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Predictors of Left Ventricular Outflow Tract Obstruction After Transcatheter Mitral Valve Replacement in Severe Mitral Annular Calcification: An Analysis of the Transcatheter Mitral Valve Replacement in Mitral Annular Calcification Global Registry

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ORIGINAL ARTICLE

Predictors of Left Ventricular Outflow Tract Obstruction After Transcatheter Mitral Valve Replacement in Severe Mitral Annular Calcification: An Analysis of the Transcatheter Mitral Valve Replacement in Mitral Annular Calcification Global Registry

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BACKGROUND: Several studies have evaluated preprocedural imaging predictors of left ventricular outflow tract obstruction (LVOTO) after transcatheter mitral valve replacement. The patient cohorts in these studies were heterogeneous and included patients with transcatheter mitral valve replacement in failed bioprostheses, annuloplasty rings, and severe mitral annular calcification (MAC). The goal of this study was to evaluate predictors of LVOTO specific to patients undergoing valve-in-MAC.

METHODS: This study included patients with severe MAC who underwent valve-in-MAC and had optimal quality preprocedural multidetector row computed tomography scans eligible for retrospective analysis. Baseline demographic, echocardiographic, and procedural data on these patients were collected. multidetector row computed tomography parameters were analyzed for association with LVOTO, defined as increase in mean LVOT gradient by ≥10 mm Hg with accompanying hemodynamic instability.

RESULTS: Seventy-one patients with optimal preprocedural computed tomography scans were included in this study (mean age, 72.5±13.5 years), 9 of which developed LVOTO (all female). Baseline mean LVOT area, neo-LVOT area (145.3 versus 270.9 mm^2; P=0.006), indexed neo-LVOT area (90.1 versus 157.4; P=0.05), and virtual transcatheter heart valve to septum distance (3.1 versus 6.9 mm; P=0.002) were lower in the LVOTO group. Expected % LVOT area reduction was higher in the latter group (58.3 versus 42.7%; P=0.008). In the univariable analysis, the baseline mean LVOT area, neo-LVOT area, indexed neo-LVOT area, and valve to septum distance were all significantly associated with LVOTO.

CONCLUSIONS: The systolic mean LVOT area, neo-LVOT area, indexed neo-LVOT, expected percentage LVOT area reduction, and the valve to septum distance were associated with LVOTO after valve-in-MAC.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: calcium ■ catheter ■ heart valve ■ mitral valve ■ tomography

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WHAT IS KNOWN

- Previous studies evaluating imaging predictors of left ventricular outflow tract (LVOT) obstruction after transcatheter mitral valve replacement in mitral annular calcification have been imprecise and hampered by the heterogeneity of patients included in the analysis.
- Patients undergoing transcatheter mitral valve replacement in failed bioprosthetic valves and annuloplasty rings were lumped with patients undergoing valve-in-mitral annular calcification.

WHAT THE STUDY ADDS

- The present study evaluated predictors of LVOT obstruction specific to patients undergoing valve-in-mitral annular calcification.
- The neo-LVOT area, indexed neo-LVOT, and expected percentage LVOT area reduction were associated with LVOT obstruction
- The virtual transcatheter heart valve to septum distance was a novel parameter associated with LVOT obstruction.

Nonstandard Abbreviations and Acronyms

AUC	area under the curve
LVOT	left ventricular outflow tract
LVOTO	left ventricular outflow tract obstruction
MAC	mitral annular calcification
MDCT	multidetector row computed tomography
THV	transcatheter heart valve
TMVR	transcatheter mitral valve replacement
ViMAC	valve-in-MAC

Severe mitral annular calcification (MAC) is a chronic degenerative condition that affects the elderly with comorbidities and presents a therapeutic challenge to mitral valve replacement.[1] Surgical mitral valve replacement in severe MAC is associated with high morbidity and mortality, in part due to the high-risk population with comorbidities, along with technical challenges from the calcium burden.[2,3] Transcatheter mitral valve replacement (TMVR) with a valve-in-MAC (ViMAC) procedure using a balloon-expandable aortic transcatheter heart valve (THV) has emerged as a therapeutic option in patients with high surgical risk and severe MAC.[4] Early experience of ViMAC procedures was obtained through the TMVR in MAC Global registry.[4] In that registry, the 30-day mortality was approaching 25%.[4] Left ventricular outflow tract obstruction (LVOTO) was the strongest independent predictor of mortality, and therefore represents an impactful target to improve procedural safety.[4]

LVOTO during TMVR is complex and involves an intricate interaction of the mitral apparatus, aortic valve, and the basal septum. Preprocedural ECG-gated multidetector row computed tomography (MDCT) has been instrumental in planning TMVR in MAC and anticipating anatomic challenges.[5] Data on predictors of LVOTO during TMVR in MAC is limited. Studies thus far have been hampered due to heterogeneous cohorts of patients. These studies have grouped TMVR in failed surgical bioprostheses, annuloplasty rings, and MAC, all into one cohort of patients, making interpretation of results challenging.[6–8] In this analysis from the TMVR in MAC Global Registry, the predictors of LVOTO specific to patients with severe MAC who underwent TMVR were evaluated.

