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ORIGINAL STUDIES

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The impact of pulmonary hypertension on outcomes of transcatheter mitral valve replacement in mitral annular calcification

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Abstract

Objectives: To assess the impact of pulmonary hypertension (PH) on outcomes of patients with severe mitral annular calcification (MAC) undergoing transcatheter mitral valve replacement (TMVR).

Background: PH is associated with poor outcomes after mitral valve surgery. Whether the presence of PH in patients with MAC undergoing (TMVR) is associated with poor outcomes, is unknown.

Methods: Retrospective evaluation of 116 patients from 51 centers in 11 countries who underwent TMVR with valve in mitral annular calcification (ViMAC) using balloon-expandable aortic transcatheter valves (THVs) from September 2012 to March 2017. Pulmonary artery systolic blood pressure (PASP) by echocardiogram was available in 90 patients. The subjects were stratified based on PASP: No PH = PASP ≤35 mmHg ($n = 11$); mild to moderate PH = PASP 36–49 mmHg ($n = 21$) and severe PH = PASP ≥50 mmHg (n = 58). Clinical, procedural, and echocardiographic outcomes were assessed.

Results: Mean age was 72.7 (±12.8) years, 59 (65.6%) were female, Society of Thoracic Surgeons score was 15.8 + 11.8% and 90.0% where in New York Heart Association (NYHA) class III–IV. There was no significant difference in all-cause mortality at 30 days (no PH = 27.3%, mild–moderate PH = 19.0%, severe PH = 31.6%; $p = 0.55$) or at 1 year (no PH = 54.5%, mild–moderate PH = 38.1%, severe PH = 56.1%; $p = 0.36$). No difference in adverse events, NYHA class or amount of residual mitral regurgitation at 1 year were observed between the groups.

Abbreviations: CT, computed tomography; MAC, mitral annular calcification; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension; THV, transcatheter heart valves; TMVR, transcatheter mitral valve replacement; ViMAC, valve in mitral annular calcification.

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Conclusion: This study suggests that the presence of PH in patients with predominantly mitral stenosis with MAC undergoing TMVR does not impact mortality or adverse events. Further studies are needed to fully understand the effect of PH in this group of patients.

KEYWORDS
mitral annular calcification, pulmonary hypertension, transcatheter mitral valve replacement

1 | INTRODUCTION

Pulmonary hypertension (PH) is an important prognostic risk factor for perioperative morbidity and mortality in cardiac surgery,[1,2] and is present in 30%–40% of patients with mitral stenosis undergoing mitral valve replacement or valvuloplasty.[3–5] Patients with symptomatic severe mitral valve disease frequently develop significant decreased net atrioventricular compliance and pulmonary venous hypertension which may further impact their outcome.[6] Patients with severe mitral annular calcification (MAC) have high surgical risk because are often elderly with multiple comorbidities[7] and technical challenges related to calcium.[8–10] Therefore, transcatheter mitral valve replacement (TMVR) with the off-label use of balloon-expandable aortic transcatheter heart valves (THVs) is emerging as an alternative to surgery for patients who are not candidates for standard mitral surgery due to high risk.[11,12] The impact of PH on outcomes of TMVR in patients with severe MAC has not been well studied. We sought to evaluate outcomes of high surgical risk patients with severe MAC complicated with PH treated with valve in mitral annular calcification (ViMAC) using balloon-expandable aortic THV in the TMVR in MAC Global registry.

2 | METHODS

A total of 116 high-risk patients from 51 centers in 11 countries from North America, Europe, and South America who underwent TMVR ViMAC with the off-label use of balloon-expandable THV between September 2012 and March 2017 were included. One-year outcomes of these patients have already been published.[11] Baseline pulmonary artery systolic pressure (PASP) estimates based on transthoracic echocardiography were available in 90 patients. The remaining 26 patients for which PASP measurements were not available, were excluded from this analysis. Severe MAC was considered if the mitral valve annulus had the presence of diffuse, almost circumferential heavy calcification assessed by cardiac computed tomography (CT; Figure 1). The severity of MAC was evaluated using the Guerrero cardiac CT-based score developed from data generated in this registry.[13] Baseline clinical and echocardiographic characteristics, cardiac CT images, procedural characteristics including hemodynamic measurements via right heart catheterization when available, postimplantation echocardiographic characteristics, procedural complications, and major adverse events were collected at discharge, 30 days and 1 year. PH was defined as the presence of PASP of >35 mmHg. Mild PH was defined as PASP 36–49 mmHg and moderate to severe as PASP of ≥50 mmHg.[2,14]

This study was conducted following ethical principles according to the Declaration of Helsinki as well as US Food and Drug Administration guidelines (Code of Federal Regulations Title 21, part 812; and Good Clinical Practices recommended by the International Organization for Standardization ISO 14155:2011). The study was approved by the Mayo Clinic Institutional Review Board and the respective institutional review boards of the participating institutions. All patients provided written informed consent.

