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ORIGINAL RESEARCH

STRUCTURAL

Transmitral Gradients and Mortality Following Transseptal Transcatheter Mitral Valve in Valve

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ABSTRACT

BACKGROUND Echocardiographic transvalvular mitral gradients (TMGs) following transcatheter mitral valve in valve (MVIV) are regarded as correlates of clinical outcomes despite limited data.

OBJECTIVES The aim of this study was to examine the association between discharge and 30-day TMGs and mortality, as well as other clinical outcomes, following MVIV.

METHODS The Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry was used to extract data for all comers undergoing MVIV from August 2015 to March 2024. Adjusted and unadjusted Cox proportional hazards regression models with cubic spline functions were used to explore the relationship between discharge TMG post-MVIV and all-cause mortality. TMG ranges included low (<4 mm Hg), intermediate (4-7 mm Hg), and high (>7 mm Hg). Kaplan-Meier estimates were generated for all-cause mortality and the composite endpoint of all-cause mortality or stroke across TMG ranges (at discharge and at 30 days), with overall curve comparisons performed using log-rank tests. Pairwise comparisons were based on adjusted HRs and corresponding *P* values from Cox proportional hazards models.

RESULTS The study included 5,401 MVIV patients, with a median follow-up duration of 377 days (Q1-Q3: 58-687 days). Compared with intermediate and high TMG, low TMG had lower invasive cardiac output (CO) ($P = 0.0003$ and $P < 0.0001$, respectively) and cardiac index ($P = 0.04$ and $P = 0.0002$, respectively). Low discharge TMG was associated with an increased 3-year all-cause mortality hazard compared with intermediate discharge TMG (adjusted HR: 1.52; 95% CI: 1.22-1.89; $P = 0.0002$) and compared with high discharge TMG (adjusted HR: 1.35; 95% CI: 1.07-1.71; $P = 0.01$; 896 mortality events for the entire cohort). Discharge and 30-day gradient groups varied and should not be interchangeable.

CONCLUSIONS Following MVIV, TMG <4 mm Hg was associated with lower CO and cardiac index and increased mortality at 3 years compared with TMG 4 to 7 mm Hg and >7 mm Hg. TMG changed significantly from discharge to 30 days. Discharge TMG should not be the sole determination of procedural outcome, valve performance, or the need for optimization following MVIV without incorporating CO. (JACC Cardiovasc Interv. 2026;19:857-870)

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ABBREVIATIONS AND ACRONYMS

CMS = Centers for Medicare and Medicaid Services

CO = cardiac output

EF = ejection fraction

HF = heart failure

KCCQ = Kansas City Cardiomyopathy Questionnaire

MG = mean gradient

MR = mitral regurgitation

MVA = mitral valve area

MVIV = mitral valve in valve

TAVR = transcatheter aortic valve replacement

TEER = transcatheter edge-to-edge repair

TMG = transvalvular mitral gradient

Echocardiographic derivation of transvalvular gradients from transvalvular velocities, through the application of the simplified Bernoulli equation, was first described in patients with mitral stenosis,[1] later expanded to patients with aortic stenosis,[2] and subsequently extrapolated to normal functioning and degenerated prosthetic valves.[3]

Despite the paucity of supporting data, low echocardiography-derived mean gradients (MGs) following transcatheter mitral valve in valve (MVIV) and transcatheter aortic valve replacement (TAVR) have been regarded as markers of procedural success and predictors of long-term clinical outcomes.[4]

Although the relationship between elevated MG after surgical aortic valve replacement and outcomes is less clear,[5] post-TAVR, no difference in clinical outcomes was demonstrated between elevated (≥20 mm Hg) and low (<20 mm Hg) echocardiographic MGs.[6-9] Moreso, the relationship between echocardiographic MG and mortality post-TAVR remains nonlinear and highly dependent on ejection fraction (EF),[10] flow, and comorbidities, where a lower MG (<10 mm Hg) was associated with lower EF, lower flow, and worse outcomes compared with higher gradients.[11] Moreover, patients with low flow following TAVR exhibit poor clinical outcomes regardless of echocardiographic MG and EF.[12]

We sought to examine the association between discharge and 30-day transvalvular mitral gradients (TMGs) and mortality, as well as other clinical outcomes, following MVIV.

METHODS

STUDY POPULATION. This is a retrospective analysis of all patients undergoing transseptal MVIV from August 2015 to March 2024 using SAPIEN 3, SAPIEN 3 Ultra, or SAPIEN 3 Ultra RESILIA (Edwards Lifesciences) balloon-expandable valves, as reported to the national Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry. The TVT Registry has been approved by a central Institutional Review Board (Advarra) and granted a waiver of the requirement to obtain informed consent by the Duke University School of Medicine Institutional Review Board under Common Rule 45 CFR 46.3. The analyses were performed on data downloaded by Edwards Lifesciences from the TVT Registry. The investigators prepared the study design, analytical plan, and manuscript.

STUDY ENDPOINTS. We assessed the relationship between post-MVIV discharge TMG (as identified in the TVT Registry data set) and 3-year all-cause mortality, as well as a 3-year composite endpoint of all-cause mortality or stroke with U.S. Centers for Medicare and Medicaid Services (CMS) linkage. In addition, we studied the relationship between 30-day gradients following MVIV and mortality and the composite endpoint of mortality or stroke at 3 years.

STATISTICAL ANALYSES. Continuous variables are presented as mean ± SD or median (Q1-Q3) and were compared between groups using the 2-sample Student's *t*-test or Wilcoxon rank sum test. Categorical variables are presented as frequencies and percentages and were compared using the chi-square or Fisher exact test.

For all-cause mortality, stroke, and the composite endpoint of mortality or stroke analyses up to 3-year follow-up, the TVT Registry was linked to CMS claims data using probabilistic matching with patient birth date, gender, and TAVR procedure date. Patients eligible for linkage were all 65 years or older with Medicare coverage, enrolled in the Medicare Parts A and B fee-for-service program. Multiple matches were removed, and only 1 unique case was used for the analysis. For 1-year outcomes, both TVT Registry follow-up and CMS claims data were leveraged to maximize completeness. When TVT Registry data lacked an observed outcome at 1 year, CMS linkage often provided additional patient outcome information. For non-CMS-eligible patients without linked CMS claims data, TVT Registry data were used up to 3-year follow-up.

Unadjusted and adjusted Cox proportional hazards regression models with cubic spline functions were constructed to explore the relationship between TMG post-MVIV, as a continuous variable, and 3-year all-cause mortality. In the study population, the first quantile of MG was observed at 2 mm Hg, and the range of 4 to 7 mm Hg corresponded to the lowest

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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mortality rate, forming a U-shaped pattern. TMG cutoffs of 4 and 7 mm Hg were selected on the basis of the graphical distribution, with knots placed at 2, 4, and 7 mm Hg. Echocardiographic gradients <4 mm Hg were considered low, gradients of 4 to 7 mm Hg were considered intermediate, and gradients >7 mm Hg were considered high. Cardiac index was obtained invasively by right heart catheterization, and a cardiac index <2.2 L/min/m^2 was considered low.

For the Cox proportional hazards models, covariates were selected for all-cause mortality and the composite endpoint of all-cause mortality or stroke adjusted HRs and spline curves on the basis of a theory-based approach that incorporated clinical relevance and evidence from prior literature, rather than relying solely on univariate *P* value thresholds for mortality or no mortality at 3 years following MVIV. Clinically important variables were retained regardless of statistical significance, and additional covariates (such as cardiac index < 2.2 L/min/m^2 and left ventricular EF <50%) were evaluated on the basis of their potential role as confounders and support in existing research. Fourteen covariates were used for determining adjusted HRs or adjusted spline curves at 3 years for mortality: cardiac index <2.2 L/min/m^2, left ventricular EF <50%, age, Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score, currently on dialysis, glomerular filtration rate, heart failure (HF) hospitalization within the past year, low hemoglobin, home oxygen use, immunocompromised status, greater than moderate mitral regurgitation (MR), greater than moderate tricuspid regurgitation, prior myocardial infarction, and cardiogenic shock within 24 hours. Nineteen covariates were used for determining adjusted HRs or adjusted spline curves at 3 years for the composite endpoint of mortality or stroke: cardiac index <2.2 L/min/m^2, left ventricular EF <50%, KCCQ overall summary score, operator reason for procedure, currently on dialysis, glomerular filtration rate, prior coronary artery bypass graft surgery, hemoglobin, home oxygen use, immunocompromised status, greater than moderate MR, atrial fibrillation or flutter, baseline NYHA functional class III or IV, cardiogenic shock within 24 hours, peripheral arterial disease, chronic lung disease, porcelain aorta, Society of Thoracic Surgeons score, and procedure status.

