Impact of Mitral Stenosis on Survival in Patients Undergoing Isolated Transcatheter Aortic Valve Implantation

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This study was performed to investigate the prevalence and impact on survival of baseline mitral stenosis (MS) in patients who underwent transcatheter aortic valve implantation (TAVI) due to the presence of severe symptomatic aortic stenosis. This retrospective study included 928 consecutive patients with severe, symptomatic aortic stenosis who underwent TAVI in 2 institutions, from January 2012 to August 2016. Mean follow-up was 40.8 ± 13.9 months. Based on the mean mitral gradient (MMG) at baseline, 3 groups were identified: MMG <5 mm Hg (n = 737, 81.7%); MMG ≥5 and <10 mm Hg (n = 147, 16.3%); MMG ≥10 mm Hg (n = 17, 1.9%). These latter were more frequently women, with a smaller body surface area, a higher prevalence of atrial fibrillation, chronic obstructive pulmonary disease, and previous history of coronary-artery bypass graft/percutaneous coronary intervention. At baseline, patients with MMG ≥10 mm Hg compared with ≥5 and <10 mm Hg and <5 mm Hg patients had a lower mitral valve area (2.4 ± 0.94 vs 2.1 ± 0.86 vs 1.5 ± 0.44 cm^2), a lower prevalence of MR ≥2+ (5.9% vs 28.6% and 15.6%, p <0.0001), a higher prevalence of severe mitral annular calcium (70.6% vs 45.6% and 13.0%, p <0.0001) and a higher systolic pulmonary arterial pressure (50.6 ± 12.1 vs 47.2 ± 14.5 and 41.6 ± 14.4, p <0.0001). Despite the low prevalence of MMG ≥10 mm Hg, these patients had higher 5-year mortality compared with the other groups (adjusted hazard ratio 2.91, 95% confidence interval 1.17 to 7.20, p = 0.02). In conclusion, severe calcific MS is uncommon in patients who underwent TAVI. Its presence is associated with higher long-term mortality whereas moderate MS is not. **(Am J Cardiol 2019;123:1314−1320)**

Degenerative aortic stenosis (AS) is characterized by calcific thickening of the aortic cusps which often involves the mitral annulus and leaflets, particularly in the elderly population.[1−4] In some patients, this leads to the concomitant presence of AS and mitral stenosis (MS; i.e., variously termed nonrheumatic, or degenerative MS). It has been reported that the prevalence of MS in patients with severe AS is around 10%.[5] Current guidelines on the management of patients with concomitant AS and MS recommend a double valve intervention when the disease is judged to be moderate or severe. Transcatheter aortic valve implantation (TAVI) is the new standard of care for patients with symptomatic severe AS who are deemed at intermediate or higher risk for surgical aortic valve replacement. Because double valve replacement increases operative risk compared with surgical aortic valve replacement alone, patients with severe AS and MS are almost always at least intermediate risk. In this population, data on the prevalence of MS and its role on survival are limited. A recent report from the Transcatheter Valve Therapy registry identified mitral valve area as a predictor of mortality at 1-year after TAVI.[6] So far this is the only available data on this topic, and it suffers from lack of long-term follow-up. Moreover, severe MS was defined by a mitral valve area <1.5 cm^2 derived from echocardiography or catheterization using various methods, which likely overestimated the proportion of patients in the severe MS group.[6] In this report, using a different definition of MS based on the resting mean mitral gradient (MMG), we sought to investigate the prevalence of MS in a cohort of TAVI patients from 2 centers and how the presence of MS impacted the 5-year survival of this population.

Methods

We retrospectively examined 928 patients with severe symptomatic AS who underwent TAVI at Baylor Heart and Vascular Hospital (Dallas, Texas) and The Heart Hospital Baylor Plano (Plano, Texas) from January 2012 to August 2016. Baseline demographics, echocardiographic, and procedural data were retrospectively collected and analyzed. Data from both medical centers were pooled and a joint database was created. Only patients with complete echocardiographic information at baseline and post-TAVI were considered for this analysis (n = 901). Primary outcome was all-cause mortality at 5-year follow-up, which was

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obtained through querying the National Death Index. The study was approved by the Baylor Institutional Review Board.