METHODS

This study was a subgroup analysis of the TMVR in MAC Global Registry. The study was approved by the Mayo Clinic Institutional Review Board, and patient consent was waived. The authors declare that all the supporting data is available within the article. This international multicenter registry included patients at high surgical risk who underwent TMVR in severe MAC using balloon-expandable aortic THVs. One hundred sixteen patients from 51 centers in 11 countries from North America, Europe, and South America were included in this registry between September 2012 and March 2017.

Inclusion criteria were adult patients (>18 years), with symptomatic severe mitral valve disease and severe MAC deemed to be high risk for conventional surgical mitral valve replacement by the heart team at their respective institutions. In the current analysis, patients in whom an MDCT, performed for purposes of preprocedural planning, was of adequate quality were eligible for the retrospective analysis. Severe MAC during enrollment phase was defined as presence of diffuse, nearly circumferential calcification of the mitral annulus as seen on preprocedural MDCT (Figure 1). MAC severity was classified using the CT MAC score developed in this registry.[9] Data was collected retrospectively using a standardized case-report form. Baseline demographics, echocardiographic characteristics were extracted from the case-report forms. Preprocedural MDCT images were acquired for centralized retrospective analysis of different parameters using 3Mensio Structural Heart Mitral Workflow version 8.1 (Pie Medical Imaging, Maastricht, the Netherlands). Procedural data acquired included THV type and size and valve delivery approach. All procedures were done according to local guidelines with standard techniques via transseptal and transapical routes. For this analysis, patients who underwent transatrial TMVR were excluded as anterior mitral leaflets were resected in these patients to decrease risk of LVOTO. None of the patients in this study underwent preemptive measures to mitigate LVOTO risk, such as alcohol septal ablation or electrosurgical anterior leaflet laceration because those were developed after this registry was initiated. One patient with predominantly posterior MAC with atypical extensive extension of the calcification into the posterior left ventricular wall and neo-LVOT area of 317 mm^2 developed LVOTO, likely from the THV being pushed anteriorly by the posterior calcium and