Kaplan-Meier estimates were generated for all-cause mortality and the composite endpoint of all-cause mortality or stroke across TMG ranges at discharge and at 30 days. Overall Kaplan-Meier curve comparisons were performed using log-rank tests. The log-rank statistics for the 1-year outcome were calculated on the basis of patients' being censored at 1 year if they were event free. For 3-year follow-up analysis, patients were censored at 3 years or at the date of last contact, whichever occurred first. Adjusted HRs and corresponding *P* values using a Cox model were further used to compare the occurrence of all-cause mortality and the composite endpoint of all-cause mortality or stroke over 3 years, stratified according to the selected TMG cutoffs at discharge or 30 days. Additionally, the proportional hazards assumption was evaluated for Cox models.

All *P* values were 2-sided, *P* values <0.05 were considered to indicate statistical significance for all tests, and no adjustment for multiple testing was undertaken. All statistical analyses were performed using SAS version 9.4 (SAS Institute).

RESULTS

STUDY POPULATION, BASELINE CHARACTERISTICS, AND POSTPROCEDURAL TRANSVALVULAR HEMODYNAMIC STATUS. The study population included 5,401 MVIV patients (Central Illustration), with a median follow-up duration of 377 days (Q1-Q3: 58-687 days). The mean age was 72.8 ± 11.4 years, with 3,139 women (58.1%) and a 1-year mortality rate of 12.9%. Among the total patient population, 491 patients (9%) had low TMGs, 3,300 patients (61%) had intermediate TMGs, and 1,610 patients (30%) had high TMGs at discharge (Supplemental Figure 1). Patients with low TMGs were older ($P < 0.0001$), were more likely to be female ($P = 0.0003$), and had smaller body mass index ($P < 0.002$) compared with patients with intermediate and high TMGs. Patients with high TMGs had a lower incidence of atrial fibrillation or flutter ($P < 0.0001$) (Table 1).

On baseline echocardiography, patients with low TMGs had smaller mitral valve areas (MVAs; $P = 0.0004$) and more moderate or severe tricuspid regurgitation ($P < 0.0001$) (Table 1).

On baseline right heart catheterization, patients with low TMGs had lower cardiac output (CO; $P < 0.0001$), had a lower cardiac index ($P = 0.0002$), had a higher percentage of low cardiac index <2.2 L/min/m^2 ($P = 0.0004$), and were more likely to receive large (29-mm) balloon-expandable valves ($P < 0.0001$) (Table 1, Supplemental Table 1).

On discharge echocardiography, patients with low TMGs were more likely to exhibit larger MVAs ($P = 0.0009$) and lower TMGs ($P < 0.0001$) (Table 2).

PATTERNS OF MORTALITY ACCORDING TO DISCHARGE TMG. Unadjusted and adjusted spline

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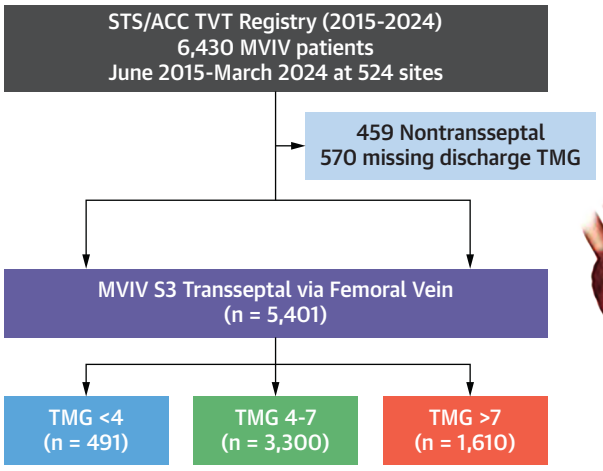
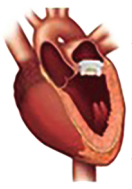
CENTRAL ILLUSTRATION Study Overview and Main Findings

Transmitral Gradients and Mortality Following Transcatheter Mitral Valve in Valve

Study Flow

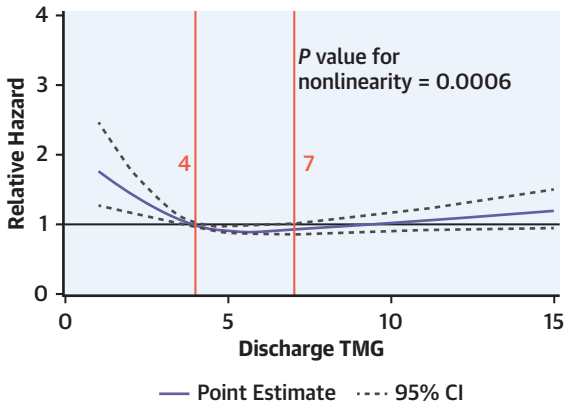


Baseline Cardiac Output/Index

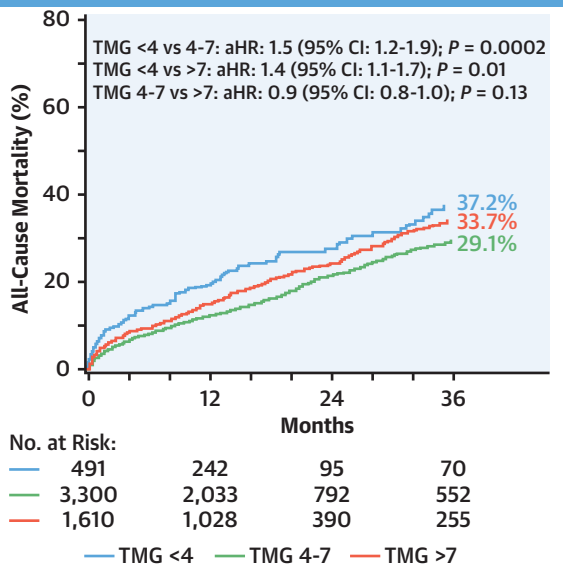


	Cardiac Output	Cardiac Index
	P < 0.0001	*P* = 0.0002
TMG <4 (n = 491)	3.9 ± 1.3	2.2 ± 0.7
TMG 4-7 (n = 3,300)	4.2 ± 1.4	2.3 ± 0.7
TMG >7 (n = 1,610)	4.6 ± 1.4	2.4 ± 0.7

Adjusted Spline Curve of Discharge TMG and 3-Year All-Cause Mortality



3-Year All-Cause Mortality by Discharge TMG



- Compared to TMG 4-7 mm Hg and TMG >7 mm Hg, TMG <4 mm Hg had lower cardiac output (*P* = 0.0003 and *P* < 0.0001, respectively) and cardiac index (*P* = 0.04 and *P* = 0.0002, respectively).
- Nonlinear relationship exists between all-cause mortality and echocardiographic TMG post MVIV.
- Discharge low TMG <4 mm Hg was associated with higher 3-year all-cause mortality.
- TMG post MVIV primarily reflects transvalvular flow as determined by cardiac output and not optimum valve hemodynamics or clinical outcomes.
- Attempts to optimize valves post MVIV based solely on echocardiographic TMG alone needs to be further explored.

Abbas AE, et al. JACC Cardiovasc Interv. 2026;19(7):857-870.

Study flowchart, cardiac output and cardiac index, adjusted spline curve of discharge transmitral gradient (TMG) and 3-year all-cause mortality, and 3-year all-cause mortality by discharge TMG. ACC = American College of Cardiology; aHR = adjusted HR; MVIV = mitral valve in valve; S3 = SAPIEN 3; STS = Society of Thoracic Surgeons; TVT = Transcatheter Valve Therapy.