2.1 | Statistical analysis

Continuous variables are described as mean (±SD) and compared using one-way analysis of variance. Categorical variables are summarized as frequency (%) and compared using a χ^2 test with Yate's continuity correction. Comparisons across time points were made

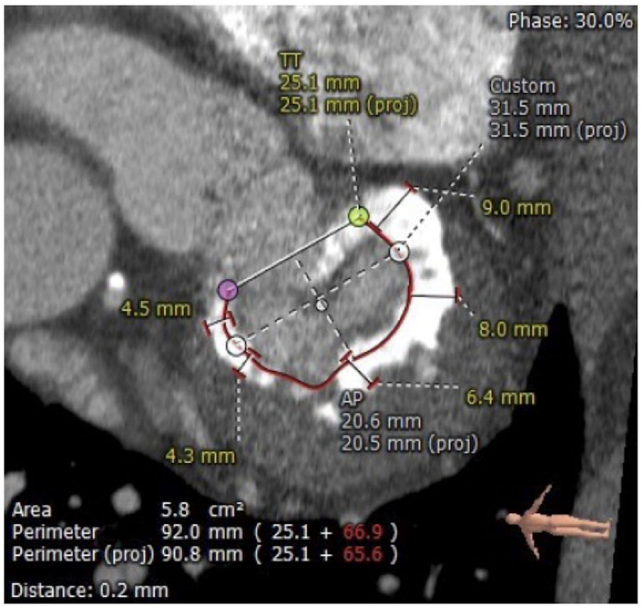

FIGURE 1 Mitral annular calcification assessed by computed tomography [Color figure can be viewed at wileyonlinelibrary.com]

using a paired *t*-test. If more than 5% of values are missing, the number of missing values was reported in the tables. Kaplan–Meier curves were created to visualize the long-term survival rate, and differences were compared using the log-rank test. All *p*-values are two-sided with a 0.05 Type I error rate. Analyses were conducted using R version 3.6.2 (R Foundation for Statistical Computing).

3 | RESULTS

Most of the 90 patients (79/90, 87.8%) who had PASP measurements by echocardiography had PH: 11 (12.2%) had PASP less than 35 mmHg (no PH group), 21 (23.3%) had PASP between 36 and 49 mmHg (mild to moderate PH group), and 58 (64.5%) exhibited PASP above or equal to 50 mmHg (severe PH group). Baseline characteristics are described in Table 1. The mean age was 72.7 ± 12.8 years and 66% were female. Multiple comorbidities were present and most patients (90%) were in NYHA functional class III or IV without differences between the groups. The Society of Thoracic Surgeons Predicted Risk of Mortality was 15.8 (±11.8).

Baseline echocardiographic characteristics are summarized in Table 2. Left ventricular ejection fraction was preserved in all groups. Mitral stenosis was the predominant pathology. Moderate or severe mitral regurgitation was more common in the severe PH group (no PH = 36.4%, mild to moderate PH = 14.3%, severe PH = 43.1%; $p = 0.02$) and mean mitral valve gradient tended to be higher in severe PH group (no PH = 8.6 (±3.4), mild to moderate PH = 11.3 (±3.9), severe PH = 12.1 (±4.5); $p = 0.05$).

There was a trend toward more moderate or severe tricuspid regurgitation in the severe PH group (28.6%, 35.3% and 58.3%; $p = 0.07$). Similarly, the presence of right ventricular dysfunction by echocardiography visual estimate of contractility was numerically higher in the severe PH group but did not reach statistical significance (12.5%, 27.8%, and 38.8%; $p = 0.29$). Baseline hemodynamic characteristics are

TABLE 1 Baseline clinical characteristics

	All	No PH PASP ≤35 mmHg (*n* = 11)	Mild–moderate PH PASP 36–49 mmHg (*n* = 21)	Severe PH PASP ≥50 mmHg (*n* = 58)	*p* Value
Age	72.7 (±12.8)	71.8 (±14.6)	71.2 (±16.3)	73.4 (±11.1)	0.78
Female	59 (65.6)	7 (63.6)	11 (52.4)	41 (70.7)	0.32
Hypertension	75 (83.3)	9 (81.8)	18 (85.7)	48 (82.8)	0.94
Diabetes	44 (49.4)	8 (72.7)	12 (57.1)	24 (42.1)	0.13
CABG	28 (31.1)	2 (18.2)	5 (23.8)	21 (36.2)	0.35
Prior MI (20 missing)	9 (12.9)	1 (16.7)	2 (11.8)	6 (12.8)	0.95
CAD (16 missing)	38 (51.4)	2 (28.6)	8 (47.1)	28 (58.6)	0.37
A fib	38 (42.2)	4 (36.4)	9 (42.9)	25 (43.1)	0.92
COPD	37 (41.6)	3 (27.3)	9 (42.9)	25 (43.9)	0.59
Oxygen use	17 (19.5)	3 (27.3)	2 (9.5)	12 (21.8)	0.38
Renal Disease	46 (51.1)	6 (54.5)	11 (52.4)	29 (50.0)	0.95
Rheumatic fever (14 missing)	11 (14.5)	0 (0)	3 (17.6)	8 (15.7)	0.46
Stroke	17 (19.1)	3 (27.3)	3 (14.3)	11 (19.3)	0.67
Heart Failure Hospitalization	63 (73.3)	8 (72.7)	14 (66.7)	41 (75.9)	0.72
Prior AVR	53 (58.9)	8 (72.7)	11 (52.4)	34 (58.6)	0.54
NYHA class					0.52
II	9 (10.0)	1 (9.1)	3 (14.3)	5 (8.6)	
III	42 (46.7)	5 (45.5)	11 (52.4)	26 (44.8)	
IV	39 (43.3)	5 (45.5)	7 (33.3)	27 (46.6)	
STS score	15.8 (±11.8)	15.0 (±9.8)	11.7 (±9.5)	17.4 (±12.8)	0.25
n-Missing	20	1	5	14	

Abbreviations: A fib, atrial fibrillation; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension; STS, Society of Thoracic Surgeons.