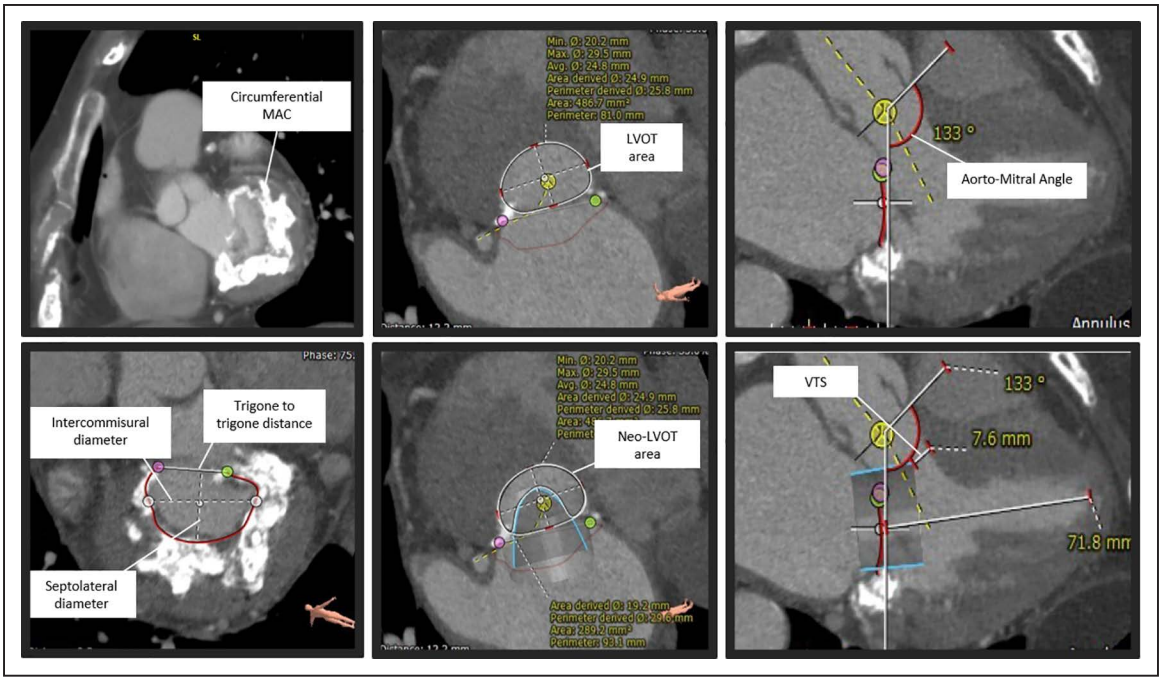


Figure 1. Preprocedural cardiac multidetector computed tomographic parameters to evaluate predictors of left ventricular outflow tract (LVOT) obstruction after transcatheter mitral valve replacement in mitral annular calcification (MAC) using 3Mensio Structural Heart Workflow (version 8.1, Pie Medical Imaging, Maastricht, the Netherlands).
VTS indicates virtual transcatheter heart valve to septum distance.

was excluded from the analysis given the unusual mechanism of LVOTO. Postprocedural echocardiographic findings were recorded. LVOT gradient was measured in a standard fashion, as recommended by the guidelines,[10] using continuous-wave Doppler. LVOT gradient was measured on preoperative and postoperative transthoracic echocardiography, as well as intraoperative transesophageal echocardiography. Procedural and in-hospital outcomes and complications were collected. Patients were grouped into those with versus without development of LVOTO.

Definition of LVOT Obstruction With Hemodynamic Compromise

For purposes of this analysis, LVOTO with hemodynamic compromise was defined as increase in mean LVOT gradient by ≥10 mm Hg with accompanying hemodynamic instability requiring treatment with intravenous medications, mechanical support, or additional cardiac procedures.[4,11] Hemodynamic instability data were extracted from patient charts including intraprocedural and postprocedural records, depending on when hemodynamic instability occurred.

Mitral Valve and LVOT MDCT Analysis

Preprocedural MDCT images were obtained from different centers. Protocols for acquiring the MDCT were according to standard practice of each center. Images were reviewed for quality check, including image quality, sufficient number of slices, contrast use, and gated electrocardiography-synchronization. MDCT images were postprocessed retrospectively at Mayo Clinic using 3Mensio Structural Heart Mitral Workflow version 8.1 (Pie Medical Imaging, Maastricht, the Netherlands). Mitral annulus dimensions and LVOT area were measured using previously described methods (Figure 1).[12–14] Aortomitral angle was determined by measuring the interior angle of the intersection between lines drawn across the aortic and mitral annulus plane during systole. Neo-LVOT was measured using a virtual valve embedded in the segmented MDCT in systole at an 80% ventricular/20% atrial position, in relation to the mitral annular plane. The size of the virtual valve was chosen according to the manufacturer's recommendation for transcatheter aortic valve replacement based on mitral annular area. The distance from ventricular edge of the virtual valve frame to the basal interventricular septum at 80/20 position was measured in systole (virtual THV to septum distance [VTS]). The percentage of LVOT area reduction was calculated (Native LVOT area–neo-LVOT area/native LVOT area). The cross-sectional planimetry of the neo-LVOT is then traced during systole and then indexed to body surface area. The length of the anterior mitral valve leaflet was measured in the 3-chamber view in diastole. End-systolic maximal septal thickness as well as septal thickness 10 to 15 mm below the aortic annulus were measured.

Statistical Analysis

Continuous variables are presented as mean±SD or median (interquartile range) and were compared using a 2-sample *t* test for normally distributed variables or the Kruskal-Wallis test for non-normal variables. Categorical variables are presented as frequency and percentage and were compared using the χ^2 test. Univariate analysis was used to determine significant risk factors contributing to LVOTO. Receiver-operating characteristics curves were plotted, and the optimal cutoff values of the predictors of LVOTO were selected as the point that maximized

Youden J statistic. A 2-tail $P<0.05$ was considered statistically significant. Statistical analysis was performed using R version 3.6.2 (R Core Team, 2019).

RESULTS

Patient Characteristics

A total of 71 patients with optimal preprocedural CT scans were included in this study. Of these, 9 patients developed LVOTO after the ViMAC procedure. The mean age was greater in the group that developed LVOTO (80.9 years versus 71.4 years; $P=0.06$). Hundred percent of patients who developed LVOTO were female compared with 61.3% in the group who did not develop LVOTO ($P=0.02$). The number of patients with a prior aortic valve replacement was similar between both groups ($P=0.4$). There were numerically more patients in the group with LVOTO who had prior TAVR compared to the group without LVOTO ($P=0.02$). New York Heart Association class ($P=0.79$) and Society of Thoracic Surgery score (21.1 versus 14.4; $P=0.08$) were similar in both groups (Table 1).