TABLE 1 Baseline, Catheterization, and Echocardiographic Characteristics

	TMG <4 mm Hg (n = 491)	TMG 4-7 mm Hg (n = 3,300)	TMG >7 mm Hg (n = 1,610)	*P* Value
Clinical characteristic				
Age, y	74.9 ± 10.5 (491)	73.7 ± 11.0 (3,300)	70.4 ± 12.1 (1,610)	<0.0001
Female	65.2 (320/491)	58.5 (1,931/3,300)	55.2 (888/1,610)	0.0003
STS score, %	8.0 (4.7-13.4)	6.9 (4.0-11.0)	6.4 (4.0-10.4)	<0.0001
BMI, kg/m^2	26.0 ± 10.4 (491)	27.5 ± 16.6 (3,290)	28.4 ± 6.4 (1,607)	0.002
Permanent pacemaker	29.1 (143/491)	27.7 (914/3,295)	22.5 (361/1,608)	0.0001
Previous ICD	11.2 (55/490)	10.9 (360/3,294)	10.4 (168/1,609)	0.83
Prior MI	14.3 (70/490)	17.0 (560/3,295)	18.4 (296/1,610)	0.10
Prior PCI	13.1 (64/490)	15.4 (507/3,297)	18.2 (293/1,609)	0.007
Prior CABG	25.5 (125/490)	29.1 (959/3,297)	32.6 (524/1,608)	0.004
Prior aortic valve procedure	21.6 (106/491)	20.8 (687/3,298)	30.0 (483/1,610)	<0.0001
MV replacement type				
Stented	89.1 (213/239)	90.5 (1,507/1,666)	90.3 (825/914)	0.81
Stentless	10.9 (26/239)	9.5 (159/1,666)	9.7 (89/914)	0.81
Prior TIA	10.2 (50/491)	9.9 (325/3,299)	8.6 (138/1,610)	0.31
Hypertension	80.5 (395/491)	83.9 (2,769/3,299)	86.0 (1,383/1,609)	0.01
Diabetes mellitus	25.1 (123/490)	26.6 (876/3,297)	30.8 (496/1,609)	0.003
Peripheral arterial disease	12.0 (59/490)	14.0 (462/3,297)	13.7 (220/1,609)	0.49
GFR, mL/min/1.73 m^2	53.6 ± 28.6 (487)	57.6 ± 24.0 (3,291)	55.8 ± 26.0 (1,605)	0.001
Heart failure hospitalization within past year	59.9 (248/414)	58.2 (1,594/2,741)	57.7 (798/1,384)	0.72
Cardiogenic shock within 24 h	5.5 (27/491)	3.5 (115/3,298)	5.1 (82/1,608)	0.009
Atrial fibrillation/flutter	76.2 (374/491)	74.5 (2,456/3,299)	68.2 (1,097/1,609)	<0.0001
Chronic lung disease	34.0 (166/489)	37.7 (1,239/3,288)	38.6 (618/1,603)	0.18
Home oxygen use	11.8 (58/490)	12.8 (421/3,297)	15.4 (248/1,608)	0.02
Positive inotropes	9.0 (44/489)	8.3 (272/3,285)	10.6 (170/1,602)	0.03
BNP, pg/mL	595.0 (295.0-1,161.0)	421.0 (217.0-910.0)	408.5 (203.0-873.5)	<0.0001
NT-proBNP, pg/mL	3,148.5 (1,276.5-6,918.5)	2,092.0 (947.0-4,828.0)	2,233.0 (966.0-5,804.0)	0.004
Hemoglobin, g/dL	11.8 ± 2.0 (488)	11.7 ± 2.0 (3,292)	11.3 ± 2.3 (1,603)	<0.0001
Operator reason for procedure				0.59
Inoperable/extreme risk	15.1 (73/484)	17.3 (562/3,256)	17.9 (285/1,597)	0.37
High risk	65.3 (316/484)	61.0 (1,985/3,256)	61.4 (980/1,597)	0.19
Intermediate risk	14.5 (70/484)	16.0 (521/3,256)	15.7 (251/1,597)	0.69
Low risk	5.2 (25/484)	5.8 (188/3,256)	5.1 (81/1,597)	0.57
NYHA functional class III/IV	82.7 (396/479)	82.6 (2,673/3,238)	79.3 (1,257/1,586)	0.02
KCCQ overall summary score	36.8 ± 23.9 (398)	37.1 ± 23.7 (2,845)	37.1 ± 24.2 (1,355)	0.98
Echocardiographic characteristics				
Mitral annular calcification	44.4 (84/189)	43.9 (512/1,167)	41.5 (243/585)	0.61
MV area, cm^2	1.0 (0.7-1.40)	1.1 (0.8-1.7)	1.2 (0.8-1.9)	<0.0001
MV mean gradient, mm Hg	12.0 (9.0-16.0)	12.0 (9.0-16.0)	13.0 (10.0-17.0)	<0.0001
LVEF, %	54.0 ± 12.5 (485)	55.0 ± 11.5 (3,269)	55.4 ± 11.9 (1,596)	0.07
Moderate mitral regurgitation	14.6 (71/487)	13.1 (428/3,270)	13.3 (212/1,598)	0.66
Moderate to severe mitral regurgitation	6.0 (29/487)	6.5 (214/3,270)	7.2 (115/1,598)	0.55
Severe mitral regurgitation	30.2 (147/487)	33.7 (1,101/3,270)	33.3 (532/1,598)	0.31
Mitral stenosis	78.3 (375/479)	75.0 (2,418/3,224)	76.2 (1,198/1,573)	0.25
Moderate or greater aortic regurgitation	11.9 (58/486)	9.2 (300/3,267)	9.4 (150/1,599)	0.15
Aortic stenosis	16.2 (79/489)	15.9 (518/3,258)	19.2 (305/1,590)	0.01
Moderate or greater tricuspid regurgitation	63.6 (311/489)	57.8 (1,899/3,283)	52.5 (842/1,604)	<0.0001
Pulmonary capillary wedge pressure, mm Hg	26.3 ± 8.5 (240)	26.0 ± 8.4 (1,570)	27.1 ± 8.6 (800)	0.01
Pulmonary artery pressure, mm Hg	39.5 ± 12.2 (240)	40.2 ± 12.4 (1,633)	42.0 ± 12.0 (828)	0.001
Right atrial pressure/CVP, mm Hg	11.5 ± 6.1 (250)	11.9 ± 6.5 (1,761)	12.4 ± 6.9 (876)	0.056
Pulmonary vascular resistance	260.0 (148.6-425.0)	258.1 (152.4-408.9)	248.7 (154.8-391.1)	0.87
Cardiac output, L/min	3.9 ± 1.3 (233)	4.2 ± 1.4 (1,573)	4.6 ± 1.4 (774)	<0.0001
Cardiac index, L/min/m^2	2.1 (1.7-2.6)	2.2 (1.8-2.6)	2.3 (1.9-2.8)	<0.0001
Cardiac index <2.2 L/min/m^2	57.1 (133/233)	50.3 (788/1,568)	43.7 (338/774)	0.0004

Values are mean ± SD (n), % (n/N), or median (Q1-Q3).

BMI = body mass index; BNP = brain natriuretic peptide; CABG = coronary artery bypass grafting; CVP = central venous pressure; GFR = glomerular filtration rate; ICD = implantable cardioverter-defibrillator; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; MG = mean gradient; MI = myocardial infarction; MV = mitral valve; NT-proBNP = N-terminal pro-brain natriuretic peptide; PCI = percutaneous coronary intervention; STS = Society for Thoracic Surgeons; TIA = transient ischemic attack; TMG = transvalvular mitral gradient.

