

Increase in Aortic Valve Mean Gradients One Day After Transcatheter Aortic Valve Implantation: The Role of Mitral Regurgitation

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Abstract

Background: Following transcatheter aortic valve implantation (TAVI), transvalvular mean gradient is known to increase from immediate to 24 h post-procedure. While anesthesia, rapid-pacing, and volume status are blamed, the true etiology is unclear. To our knowledge, no prior studies have evaluated the effects of mitral regurgitation (MR) on the rise in post-TAVI transvalvular mean gradient.

Methods: A single-center, retrospective analysis of patients who underwent TAVI at our institution between 2011 to 2020 was performed (n = 378, males = 206). Patients were divided into two groups, no-to-mild MR (n = 327) and moderate-to-severe MR (n = 51) based on echocardiograms obtained prior to TAVI. Transvalvular gradients were compared between immediate and 24-h post-TAVI echocardiograms.

Results: The average age of no-to-mild MR patients (77 years (interquartile range (IQR): 71 - 84)) was similar to moderate-to-severe MR patients (79 years (IQR: 76 - 85), p=0.13). Both groups had similar procedural blood pressures and peri-procedural medication use. The change in 24-h post-TAVI mean transvalvular gradient was +6 mm Hg (IQR: 3.7 - 9) in the moderate-to-severe MR group and +6 mm Hg (IQR: 3.4 - 9) in the no-to-mild MR group (P = 0.87).

Conclusions: In this study, we evaluated the impact of preexisting MR on changes in transvalvular gradients following TAVI. We observed no statistically significant difference in 24-h post-TAVI gradient changes between patients with moderate-to-severe MR and those

with no-to-mild MR. These findings suggest that baseline MR may not be a major determinant of early post-TAVI hemodynamics; however, further prospective studies are needed to confirm this observation.

Keywords: Transcatheter aortic valve implantation; Transvalvular gradient; Mitral regurgitation

Introduction

Transthoracic echocardiogram (TTE) has an important role in transcatheter aortic valve implantation (TAVI) from pre-procedural planning to long-term post-procedural follow-up. Immediately following TAVI, TTE is used to determine post-procedural success including appropriate TAVI valve placement and function, as well as identification of paravalvular leak and/or complications [1, 2]. Obtaining mean and max transvalvular gradients are a key component to assessing TAVI function [2]. While some studies have demonstrated that elevated long-term post-TAVI gradients are associated with worse outcomes and greater mortality [3], others have found no linear correlation between mortality and high post-TAVI gradients [4, 5].

Following TAVI, there is a notable increase in mean and max transvalvular gradients when comparing immediate to 24-h post-TAVI echocardiograms. Prior studies have attributed this phenomenon to a low-flow state in the intra-procedural and immediate post-procedural setting [6]. Multiple procedural factors have been considered “low-flow state inducers” including sedation or anesthesia, rapid pacing-induced ischemia, and fasting-related hypovolemia [7]. However, to our knowledge, no prior studies have considered the impact of baseline mitral regurgitation (MR) on the 24-h transvalvular gradient change phenomenon.

The effect of concomitant MR and aortic stenosis (AS) on post-TAVI outcomes has been well presented in the current literature [8-12]. Prior studies have also demonstrated significant improvement in baseline MR with the resolution of forward flow obstruction following TAVI [12, 13]. We sought to assess whether patients with moderate-to-severe MR at the time of TAVI had a greater increase in transvalvular gradients at 24 h post-TAVI compared to patients with no-to-mild MR.

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Materials and Methods

Study design

We retrospectively reviewed patients who underwent TAVI at our institution between 2011 and 2020. The study was approved by the Institutional Review Board (IRB) (IRB registration number: 00005012). Informed consent was waived by our institution's IRB, given this is a retrospective study. The study was conducted in compliance with the ethical standards of our institution and the revised Helsinki Declaration.

