has led to close tracking of moderate-to-severe PVL after TAVR as a quality metric.[20] These adverse

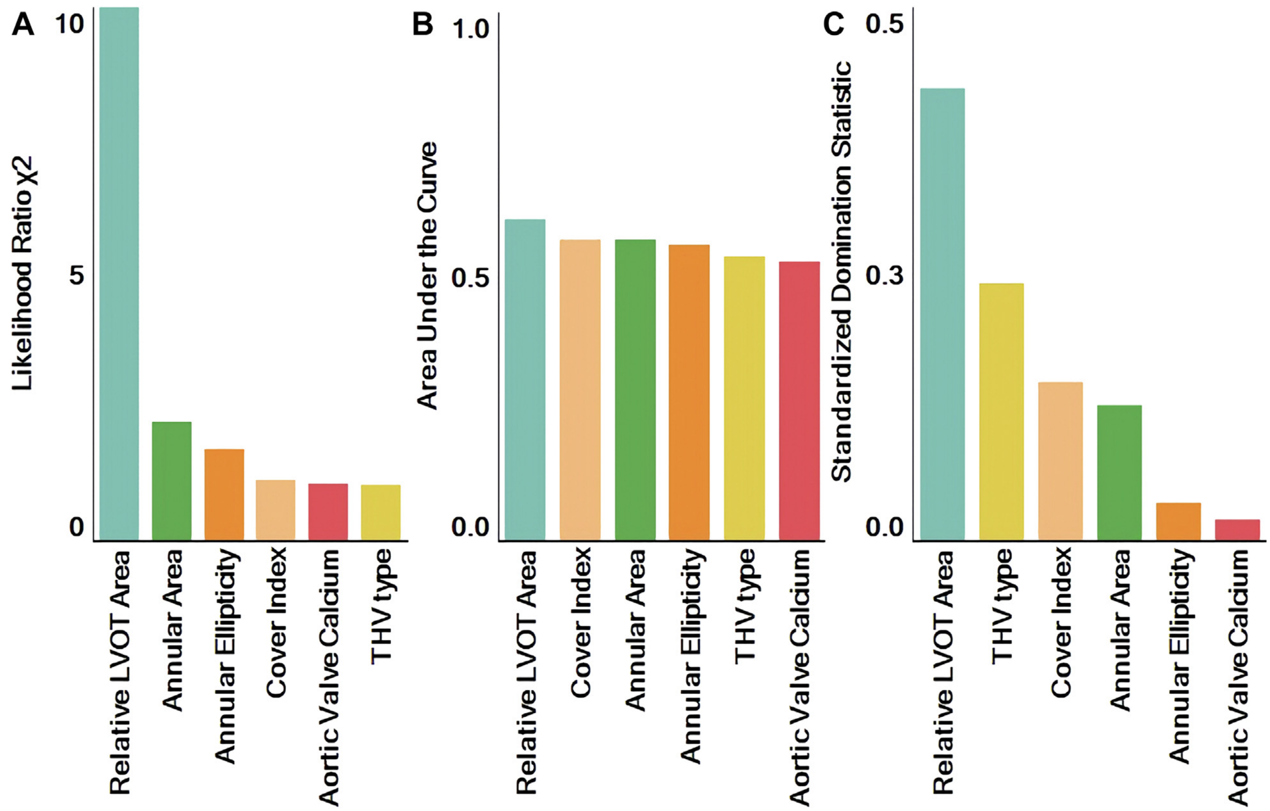


Figure 2.
Relative predictive value of variables used in the multivariable model to predict post-TAVR mild-to-moderate aortic insufficiency (AI) using likelihood ratio (A), area under the curve (B), and domination analyses (C). Annular distensibility was defined as (annular area in systole – annular area in diastole/annular area in systole, annular ellipticity was defined as (maximum-minimum annulus diameter in systole) maximum annulus diameter in systole, relative left ventricle outflow tract (LVOT) area was defined as LVOT area/annular area in systole. TAVR, transcatheter aortic valve replacement.