TABLE 2 Echocardiographic Outcomes at Discharge, 30 Days, and 1 Year

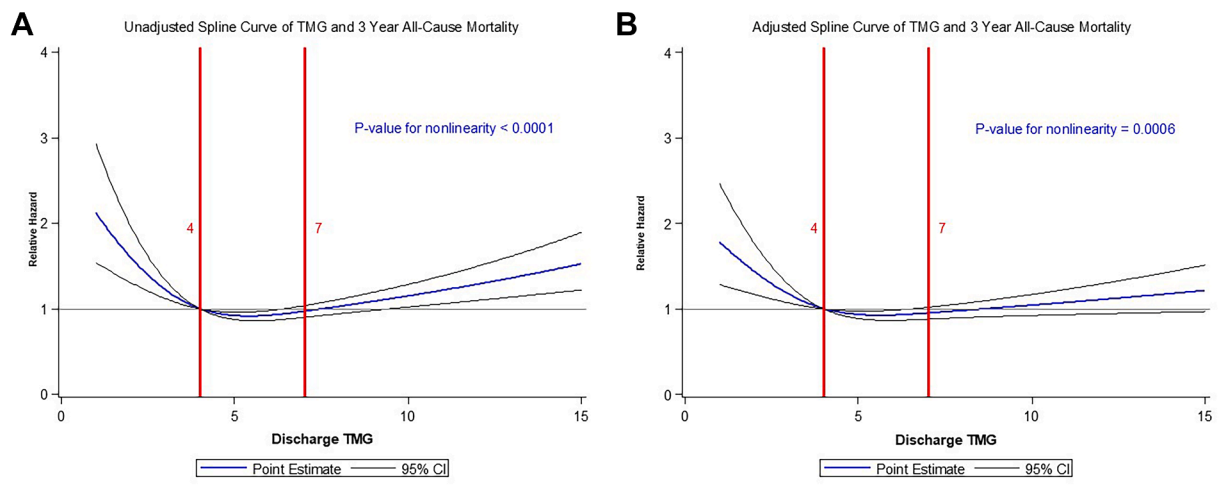
	TMG <4 mm Hg (n = 491)	TMG 4-7 mm Hg (n = 3,300)	TMG >7 mm Hg (n = 1,610)	*P* Value
Discharge				
MV area, cm^2	2.2 ± 1.0 (190)	2.0 ± 1.0 (1,707)	1.9 ± 0.9 (889)	0.0009
MV mean gradient, mm Hg	2.6 ± 0.6 (491)	5.5 ± 1.1 (3,300)	9.8 ± 2.4 (1,610)	<0.0001
Moderate or greater PVL	0.2 (1/425)	0.1 (4/2,781)	0.4 (5/1,327)	0.33
Moderate or greater mitral regurgitation	0.2 (1/486)	0.4 (12/3,281)	1.1 (17/1,591)	0.005
Moderate or greater tricuspid regurgitation	41.1 (122/297)	37.9 (709/1,871)	36.0 (303/841)	0.29
30 d				
MV area, cm^2	2.0 ± 1.0 (157)	1.9 ± 1.0 (1,298)	1.9 ± 1.0 (647)	0.12
MV mean gradient, mm Hg	5.6 ± 2.5 (293)	6.9 ± 2.6 (2,309)	9.0 ± 3.2 (1,100)	<0.0001
LVEF, %	52.5 ± 11.8 (298)	54.0 ± 11.2 (2,352)	54.4 ± 11.7 (1,114)	0.04
Moderate or greater PVL	0.0 (0/251)	0.2 (3/1,944)	0.4 (4/936)	0.26
Moderate or greater mitral regurgitation	1.3 (4/299)	0.7 (16/2,337)	0.7 (8/1,119)	0.46
Moderate or greater tricuspid regurgitation	44.3 (131/296)	40.3 (940/2,332)	33.6 (372/1,106)	0.0001
1 y				
MV area, cm^2	2.0 ± 1.6 (54)	1.9 ± 1.0 (550)	1.8 ± 0.8 (320)	0.03
MV mean gradient, mm Hg	5.8 ± 2.5 (120)	7.0 ± 3.0 (1,046)	8.7 ± 3.4 (567)	<0.0001
LVEF, %	53.5 ± 11.3 (126)	53.8 ± 11.3 (1,091)	54.5 ± 11.3 (599)	0.39
Moderate or greater PVL	0.0 (0/96)	0.4 (3/844)	0.6 (3/472)	0.61
Moderate or greater mitral regurgitation	0.8 (1/127)	0.7 (7/1,078)	1.6 (9/571)	0.18
Moderate or greater tricuspid regurgitation	40.0 (50/125)	34.8 (371/1,066)	30.6 (180/589)	0.07

Values are mean ± SD (n) or % (n/N).
LV = left ventricular; PVL = paravalvular leak; other abbreviations as in Table 1.

curves were used to explore the relationship between TMG post-MVIV and 3-year all-cause mortality (Figures 1A and 1B).

Prior to adjustment, the relationship between TMG and mortality at 3 years was nonlinear (*P* for nonlinearity < 0.0001). Excess mortality occurred in patients with low TMGs, a decrease in mortality in patients with intermediate TMGs, and a slow relative incline in mortality at higher TMGs, reaching significance at TMG >10 mm Hg.

FIGURE 1 MVIV Relationship Between DMG and 3-Year All-Cause Mortality



Covariates used for adjusted spline curves: Cardiac Index < 2.2, LVEF < 50, age, KCCQ-OS, currently on dialysis, GFR, heart failure hospitalization within past year, hemoglobin, home oxygen, immunocompromised state, ≥ moderate mitral regurgitation, ≥ moderate tricuspid regurgitation, prior myocardial infraction, and cardiogenic shock within 24 hours

(A) Unadjusted spline curve of discharge mean gradient (DMG) and 3-year all-cause mortality for mitral valve in valve (MVIV). (B) Adjusted spline curve of DMG and 3-year all-cause mortality for MVIV. GFR = glomerular filtration rate; KCCQ-OS = Kansas City Cardiomyopathy Questionnaire overall summary score; LVEF = left ventricular ejection fraction; TMG = transvalvular mitral gradient.

After adjustment, the *P* value for nonlinearity remained significant ($P = 0.0006$) at 3 years. Low TMG was associated with increased mortality, and intermediate TMG was associated with decreased mortality. However, there was no increase in mortality with high TMG.

IMPACT OF ECHOCARDIOGRAPHIC GRADIENT ON CLINICAL OUTCOMES. Discharge TMG. At 1 year, compared with high TMG, intermediate TMG was associated with less advanced NYHA functional class III or IV ($P = 0.0003$) and a better composite safety outcome ($P = 0.005$). One-year results also showed that compared with low TMG, intermediate TMG was associated with lower all-cause mortality ($P < 0.0001$), the composite endpoint of all-cause mortality or stroke ($P = 0.0003$), cardiac mortality ($P = 0.001$), less advanced NYHA functional class III or IV ($P = 0.05$), and a better composite safety outcome ($P = 0.0008$) (Table 3). There were no differences in KCCQ overall summary score ($P = 0.14$), any readmissions ($P = 0.30$), and HF-related readmissions ($P = 0.11$) between groups at 1 year (Table 3).

Kaplan-Meier curves showing the cumulative incidence of outcomes demonstrated a significant overall difference among the 3 groups over a 3-year follow-up period (896 mortality events for entire cohort; log-rank $P < 0.0001$) (Figures 2 and 3). Low discharge TMG was associated with increased risk for 3-year all-cause mortality compared with intermediate discharge TMG (adjusted HR: 1.52; 95% CI: 1.22-1.89; $P = 0.0002$) and high discharge TMG (adjusted HR: 1.35; 95% CI: 1.07-1.71; $P = 0.01$) (Figure 2, Central Illustration). The risk for the composite endpoint of all-cause mortality or stroke was also higher in the low discharge TMG group compared with the intermediate discharge TMG group (adjusted HR: 1.36; 95% CI: 1.11-1.68; $P = 0.004$). No difference was observed between the low discharge TMG and high discharge TMG groups (adjusted HR: 1.21; 95% CI: 0.97-1.51; $P = 0.09$) or between the intermediate and high discharge TMG groups (adjusted HR: 0.89; 95% CI: 0.78-1.02; $P = 0.08$) in the 3-year composite endpoint of all-cause mortality or stroke (Figure 3).

30-DAY TMG. To estimate the impact of gradients in patients who survived to 30 days, we studied the relationship between 30-day TMG and 3-year clinical outcomes (Figures 4A and 4B). Compared with high TMG, intermediate TMG had lower 3-year all-cause mortality (adjusted HR: 0.68; 95% CI: 0.57-0.82; $P < 0.0001$) and a reduced risk for the composite endpoint of all-cause mortality or stroke (adjusted HR: 0.70; 95% CI: 0.59-0.83; $P < 0.0001$). In this analysis, the proportional hazards assumption was violated. This may have been due to the limited patient number in the low TMG group during extended follow-up; conclusions for this subgroup therefore remain exploratory. The distribution of 30-day MG is shown in Supplemental Figure 2.

Discharge to 30-day TMG. We also studied the change in TMG from discharge to 30 days. At 30 days, among the 322 patients in the low TMG group, 29 (9.0%) had died, 54 (16.8%) maintained low TMGs, 189 (58.7%) had intermediate TMGs, and 50 (15.5%) had high TMGs. Among the 2,388 patients in the intermediate TMG group, 81 (3.4%) had died, 78 (3.3%) had low TMG, 1,464 (61.3%) maintained intermediate TMGs, and 765 (32.0%) had high TMGs. Among 1,159 patients with high TMGs at discharge, 59 (5.1%) had died, 8 (0.7%) had low TMGs, 382 (33.0%) had intermediate TMGs, and 710 (61.3%) maintained high TMGs (Supplemental Figure 3).