Patient population

Patients with severe AS that underwent TAVI between January 2011 to August 2020 at our institution were included in this retrospective study. Patients in the study underwent a thorough, standardized evaluation by our multidisciplinary heart team prior to TAVI. All forms of AS (normal flow-low gradient, low flow-low gradient, paradoxical low flow-low gradient and classical normal flow-high gradient) were included in the study. All patients in the study received Edwards SAPIEN balloon-expandable valves [14]. Prior studies have demonstrated variations in gradients when comparing self-expanding TAVI valves and balloon-expanding valves [15, 16]. Given these known gradient discrepancies, patients that received self-expanding TAVI valves were excluded from the study. Patients with significant paravalvular leak following TAVI were excluded from the study given the potential effects of post-TAVI transvalvular gradients. Patients in the study must have had a TTE immediately and 24 h post-TAVI. Those who had TTE performed outside the 24-h window or at an outside facility were excluded from the study. Patients who underwent concomitant MV therapy were excluded. Additionally, patients with mechanical or bioprosthetic valves were excluded from the study.

As discussed, several factors have been previously considered to explain the low-flow state and transvalvular gradient changes. We considered these factors in the pre-, peri- and post-procedural settings. Pre- and post-procedural blood pressures and weight were compared between the two groups as a surrogate to volume status. Additionally, intravenous fluids received were also taken into consideration. Procedural and anesthesia documentation were reviewed to record the use of inhaled anesthetics, vasopressors, and total dosage of midazolam, propofol and fentanyl administered during TAVI.

Doppler-echocardiographic measurements - TAVI valve

All echocardiograms were interpreted in accordance with the American Society of Echocardiography (ASE) clinical recommendations. Pre-TAVI TTE was obtained to assess the severity of AS. With the utilization of continuous-wave Doppler ultrasound, the peak velocity across aortic valve was measured in the apical five-chamber view and apical long axis view. Aortic

valve area (AVA) was calculated using the continuity equation. The left ventricular outflow tract (LVOT) diameter was measured from the inner edge to inner edge in the parasternal long axis view with zoom. LVOT velocity was assessed using pulse-wave Doppler in the apical long axis view. Peak gradient, mean gradient and continuous wave velocity was obtained in the apical five-chamber and/or apical long axis view for immediate and 24-h post-TAVI TTEs. For patients with atrial fibrillation, an average of three beats were obtained.

Doppler-echocardiographic measurements - mitral valve (MV)

Echocardiographic assessment of MR was performed in accordance with the most current guidelines provided by the ASE at the time of analysis [17]. For consistency, all TTEs were independently re-reviewed by a study investigator. None of the original echocardiographic report data were used. MR severity was classified based on direct image reassessment using standardized quantitative and semi-quantitative parameters, including vena contracta (VC), effective regurgitant orifice area (EROA) by proximal isovelocity surface area (PISA), and regurgitant volume.

VC

VC was measured in all patients at the narrowest portion of the mitral regurgitant flow at or immediately downstream of the regurgitant orifice. Patients with VC measurements < 0.3 cm were considered to have no-to-mild MR, while patients with VC widths > 0.3 cm were considered to have moderate-to-severe MR for the purposes of this study. Great effort was placed into measuring the smallest flow area for accurate VC given that small errors can lead to misclassification of MR severity.

EROA by flow convergence method (PISA)

PISA radius measurement was performed for each patient in the study if an appropriate color frame corresponding to the maximal jet velocity was obtainable. The PISA radius was then used to calculate a PISA ($2\pi r_{\text{PISA}}^2$). The PISA was then used to calculate the regurgitant flow (Reg flow = PISA \times aliasing velocity). The regurgitant flow could then be divided by the peak velocity of the regurgitant MR jet to provide the EROA ($\text{EROA} = \text{Reg flow}/V_{\text{Max}}$). Patients with an EROA < 0.20 cm² were considered no-to-mild MR, and patients with EROA > 0.20 cm² were considered moderate-to-severe MR.

Regurgitant volume and EROA by continuity method

The MV annulus diameter and the LVOT diameter were obtained for calculation of the MV area and LVOT area, respectively (area = π (diameter/2)²). Once the area was calculated for both the MV and LVOT, the regurgitant volume was cal-

culated using the following equation, $(MV \text{ area} \times MV \text{ VTI}) - (LVOT \text{ area} \times LVOT \text{ VTI})$. Patients with regurgitant volumes > 30 mL were considered moderate-to-severe MR. Patients with regurgitant volumes < 30 mL were put in the no-to-mild MR group. Patients with an EROA < 0.20 cm² were considered no-to-mild MR, and patients with EROA > 0.20 cm² were considered moderate-to-severe MR.