prognostic implications inspired a newer generation of valves to improve annular seal and reduce PVL. The SAPIEN 3 valve has an added external fabric seal with a taller stent frame as compared with the previous generation of SAPIEN valves.[21] The CoreValve Evolut R model has a shortened nitinol frame and a longer inner porcine pericardial sealing skirt.[22] The operator experience and preprocedural imaging have also improved with time.[7] With all these variables, there has been a significant reduction in post-TAVR PVL.[23]

We found that despite the linear correlation between the absolute annular and LVOT area, when broken into tiers, a relatively smaller LVOT had a higher incidence of mild or greater PVL. These results vary from a previous study by Tang et al,[24] where patients with relatively larger LVOT sizes had a higher incidence of mild or greater PVL (38.5% vs 15.2%). This observational study evaluated PVL incidence in 74 patients with extremely large annulus (>683 mm^2) who received a 29-mm SAPIEN 3 valve.[24] The discrepant results may be related to a cohorting of the largest size annuli, which may have led to a greater number of more significantly undersized valves. The study by Tang et al[24] also reported a significant association of mild or greater PVL with absolute annular and LVOT area, and annular eccentricity in univariate analysis which was also not seen in our study. It is difficult to account for these types of patient-specific differences in technique (degree of postdilation), valve size selection (percentage of over/undersizing), variability, or variability in interobserver quantification of PVL.

The LVOT is an integral component of the aortic root and THV landing zone. A nontubular LVOT was first defined by Condado et al[13] in 2016 if the valve size selection according to the manufacturer's recommendation differed based on annulus or LVOT measurements. In 2016, Condado et al[13] defined 3 types of LVOT depending on relative LVOT dimension 4 mm below the aortic annulus. If the valve size using annulus and LVOT dimension was the same, it was classified as type A (tubular). If the valve size selection by LVOT was smaller, it was classified as type B (funnel). If the valve size selection by LVOT was bigger it was classified as type C (trumpet).[13] The authors used this categorical classification of LVOT in a study of 316 consecutive patients undergoing balloon-expandable TAVR and reported that in a multivariable model, nontubular LVOT was independently associated with a higher risk of mild or greater PVL at 30 days after TAVR.[16] The association was adjusted for STS score, type of valve, membranous septum length, annular ellipticity, area cover index, and annular calcification. The authors did not assess the continuous association of relative LVOT area, or how narrower or wider LVOT impacts PVL.[16] Our findings are additive to the current knowledge base by reporting a continuous and significant inverse association between relative LVOT area and increased risk of mild or greater PVL. We also report that relative LVOT area may be more important than the valvular calcium burden, annular eccentricity, or type of THV.

Current studies evaluating the association of LVOT with PVL have used different multivariable models. Most of these variables (annular area, LVOT area, and burden of calcium) likely result from the same pathophysiological mechanism that underlies severe AS. Thus, these variables likely correlate with each other which makes the task of finding independent association difficult.

The incidence of mild or greater PVL with SAPIEN 3 at discharge (21.8%) is similar to another observational study (n = 206), where the incidence at discharge was 18%.[25] In the real-world SOURCE 3 registry (n = 1695), all patients received the SAPIEN 3 valve, and the incidence of mild or greater PVL at 30 days was 26.4%.[21] Our reported incidence with CoreValve (31.5%) is significantly lower than reported in the above observational study (46%, n = 44) and similar to another small observational study 35.7% (n = 56).[25,26] This variation in the incidence of post-TAVR PVL has been previously reported with older generations of THV as well and could be because of differences in the volume of cases, predilation and postdilation, valve over/undersizing, and reporting of PVL.[23] For this study we did not have data on frequency and degree of predilation and postdilation. Sample size precluded analysis of the impact of annulus sizes which were between manufacturer-recommended THV sizes.