There was no difference in patients who exhibited low or intermediate TMGs at discharge and high TMGs at 30 days and those with high TMGs at both discharge and 30 days regarding all-cause mortality over 3 years (log-rank $P = 0.66$) (Figure 5).

DISCUSSION

Post-MVIV: 1) The relationship between all-cause mortality and post-MVIV echocardiography-derived TMG is complex and nonlinear; 2) At 3 years post-MVIV, low echocardiography-derived TMG (<4 mm Hg) at discharge was associated with higher all-cause mortality compared with intermediate (4-7 mm Hg) and high (>7 mm Hg) TMGs; 3) low TMG was associated with reduced CO and cardiac index compared with intermediate and high TMGs; 4) intermediate TMG was associated with less advanced NYHA functional class III or IV compared with high and low TMGs; 5) intermediate TMG at 30 days was associated with lower all-cause mortality and the composite endpoint of all-cause mortality or stroke at 3 years compared with high TMG, with no difference in outcomes between high and low TMGs; 6) there was a significant change in TMG between discharge and 30-day follow-up; and 7) there was no difference in 3-year all-cause mortality between patients who exhibited high TMG both at discharge and at 30 days and those with low and intermediate TMGs at discharge but developed high TMGs at 30 days.

This study highlights the complex association between TMG following MVIV, at discharge and 30 days, and clinical outcomes. It also extends the previous findings noted post-TAVR regarding the relation of postprocedural valvular gradients to flow and mortality. In addition, it argues against the use of

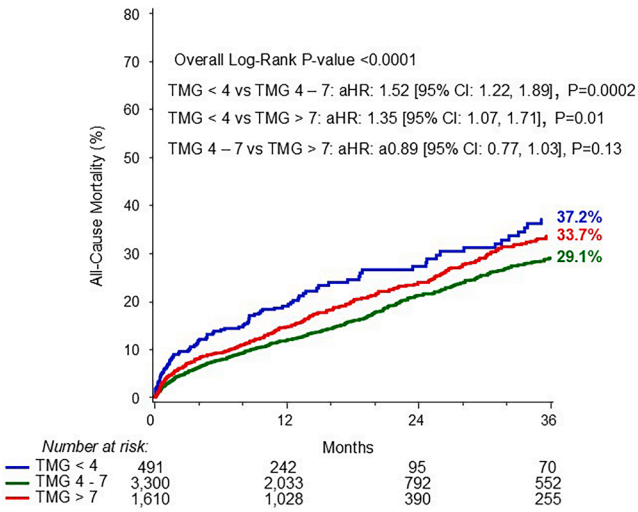
TABLE 3 In-Hospital, 30-Day, and 1-Year Outcomes

	TMG <4 mm Hg (n = 491)	TMG 4-7 mm Hg (n = 3,300)	TMG >7 mm Hg (n = 1,610)	*P* Value
In hospital				
All-cause mortality	4.3 (21/491)	1.5 (50/3,300)	2.9 (46/1,610)	<0.0001
All-cause mortality or stroke				
Cardiac death	2.0 (10/491)	0.7 (23/3,300)	1.3 (21/1,610)	0.007
Mitral valve reintervention	0.4 (2/491)	0.2 (7/3,300)	0.6 (9/1,610)	0.13
Major vascular complication	1.6 (8/491)	0.7 (24/3,300)	1.4 (23/1,610)	0.03
Life-threatening bleeding	2.0 (10/491)	0.9 (31/3,300)	1.1 (18/1,610)	0.09
New requirement for dialysis	1.4 (7/491)	0.8 (26/3,300)	1.4 (22/1,610)	0.11
Myocardial infarction	0.6 (3/491)	0.0 (1/3,300)	0.2 (3/1,610)	0.003
New pacemaker without baseline pacemaker	1.4 (5/348)	1.2 (29/2,386)	1.0 (13/1,249)	0.81
New onset of atrial fibrillation	2.8 (7/248)	1.2 (22/1,909)	1.7 (18/1,040)	0.08
Stroke	1.0 (5/491)	0.7 (22/3,300)	1.6 (26/1,610)	0.007
TIA	0.6 (3/491)	0.1 (2/3,300)	0.0 (0/1,610)	0.0003
LVOT obstruction	0.4 (2/491)	0.3 (9/3,300)	0.8 (12/1,610)	0.058
Device thrombosis	0.0 (0/491)	0.2 (6/3,300)	0.3 (4/1,610)	0.53
Cardiac perforation	1.2 (6/491)	0.3 (10/3,300)	0.3 (5/1,610)	0.008
ASD closure	9.2 (45/491)	9.2 (302/3,300)	7.9 (127/1,610)	0.32
Any readmission	0.2 (1/491)	0.2 (7/3,300)	0.3 (5/1,610)	0.79
Cardiac readmission	0.0 (0/491)	0.2 (5/3,300)	0.1 (1/1,610)	0.50
Heart failure readmission	0.0 (0/491)	0.1 (2/3,300)	0.0 (0/1,610)	0.53
30 d				
All-cause mortality	6.1 (29) (4.3-8.7)	2.6 (82) (2.1-3.2)	3.8 (60) (3.0-4.9)	<0.0001
Stroke	1.2 (6) (0.6-2.7)	1.3 (43) (1.0-1.8)	2.5 (39) (1.8-3.4)	0.006
All-cause mortality or stroke	6.5 (31) (4.6-9.1)	3.7 (119) (3.1-4.4)	5.8 (91) (4.7-7.0)	
Cardiac death	2.9 (13)(1.7-4.9)	1.0 (30) (0.7-1.4)	1.8 (27) (1.2-2.6)	0.001
Mitral valve reintervention	0.4 (2) (0.1-1.7)	0.3 (9) (0.1-0.5)	0.7 (11) (0.4-1.3)	0.11
Major vascular complication	1.7 (8) (0.8-3.3)	0.9 (28) (0.6-1.2)	1.7 (27) (1.2-2.5)	0.02
Life-threatening bleeding	1.6 (7) (0.8-3.3)	1.3 (39) (0.9-1.7)	0.9 (14) (0.5-1.5)	0.44
New requirement for dialysis	1.5 (7) (0.7-3.1)	1.0 (31) (0.7-1.4)	1.6 (24) (1.0-2.3)	0.19
Myocardial infarction	0.8 (4) (0.3-2.2)	0.1 (4) (0.0-0.3)	0.3 (5) (0.1-0.8)	0.009
New pacemaker without baseline pacemaker	2.2 (7) (1.1-4.6)	1.5 (35) (1.1-2.1)	1.1 (14) (0.7-1.9)	0.39
New onset of atrial fibrillation	3.5 (8) (1.8-6.9)	1.5 (28) (1.0-2.2)	1.9 (19) (1.2-2.9)	0.11
TIA	0.6 (3) (0.2-2.0)	0.2 (6) (0.1-0.4)	0.1 (1) (0.0-0.5)	0.04
LVOT obstruction	0.4 (2) (0.1-1.6)	0.3 (9) (0.1-0.5)	0.8 (12) (0.4-1.3)	0.06
Device thrombosis	0.0 (0) (0.0-0.0)	0.2 (7) (0.1-0.5)	0.3 (5) (0.1-0.8)	0.44
ASD closure	9.2 (45) (7.0-12.1)	9.3 (306) (8.4-10.3)	8.0 (128) (6.7-9.4)	0.30
Any readmission	9.1 (40) (6.7-12.2)	9.3 (288) (8.3-10.4)	8.8 (133) (7.5-10.4)	0.87
Cardiac readmission	2.1 (9) (1.1-3.9)	1.7 (52) (1.3-2.2)	1.7 (25) (1.1-2.4)	0.84
Heart failure readmission	2.3 (10) (1.2-4.2)	2.3 (71) (1.8-2.9)	2.1 (32) (1.5-3.0)	0.93
1 y				
All-cause mortality	19.1 (71) (15.3-23.6)	11.9 (311) (10.7-13.2)	14.8 (199) (13.0-16.8)	<0.0001
Stroke	3.9 (13) (2.2-6.7)	3.6 (93) (2.9-4.4)	4.9 (67) (3.8-6.2)	0.13
All-cause mortality or stroke	20.5 (76) (16.6-25.1)	14.4 (381) (13.1-15.8)	17.8 (244) (15.8-19.9)	<0.001
Cardiac death	7.1 (24) (4.7-10.6)	3.8 (88) (3.1-4.7)	4.6 (56) (3.5-5.9)	0.005
Mitral valve reintervention	0.8 (3) (0.2-2.4)	1.0 (24) (0.7-1.6)	2.3 (27) (1.5-3.3)	0.010
Major vascular complication	2.1 (9) (1.1-4.0)	1.1 (34) (0.8-1.6)	1.9 (29) (1.3-2.7)	0.051
Life-threatening bleeding	3.9 (14) (2.3-6.6)	2.0 (55) (1.5-2.6)	2.6 (32) (1.8-3.7)	0.11
New requirement for dialysis	1.8 (8) (0.9-3.5)	1.5 (42) (1.1-2.1)	2.4 (33) (1.7-3.4)	0.13
Myocardial infarction	0.8 (4) (0.3-2.2)	0.7 (15) (0.4-1.1)	0.8 (10) (0.4-1.6)	0.43
New pacemaker without baseline pacemaker	3.4 (9) (1.7-6.7)	3.4 (62) (2.7-4.4)	2.2 (23) (1.5-3.4)	0.25
New onset of atrial fibrillation	5.5 (11) (3.0-9.9)	2.9 (45) (2.1-3.9)	3.6 (31) (2.5-5.1)	0.09
TIA	1.1 (4) (0.4-3.0)	0.5 (11) (0.3-0.9)	0.7 (7) (0.3-1.4)	0.19
Safety composite[a]	20.2 (70) (16.2-25.1)	14.3 (343) (12.9-15.8)	17.1 (219) (15.1-19.4)	0.0005
LVOT obstruction	0.4 (2) (0.1-1.6)	0.3 (9) (0.1-0.5)	0.8 (12) (0.4-1.3)	0.06
Device thrombosis	0.0 (0) (0.0-0.0)	0.4 (11) (0.2-0.7)	0.7 (9) (0.4-1.4)	0.20
ASD closure	11.4 (51) (8.7-14.9)	9.8 (316) (8.8-10.9)	8.8 (137) (7.5-10.3)	0.31
Any readmission	34.5 (109) (29.3-40.4)	31.4 (743) (29.5-33.5)	33.8 (402) (9.8-13.6)	0.30
Cardiac readmission	9.1 (27) (6.2-13.2)	8.2 (183) (7.1-9.5)	9.6 (106) (7.9-11.5)	0.51
Heart failure readmission	14.2 (41) (10.5-19.0)	9.9 (228) (8.7-11.2)	11.6 (133) (9.8-13.6)	0.11
NYHA functional class III/IV	16.9 (24/142)	11.2 (119/1,067)	17.5 (99/566)	0.0009
KCCQ overall summary score	79.8 ± 20.7 (128)	78.6 ± 21.7 (1,065)	76.7 ± 22.6 (581)	0.14
3 y				
All-cause mortality	37.2 (98) (30.7-44.7)	29.1 (496) (26.7-31.7)	33.7 (302) (30.2-37.5)	
All-cause mortality or stroke	41.1 (106) (34.2-48.8)	33.6 (589) (31.0-36.3)	38.9 (358) (35.2-42.8)	