Primary and secondary endpoint measurements

The primary outcome assessed in this study was the numerical change (delta) in mean and max transvalvular gradients from immediate and 24 h post-TAVI echocardiograms.

Statistical analysis

The MR groups (no-to-mild vs. moderate-to-severe) were compared on baseline demographic and clinical characteristics, and echocardiographic characteristics. Chi-square or Fisher's exact tests were used for categorical parameters, and Mann-Whitney U tests were used for continuous variables that violated normality, as determined by Shapiro-Wilk tests. Frequency and percentage statistics were used to give context to the Chi-square analyses, and medians with interquartile range (IQR) were reported for the group comparisons using Mann-Whitney U tests. Statistical significance was assumed at an alpha value of 0.05, and all analyses were performed using SPSS Version 29 (Armonk, NY: IBM Corp.).

Results

A total of 378 patients that underwent TAVI between January 2011 and December 2020 with an Edwards SAPIEN valve were included in the study. Of those, 327 patients had no-to-mild MR and 51 patients had moderate-to-severe MR (Table 1).

Baseline clinical characteristics

All patients received balloon-expandable Edwards SAPIEN valves in the study with the most common valve being the Edwards SAPIEN 3 valve (84.7%). The mean age of patients with no-to-mild MR was 77 years (IQR: 71 - 84) and 177 (54.1%) were males. The mean age of the moderate-to-severe MR population was 79 years (IQR: 76 - 85) and 29 (56.9%) were males. The baseline clinical data for the patients included in this study are summarized in Table 1. All baseline clinical history was similar between the no-to-mild MR and moderate-to-severe MR groups, except prior coronary artery bypass grafting (CABG), chronic kidney disease, and body mass index (BMI). Patients with moderate-to-severe MR had a greater frequency of chronic kidney disease ($n = 33$, 64.7%) with statistically significant lower glomerular filtration rate (GFR) of 48.5 mL/min (IQR: 32.7 - 65.1) compared to 62.9

mL/min (IQR: 43.3 - 78) in the no-to-mild MR group. Patients with moderate-to-severe MR also had a greater history of prior CABG ($n = 20$, 39.2%) and BMI 26.4 (IQR: 23.9 - 30) compared to patients with no-to-mild MR ($n = 64$, 19.6% and 29 (IQR: 25 - 34.8), respectively. Most patients in both groups had New York Heart Association (NYHA) class III-IV symptoms prior to TAVI (94.8% in the no-to-mild MR group vs. 94.1% in the moderate-to-severe MR group).

Pre-, peri-, and post-procedural characteristics

Patients with no-to-mild MR had higher pre- and post-TAVI body weights compared to those with moderate-to-severe MR ($P = 0.005$ and $P = 0.006$, respectively). However, both groups demonstrated an average weight increase of less than 0.5 kg following the procedure (no-to-mild MR $P = 0.006$ and moderate-to-severe MR $P = 0.005$). There were no significant differences between groups in terms of pre-, peri-, or post-procedural fluid administration. Additionally, pre- and post-procedural blood pressures were comparable. As shown in Table 2, the use of vasopressors, inhaled anesthetics, and peri-procedural medication dosages was similar between groups.

Baseline echocardiographic characteristics, TAVI gradient delta and MR

Immediate and 24-h echocardiogram comparisons between the two groups are outlined in Table 3. Following TAVI, both groups were noted to have improvement in MR severity when comparing pre-TAVI to post-TAVI echocardiograms. The quantitative MR data for both pre- and post-TAVI assessments are summarized in Table 4. Patients in the no-to-mild MR group did not have sufficiently measurable MR jets to permit reliable quantification, and values in this cohort are therefore reported categorically as below the established thresholds for moderate MR.

Additionally, both groups were noted to have a statistically significant increase in transvalvular gradients in 24 h following TAVI. However, the 24-h change in post-TAVI mean and peak transvalvular gradients did not significantly differ between patients with no-to-mild MR and patients with moderate-to-severe MR (Figs. 1, 2). Furthermore, a scatter plot of change in regurgitant volume and change in transvalvular gradient (Supplementary Material 1, cr.elmerpub.com) showed no apparent correlation between changes in MR severity and changes in mean aortic gradient following TAVI.