Note: Values are *n* (%) or mean (±SD).

TABLE 2 Baseline echocardiographic characteristics

	All	No PH PASP ≤35 mmHg (*n* = 11)	Mild–moderate PH PASP 36–49 mmHg (*n* = 21)	Severe PH PASP ≥50 mmHg (*n* = 58)	*p* Value
LV ejection fraction	60.3 (±10.2)	57.7 (±7.3)	61.3 (±12.1)	60.4 (±10.1)	0.63
Mitral valve area (cm^2)	1.32 (±0.73)	1.39 (±0.69)	1.91 (±0.46)	1.37 (±0.83)	0.64
n-Missing	15	2	1	12	
MV gradient (mean, mmHg)	11.5 (±4.4)	8.6 (±3.4)	11.3 (±3.9)	12.1 (±4.5)	0.05
Mitral regurgitation					0.02
N (%)					
None	9 (10.0)	0 (0)	3 (14.3)	6 (10.3)	
Trace	15 (16.7)	1 (9.1)	7 (33.3)	7 (12.1)	
Mild	34 (37.8)	6 (54.5)	8 (38.1)	20 (34.5)	
Moderate	18 (20.0)	3 (27.3)	3 (14.3)	12 (20.7)	
Severe	14 (15.6)	1 (9.1)	0 (0)	13 (22.4)	
Pulmonary artery systolic pressure (mmHg) mean (SD)	57.9 (19.2)	30.7 (3.7)	42.9 (3.6)	68.6 (15.0)	<0.001
Tricuspid regurgitation					0.07
None	0 (0)	0 (0)	0 (0)	1 (2.1)	
Trace	14 (19.4)	2 (28.6)	6 (35.3)	6 (12.5)	
Mild	21 (29.2)	3 (42.9)	5 (29.4)	13 (27.1)	
Moderate	25 (34.7)	1 (14.3)	6 (35.3)	18 (37.5)	
Severe	11 (15.3)	1 (14.3)	0 (0)	10 (20.8)	
n-Missing	18	4	4	10	
Right ventricular dysfunction	25 (33.3)	1 (12.5)	5 (27.8)	19 (38.8)	0.29
n-Missing	15	3	3	9	

Note: Values are *n* (%) or mean (±SD).

Abbreviations: LV, left ventricle; MV, mitral valve; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension.