Transthoracic echocardiography was performed using a commercially available system (iE33 or Epiq, Koninklijke Philips Electronics N.V.). Images of the standard parasternal and apical views were obtained with the patient in the left lateral decubitus position. Left ventricular (LV) dimensions and function, left atrium diameters were measured according to the current guidelines.[7,8] MR was evaluated pre- and post-TAVI on the basis of the integration of multiple parameters, including color Doppler jet area, vena contracta width, and effective regurgitant orifice area and regurgitant volume by proximal isovelocity surface area and volumetric methods and graded as no/trivial, mild, moderate, or severe per guideline recommendations.[9] MMG was determined pre- and post-TAVI from the Doppler diastolic mitral flow; based on MMG at baseline, 3 groups of patients were identified, MMG <5 mm Hg; MMG ≥5, and <10 mm Hg; MMG ≥10 mm Hg.[10] Mitral annular calcium (MAC) was defined by the presence of echodense calcium deposits either limited to the true mitral annulus behind the posterior mitral leaflet[11,12] (posterior) or extending anteriorly onto the aorto-mitral curtain (anterior). MAC grade was reported as none, mild (<25% of mitral annulus), moderate (25% to 50% of mitral annulus), and severe (≥50% of mitral annulus).

Continuous variables were presented as mean ± standard deviation. Categorical data were reported as frequencies and percentages. Differences in continuous variables between MMG groups were compared using the one-way analysis of variance or the Mann-Whitney *U*-test, as appropriate. Differences in categorical variables between MMG groups were compared using the chi-square test. Unadjusted, cumulative long-term mortality was compared across the 3 MMG groups using Kaplan-Meier approach and the log-rank test. Due to the small number of patients (n = 17) in the largest MMG group, inclusion of additional covariates for adjustment would have been inappropriate due to the lack of adequate overlap in characteristics between comparison groups. Therefore, to adjust for potential confounding due to preoperative patient characteristics, we formed a risk-adjusted Cox Proportional Hazards time-to-mortality model by including the US-TAVI score (modeled using a 3-knot restricted cubic spline function) as an adjustment covariate along with MMG group. The proportional hazards assumption was confirmed by the chi-squared test of the interaction between MMG group and survival time (p = 0.67). For all tests, a p value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS software version 20.0 (IBM, Armonk, New York) 13 and SAS 9.4 (SAS Inc., Cary, North Carolina).[13]

Results

During the study period from January 2012 to August 2016, a total of 928 patients underwent TAVI. Of those, complete echocardiographic and survival data were available for 901 patients (97%). Table 1 displays the baseline characteristics for the study population according to baseline MMG. Most had MMG <5 mm Hg at baseline (n = 737, 81.7%); 147 patients (16.3%) had MMG ≥5 and <10 mm Hg, and only 17 patients (1.9%) had a baseline MMG ≥10 mm Hg. As shown in Table 1, patients with a baseline MMG ≥10 mm Hg tended to be more frequently women (76.5% vs 41.5% and 72.15, p <0.0001) and a smaller body surface area (1.8 ± 0.22 vs 1.9 ± 0.25 and 1.8 ± 0.25, p = 0.001). Compared with patients with MMG <10 mm Hg, those with baseline MMG ≥10 mm Hg had a higher prevalence of atrial fibrillation (35.3% vs 32.7% and 22.4%, p = 0.046), chronic obstructive pulmonary disease (47.1% vs 21.4% and 22.4%, p = 0.041) and previous history of coronary-artery bypass graft/percutaneous coronary intervention (70.6% vs 50.2% and 36.7%, p = 0.002). The 3 groups were similar for procedural characteristics apart from the use of smaller aortic valve prosthesis in the group of patients with baseline MMG ≥10 mm Hg (p <0.0001; Table 1). As reported in Table 2, patients with baseline MMG ≥10 mm Hg showed higher LV ejection fraction compared with the other 2 groups (60.6 ± 13.2 vs 53.7 ± 13.1 and 58.5 ± 13.1, p <0.0001). This latter group also showed higher aortic valve mean gradients (47.8 ± 10.8 vs 43.8 ± 13.4 and 48.8 ± 16.4, p <0.0001) and peak velocity (4.6 ± 0.5 vs 4.3 ± 0.62 and 4.5 ± 0.65, p = 0.001). Consistently, they had higher mitral mean gradients (11.8 ± 1.7 vs 2.3 ± 1.0 and 6.2 ± 1.3, p <0.0001), smaller mitral valve area (1.5 ± 0.44 vs 2.4 ± 0.94 and 2.1 ± 0.86, p <0.0001) and a higher prevalence of severe MAC (64.7% vs 13.0% and 45.6%, p <0.0001), which was more frequently localized both anteriorly and posteriorly (41.2% vs 11.7% and 31.7%, p <0.0001). Finally, patients with baseline MMG ≥10 mm Hg had a significantly lower prevalence of MR ≥2 + (5.9% vs 15.6% and 28.6%, p <0.0001) and a higher systolic pulmonary arterial pressure (50.6 ± 12.1 vs 41.6 ± 14.4 and 47.2 ± 14.5, p <0.0001) compared with the other 2 groups. After TAVI, patients with baseline MMG ≥10 mm Hg had a persistently higher left ventricle ejection fraction (61.9 ± 6.6 vs 54.8 ± 11.9 and 56.9 ± 10.6, p = 0.012), slightly higher aortic mean gradient (10.2 ± 5.4 vs 8.3 ± 4.1 and 9.3 ± 4.5, p = 0.004). Patients starting with MMG ≥10 mm Hg also displayed higher MMG post-TAVI (8.7 ± 4.5 vs 3.0 ± 1.56 and 5.1 ± 2.3, p <0.0001, Table 3). No differences were observed for all the other hemodynamic variables.