Discussion

In this study we compared changes in mean and peak transvalvular gradients following TAVI in patients with no-to-mild MR and moderate-to-severe MR. The main findings of this study were: 1) There was an increase in mean and max transvalvular gradients 24 h post-TAVI regardless of baseline MR severity; 2) There was a statistically significant improvement in MR

Table 1. Comparing Baseline Clinical Characteristics Between Patients With No-to-Mild MR and Patients With Moderate-to-Severe MR

Baseline clinical characteristics of the patients	No-to-mild MR (n = 327)	Moderate-to-severe MR (n = 51)	P value
Age (years)	77 (71 - 84)	79 (76 - 85)	0.01
Gender (male)	177 (54.1%)	29 (56.9%)	0.01
Clinical history			
Diabetes mellitus	160 (48.9%)	22 (43.1%)	0.44
Hypertension	292 (89.3%)	48 (94.1%)	0.29
Hyperlipidemia	270 (82.6%)	40 (78.4%)	0.47
Peripheral vascular disease	102 (31.2%)	15 (29.4%)	0.80
Stroke/TIA	54 (16.5%)	14 (27.5%)	0.06
COPD	72 (22%)	10 (19.6%)	0.70
Atrial fibrillation	102 (31.2%)	23 (45.1%)	0.05
Previous permanent pacemaker	38 (11.6%)	10 (19.6%)	0.11
Chronic kidney disease	155 (47.4%)	33 (64.7%)	0.02
Coronary artery disease	210 (64.2%)	35 (68.6%)	0.54
Previous myocardial infarction	72 (22%)	8 (15.7%)	0.30
Previous CABG	64 (19.6%)	20 (39.2%)	0.002
Obstructive sleep apnea	70 (21.4%)	7 (13.7%)	0.21
BMI (kg/m ²)	29 (25 - 34.7)	26.37 (23.96 - 30)	0.002
NYHA class III-IV symptoms	309 (94.8%)	48 (94.1%)	0.96
CHA2DS2-VASc score	4 (4 - 5)	5 (4 - 6)	0.002
Type of TAVI valve			
SAPIEN	34 (10.4%)	9 (17.6%)	0.19
SAPIEN XT	3 (0.9%)	2 (3.9%)	0.19
SAPIEN 3	286 (87.5%)	40 (78.5%)	0.19
SAPIEN 3 Ultra	4 (1.2%)	0	0.19

Data are expressed as median (IQR, 25th - 75th percentile) or proportion (percentages). P < 0.05 indicates the difference between the two groups is statistically significant. BMI: body mass index; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; MR: mitral regurgitation; NYHA: New York Heart Association; TAVI: transcatheter aortic valve implantation; TIA: transient ischemic attack; IQR: interquartile range.

severity in all patients with baseline MR following TAVI; 3) There was no significant difference in 24-h post-TAVI mean and peak transvalvular gradient deltas between patients with moderate-to-severe MR and patients with no-to-mild MR.

We considered our findings in the context of prior research evaluating 24-h post-TAVI increases in transvalvular gradients. Changes in 24-h post-TAVI transvalvular gradients are thought to be due to an induced low flow state during the procedure. Prior studies have considered medications, pre-procedural *nil per os* (NPO) status, and rapid-pacing transient ischemia as potential factors that may induce a low flow state [7]. The current study considered these various factors, in addition to blood pressure recordings, baseline ejection fraction, medication dosages, use of vasopressors, and administered fluids. To our knowledge, no prior studies have considered pre-existing MV disease when evaluating transvalvular gradient changes following TAVI. Our study aimed to determine the effects of pre-existing MV disease on transvalvular gradient changes following TAVI.

The observed increase in transvalvular gradients at 24 h post-TAVI may reflect early hemodynamic adaptations rather than procedural complications. While transient low-flow states immediately following TAVI have been proposed as a contributing factor, they may not fully account for the magnitude of change. Prior work by Naidu et al [7] similarly reported an increase in transvalvular gradients from immediate to early post-TAVI follow-up, noting that this rise was not proportional to changes in stroke volume. Their findings support the notion that both low-flow physiology and evolving post-procedural ventricular loading conditions may influence early gradient measurements.