Echocardiographic Characteristics

Patients in both groups had similar baseline LVOT systolic gradients (15.0 versus 4.1; $P=0.08$), ejection fraction (64.1 versus 61.4%; $P=0.4$), mean baseline mitral gradients (10.9 versus 12.4; $P=0.4$), and severe tricuspid regurgitation (12.5% versus 17.1%; $P=0.75$; Table 1).

Procedural Data

There was no difference in the valve type, size, and access between the 2 groups (Table 2).

MDCT Parameters

Mitral annular diastolic dimensions were similar between both groups. Average MAC thickness (8.4 versus 8.3 mm; $P=0.93$), maximum MAC thickness (11.8 versus 12.8 mm; $P=0.59$) and CT-based MAC score were similar between both groups (7.9±0.8 versus 7.7±1.5; $P=0.72$). The mean length of the anterior mitral leaflet was shorter in the group with LVOTO (18.6 versus 22.4 mm; $P=0.02$).

The mean LVOT area in systole was lower in the group with LVOTO (331.1 versus 451.9 mm^2; $P=0.03$). Similarly, the neo-LVOT (145.3 versus 270.9; $P=0.006$) and the indexed neo-LVOT (90.1 versus 157.4; $P=0.05$) were also lower in the group with LVOTO, and the expected % LVOT area reduction was higher in this group (58.3 versus 42.7%; $P=0.008$). The VTS was lower in the group with LVOTO (3.1 versus 6.9 mm; $P=0.002$; Table 3).

Table 1. Baseline Demographics

	No LVOT obstruction; N=62	LVOT obstruction; n=9	*P* value
Age, y	71.4±13.4	80.9±12.1	0.06
Female	38/62 (61.3%)	9/9 (100%)	0.02
Diabetes	25/54 (46.3%)	04/8 (50.0%)	0.85
Hypertension	44/55 (80.0%)	8/8 (100%)	0.16
Atrial fibrillation	22/51 (43.1%)	05/9 (55.6%)	0.49
Peripheral artery disease	9/54 (16.7%)	01/7 (14.3%)	0.87
COPD	19/54 (35.2%)	05/8 (62.5%)	0.14
CKD	31/56 (55.4%)	06/9 (66.7%)	0.53
CVA	10/54 (18.5%)	04/8 (50.0%)	0.05
Prior CABG	23/56 (41.1%)	02/9 (22.2%)	0.28
Prior PCI	8/42 (19.0%)	01/7 (14.3%)	0.76
Prior AVR	35/59 (59.3%)	04/9 (44.4%)	0.40
TAVR	7/35 (20%)	3/4 (75%)	0.02
SAVR	28/35 (80%)	1/4 (25%)	
Mechanical	11/27 (40.7%)	1/1 (100%)	0.24
Bioprosthesis	16/27 (59.3%)	0/1 (0%)	
Prior pacemaker	19/53 (35.8%)	03/8 (37.5%)	0.93
Hospit-n due to heart failure within 12 mo	39/51 (76.5%)	7/8 (87.5%)	0.48
STS score	14.4±10.2	21.1±10.5	0.08
NYHA functional class			0.79
II	5/58 (8.6%)	1/9 (11.1%)	
III	25/58 (43.1%)	4/9 (44.4%)	
IV	28/58 (48.3%)	4/9 (44.4%)	
Echocardiographic data			
Mitral regurgitation			
None	76/55 (10.9%)	1/8 (12.5%)	0.12
Trace	7/55 (12.7%)	4/8 (50.0%)	
Mild	21/55 (38.2%)	1/8 (12.5%)	
Moderate	11/55 (20.0%)	2/8 (25.0%)	
Severe	10/55 (18.2%)	0/8 (0.0%)	
Mitral valve area, cm^2	1.16±0.50	1.26±0.49	0.60
LVEF	61.1±10.0	64.1±6.6	0.40
Peak LVOT mean systolic gradient, median (IQR)	4.1±5.3	15.0±21.2	0.08
Mean mitral valve diastolic gradient	12.4±4.9	10.9±2.8	0.40
Severe TR	07/41 (17.1%)	1/8 (12.5%)	0.75
RV dysfunction	13/42 (31.0%)	3/8 (37.5%)	0.72

AVR indicates aortic valve replacement; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; Hospit-n, hospitalization; IQR, interquartile range; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; RV, right ventricular; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgery; TAVR, transcatheter aortic valve replacement; and TR, tricuspid regurgitation.