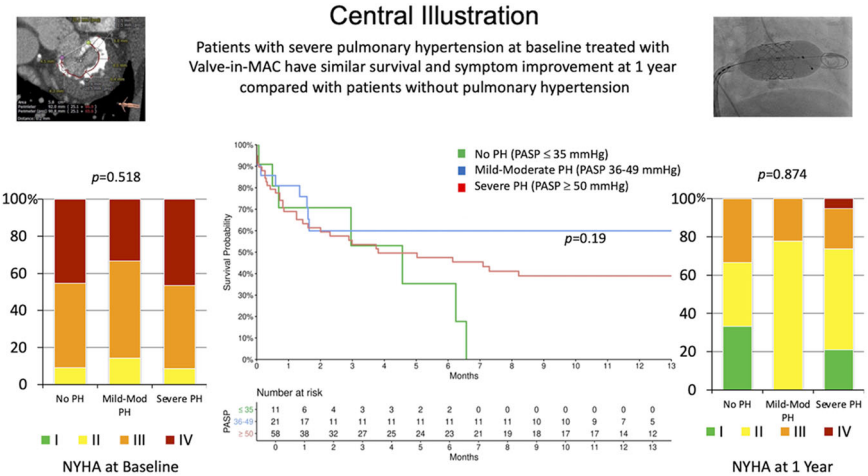

TABLE 3 Baseline hemodynamic assessments

	All	No PH PASP ≤35 mmHg (*n* = 11)	Mild–moderate PH PASP 36–49 mmHg (*n* = 21)	Severe PH PASP ≥50 mmHg (*n* = 58)	*p* Value
Right atrial pressure (mmHg)	12.1 (±7.3)	8.0 (±2.2)	9.9 (±5.4)	13.9 (±8.3)	0.212
n-Missing	60		13	40	
Right ventricular systolic pressure (mmHg)	57.7 (±19.8)	50.	52.4 (±9.5)	61.4 (±14.5)	0.61
n-Missing	70	10	14	46	
Left atrial pressure (mmHg)	24.0 (±7.1)	22.0 (±4.1)	24.2 (±4.2)	24.4 (±8.8)	0.84
n-Missing	66	7	15	44	
Pulmonary artery systolic pressure (mmHg)	60.7 (±20.0)	47.5 (±6.1)	52.3 (±14.0)	67.1 (±21.2)	0.06
n-Missing	57	7	12	38	
Pulmonary artery diastolic pressure (mmHg)	24.4 (±8.3)	21.3 (±5.6)	22.8 (±5.7)	25.8 (±9.6)	0.51
n-Missing	60	7	13	40	
Pulmonary artery mean pressure	40.4 (±10.5)	31.2 (±6.7)	35.3 (±8.4)	44.4 (±8.8)	0.02
n-Missing	62	7	12	40	
Pulmonary capillary wedge pressure (mmHg)	26.3 (±9.1)	22.0 (NA)	24.0 (±6.2)	27.6 (±10.3)	0.64
n-Missing	66	10	14	42	
Left ventricular end-diastolic pressure (mmHg)	14.2 (±5.0)	15.0 (±6.1)	14.2 (±4.2)	13.9 (±5.4)	0.95
n-Missing	70	8	16	46	
Cardiac output, Fick		4.8 ± 2.0 (*n* = 3)	5.2 ± 1.1 (*n* = 5)	5.4 ± 2.3 (*n* = 8)	
Cardiac index, Fick		2.7 ± 0.9 (*n* = 3)	2.8;± 0.8 (*n* = 4)	2.8 ± 1 (*n* = 8)	
Cardiac output, TD		4.6 (*n* = 1)	4.1 (*n* = 1)	4.8 ± 1.7 (*n* = 10)	
Cardiac index, TD		2.2 (*n* = 1)	2.2 (*n* = 1)	2.5 ± 0.7 (*n* = 9)	
Systolic aortic pressure		118.2 ± 28.6 (*n* = 6)	120.8 ± 21.7 (*n* = 9)	123.2 ± 35.0 (*n* = 26)	
Diastolic aortic pressure		58.6 ± 21.7 (*n* = 6)	54.4 ± 13.0 (*n* = 9)	57.3 ± 14.8 (*n* = 26)	
Mean aortic pressure		83.0 ± 26.0 (*n* = 6)	79.8 ± 19.4 (*n* = 7)	81.5 ± 14.5 (*n* = 21)	

Note: Values are *n* (%) or mean (±SD).

Abbreviations: PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension; TD, thermodilution.

summarized in Table 3. There were no significant differences in left ventricular end-diastolic pressure or left atrial pressure at baseline. However, the frequency of missing values was high. Intraprocedural outcomes are presented in Table 4. There were no significant differences in rates of valve implantation success, need for a second valve, conversion to open surgery, use of hemodynamic mechanical assist devices, occurrence of intraprocedural left ventricular outflow obstruction with hemodynamic compromise or device migration events.

In-hospital outcomes are summarized in Table 5. There was no significant difference in all-cause mortality (no PH = 27.3%, mild to moderate PH = 19.0%, severe PH = 27.6%; $p = 0.74$), other adverse events, length of hospital stay or NYHA class at discharge.

30 Days outcomes are presented in Table 6. All-cause mortality was similar among the groups (no PH = 27.3%, mild to moderate PH = 19.0%, severe PH = 31.6%; $p = 0.55$),

The PASP by transthoracic echocardiogram was numerically higher in the severe PH group (no PH = 45.0 ± 7.1 mmHg, mild–moderate PH = 36.1 ± 13.9 mmHg, severe PH = 52.8 ± 17.2 mmHg; $p = 0.09$), but lower compared with baseline 68.6 ± 15.0 mmHg; $p = 0.02$.

TABLE 4 Intraprocedural outcomes

	All	No PH PASP ≤35 mmHg (*n* = 11)	Mild–moderate PH PASP 36–49 mmHg (*n* = 21)	Severe PH PASP ≥50 mmHg (*n* = 58)	*p* Value
Access route					0.15
Transseptal	45 (50.0)	8 (72.7)	12 (57.1)	25 (43.1)	
Transapical	29 (32.2)	1 (9.1)	9 (42.9)	19 (32.8)	
Transatrial	16 (17.8)	2 (18.2)	0 (0)	14 (24.1)	
Device band					0.94
Edwards					
Sapien	5 (5.6)	1 (9.1)	2 (9.5)	2 (3.4)	
Sapien XT	33 (36.7)	2 (18.2)	7 (33.3)	24 (41.4)	
Sapien 3	50 (55.6)	8 (72.7)	11 (52.4)	31 (53.4)	
Inovare	2 (2.2)	0 (0)	1 (4.8)	1 (1.7%)	
Valve size (mm)					0.94
23	6 (6.7)	1 (9.1)	1 (4.8)	4 (6.9)	
26	32 (35.6)	3 (27.3)	11 (52.4)	18 (31.0)	
29	50 (55.6)	7 (63.6)	8 (38.1)	35 (60.3)	
25	0 (0)	0 (0)	0 (0)	0 (0)	
30	2 (2.2)	0 (0)	1 (4.8)	1 (1.7)	
Successful implantation of mitral valve	80 (89.9)	10 (90.9)	19 (90.5)	51 (89.5)	0.98
Technical success by MVARC criteria					0.58
Yes	67 (74.4)	7 (63.6)	15 (71.4)	45 (77.6)	
No	23 (25.6)	4 (36.4)	6 (28.6)	13 (22.4)	
Need for the second valve	14 (15.6)	1 (9.1)	3 (14.3)	10 (17.2)	0.79
Conversion to open surgery	3 (3.3)	1 (9.1)	1 (4.8)	1 (1.7)	0.42
Mechanical assist device requirement	11 (12.8)	0 (0)	3 (14.3)	8 (14.8)	0.40
Mechanical assist device type					0.99
IABP	1 (12.5)	0 (0)	0 (0)	1 (20.0)	
Impella	2 (25.0)	0 (0)	1 (33.3)	1 (20.0)	
Tandem heart	0 (0)	0 (0)	0 (0)	0 (0)	
ECMO	5 (62.5)	0 (0)	2 (66.7)	3 (60.0)	
n-Missing	3	0	0	3	
LVOT obstruction with hemodynamic compromise	11 (12.2)	1 (9.1)	4 (19.0)	6 (10.3)	0.55
Device migration	9 (10.0)	2 (18.2)	0 (0)	7 (12.1)	0.18