As reported in Table 4, the 3 groups did not differ for any of the listed outcomes, apart from the prevalence of mitral valve interventions at follow-up which occurred more frequently in the group of patients with baseline MMG ≥10 mm Hg (5.9% vs 0.2% and 0.7%, p = 0.003). Figure 1 shows unadjusted Kaplan-Meier cumulative survival (with shaded 95% confidence intervals [CI]) and unadjusted hazard ratios (HR) by MMG (<5, 5≤ MMG <10, and MMG ≥10) for 901 patients with complete MMG and follow-up data. There were 102 total deaths matched with data from the National Death Index over 5 years (60 months) of follow-up. The mean follow-up was 40.8 ± 13.9 months. Those with a baseline MMG ≥10 experienced nearly 3 times the risk of long-term mortality compared with those with baseline MMG <5 (unadjusted HR 3.11, 95% CI 1.26 to 7.68, p = 0.01; TAVI-risk adjusted HR 2.91, 95% CI 1.17 to 7.20, p = 0.02). When the population was stratified according to mitral valve area, no difference

Table 1
Baseline characteristics of the study population according to baseline mean mitral gradients (MMG)

	Mean mitral gradient (mm Hg)			
	<5 (n = 737)	5 to 9 (n = 147)	≥ 10 mm Hg (n = 17)	p
Variable				
Age, yrs	81.4 ± 7.9	81.2 ± 8.3	79.5 ± 8.8	0.613
Female	306 (41.5%)	106 (72.1%)	13 (76.5%)	**<0.0001**
Body mass index (Kg/m^2)	27.7 ± 6.6	28.6 ± 7.2	27.0 ± 5.0	0.338
Body Surface area (m^2)	1.9 ± 0.25	1.8 ± 0.24	1.8 ± 0.22	**0.001**
STS score (%)	7.7 ± 4.3	8.0 ± 4.3	8.9 ± 5.8	0.469
TAVR risk score (%)	4.7 ± 2.2	5.1 ± 2.1	5.4 ± 2.3	0.123
Hypertension	638 (86.6%)	125 (85.0%)	14 (82.4%)	0.793
Hyperlipidemia	550 (74.6%)	112 (76.2%)	11 (64.7%)	0.585
Diabetes mellitus	286 (38.8%)	65 (44.2%)	8 (47.1%)	0.392
Chronic kidney disease	560 (76.0%)	147 (75.5%)	10 (58.8%)	0.266
End stage renal disease	25 (3.4%)	5 (3.4%)	0 (0%)	0.742
Coronary artery disease	537 (72.9%)	95 (64.6%)	14 (82.4%)	0.079
Peripheral artery disease	234 (31.8%)	45 (30.6%)	8 (47.1%)	0.383
Chronic Obstructive Pulmonary Disease	158 (21.4%)	33 (22.4%)	8 (47.1%)	**0.041**
Atrial fibrillation	241 (32.7%)	33 (22.4%)	6 (35.3%)	**0.046**
Previous coronary-artery bypass graft/percutaneous coronary intervention	370 (50.2%)	54 (36.7%)	12 (70.6%)	**0.002**
Previous cerebrovascular accident	151 (20.5%)	29 (19.7%)	4 (23.5%)	0.929
Permanent pacemaker	156 (21.2%)	29 (19.7%)	2 (11.8%)	0.605
Procedural characteristics				