Predictors of LVOT Obstruction

In univariable analysis, LVOT obstruction was associated with the LVOT area ($R^2=0.14$; $P=0.03$), neo-LVOT

Table 2. Procedural Outcomes

	No LVOT obstruction; n=62	LVOT obstruction; n=9	*P* value
Device type			
SAPIEN	05/62 (8.1%)	0/9 (0%)	0.38
SAPIEN XT	27/62 (43.5%)	5/9 (55.6%)	0.50
SAPIEN S3	29/62 (46.8%)	4/9 (44.4%)	0.90
Inovare	01/62 (1.6%)	0/9 (0%)	0.70
Device size			
23	05/62 (8.1%)	2/9 (22.2%)	0.18
26	26/62 (41.9%)	3/9 (33.3%)	0.62
29	30/62 (48.4%)	4/9 (44.4%)	0.83
30 (Inovare)	01/62 (1.6%)	0/9 (0%)	0.70
Access			
Transapical	29/62 (46.8%)	5/9 (55.6%)	0.62
Transseptal	29/62 (46.8%)	3/9 (33.3%)	0.45
Transseptal wire externalized via LV	04/62 (6.5%)	1/9 (11.1%)	0.61
AVR during procedure	4/61 (14.4%)	1/8 (11.1%)	0.54
TAVR	4/4 (0%)	1/1 (100%)	
SAVR	0/4 (100%)	0/1 (0%)	
Technical success*	48/62 (77.4%)	2/9 (22.2%)	<0.001
In-hospital death	10/62 (16.1%)	6/9 (66.7%)	<0.001
Conversion to open heart surgery	04/58 (6.9%)	0/9 (0%)	0.44
Residual ≥3+MR	01/62 (1.6%)	0/9 (0%)	0.70
Need for second valve	10/62 (16.1%)	3/9 (33.3%)	0.21
Hemolytic anemia	01/57 (1.8%)	0/9 (0%)	0.69
Post-mean MVG	3.8±1.7	3.5±5.0	0.90

AVR indicates aortic valve replacement; LV, left ventricle; LVOT, left ventricular outflow tract; MR, mitral regurgitation; MVARC, Mitral Valve Academic Research Consortium; MVG, mean valve gradient; SAVR, surgical aortic valve replacement; and TAVR, transcatheter aortic valve replacement.

*Technical success was defined according to the MVARC criteria.

area (R^2=0.18; *P*=0.02), neo-LVOT area index (R^2=0.15; *P*=0.07), and VTS distance (R^2=0.22; *P*=0.008). There was inverse correlation between estimated neo-LVOT area and the VTS and the measured peak LVOT gradient after implantation of the THV. The small sample size and few events prevented the conducting of a multivariable analysis.

Discriminatory Values of LVOT Obstruction Predictors

The value of several MDCT variables in predicting LVOTO were evaluated (Figure 2). The optimal discriminatory cutoff valve for VTS was 5.5 mm (area under the curve [AUC], 0.86; sensitivity, 0.72; specificity, 0.68; and accuracy, 0.68), whereas the cutoff for neo-LVOT area was 173.4 mm^2 (AUC, 0.86; sensitivity, 0.8; specificity, 0.87; and accuracy, 0.81), mean LVOT area was 371.5 mm^2 (AUC, 0.76; sensitivity, 0.67; specificity, 0.87; and accuracy, 0.54), indexed Neo-LVOT was 127.5 mm^2/m^2 (AUC, 0.83; sensitivity, 0.68; specificity, 1; and accuracy, 0.73), and the expected % LVOT area reduction cutoff was 63.5% (AUC, 0.80; sensitivity, 0.72; specificity, 0.68; and accuracy, 0.68).

DISCUSSION

This substudy from the TMVR in MAC Global Registry evaluated predictors of LVOT obstruction after ViMAC. The principal findings of this analysis are (1) female sex was strongly associated with LVOTO; (2) LVOTO occurrence was independent of baseline echocardiographic parameters included in this analysis, device choice, and procedural approach; (3) neo-LVOT area and related parameters including systolic mean LVOT area, indexed neo-LVOT area, and expected % LVOT area reduction were all associated with LVOTO; and (4) a new parameter-the VTS was also predictive of LVOTO (Figure 3).

LVOTO remains an Achilles heel of ViMAC. In the TMVR in MAC Global Registry, 13 (11.2%) patients with severe MAC undergoing TMVR using balloon-expandable transcatheter aortic valves developed LVOTO. In that study, LVOTO was a strong predictor of 30-day and 1-year mortality, despite salvage attempts including kissing balloon valvuloplasty, emergent surgery, and emergent alcohol septal ablation.[4] Prediction of LVOTO risk as part of procedural planning is therefore fundamental to avoid this catastrophic complication.