While prior studies have focused on procedural factors that induce low-flow states during TAVI, few have evaluated the effects of pre-existing MV disease on transvalvular gradient changes following the procedure. Concomitant MR and severe AS are frequently encountered in patients undergoing TAVI [18, 19]. In the setting of severe AS, functional MR (FMR) is more commonly observed than primary (degenera-

Table 2. Comparing Various Factors Considered to Be Low-Flow State Inducers Between Patients With No-to-Mild MR and Patients With Moderate-to-Severe MR

Low-flow state factors	No-to-mild MR (n = 327)	Moderate-to-severe MR (n = 51)	P value
Volume status			
Pre-TAVI weight (kg)	83.9 (71 - 99.2)	75.7 (65.8 - 88.3)	0.005
Post-TAVI weight (kg)	84.1 (70.48 - 100)	76.2 (65 - 90)	0.006
Pre-TAVI systolic blood pressure (mm Hg)	155 (139 - 173)	146 (129 - 163.5)	0.055
Pre-TAVI diastolic blood pressure (mm Hg)	67 (59 - 76.5)	64 (55 - 74.5)	0.175
Immediate post-TAVI systolic blood pressure (mm Hg)	126 (114 - 141.5)	130 (118.5 - 139)	0.62
Immediate post-TAVI diastolic blood pressure (mm Hg)	54 (47 - 62.5)	54 (46 - 63.5)	0.813
24-h post-TAVI systolic blood pressure (mm Hg)	127 (115 - 138)	124 (118 - 139)	0.664
24-h post-TAVI diastolic blood pressure (mm Hg)	57 (50 - 65)	56 (46 - 64.5)	0.451
Peri-procedural fluids (mL)	575 (200 - 800)	550 (125.5 - 950)	0.411
Post-procedural fluids (mL)	394 (0 - 970)	450 (0 - 1,050)	0.869
Medications			
Total fentanyl dose (mg)	100 (50 - 250)	100 (50 - 250)	0.733
Total propofol dose (g)	0	0	0.945
Total versed dose (g)	1 (0 - 2)	1 (0 - 2)	0.587
Total dexmedetomidine dose (µg)	16.8 (0 - 83.35)	26.5 (0 - 63.45)	0.669

Data are expressed as median (IQR, 25th - 75th percentile) or proportion (percentages). P < 0.05 indicates the difference between the two groups is statistically significant. MR: mitral regurgitation; TAVI: transcatheter aortic valve implantation; IQR: interquartile range.

tive) MR [20]. Prior studies have suggested that MR may be a significant hemodynamic determinant of a low-flow state in this population [21]. This theory is supported by data showing that moderate-to-severe MR can lead to underestimation of AS severity [18]. It has been proposed that FMR in the context of AS may arise from direct aortic valve obstruction and elevated left ventricular (LV) pressure [22]. However, more recent lit-

erature indicates that FMR is more likely related to impaired longitudinal LV function and adverse ventricular remodeling [20].

These pathophysiologic mechanisms were considered in the present study. Among patients with moderate-to-severe MR, we assessed the etiology and found that 49 of 51 patients (96%) had degenerative MR, while only two patients (4%) had

Table 3. Comparing Echocardiographic Characteristics Between Patients With No-to-Mild MR and Patients With Moderate-to-Severe MR

Echocardiographic characteristics of the patients	No-to-mild MR (n = 327)	Moderate-to-severe MR (n = 51)	P value
Pre-TAVI			
Left ventricular ejection fraction (%)	58 (55 - 62.5)	51 (45 - 57.1)	< 0.001
Aortic valve area (cm ²)	0.78 (0.66 - 0.90)	0.77 (0.69 - 0.85)	0.002
Aortic valve mean gradient (mm Hg)	41.1 (32.9 - 48.11)	34.5 (24.3 - 45)	0.017
Immediate post-TAVI			
Transvalvular mean gradient (mm Hg)	4.5 (3 - 6)	3.3 (2.5 - 4.7)	< 0.001
Transvalvular peak gradient (mm Hg)	9.4 (7 - 13)	7 (5.9 - 10)	< 0.001
24-h post-TAVI			
Transvalvular mean gradient (mm Hg)	11 (8 - 14.7)	9.05 (7 - 13)	< 0.001
Transvalvular peak gradient (mm Hg)	22 (16.3 - 29.1)	18 (13.4 - 24.3)	< 0.001
Deltas (24-h - immediate)			
Transvalvular mean gradient delta (mm Hg)	6 (3.7 - 9)	6 (3.4 - 9)	0.87
Transvalvular peak gradient delta (mm Hg)	12.2 (6.8 - 18)	12 (5.5 - 15.9)	0.41