Type of valve				0.333
Balloon-expandable	304 (41.2%)	51 (34.7%)	7 (41.2%	
Self-expandable	433 (58.8%)	96 (65.3%)	10 (58.8%)	
Approach				0.528
Trans-femoral	654 (88.7%)	127 (86.4%)	14 (82.4%)	
Transapical	55 (7.5%)	13 (8.8%)	1 (5.9%)	
Transaortic	23 (3.1%)	5 (3.4%)	2 (11.8%)	
Subclavian	5 (0.7%)	2 (1.4%)	0 (0%)	
Valve Size (mm)				**<0.0001**
20	9 (1.2%)	5 (3.4%)	1 (5.9%)	
23	137 (18.6%)	52 (35.4%)	6 (35.3%)	
25	11 (1.5%)	2 (1.4%)	0 (0%)	
26	257 (34.9%)	59 (40.1%)	5 (29.4%)	
27	11 (1.5%)	1 (0.7%)	0 (0%)	
29	242 (32.8%)	25 (17.0%)	5 (29.4%)	
31	67 (9.1%)	3 (2.0%)	0 (0%)	
34	3 (0.4%)	0 (0%)	0 (0%)	
Balloon predilate	506 (68.7%)	95 (64.6%)	11 (64.7%)	0.608
Balloon postdilate	352 (47.8%)	77 (52.4%)	6 (35.3%)	0.330

Statistically significant values are bold.
Values are mean ± SD, n (%).
Abbreviations: CABG = coronary artery by-pass graft; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; LVEF = left ventricle ejection fraction; PCI = percutaneous coronary intervention; SD = standard deviation.

in long-term mortality was observed between patients with mitral valve area >1.5 cm^2 and those with mitral valve area ≤1.5 cm^2 (TAVI-risk adjusted HR 1.08, 95% CI 0.62 to 1.85, p = 0.81, Figure 2). Mortality was additionally assessed by stratifying the population as follows: patients with baseline and post-TAVI MMG <10 mm Hg; patients with baseline MMG <10 mm Hg and post-TAVI MMG ≥10 mm Hg; patients with baseline MMG ≥10 mm Hg and post-TAVI MMG ≥10 mm Hg; patients with baseline MMG ≥10 mm Hg and post-TAVI MMG <10 mm Hg. Having a MMG ≥10 mm Hg at baseline and post-TAVI was extremely rare (n = 3) but portended a detrimental long-term survival (TAVI-risk adjusted HR 7.09, 95% CI 1.74 to 28.9, p = 0.03, Figure 3).

Discussion

To the best of our knowledge, this is the first registry assessing the prevalence and role on survival at 5 years after TAVI of MS. The main findings of this study are the following: (1) the prevalence of severe MS, defined as MMG ≥10 mm Hg, in this cohort of severe AS patients is low, approximately 2%. (2) Patients with baseline MMG ≥10 mm Hg are frequently women, with a worse baseline risk profile compared with the other groups. (3) Despite the low prevalence of MMG ≥10 mm Hg before TAVI, patients in this group experienced a nearly 3 times higher mortality at 5 years after the procedure compared with other groups.