LVOT area after ViMAC is determined by the interaction of the basal left ventricular septum, aortic valve, anterior mitral valve leaflet, and transcatheter valve frame.[14] Patients with MAC often have a hypertrophic basal septum, due to comorbidities such as hypertension and chronic kidney disease.[15,16] Displacement of the anterior mitral leaflet during valve deployment, along with direct valve frame interaction, can further narrow the LVOT.[17] The most commonly used parameter to determine the risk of LVOTO during TMVR has been the neo-LVOT area.[13,14] Neo-LVOT area is determined by inserting a virtual transcatheter valve in the mitral position on MDCT using dedicated software, followed by tracing the LVOT area delineated by the interventricular septum and virtual valve frame in cross-sectional view. A study by Wang et al[7] evaluated 38 patients who underwent TMVR (9 ViMAC, 12 valve-in-ring, and 17 valve-in-valve). This study showed that a neo-LVOT surface area of ≤189.4 mm^2 was associated with LVOTO with 100% sensitivity and 96.8% specificity. Moreover, in this study, preprocedural MDCT predictors before TMVR were validated using postprocedural MDCT, showing excellent correlation (R^2=0.8169; *P*<0.0001).[7] A subsequent larger study by Yoon et al[8] included a cohort of 194 patients undergoing TMVR for valve-in-valve (n=107), valve-in-ring (50 patients), and ViMAC (37 patients). Twenty-six patients in that study had LVOTO. The predictive value of several echocardiographic and MDCT variables was evaluated,

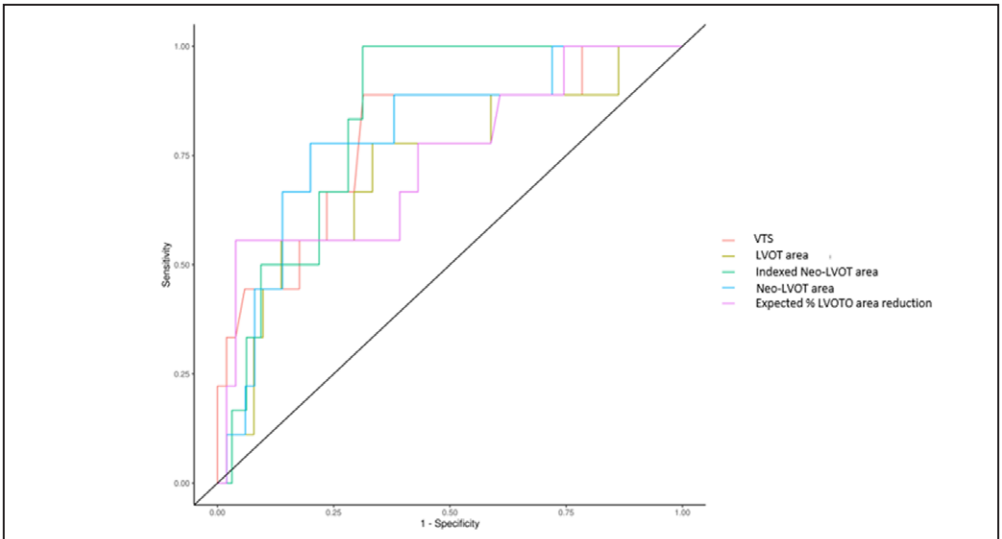
Table 3. Preprocedural Multidetector Computed Tomographic Data