Data are expressed as median (IQR, 25th - 75th percentile) or proportion (percentages). P < 0.05 indicates the difference between the two groups is statistically significant. MR: mitral regurgitation; TAVI: transcatheter aortic valve implantation; IQR: interquartile range.

Table 4. Quantitative Echocardiographic Measurements of MR Before and After TAVI, Stratified by MR Severity Groups

MR severity quantification by TTE	Pre-TAVI	Post-TAVI	P value
No-to-mild MR patients (n = 327)			
MR vena contracta (cm)	< 0.30	< 0.30	-
MR EROA - PISA (cm ²)	< 0.20	< 0.20	-
MR EROA - continuity (cm ²)	< 0.20	< 0.20	-
Regurgitant volumes (mL)	< 30	< 30	-
Moderate-to-severe MR patients (n = 51)			
MR vena contracta (cm)	0.50 (0.41 - 0.71)	0.3 (0.30 - 0.30)	< 0.001
MR EROA - PISA (cm ²)	0.40 (0.34 - 0.57)	0.20 (0.20 - 0.20)	< 0.001
MR EROA - continuity (cm ²)	0.41 (0.35 - 0.61)	0.20 (0.20 - 0.20)	< 0.001
Regurgitant volumes (mL)	73.94 (58.26 - 114.61)	30 (30 - 30)	< 0.001

Quantitative metrics include MR vena contracta, EROA measured by both PISA and continuity methods, and regurgitant volume. In the no-to-mild MR group, quantitative values are uniformly reported below ASE guideline-based thresholds for moderate MR due to the absence of sufficiently measurable MR jets, a limitation inherent to the minimal severity in this cohort. As such, statistical comparisons are not applicable for this group. In contrast, patients with moderate-to-severe MR demonstrated significant reductions in all quantitative parameters post-TAVI. Data are expressed as median (IQR, 25th - 75th percentile) or proportion (percentages). $P < 0.05$ indicates the difference between the two groups is statistically significant. EROA: effective regurgitant orifice area; TTE: transthoracic echocardiogram; MR: mitral regurgitation; PISA: proximal isovelocity surface area; TAVI: transcatheter aortic valve implantation; ASE: American Society of Echocardiography; IQR: interquartile range.

FMR. Due to the minimal MR burden in the no-to-mild MR group, etiology was not further classified in that cohort. The predominance of degenerative MR in our population may help explain the absence of a significant difference in post-TAVI transvalvular gradient changes between groups, in contrast to prior studies that focused on FMR and its potential contribution to low-flow physiology.

Although MR severity may improve rapidly following TAVI [12, 13, 23], we hypothesized that the decrease in LV pressure and recovery of ventricular function and remodeling do not occur immediately. Rather, transvalvular gradient changes are likely to evolve over the early post-TAVI period.

Based on this hypothesis, we expected that patients with moderate-to-severe MR would exhibit a more pronounced increase in transvalvular gradients at 24 h post-TAVI compared to those with no-to-mild MR. However, our findings demonstrated no statistically significant difference in 24-h mean or peak transvalvular gradient changes between the two groups. While we found no significant difference in the 24-h transvalvular gradient changes between the two groups, the measurable effects of TAVI on LV function, LV remodeling, and MR may take more than 24 hours. In the study performed by Naidu et al [7], they demonstrated that transvalvular gradients were high at day 1 and at day 30 post TAVI when compared to immediate