Table 2
Baseline echocardiographic findings according to baseline mean mitral gradients

	Mean mitral gradient (mm Hg)			
	<5 (n = 737)	5 to 9 (n = 147)	≥ 10 (n = 17)	p
Variable				
Heart Rate (bpm)	68.2 ± 13.4	77.4 ± 7.9	68.7 ± 11.0	0.154
LVEF (%)	53.7 ± 13.1	58.5 ± 12.1	60.6 ± 13.2	**<0.0001**
Stroke Volume indexed (ml/beat/m^2)	37.5 ± 12.2	38.1 ± 10.5	40.5 ± 9.1	0.523
Aortic valve mean gradient (mm Hg)	43.8 ± 13.4	48.8 ± 16.4	47.8 ± 10.8	**<0.0001**
Aortic valve area (cm^2)	0.69 ± 0.19	0.66 ± 0.18	0.67 ± 0.15	0.246
Aortic peak velocity (m/sec)	4.3 ± 0.62	4.5 ± 0.65	4.6 ± 0.50	**0.001**
Mitral valve mean gradient (mm Hg)	2.3 ± 1.0	6.2 ± 1.3	11.8 ± 1.7	**<0.0001**
Mitral Valve Area (cm^2)	2.4 ± 0.94	2.1 ± 0.86	1.5 ± 0.44	**<0.0001**
Mitral annular calcium grade				**0.001**
None	108 (14.7%)	7 (4.8%)	0 (0%)	**<0.0001**
Mild	290 (39.3%)	16 (10.9%)	2(11.8%)	**<0.0001**
Moderate	243 (33.0%)	57 (38.8%)	4 (23.5%)	**<0.0001**
Severe	96 (13.0%)	67 (45.6%)	11 (64.7%)	**<0.0001**
Mitral annular calcium location				
Anterior OR posterior	537 (88.3%)	95 (68.3%)	10 (58.8%)	**<0.0001**
Anterior AND posterior	71 (11.7%)	44 (31.7%)	7 (41.2%)	**<0.0001**
Mitral regurgitation ≥2+ (%)	115 (15.6%)	42 (28.6%)	1 (5.9%)	**<0.0001**
Aortic regurgitation ≥2+(%)	73 (9.9%)	22 (15.0%)	3 (17.6%)	0.131
Tricuspid regurgitation ≥2+ (%)	85 (11.5%)	21 (14.3%)	3 (17.6%)	0.503
Systolic Pulmonary Arterial Pressure (mm Hg)	41.6 ± 14.4	47.2 ± 14.5	50.6 ± 12.1	**<0.0001**
Left atrial volume (ml)	82.7 ± 30.6	88.9 ± 35.0	88.6 ± 26.6	0.173

Statistically significant values are bold.
Values are mean ± SD, median (minimum-maximum), n (%).
Abbreviations: LVEF = left ventricle ejection fraction.

The prevalence of MS in patients with AS has been reported to be around 10% and generally the outcome of these patients is very poor once they develop symptoms.[5] The American College of Cardiology/American Heart Association guidelines for valve disease recommend double valve intervention in these cases, although it carries a high operative risk.[2,14] Moreover, mitral valve replacement in cases of MS with severe MAC might be particularly challenging with a high risk of postoperative paravalvular leakage and complications. The development of TAVI in the last decade has drastically reduced the operative risk and improved survival of high to intermediate-risk or inoperable patients, and might represent a valid alternative also for patients with concomitant MS. However, data about MS in the TAVI era are scarce. A recent report from the TVT registry documented that severe MS (as defined by a mitral valve area ≤1.5 cm^2) is a predictor of mortality and rehospitalization for heart failure at 1 year after-TAVI.[6] In this study, the authors reported a prevalence of MS around 3%, similar to what we found in our population (1.9%).

Table 3
Post-TAVR echocardiographic findings according to baseline mean mitral gradients

	Mean mitral gradient (mm Hg)			
	<5 (n = 737)	5 to 9 (n = 147)	≥10 (n = 17)	p
Variable				
Heart rate (bpm)	73.6 ± 12.6	75.7 ± 12.7	72.3 ± 8.5	0.135
LVEF (%)	54.8 ± 11.9	56.9 ± 10.6	61.9 ± 6.6	**0.012**
Stroke Volume indexed (ml/beat/m^2)	22.9 ± 19.1	25.2 ± 16.8	26.2 ± 18.1	0.309
Aortic valve mean gradient (mm Hg)	8.3 ± 4.1	9.3 ± 4.5	10.2 ± 5.4	**0.004**
Aortic valve area (cm^2)	2.0 ± 0.60	1.8 ± 0.53	1.8 ± 0.37	**0.014**
Aortic peak velocity (m/sec)	2.0 ± 0.47	2.1 ± 0.44	2.2 ± 0.51	0.096
Mitral valve mean gradient (mm Hg)	3.0 ± 1.56	5.1 ± 2.3	8.7 ± 4.5	**<0.0001**
Mitral regurgitation ≥2+ (%)	53 (9.3%)	16 (10.9%)	1 (5.9%)	0.462
Paravalvular regurgitation ≥2+ (%)	27 (3.7%)	10 (6.8%)	1 (5.9%)	0.315
Left atrial volume (ml)	87.4 ± 30.6	92.4 ± 32.9	76.0 ± 33.9	0.575