	No LVOT obstruction; n=62	LVOT obstruction; n=9	*P* value
Septolateral diameter, mm (diastole)	22.0±3.6	21.3±1.2	0.60
Intercommisural diameter, mm (diastole)	31.6±4.2	30.1±4.3	0.35
Trigone to trigone distance diastole, mm (diastole)	23.4±3.8	22.0±3.7	0.32
Average MAC thickness	8.3±2.3	8.4±2.2	0.93
Minimal MAC thickness (diastole)	4.7±1.5	4.8±1.3	0.94
Maximal MAC thickness (systole)	12.8±5.4	11.8±3.4	0.59
Caseous MAC	17/62 (27.4%)	3/9 (33.3%)	0.71
Continuous MAC	39/62 (62.9%)	6/9 (66.7%)	0.83
MAC distribution			0.54
<180	06/62 (9.7%)	0/9 (0%)	
180–270	17/62 (27.4%)	2/9 (22.2%)	
>270	39/62 (62.9%)	7/9 (77.8%)	
MAC score	7.7±1.5	7.9±0.8	0.72
Anterior mitral valve calcification	55/62 (88.7%)	9/9 (100%)	0.29
Length of anterior MV leaflet in 3-chamber view in diastole, mm	22.4±3.9	18.6±4.6	0.02
Maximum septum thickness 10–15 mm below annulus (end-systolic), mm	15.6±2.9	16.5±2.8	0.45
Septal bulge (>15 mm)	27/62 (43.5%)	6/8 (75%)	0.27
Aortomitral angle	126.75±7.9	124.5±7.9	0.46
VTS	6.9±3.2	3.1±1.9	0.002
LVOT area systole, mm^2	451.9±146.1	331.1±117	0.03
Neo-LVOT area systole	270.9±122.8	145.3±45.5	0.006
Indexed neo-LVOT area systole	157.4±78.1	90.1±26.9	0.05
Sapien size and type for neo-LVOT			
23 S3 (TA)	1/62 (1.6%)	0/9 (0%)	0.35
23 XT (TA)	1/62 (1.6%)	2/9 (22.2%)	
23 S3 (TS)	2/62 (3.2%)	1/9 (11.1%)	
26 XT (TA)	8/62 (12.9%)	1/9 (11.1%)	
26 XT (TS)	5/62 (8.1%)	1/9 (11.1%)	
26 S3 (TA)	2/62 (3.2%)	0/9 (0%)	
26 S3 (TS)	4/62 (6.5%)	0/9 (0%)	
29 XT (TS)	5/62 (8.1%)	1/9 (11.1%)	
29 S3 (TS)	9/62 (14.5%)	1/9 (11.1%)	
29 S3 (TA)	7/62 (11.3%)	2/9 (22.2%)	
29 XT (TA)	7/62 (11.3%)	0/9 (0%)	
30 mm Inovare	1/62 (1.6%)	0/9 (0%)	
Expected %LVOT area reduction	42.7±15.2	58.3±12.9	0.008

LVOT indicates left ventricular outflow tract; MAC indicates mitral annular calcification; TA, transapical; TS, transseptal; and VTS, virtual transcatheter heart valve to septum distance.

with a satisfactory intraobserver and interobserver variability. For the overall cohort, a smaller neo-LVOT area and indexed neo-LVOT area were associated with LVOT obstruction, with cutoff values of 170 mm^2 and 0.92 cm^2/m^2, respectively.[8]

Complimentary to the advancements in preprocedural, several procedural techniques have been developed to preemptively mitigate the risk of LVOTO during TMVR. Such techniques include alcohol septal ablation before TMVR,[18] anterior leaflet laceration during TMVR



	AUC	Cutoff Value	Accuracy	Sensitivity	Specificity
LVOT area	0.76	371.5 mm²	0.54	0.67	0.87
Neo-LVOT area	0.86	173.4 mm²	0.81	0.8	0.87
Indexed Neo-LVOT area	0.83	127.5 mm²/m²	0.73	0.68	1
Expected % LVOT area reduction	0.80	63.5%	0.91	0.62	0.96
VTS	0.86	5.5 mm	0.68	0.72	0.68

Figure 2. Receiver-operating characteristic curves for multidetector row computed tomographic parameters to predict left ventricular outflow tract (LVOT) obstruction (LVOTO) post-transcatheter mitral valve replacement in mitral annular calcification. VTS indicates virtual transcatheter heart valve to septum distance.

(LAMPOON technique),[19] adoption of more invasive transatrial approach with anterior leaflet resection or septal myectomy during TMVR,[20] and radiofrequency ablation of the basal ventricular septum.[21] A recent single-center study evaluated the outcomes of TMVR in patients with MAC and failed ring repairs using all these techniques to mitigate the risk of LVOTO. They found that despite the advancements, the risk of LVOTO was still high at 13%.[22]

A major limitation of all previous studies has been the heterogeneity of the population studied. These studies