Note: Values are *n* (%) or mean (±SD).

Abbreviations: ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVOT, left ventricular tract; MVARC, Mitral Valve Academic Research Consortium; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension.

TABLE 5 In-hospital outcomes

	All	No PH PASP ≤35 mmHg (*N* = 11)	Mild–moderate PH PASP 36–49 mmHg (*N* = 21)	Severe PH PASP ≥50 mmHg (*N* = 58)	*p* Value
All-cause death	23 (25.6)	3 (27.3)	4 (19.0)	16 (27.6)	0.74
Cardiovascular	15 (65.2)	2 (66.7)	3 (75.0)	10 (62.5)	0.85
Noncardiovascular	8 (34.8)	1 (33.3)	1 (25.0)	6 (37.5)	0.85
Emergent cardiac surgery	5 (6.0)	1 (9.1)	1 (5.0)	3 (5.7)	0.89
n-Missing	6	0	1	5	
Pacemaker requirement	14 (16.3)	1 (9.1)	5 (23.8)	8 (14.8)	0.50
n-Missing	4	0	0	4	
Device embolization	4 (4.4)	2 (18.2)	0 (0)	2 (3.4)	0.05
Device migration	7 (8.3)	2 (18.2)	1 (5.0)	4 (7.5)	0.42
n-Missing	6	0	1	5	
Device thrombosis	0 (0)	0 (0)	0 (0)	0 (0)	1
n-Missing	5	0	1	4	
Stroke ischemic	4 (4.7)	2 (18.2)	0 (0)	2 (3.7)	0.06
n-Missing	5	0	1	4	
Red blood cell transfusion	35 (53.8)	3 (50.0)	7 (53.8)	25 (54.3)	0.98
n-Missing	25	5	8	12	
NYHA functional class at discharge					0.22
I	13 (22.8)	2 (28.6)	5 (35.7)	6 (16.7)	
II	24 (42.1)	2 (28.6)	6 (42.9)	16 (44.4)	
III	16 (28.1)	3 (42.9)	3 (21.4)	10 (27.8)	
IV	4 (7.0)	0 (0)	0 (0)	4 (11.1)	
n-Missing	33	4	7	22	
Hospital length of stay days	13.7 (±11.9)	15.3 (±13.5)	14.2 (±12.8)	13.1 (±11.3)	0.85
n-Missing	16	1	2	13	
Destination at discharge					0.79
Home, *N* (%)	25 (52.1)	3 (42.9)	7 (58.3)	15 (51.7)	
Extended care	20 (41.7)	3 (42.9)	5 (41.7)	12 (41.4)	
NH/rehab/other	3 (6.2)	1 (14.3)	0 (0)	2 (6.9)	
n-Missing	42	4	9	29	

Note: Values are *n* (%) or mean (±SD).

Abbreviations: LV, left ventricle; NH, Nursing Home; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension; Rehab, rehabilitation center.

There was no difference in adverse events, left ventricular ejection fraction, amount of residual mitral regurgitation, or functional class between the groups.

One-year outcomes are shown in Table 7. All-cause mortality was similar in the groups (no PH = 54.5%, mild–moderate PH = 38.1%, severe PH = 56.1%; $p = 0.36$), Kaplan–Meier survival curves are shown in the central illustration. No differences in adverse events, left ventricular ejection fraction, amount of residual mitral regurgitation, or functional class were found at 1 year among the groups. THV function remained stable (Figure 2) and symptoms improved in all groups (NYHA class is presented in Figure 3).