Statistically significant values are bold.
Values are mean ± SD, median (minimum-maximum), n (%).
Abbreviations: LVEF = left ventricle ejection fraction.

Table 4
Outcomes after transcatheter aortic valve implantation according to baseline mean mitral gradient

	Mean mitral gradient (mm Hg)			
	<5 (n = 737)	5 to 9 (n = 147)	≥10 (n = 17)	p
Acute Kidney Injury	40 (5.4%)	2 (1.4%)	0 (0%)	0.066
Vascular complication	47 (6.4%)	14 (9.5%)	0 (0%)	0.206
Minor bleeding	91 (12.3%)	19 (12.9%)	3 (17.6%)	0.333
Major or life-threatening bleeding	21 (2.8%)	5 (3.4%)	1 (5.9%)	0.333
Stroke	26 (3.5%)	3 (2.0%)	1 (5.9%)	0.516
Valve-in-Valve	14 (1.9%)	2 (1.4%)	0 (0%)	0.695
Permanent pacemaker implantation	140 (18.9%)	29 (19.7%)	2 (11.8%)	0.716
New-onset atrial fibrillation	67 (9.0%)	17 (11.6%)	1 (5.9%)	0.570
Mitral valve intervention	2 (0.2%)	1 (0.7%)	1 (5.9%)	**0.003**
Immediate postprocedural mortality	6 (0.8%)	1 (0.7%)	0 (0%)	0.919
30-day cardiovascular mortality	19 (2.6%)	1 (0.7%)	1 (5.9%)	0.240
30-day All-cause mortality	23 (3.1%)	2 (1.4%)	1 (5.9%)	0.390
1-year All-cause mortality	60 (8.1%)	12 (8.2%)	3 (17.6%)	0.573

Statistically significant values are bold.
Values are mean ± SD, median (minimum-maximum), n (%).

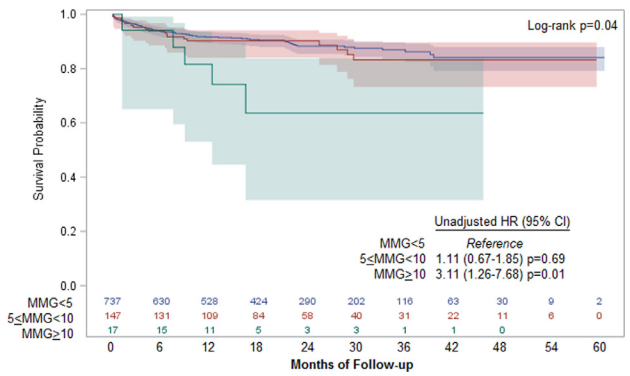

Figure 1. Kaplan-Meier curves for 5-year survival according to MMG. Unadjusted Kaplan-Meier cumulative survival (with shaded 95% confidence intervals) and TAVI score risk-adjusted Hazard Ratios by MMG (MMG <5, 5≤ MMG <10, and MMG ≥10) for 901 patients with complete MMG and follow-up data.

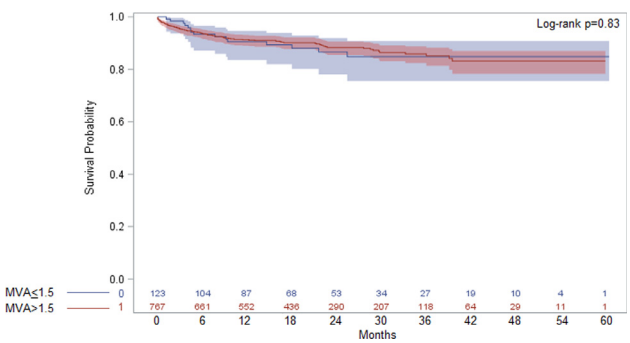

Figure 2. Kaplan-Meier curves for 5-year survival according to mitral valve area. Unadjusted Kaplan-Meier cumulative survival (with shaded 95% confidence intervals) and unadjusted hazard ratios by mitral valve area [(mitral valve area): ≤1.5 cm^2, mitral valve area >1.5 cm^2] for 890 patients with complete mitral valve area and follow-up data.