Values are % (n/N), Kaplan-Meier estimate % (number of events) (95% CI) for 30-day and 1-year outcomes, or mean ± SD (n). [a]The safety composite was defined as all-cause mortality, stroke, and mitral valve reintervention.

ASD = atrial septal defect; LVOT = left ventricular outflow tract; other abbreviations as in Table 1.

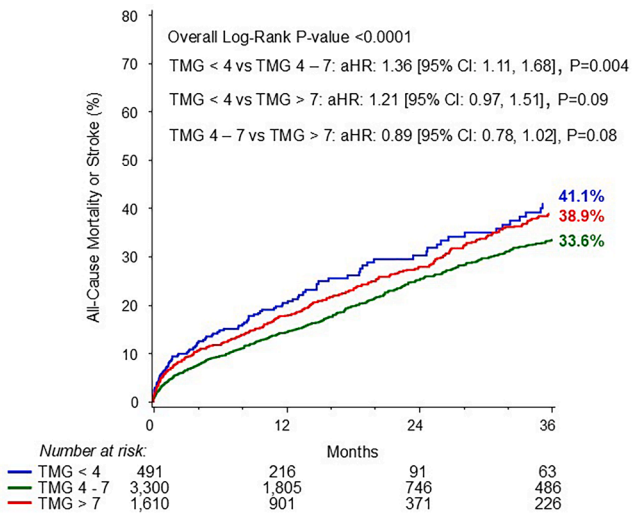
FIGURE 2 MVIV 3-Year All-Cause Mortality by DMG Status



Hazard ratios adjusted be following covariates: Cardiac Index < 2.2, LVEF < 50, age, KCCQ-OS, currently on dialysis, GFR, heart failure hospitalization within past year, hemoglobin, home oxygen, immunocompromised state, ≥ moderate mitral regurgitation, ≥ moderate tricuspid regurgitation, prior myocardial infraction, and cardiogenic shock within 24 hours

MVIV 3-year all-cause mortality by DMG status. aHR = adjusted HR; other abbreviations as in Figure 1.

FIGURE 3 MVIV 3-Year All-Cause Composite Endpoint of Mortality or Stroke by DMG Status



Hazard ratios adjusted be following covariates: Cardiac Index < 2.2, LVEF < 50, KCCQ-OS, operator reason for procedure, currently on dialysis, GFR, prior coronary artery bypass graft (CABG), hemoglobin, home oxygen, immunocompromised, ≥ moderate mitral regurgitation (MR), atrial fibrillation/flutter, baseline New York Heart Association (NYHA) class III/IV, cardiogenic shock within 24 hours, peripheral arterial disease, chronic lung disease, porcelain aorta, STS score, and procedure status.

MVIV 3-year composite endpoint of all-cause mortality or stroke by DMG status. STS = Society of Thoracic Surgeons; other abbreviations as in Figures 1 and 2.