4 | DISCUSSION

In this group of high-risk patients with MAC who underwent TMVR with a ViMAC procedure, the presence of PH was not associated with an increase in all-cause mortality, worse mitral

TABLE 6 30 Days outcomes

	All	No PH PASP ≤35 mmHg (*n* = 11)	Mild–moderate PH PASP 36–49 mmHg (*n* = 21)	Severe PH PASP ≥50 mmHg (*n* = 58)	*p* Value
All-cause death	25 (27.8)	3 (27.3)	4 (19.0)	18 (31.0)	0.58
Cardiovascular	3 (12.0)	1 (33.3)	1 (25.0)	1 (5.6)	0.86
Noncardiovascular	22 (88.0)	2 (66.7)	3 (75.0)	17 (94.4)	0.86
NYHA functional class					0.56
I	12 (30.0)	1 (20.0)	3 (30.0)	8 (32.0)	
II	13 (32.5)	1 (20.0)	3 (30.0)	9 (36.0)	
III	11 (27.5)	2 (40.0)	3 (30.0)	6 (24.0)	
IV	4 (10.0)	1 (20.0)	1 (10.0)	2 (8.0)	
n-Missing	24	3	7	14	
LV ejection fraction	60.9 (±8.1)	60.4 (±4.4)	58.8 (±7.1)	61.3 (±9.2)	0.70
n-Missing	23	2	5	16	
Mean mitral gradient	5.7 (±1.9)	6.4 (±1.4)	5.2 (±1.5)	5.7 (±2.1)	0.49
n-Missing	26	2	7	17	
Mitral regurgitation					0.59
None	21 (51.2)	3 (50.0)	6 (50.0)	12 (52.2)	
Trace	13 (29.3)	3 (50.0)	3 (25.0)	7 (26.1)	
Mild	5 (12.2)	0 (0)	1 (8.3)	4 (17.4)	
Moderate	2 (4.9)	0 (0)	1 (8.3)	1 (4.3)	
Severe	1 (2.4)	0 (0)	1 (8.3)	0 (0)	
n-Missing	23	2	5	16	
Paravalvular MR					0.35
None	15 (50.0)	2 (50.0)	3 (33.3)	10 (58.8)	
Trace	7 (23.3)	2 (50.0)	3 (33.3)	2 (11.8)	
Mild	5 (16.7)	0 (0)	1 (11.1)	4 (23.5)	
Moderate	2 (6.7)	0 (0)	1 (11.1)	1 (5.9)	
Severe	1 (3.3)	0 (0)	1 (11.1)	0 (0)	
n-Missing	34	4	8	22	
Pulmonary artery systolic pressure (mmHg)	46.0 (±16.9)	45.0 (±7.1)	36.1 (±13.9)	52.8 (±17.2)	0.09
n-Missing	42	6	9	27	
LVOT gradient (mmHg)	9.8 (±11.9)	4.7 (±5.7)	14.5 (±18.8)	8.9 (±7.5)	0.32
n-Missing	34	3	8	23	

Note: Values are *n* (%) or mean (±SD).

Abbreviations: LVOT, left ventricular outflow tract; MR, mitral regurgitation; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension.

valve function, or worse NYHA class at 30 days and 1 year compared with those patients without PH.

These findings are different than prior surgical reports or transcatheter mitral valve edge-to-edge repair with MitraClip reports. Historically, in patients with mitral stenosis undergoing surgical intervention, the presence of PH has been found to be associated with higher mortality rates ranging from 3% to 31%.[15–18] In a retrospective analysis of 1571 patients who underwent first-time mitral valve surgery between April 2004 and December 2013, patients were stratified into PH groups of none (<35 mmHg); moderate (35–49); severe (50–79); and extreme (>80)

TABLE 7 1-Year outcomes

	All	No PH PASP ≤35 mmHg (*n* = 11)	Mild PH PASP 36–49 mmHg (*n* = 21)	Severe PH PASP ≥50 mmHg (*n* = 58)	*p* Value
All-cause death	47 (52.2)	6 (54.5)	8 (38.1)	33 (56.9)	0.33
Cardiovascular	11 (23.4)	1 (16.7)	1 (12.5)	9 (27.3)	0.62
Noncardiovascular	36 (76.6)	5 (83.3)	7 (87.5)	24 (72.7)	0.62
NYHA functional					0.87
I *N* (%)	5 (16.1)	1 (33.3)	0 (0)	4 (21.1)	
II	18 (58.1)	1 (33.3)	7 (77.8)	10 (52.6)	
III	7 (22.6)	1 (33.3)	2 (22.2)	4 (21.1)	
IV	1 (3.2)	0 (0)	0 (0)	1 (5.3)	
n-Missing	12	2	4	6	
LV ejection fraction	62.3 (±9.5)	66.7 (±7.6)	59.3 (±7.4)	63.0 (±10.8)	0.48
n-Missing	17	2	5	10	
Mean mitral gradient	6.0 (±1.9)	6.5 (±0.6)	5.7 (±0.9)	6.0 (±2.4)	0.84
n-Missing	17	2	6	9	
Mitral regurgitation					0.99
None	18 (78.3)	0 (0)	4 (44.4)	10 (66.7)	
≤1 (+)	4 (17.4)	0 (0)	4 (44.4)	4 (26.7)	
2 (+)	0 (0)	0 (0)	0 (0)	0 (0)	
3 (+) or greater	1 (4.3)	0 (0)	0 (0)	1 (6.7)	
n-Missing	20	5	5	10	
LVOT gradient (mmHg)					0.95
Mean (SD)	6.4 (±9.2)	5.3 (±1.8)	5.8 (±9.7)	7.1 (±10.6)	
n-Missing	23	2	7	14	

Note: Values are *n* (%) or mean (±SD).

Abbreviations: LV, left ventricle; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension.