However, this was based on site-reported mitral valve area using variable methodologies and MMG was not reported. Although the latest US and European guidelines on valvular disease define MS based on mitral valve area as measured by planimetry, this recommendation is based on rheumatic heart disease.[15,16] When the mitral valve is calcified, planimetry is limited by shadowing and blooming artifact[17] (Figure 4). Mitral valve area by pressure half-time is strongly affected by the net compliance of the LV and left atrium, which are altered in AS.[18] By defining calcific MS as MMG ≥10 mm Hg, we selected a group with a high specificity for severe MS and elevated left atrium pressures at rest with normal heart rate (68.7 ± 11.0 bpm). Indeed, when we stratified our population according to mitral valve area, the group with MS (mitral valve area ≤1.5 cm^2, n = 123) did not experience a higher mortality up to 5 years

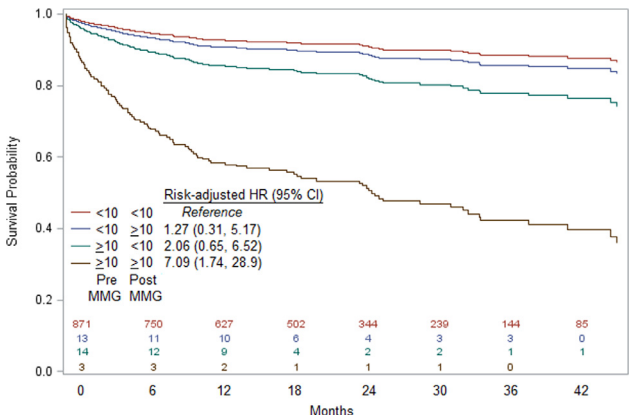

Figure 3. Kaplan-Meier curves for 5-year survival according to MMG. Unadjusted Kaplan-Meier cumulative survival (with shaded 95% confidence intervals) and unadjusted hazard ratios by MMG (both pre- and post-TAVI MMG: <10, either pre- and/or post-TAVI MMG ≥10) for 901 patients with complete MMG and follow-up data.