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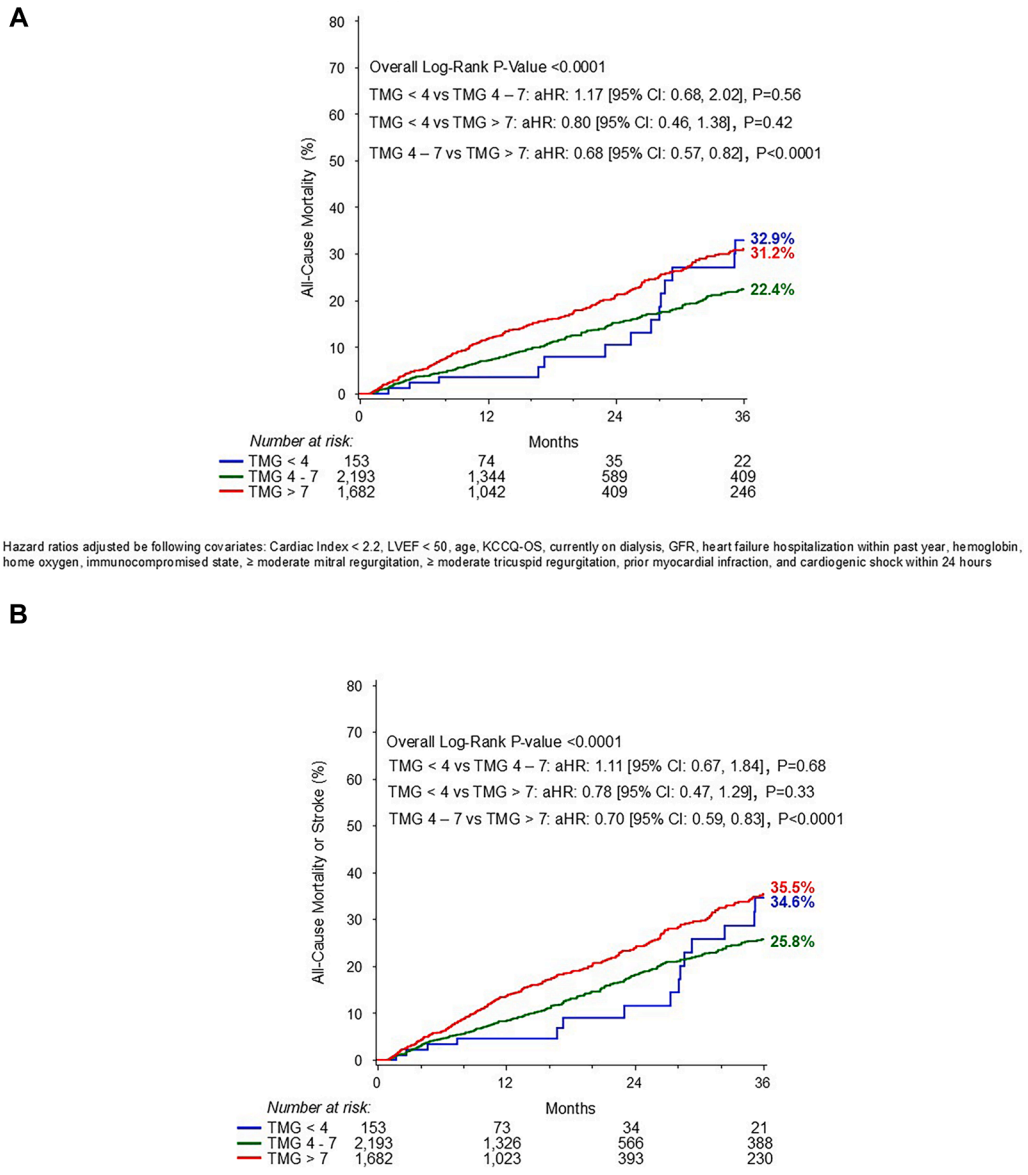
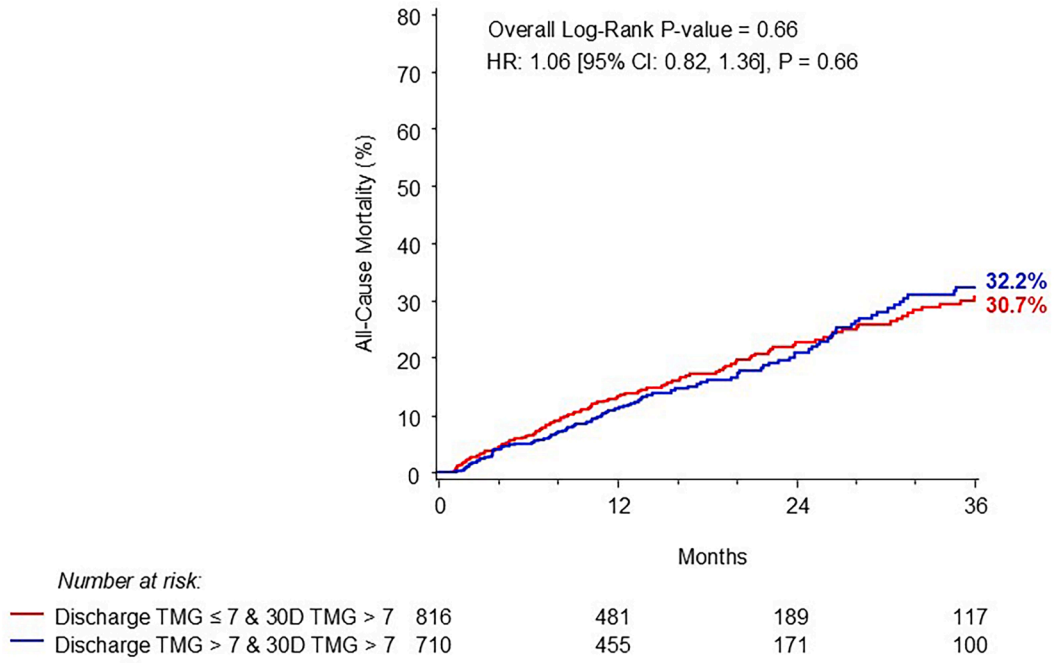
FIGURE 4 MVIV 3-Year All-Cause Mortality and 3-Year Composite Endpoint of All-Cause Mortality or Stroke by 30-Day MG Status



(A) MVIV 3-year all-cause mortality by 30-day mean gradient (MG) status. (B) MVIV 3-year composite endpoint of all-cause mortality or stroke by discharge MG status. *Because of the limited patient number in the low TMG group during extended follow-up, conclusions for this subgroup remain exploratory. Abbreviations as in Figures 1 to 3.

FIGURE 5 Mitral Valve in Valve 3-Year All-Cause Mortality by Change in Discharge to 30-Day Mean Gradient Status



Mitral valve in valve 3-year all-cause mortality by change in discharge to 30-day mean gradient status. TMG = transvalvular mitral gradient.

discharge and 30-day gradients interchangeably post-MVIV, as there was a significant shift of gradients from discharge to 30 days.

TRANSVALVULAR GRADIENTS AND MORTALITY WITH OTHER TRANSCATHETER VALVE THERAPIES. Other therapies have also shown similar findings regarding the relationship between clinical outcomes, gradient, flow post-TAVR and transcatheter edge-to-edge repair (TEER), as noted in the following discussion.

Following TAVR, previous studies have failed to demonstrate an association between an elevated echocardiographic MG (≥20 mm Hg) and mortality.[7-9,12,13] Echocardiographic gradients also demonstrated a nonlinear and complex relationship with 2-year mortality. Low (<10 mm Hg) echocardiographic gradients were associated with worse survival at 2 years[11] and 3 years[10] and were associated with lower echocardiographic stroke volume index and EF.

Post-TEER, TMGs have demonstrated variable relationships with clinical outcomes. However, no studies factored in transvalvular flow and EF.

In one study, high gradients following degenerative MR therapy, but not functional MR, were associated with poor outcomes. There was no difference in EF among TMGs in the degenerative MR group, but EF was lower in patients with TMGs <5 mm Hg in the functional MR group.[13]

Another study suggested increased mortality post-TEER with TMG >5 mm Hg in patients with severe HF.[14] Conversely, in the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) trial, different quartiles of low, intermediate, and elevated TMGs post-TEER were not associated with increased mortality or worse functional status, and there was a trend toward lower EF in patients with lower TMGs post-TEER.[15]

POSSIBLE EXPLANATIONS FOR THE NONLINEAR ASSOCIATION OF TMG AND MORTALITY. In convective acceleration, the primary cause of the increase in blood velocity with reduced valve area, there is a quadratic relationship between transaortic velocity and pressure gradient. Hence, in native or prosthetic valve stenosis, the transvalvular velocity and echocardiography-derived gradient, by the simplified Bernoulli equation, are primarily a function of valvular hemodynamic status and, to a lesser extent, flow and fluid dynamics. However, in the absence of valve stenosis, as in normal prosthetic

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valves, the transvalvular velocity and echocardiographic gradient largely reflect flow and fluid dynamics rather than valvular hemodynamic status.[16-18]

Low flow has been associated with lower MG and worse outcomes following TAVR.[11] This study suggests that post-MVIV, a low discharge TMG may primarily reflect transvalvular flow as determined by CO and cardiac index, rather than indicating optimal valve hemodynamic status or suggesting better clinical outcomes. Intermediate TMG patients also had better NYHA functional class at 1 year compared with those with low or high TMGs. Accordingly, post-MVIV, echocardiography-derived valve hemodynamic status should not be taken in isolation as a reflection of clinical outcomes and the need for "optimization" techniques but rather considered together with cardiac function, flow, and comorbidities. Additionally, although intermediate TMG at 30 days was associated with lower all-cause mortality and the composite endpoint of all-cause mortality or stroke at 3 years compared with high TMG, there were no differences in outcomes between high and low TMG. Thus, it is likely that low flow, reflected by CO and cardiac index, may have affected both discharge TMG and clinical outcomes. Also, the significant changes in TMG from discharge to 30 days and the similar outcomes in those with high discharge and 30-day TMGs reflect the complex relationship between TMG and clinical outcomes.