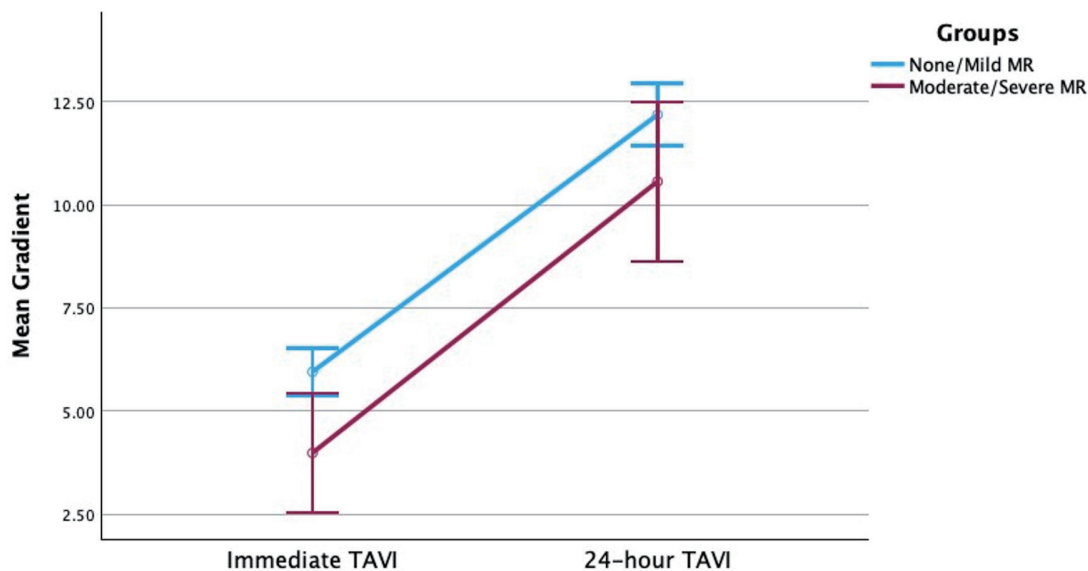


Figure 1. Change in transvalvular mean gradient across time for patients with no-to-mild MR and patients with moderate-to-severe MR. MR: mitral regurgitation; TAVI: transcatheter aortic valve implantation.

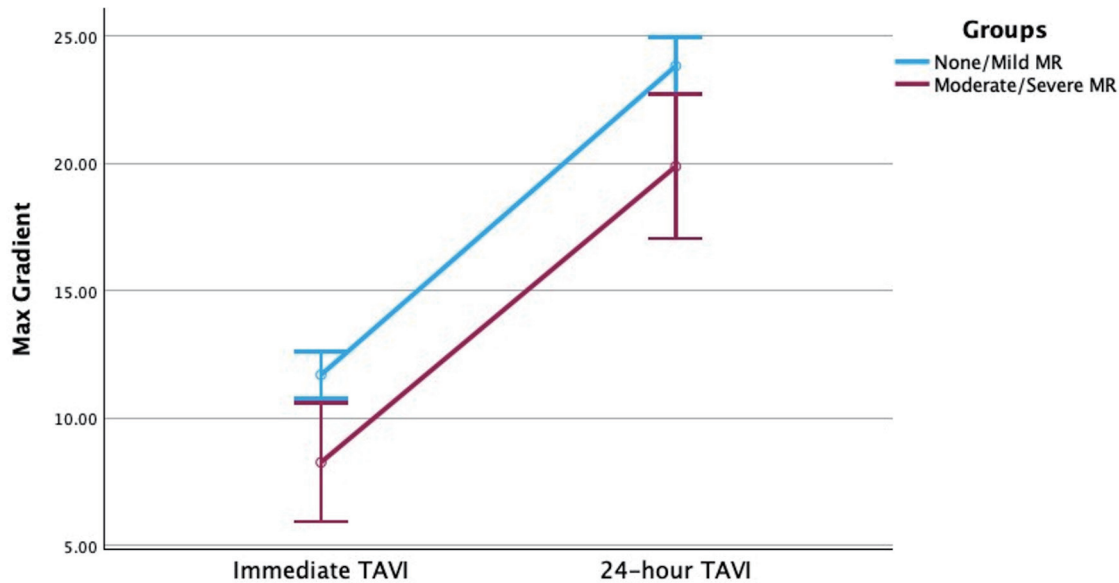


Figure 2. Change in transvalvular max gradient across time for patients with no-to-mild MR and patients with moderate-to-severe MR. MR: mitral regurgitation; TAVI: transcatheter aortic valve implantation.