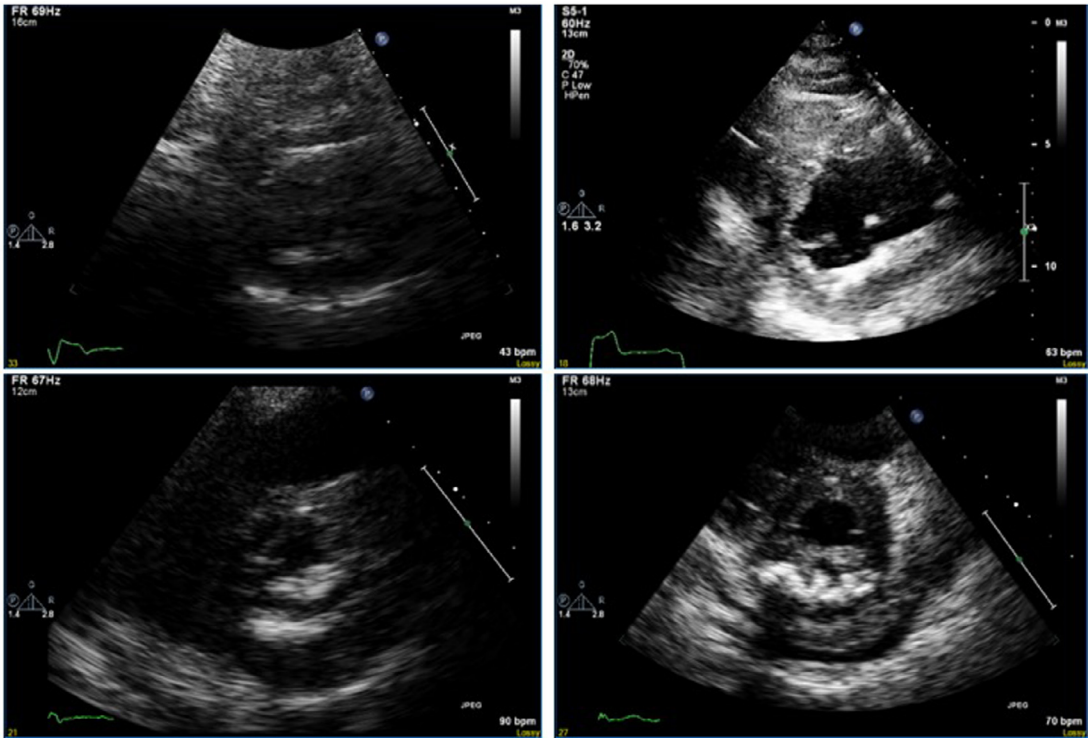

Figure 4. Examples of short-axis view of the mitral valve. Quantification of the mitral valve area by planimetry is compromised by the amount of calcium on the mitral annulus generating a blooming artifact and/or by the high acoustic thoracic impedance.

after TAVI compared with patients with mitral valve area >1.5 cm^2. Because MMG is flow and heart rate dependent, it is possible that more patients would have been classified as severe MS, had they undergone exercise testing; however; there was no clinical indication to do such in this population with severe symptomatic AS.

As to why patients with MMG ≥10 mm Hg experience a poor prognosis compared with the other 2 groups, some hypothesis might be generated. First, it is likely that in our population the etiology of MS is degenerative given the older age, the higher prevalence of atherosclerosis in this group, as testified by the higher prevalence of coronary-artery bypass graft/percutaneous coronary interventions and the higher prevalence of severe MAC. In turn, the higher atherosclerotic burden could explain, at least in part, the worse outcome. Previous studies have reported that patients with calcification of the aortic and mitral annulus frequently have calcified LV outflow tract which independently predict post-TAVI aortic regurgitation.[19] Although the presence of post-TAVI paravalvular leak has been associated with worse outcomes, we did not find differences in its prevalence in our population. Additionally, the group of patients with MMG ≥10 mm Hg had a higher prevalence of atrial fibrillation and higher systolic pulmonary arterial pressure; if, on the one hand, both conditions might be a direct result of the severe MS, in contrast, it has been widely shown that their presence is a marker of impaired prognosis.[13,20,21] Taken together these observations suggest that the increased baseline risk profile for patients with severe MS who underwent TAVI could potentially explain the increased rates of 5-year mortality. The results of this study indicate that patients with severe MS are a minority of those who underwent TAVI and that these patients experience a bad outcome at 5 years follow-up compared with patients with normal MMG. This does not mean that patients with severe AS and MS should not be offered a TAVI, but that such patients will need a more comprehensive approach that possibly includes the discussion and timing for mitral valve intervention. Indeed, with advances in transcatheter valve therapies, a percutaneous approach may become a viable alternative to conventional open-heart surgery in selected high-risk patients with concomitant severe AS and MS. As of today, we are still very limited in the way we can approach these patients. Transcatheter mitral valve replacement is often not doable in small hearts due to the significant risk of left ventricle outflow tract obstruction.

First, this study suffers from the intrinsic limitations of a retrospective design. Second, complete echocardiographic data were not available or not accurate for 2.9% of the population, which was therefore excluded from this analysis. Third, in this study we categorized MS according to MMG, which has the advantage of being a direct measurement, unlike calculated mitral valve area derived from pressure half-time measurement or continuity equation. Mitral valve area by pressure half-time is prone to error resulting from LV/left atrium compliance and aortic regurgitation,[10] both of which are common in TAVI patients. Direct planimetry of mitral valve area is recommended in rheumatic MS but is challenging in degenerative MS due to shadowing and blooming artifact from annular and leaflet calcium. Although MMG is influenced by heart rate and cardiac output, a high value reflects elevated left atrial pressure which may limit symptomatic improvement after TAVI. All the

echocardiographic measurements of the included patients have been done at a heart rate <100 bpm; also, the group of patients with MMG ≥10 mm Hg showed the lower prevalence of MR ≥2+, such the increased MMG cannot be explained by significant MR. Finally, the small number of patients with a MMG ≥10 mm Hg has to be acknowledged as a potential limitation of our study.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.01.017.

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