ROLE OF ECHOCARDIOGRAPHIC GRADIENT ASSESSMENT AFTER TRANSCATHETER MITRAL VALVE REPLACEMENT. Echocardiography remains the primary tool to assess prosthetic valve function post-MVIV and provides information regarding left ventricular function, MR, TMG, and temporal changes in valve function. However, this study calls into question the utility of a single echocardiographic measurement of an elevated gradient post-MVIV in evaluating prosthetic valve hemodynamic and function. Given the nonlinear relation of TMG to outcomes and its relationship to CO and cardiac index, clinical outcomes and procedure success based on postoperative echocardiographic gradient alone, without including left ventricular function and flow, may not be appropriate.

Results from this study showed a significant change in TMG between discharge and 30 days. However, there was no difference in 3-year mortality between patients with low TMGs and those with high TMGs at 30 days and improved mortality in patients with intermediate TMGs at 30 days compared with those with high TMGs. There was no difference in 3-year mortality in those who maintained elevated gradients from discharge to 30 days vs those with increased TMGs during the first 30 days from low to high. These findings suggest that both low and elevated TMGs at discharge or at 30 days are associated with worse outcomes at 3 years.

A paper published in 2022 suggested structural deterioration of transcatheter mitral valve replacement valves through the following hemodynamic changes: an increase in Doppler velocity index ≥0.4 mm Hg or ≥20% resulting in a Doppler velocity index ≥2.2, a decrease in MVA ≥0.5 cm^2 or 25% resulting in MVA <1.5 cm^2 and generally associated with a TMG ≥5 mm Hg, or occurrence of or increase in a grade of transprosthetic MR resulting in moderate or greater MR.[19]

Interestingly, a lower incidence of atrial fibrillation or flutter and younger age were observed in patients with high TMGs following MVIV, suggesting that impaired atrial contractile function and older age may reduce transmitral flow velocity and account for lower gradients.

STUDY LIMITATIONS. Echocardiographic hemodynamic parameters were determined at each institution and were not core laboratory adjudicated. No flow data were reported by echocardiography but only by invasive measurements. The method used to perform the CO measurement was determined by the site and is not reported to the TVT Registry. However, it is typically the Fick method that is used more frequently. Moreso, CO was missing in a significant portion of patients. There was no independent adjudication of adverse events, with a potential for underreporting. There was no invasive corroboration of TMG. Finally, no adjustments were made for multiple comparisons, because of the nature of the study design and its exploratory intent. This approach is consistent for retrospective analyses in which findings are intended to inform future research rather than provide definitive conclusions.

CONCLUSIONS

The relationship between all-cause mortality and echocardiographic TMG post-MVIV is complex and nonlinear. Compared with intermediate TMG (4-7 mm Hg) and high TMG (>7 mm Hg), post-MVIV, discharge TMG <4 mm Hg is associated with higher 3-year all-cause mortality. TMG changed significantly from discharge to 30 days, and values cannot be used interchangeably. Discharge TMG primarily reflects transvalvular flow as determined by CO or cardiac index and should not be the sole determination of

procedural outcome, valve performance, or the need for optimization without incorporating CO.

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PERSPECTIVES

WHAT IS KNOWN? After transcatheter mitral valve replacement, the relationship between echocardiographic discharge gradients is nonlinear, with lower gradients associated with lower EF, lower flow, and increased mortality.

WHAT IS NEW? After transcatheter MVIV, the relationship between echocardiographic discharge gradients is also nonlinear, such that lower gradients are associated with lower flow and increased mortality, suggesting that lower flow may be contributing to worse outcomes. Discharge and 30-day gradients vary widely and cannot be used interchangeably.

WHAT IS NEXT? The association of low gradients post-MVIV with low flow and worse clinical outcomes should be further explored in long-term follow-up. Attempts to "optimize" valves on the basis of discharge echocardiographic gradients need to be further explored. The impact of change in gradients vs single-level gradients needs to be explored.

REFERENCES

1. Hatle L, Brubakk A, Tromsdal A, Angelsen B. Noninvasive assessment of pressure drop in mitral stenosis by Doppler ultrasound. *Br Heart J*. 1978;40:131–140.

2. Hatle L, Angelsen BA, Tromsdal A. Non-invasive assessment of aortic stenosis by Doppler ultrasound. *Br Heart J*. 1980;43:284–292.

3. Burstow DJ, Nishimura RA, Bailey KR, et al. Continuous wave Doppler echocardiographic measurement of prosthetic valve gradients. A simultaneous Doppler-catheter correlative study. *Circulation*. 1989;80:504–514.

4. Généreux P, Piazza N, Alu MC, et al. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *J Am Coll Cardiol*. 2021;77:2717–2746.

5. Playford D, Stewart S, Celermajer D, et al. Poor survival with impaired valvular hemodynamics after aortic valve replacement: the National Echo Database Australia Study. *J Am Soc Echocardiogr*. 2020;33:1077–1086.e1.

6. Abbas AE, Mando R, Kadri A, et al. Comparison of transvalvular aortic mean gradients obtained by intraprocedural echocardiography and invasive measurement in balloon and self-expanding transcatheter valves. *J Am Heart Assoc*. 2021;10(19):e021014.

7. Eng MH, Abbas AE, Hahn RT, et al. Real world outcomes using 20 mm balloon expandable SAPIEN 3/Ultra valves compared to larger valves (23, 26, and 29 mm)—a propensity matched analysis. *Catheter Cardiovasc Interv*. 2021;98:1185–1192.

8. Bleiziffer S, Simonato M, Webb JG, et al. Long-term outcomes after transcatheter aortic valve implantation in failed bioprosthetic valves. *Eur Heart J*. 2020;41:2731–2742.

9. Kaneko T, Makkar RR, Krishnaswami A, et al. Valve-in-surgical-valve with SAPIEN 3 for transcatheter aortic valve replacement based on Society of Thoracic Surgeons Predicted Risk of Mortality. *Circ Cardiovasc Interv*. 2021;14:e010288.

10. Eng MH, Khalili H, Vavalle J, et al. 3-Year outcomes of balloon-expandable valves: 20-mm vs larger valves (≥23 mm). *JACC Cardiovasc Interv*. 2024;17:2041–2051.

11. Khalili H, Pibarot P, Hahn RT, et al. Transvalvular pressure gradients and all-cause mortality following TAVR: a multicenter echocardiographic and invasive registry. *JACC Cardiovasc Interv*. 2022;15:1837–1848.

12. Herrmann HC, Pibarot P, Hueter I, et al. Predictors of mortality and outcomes of therapy in low-flow severe aortic stenosis: a Placement of Aortic Transcatheter Valves (PARTNER) trial analysis. *Circulation*. 2013;127:2316–2326.

13. Koell B, Ludwig S, Weimann J, et al. Long-term outcomes of patients With elevated mitral valve pressure gradient after mitral valve edge-to-edge repair. *JACC Cardiovasc Interv*. 2022;15:922–934.

14. Neuss M, Schau T, Isotani A, Pilz M, Schopp M, Butter C. Elevated mitral valve pressure gradient after MitraClip implantation deteriorates long-

term outcome in patients with severe mitral regurgitation and severe heart failure. *JACC Cardiovasc Interv*. 2017;10:931–939.

15. Halaby R, Herrmann HC, Gertz ZM, et al. Effect of mitral valve gradient after MitraClip on outcomes in secondary mitral regurgitation: results from the COAPT trial. *JACC Cardiovasc Interv*. 2021;14:879–889.

16. Donati F, Myerson S, Bissell MM, et al. Beyond Bernoulli: improving the accuracy and precision of noninvasive estimation of peak pressure dops. *Circ Cardiovasc Imaging*. 2017;10:e005207.

17. Firstenberg MS, Abel EE, Papadimos TJ, Tripathi RS. Nonconvective forces: a critical and often ignored component in the echocardiographic assessment of transvalvular pressure gradients. *Cardiol Res Pract*. 2012;2012:383217.

18. Abbas AE, Mando R, Hanzel G, Goldstein J, Shannon F, Pibarot P. Hemodynamic principles of prosthetic aortic valve evaluation in the transcatheter aortic valve replacement era. *Echocardiography*. 2020;37:738–757.

19. Pibarot P, Herrmann HC, Wu C, et al. Standardized definitions for bioprosthetic valve dysfunction following aortic or mitral valve replacement: *JACC* state-of-the-art review. *J Am Coll Cardiol*. 2022;80:545–561.

KEY WORDS mitral valve in valve, transcatheter mitral valve replacement, transvalvular mitral gradient

APPENDIX For a supplemental table and figures, please see the online version of this paper.