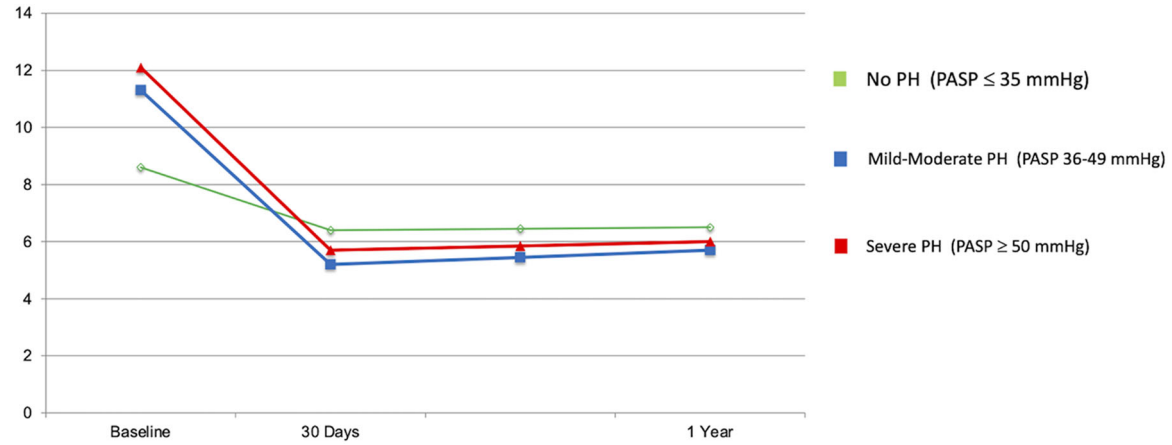

FIGURE 2 Mean mitral valve gradient at 1 year. PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension [Color figure can be viewed at wileyonlinelibrary.com]

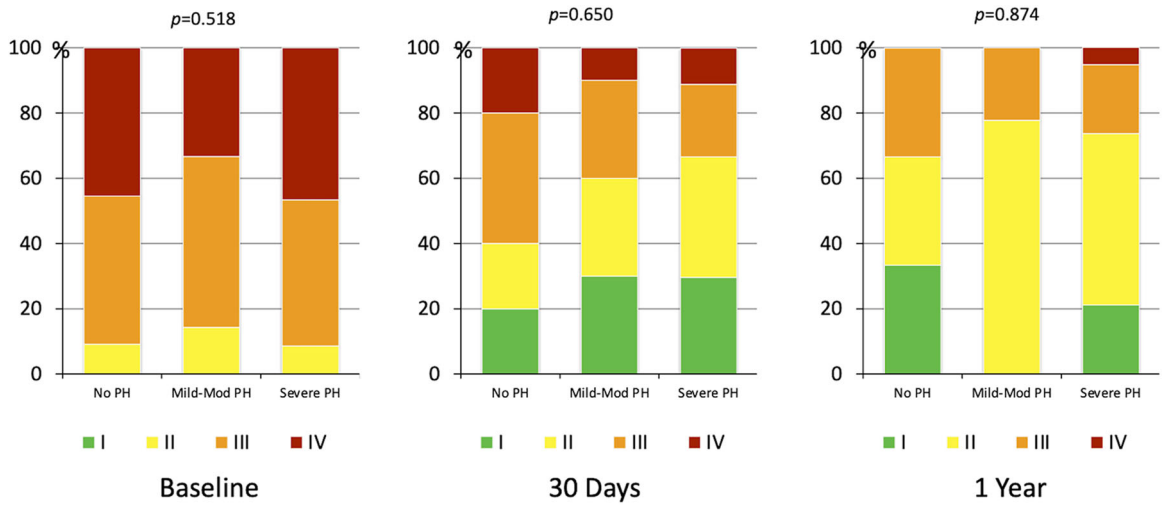

FIGURE 3 New York Heart Association Functional Class [Color figure can be viewed at wileyonlinelibrary.com]

by echocardiographic PASP measurements. In propensity-score-matched groups, no differences in mortality were found at 30 days in all groups of PH. However, 5-year survival was lower in patients with PH,75% versus 91.5% in patients without PH.[14] A similar study involving 317 consecutive patients with mitral stenosis who underwent mitral surgery, stratified patients according to PASP by echocardiogram as mild PH (35–40 mmHg); moderate PH (45–59 mmHg), or severe PH (>60 mmHg). Patients with severe PH had a 30-day mortality of 9% with no differences among groups. However, the 10- and 12-year survival was significantly worse in the moderate and severe PH groups (58% and 79%, respectively) compared with the normal and mild PH groups (83% and 79%, respectively).[19] The European System for Cardiac Operative Risk Evaluation (EuroSCORE) considers that the presence of PH poses a higher risk for mortality in the perioperative period.[20] This has been further validated by the EuroSCORE II with a more contemporary experience in cardiac surgery and in spite of better overall outcomes, continues to identify the presence of PH as a significant factor associated with increased mortality risk.[21]