post-TAVI transvalvular gradients. Following TAVI, the improvement in MR may not demonstrate significant effects on transvalvular gradients for multiple days to weeks post-TAVI as the left ventricle undergoes progressive remodeling. More studies are needed to determine the effects of baseline MR on the change in transvalvular gradients in the short-term and long-term post-TAVI setting.

Another important consideration in patients with severe AS and elevated left ventricular end diastolic pressure (LVEDP) is the effects of microvascular dysfunction. Studies have shown that microvascular remodeling is frequently found in patients with severe AS and elevated LVEDP [24-26]. Ischemic MR should be considered in patients with microvascular dysfunction in the setting of AS and elevated LVEDP. The reduction in LVEDP and improvement in microvascular function following TAVI is likely observed indirectly by the post-procedural improvement in MR severity. While there is a measurable improvement in MR severity immediately post TAVI, the impact of microvascular dysfunction on post-TAVI transvalvular gradients remains unclear.

The current study's limitations are discussed below. The results of this single-center study should be interpreted considering its smaller sample size and its retrospective nature. Although retrospective in nature, this study utilized uniform re-analysis of all echocardiograms using current ASE guidelines to mitigate inconsistencies related to evolving measurement criteria over the study period. Patients included in this study only received Edwards SAPIEN balloon-expandable valves and therefore the results should not be applied to self-expanding TAVI valves. In the current study, MR valve measurements and MR severity grading were performed by an independent reader who was not blinded, which could present potential bias. Most patients included in the study were suspected to have FMR in the setting of severe AS, however the etiology

of the MR was not differentiated. As previously discussed, immediate and 24-h post-TAVI echocardiograms were reviewed and therefore the effects of MR on transvalvular gradients after this period were not accounted for in the study. More studies are needed to evaluate the etiology behind the increase in post-TAVI transvalvular gradients and the effects of baseline concomitant valvular disease on transvalvular gradients.

Conclusions

In this retrospective analysis, we directly evaluated the role of MR in early post-TAVI transvalvular gradient changes and found that moderate-to-severe MR did not significantly influence the 24-h gradient increase compared to no-to-mild MR. Despite prior hypotheses suggesting a potential role for MR as a contributor to low-flow states and gradient dynamics following TAVI, our findings indicate that baseline MR severity does not appear to independently affect early post-TAVI transvalvular hemodynamics. These results suggest that other factors, such as intraprocedural hemodynamics, myocardial remodeling, and microvascular function, may play more prominent roles in the observed gradient changes. Future prospective studies with longer-term follow-up are warranted to further elucidate the interaction between baseline MR, LV remodeling, and transvalvular gradients in the post-TAVI period.

Supplementary Material

Suppl 1. Scatter plot depicting the relationship between the change in MR severity - quantified by regurgitant volume (ΔRV) - and the change in mean aortic transvalvular gradient (Δ Gradient) from immediately post-TAVI to 24 h post-TAVI.

Each point represents an individual patient with moderate-to-severe MR. Visual assessment using quantitative MR data demonstrates no clear correlation between ΔRV and Δ Gradient, suggesting that early post-procedural changes in transvalvular gradients are not significantly influenced by concurrent MR severity.

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Financial Disclosure

None to declare.

Conflict of Interest

The authors report no conflict of interest regarding the content herein.

Informed Consent

Informed consent was waived by our institution's IRB, as this is a retrospective study.

Author Contributions

Benjamin Fogelson: methodology, conceptualization, investigation, writing - original draft, review and editing. Raj Baljepally: methodology, conceptualization, writing, review, editing, and supervision. Eric Heidel: biostatistics, formal analysis, writing, review and editing. Steve Ferlita: investigation, validation. Travis Moodie: investigation, validation. Aladen Amro: investigation, validation, Stefan Weston: investigation, validation.

Data Availability

The data supporting these findings of this study are available from the corresponding author upon reasonable request.

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