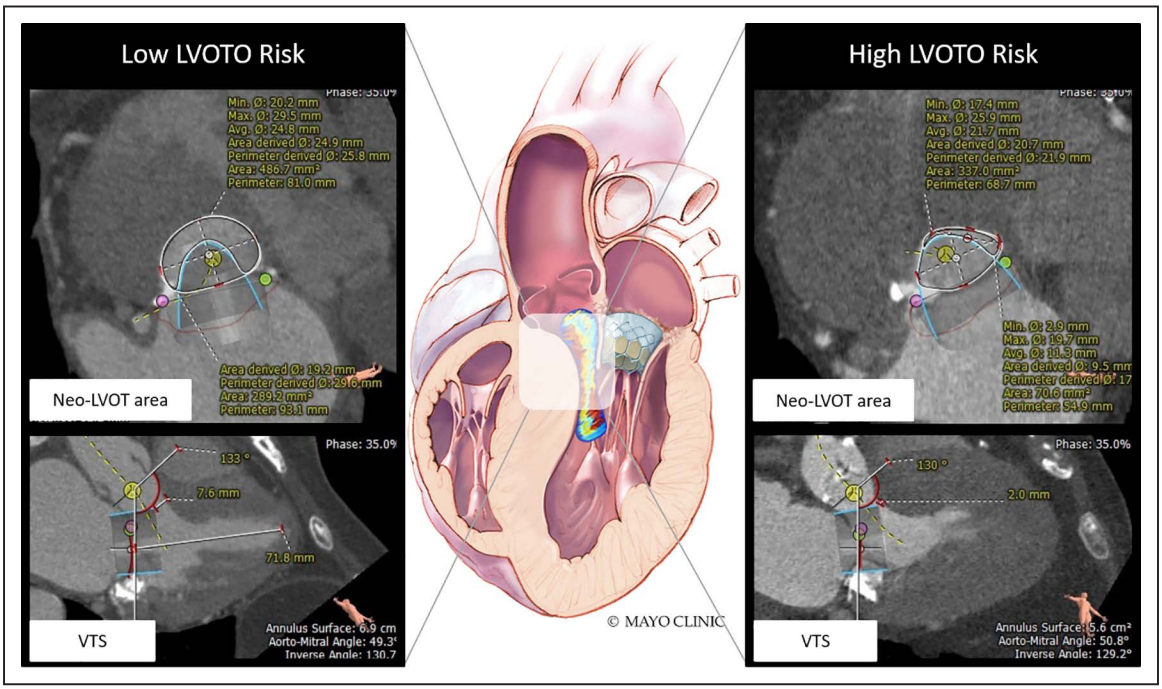


Figure 3. Multidetector computed tomography analysis using 3Mensio Structural Heart Workflow (version 10.0, Pie Medical Imaging, Maastricht, the Netherlands), showing neo–left ventricular outflow tract (LVOT) and virtual transcatheter heart valve to septum distance (VTS) in low LVOT obstruction risk (LVOTO; left) and high LVOT obstruction (right).

have included patients undergoing valve-in-valve, valve-in-ring, and ViMAC procedures. These are very different procedures with different anatomic considerations; as such, extrapolating the results of these studies to each procedure separately may be limited. This study assessed the risk of LVOTO specific to ViMAC. The core lab adjudication of the MDCT's is a major strength of this study. The neo-LVOT area was significantly associated with LVOTO with a cutoff value of 173.4 mm^2 (AUC, 0.86; sensitivity, 0.8; specificity, 0.87). Given that the neo-LVOT area integrates baseline LVOT area with the virtual valve frame, the association between systolic mean LVOT area, indexed neo-LVOT area, and expected % LVOT area reduction and LVOTO was not surprising. These findings corroborate data from the prior studies. The lack of independent association of the septal bulge diameter and anterior leaflet length with LVOTO supports the notion that the latter is determined by the complex anatomic interactions rather than individual anatomic parameters. The association of the VTS with LVOTO at a cutoff of 5.5 mm was a novel finding. This measurement can be more rapidly and predictably obtained compare to the neo-LVOT area. Due to this, it may have a role in screening those at high risk of LVOTO before TMVR.

Using these findings on MDCT would allow for a comprehensive risk assessment for LVOTO in patients undergoing ViMAC. This is particularly important for female patients because female sex was shown in this analysis to be associated with the risk of LVOTO. The low incidence of LVOTO in the current study may limit the predictive power of the cutoff values identified in this study. Larger and more definitive studies are needed for further validation of these findings.

Study Limitations

This was a retrospective and observational substudy of the global ViMAC registry. All the limitations of such a study such as selection bias, confounding, and referral bias are applicable. The sites were experienced centers and the cases enrolled were carefully vetted by the heart team of the individual sites. This selection bias cannot be understated and may limit the more general applicability of the findings. The small sample size and low event rates limit analysis adjusted to gender as well as the performance of the cutoff values of the LVOTO predictors. Moreover, significant associations between other variables and LVOT obstruction could have been underreported due to the low number of total events.

Conclusions

The systolic mean LVOT area, Neo-LVOT area, indexed Neo-LVOT, expected percentage LVOT area reduction, and the VTS were associated with LVOTO after ViMAC. Larger studies are needed to further explore and validate the predictive performance of the cutoff values reported in this study.

ARTICLE INFORMATION

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