The presence of severe PH has also been associated with increased mortality after transcatheter mitral valve repair with MitraClip. An analysis of 4071 patients who underwent transcatheter mitral edge-to-edge repair with MitraClip between November 2013 and March 2017 and were included in the Society of Thoracic Surgeons/American College of Cardiology/Transcatheter Valve Therapies Registry, found higher all-cause mortality in patients with severe PH at baseline. The patients were divided in 4 groups according the baseline mean pulmonary artery pressure (mPAP): Group 1 = No PH (mPAP < 25 mmHg, $n = 1103$); Group 2 = mild PH (mPAP: 25–34 mmHg, $n = 1399$); Group 3 = moderate PH (mPAP: 35–44 mmHg, $n = 1011$); and Group 4 = severe PH (mPAP ≥ 45 mmHg, $n = 558$). Progressively higher all-cause 30-day mortality rates were observed across PH groups (1.5% for Group 1 vs. 4.3% in Group 4, $p = 0.004$). At 1-year, all-cause mortality was higher in patients with higher severity of PH (Group 1 = 16.3%, Group 2 = 19.8%, Group 3 = 22.4%, and Group 4 = 27.8%; $p < 0.001$). In multivariable analysis, the association of PH was independently associated with an increased rate of composite of 1-year mortality and heart failure hospitalization (hazard ratio for Group 4 vs. 1, 1.44; 95% confidence interval: 1.16–1.79; $p < 0.001$).[22]

The report we present is the first large multicenter study that provides information on outcomes according to the presence and severity of PH at baseline in high-risk patients with severe MAC undergoing ViMAC procedures. For many years, the presence of severe PH has influenced surgical decisions on not to intervene due to the associated mortality and morbidity. The findings in this study suggest that PH in and of itself, may not necessarily be a relative or absolute contraindication for TMVR in patients with MAC. This is important as we enter a new era of TMVR and this finding may result in more patients being considered candidates for this treatment option. While we cannot offer a direct explanation on why in this severe group of patients PH does not affect measured outcomes up to a year of follow up, poorer outcomes may be seen in longer surveillance as noted in other studies based on echocardiographic measurement of pulmonary pressures. Careful global assessment of right ventricular function in addition to pulmonary pressures needs to be incorporated in the evaluation of each individual patient as the presence of right ventricular dysfunction may result in different outcomes. Prospective studies such as MITRAL I (Mitral Implantation of TRAnscatheter vaLves, NCT NCT 02370511) and MITRAL (NCT 04408430), may provide further insights.

5 | STUDY LIMITATIONS

The small sample size, selection bias, limitations associated with retrospective analysis of self-reported data are all limitations of this study and are acknowledged by the authors. The lack of an echocardiographic core laboratory and a clinical adjudication committee are other limitations. Right heart catheterization and direct measurement of pulmonary pressure is the gold standard for the determination of pulmonary pressures. In this data set, there were large chunks of missing right heart hemodynamic data making it impossible to correlate the echocardiographic

estimated measurements with the right heart hemodynamics. In addition, pulmonary pressures vary with stroke volume and the spuriously low PASP from concomitant right ventricular dysfunction could not be sorted from true normal pulmonary pressures.

Prospective studies with a larger number of non-heterogenous patients are needed to answer the question if the presence of PH confers additive risk to TMVR in the same way that it does for open surgical mitral valve replacement.

6 | CONCLUSIONS

The presence of PH measured by echocardiography in patients with severe MAC undergoing TMVR with balloon-expandable aortic transcatheter valves was not associated with increased all-cause mortality at 1 year compared with patients without PH.

6.1 | Clinical perspectives

6.1.1 | What is known?

PH is associated with poor outcomes after mitral valve surgery. Whether the presence of PH in patients with (MAC) undergoing (TMVR) is associated with poor outcomes, has not been evaluated.

6.1.2 | What is new?

Among high-risk patients with severe MAC treated with a ViMAC procedure, patients with severe PH at baseline had similar outcomes as patients without PH.

6.1.3 | What is next?

Further studies are needed to evaluate the long-term outcomes of ViMAC in patients with severe PH at baseline.

CONFLICT OF INTERESTS

Dr. Guerrero has received research grant support from Edwards Lifesciences. Dr. Wang has served as a consultant for Edwards Lifesciences, Boston Scientific, and Materialise. Dr. George is a consultant for MitreMedical, CardioMech, WL Gore, Atricure, Neptune Medical. Dr. Leon reports institutional research support (no direct financial compensation) from Edwards Lifesciences, Medtronic, Boston Scientific, Abbott. Consultant/Advisory Board for Medtronic, Boston Scientific, Gore, Meril Lifesciences, and Abbott. Kodali reports institutional research support (no direct financial compensation) from Edwards Lifesciences, Medtronic, Abbott. Consultant for Abbott, Admedus, Meril Lifesciences. Equity options from Biotrace Medical and Thubrikar Aortic Valve, Inc. Dr. Chakravarty has been a consultant for Abbott, Edwards Lifesciences, Boston Scientific, and Medtronic. Dr. O'Hair is a consultant and proctor for Medtronic. Dr. Jones reports proctoring and consulting for Medtronic Inc. and Edwards Lifesciences, and consulting for Boston Scientific. Dr. Makkar reports research grants from Edwards Life Sciences, Abbott, Medtronic, and Boston Scientific; personal proctoring fee from Edwards Life Sciences; and travel support from Edwards, Abbott, and Boston Scientific. Dr. O'Neill is a consultant forAbiomed, Edwards Lifesciences, and Medtronic.

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