With the improved design of valves and better implanter experience, it is also unknown if the previously reported variables thought to be associated with PVL remain relevant. These previously known variables include prosthesis mismatch (larger annulus than prosthesis),[3,4,27] valve type (higher incidence with self-expanding CoreValve Evolut model vs balloon-expandable Edwards SAPIEN valve),[5,28] higher aortic valve calcium burden,[29,30] LVOT calcification[10,31,32] and LVOT non-tubularity.[16] These older studies were limited by variable statistical models, and different classification schemas to report post-TAVR PVL.[4] We explored this knowledge gap and reported an independent association of the relative LVOT area with post-TAVR mild or greater PVL in a robust multivariable model, including previously studied variables.

This inverse association can be due to several reasons. Patients with a disproportionately smaller LVOT compared to aortic annulus (lowest tertile) had higher dynamism of annulus (difference in systolic and diastolic area). Patients also had a higher LVEF (65% in the lowest tertile vs 57% in the highest tertile). The accentuated change in the diastolic annular area in these patients and increased contractility could theoretically increase the risk of post-TAVR PVL via increased valve recoil and is an important avenue to explore in future analysis. Results may also be disproportionally impacted by multidisciplinary committee decisions on valve size selection in patients who fall between manufacturer-recommended valve sizes. Patients with increased LVOT calcium have an increased risk of post-TAVR PVL.[10,31,32] We do not routinely perform noncontrast CT scans and cannot quantify LVOT calcification via Agatston scoring. However, it is possible that patients with higher calcium burden had the LVOT area underestimated as compared with the aortic annulus compared to institutions that perform annular and LVOT measurements which fully exclude calcium from the planimetered region of interest.

To the best of our knowledge, this is the first study that has defined the characteristics of the LVOT in a large cohort of patients undergoing TAVR that reports an inverse association between its relative size and mild or greater PVL. We report that relative LVOT area might be more important than conventional variables currently associated with PVL. The poor AUC of the multivariable model suggests that many other putative variables of interest remain unknown. If the results of our study are replicated in other cohorts, future studies should investigate the underlying mechanisms behind this association.

There are several limitations to our observations. Our results are from a single center and need to be replicated in other multicenter data series. Predischarge TTE were assessed by different readers who were unblinded and potentially aware of the procedural characteristics. Data on comorbidities were extracted through registry data. There was only a qualitative assessment of aortic valve calcification, and this may be subject to interobserver or intraobserver variability. During TAVR, balloon postdilation is commonly performed to optimize THV expansion, increase apposition to the aortic wall, and thereby reduce the risk of PVL.[33] We did not have consistently reported data for the postdilation procedure, and the balloon fill volume used to delineate this relationship. Finally, as a large referral population, longitudinal follow-up data were limited.

Conclusion

In patients undergoing TAVR using the SAPIEN 3 or CoreValve Evolut model, a smaller LVOT relative to the annulus is associated with an increased risk of mild or greater PVL before discharge.

Declaration of competing interest

Pedro Villablanca is a consultant for Edwards Lifesciences and Teleflex. Dee Wang is a consultant for Abbott, Boston Scientific, and Edwards Lifesciences. Dee Dee Wang receives research grant support from Boston Scientific assigned to her employer Henry Ford Health. Brian O'Neill is a consultant to Abbott, Edwards Lifesciences, and Medtronic, and receives research support from Edwards Lifesciences assigned to employer Henry Ford Health. Tiberio Frisoli is a clinical proctor for Edwards Lifesciences, Abbott, Boston Scientific, and Medtronic. William W. O'Neill is a consultant to Abiomed, Medtronic, and Boston Scientific. The other authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics statement and patient consent

The study was performed in compliance with relevant laws and institutional guidelines and was approved by the institutional review board. Individual patient consent was not required for retrospective chart review. The study was approved on March 2, 2019 under project number 12790.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the Journal of the Society for Cardiovascular Angiography & Interventions at 10.1016/j.jscai.2023.101294.

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