1-26-2024

Echocardiographic Parameters Associated With Less Reverse Left Ventricular Remodeling After Transcatheter Aortic Valve Implant in Subjects With Prosthesis Patient Mismatch

Andrew C. Peters

Fei Fei Gong

Ashvita Ramesh

Adin Andrei

Madeline Jankowski

See next page for additional authors

Authors
Andrew C. Peters, Fei Fei Gong, Ashvita Ramesh, Adin Andrei, Madeline Jankowski, Eric Cantey, Vincent Chen, James D. Thomas, James D. Flaherty, S. Christopher Malaisrie, and Kameswari Maganti

Received: 28 March 2023 | Revised: 15 August 2023 | Accepted: 16 September 2023

DOI: 10.1111/echo.15698

ORIGINAL ARTICLE

Echocardiography WILEY

Echocardiographic parameters associated with less reverse left ventricular remodeling after transcatheter aortic valve implant in subjects with prosthesis patient mismatch

Andrew C. Peters MD[1,2] | Fei Fei Gong MD[1] | Ashvita Ramesh BS[1] | Adin Andrei PhD[1] | Madeline Jankowski RDCS[1] | Eric Cantey MD[1] | Vincent Chen MD[1] | James D. Thomas MD[1] | James D. Flaherty MD[1] | S. Christopher Malaisrie MD[1] | Kameswari Maganti MD[1]

[1]Northwestern University Feinberg School of Medicine, Chicago, USA

[2]Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, USA

Correspondence
Kameswari Maganti MD, Associate Professor of Medicine, Department of Cardiology, 251 E. Huron Street. Suite 8–503 G, Chicago, IL 60611, USA.
Email: kmaganti5@gmail.com

Subject Terms: Valvular Heart Disease

Abstract

Background: Transaortic valve implant (TAVI) is the treatment of choice for severe aortic stenosis (AS). Some patients develop prosthesis patient mismatch (PPM) after TAVI. It is challenging to determine which patients are at risk for clinical deterioration.

Methods: We retrospectively measured echocardiographic parameters of left ventricular (LV) morphology and function, prosthetic aortic valve effective orifice area (iEOA) and hemodynamics in 313 patients before and 1 year after TAVI. Our objective was to compare the change in echocardiographic parameters associated with left ventricular reverse modeling in subjects with and without PPM. Our secondary objective was to evaluate echo parameters associated with PPM and the relationship to patient functional status and survival post-TAVI.

Results: We found that 82 (26.2%) of subjects had moderate and 37 (11.8%) had severe PPM post-TAVI. There was less relative improvement in LVEF with PPM (1.9 ± 21.3% vs. 8.2 + 30.1%, $p = .045$). LV GLS also exhibited less relative improvement in those with PPM (13.4 + 34.1% vs. 30.9 + 73.3%, $p = .012$). NYHA functional class improved in 84.3% of subjects by one grade or more. Echocardiographic markers of PPM were worse in those without improvement in NYHA class (mean AT/ET was .29 vs. .27, $p = .05$; DVI was .46 vs. .51, $p = .021$; and iEOA was .8 cm/m^2 vs. .9 cm/m^2, $p = .025$). There was no association with PPM and survival.

Conclusions: There was no improvement in LVEF and less improvement in LV GLS in those with PPM post-TAVI. Echocardiographic markers of PPM were present in those with lack of improvement in NYHA functional class.

KEYWORDS
myocardial strain, prosthesis-patient mismatch, transcatheter aortic valve implant

Abbreviations: AT, Acceleration time; AV, Aortic valve; AVA, Aortic valve area; CW, Continuous wave; DVI, dimensionless valve index; EDV, End-diastolic volume; EOA, Effective orifice area; ESV, End-systolic volume; ET, Ejection Time; LAVI, left atrial volume index; LV, left ventricle; LV GLS, left ventricular global longitudinal strain; LVMI, Left ventricular mass index; PPM, Prosthesis-patient mismatch; RVSP, Right ventricular systolic pressure; SAVR, Surgical aortic valve replacement; TAVI, Transaortic valve implant; TTE, Transthoracic echocardiogram.

1 | INTRODUCTION

Transcatheter aortic valve implant (TAVI) has become the treatment of choice for severe aortic stenosis (AS).[1–3] Improved hemodynamics following TAVI result in reverse left ventricular (LV) remodeling including reduced LV mass, LV volumes, and improved left ventricular global longitudinal strain (LV GLS).[4] The benefit of reverse LV remodeling after TAVI is not realized in those with prosthesis-patient mismatch (PPM).[4] PPM occurs when the effective orifice area (EOA) of an implanted prosthetic valve is too small in relation to the patient's body surface area resulting in residual flow obstruction. The occurrence of PPM remains high following TAVI.[5] The incidence of moderate and severe PPM from the TVT registry of cases between 2014 and 2017 was 25% and 12%, respectively.[6] Severe PPM was associated with an increased risk of heart failure hospitalization and death in the year following TAVI.[6]

Despite the definition of PPM being linked to iEOA, the diagnosis of PPM remains challenging. This is due to inherent error introduced into the valve area calculation in using 2D measurements to estimate the area of an ellipsoid left ventricular outflow tract (LVOT). The European Association of Cardiovascular Imaging and American Society of Echocardiography (ASE) have recommended an integrated approach to diagnose prosthetic valve dysfunction. Beyond the iEOA, they recommend evaluating hemodynamic parameters that indicate obstruction including an aortic valve acceleration time (AT) (abnormal > 100 ms), a ratio of aortic valve acceleration to ejection time (AT/ET) (possibly abnormal .32–.37, abnormal > .37), and a dimensionless valve index (DVI) (possibly abnormal < .3, abnormal < .25).[7,8] These echo parameters are independent of Doppler beam angulation and less prone to measurement error. Recent studies have shown that in native valve AS an AT/ET > .36 is associated with increased mortality.[9,10] In prosthetic aortic valves, an AT/ET > .37 is reported to have a sensitivity of 96% and specificity of 82% for prosthetic stenosis.[11]

Our primary objective was to determine the association of echo parameters with lack of reverse remodeling in those with PPM post TAVI. Our secondary objective was to evaluate echo parameters associated with PPM and the relationship to patient functional status and survival post-TAVI.

2 | METHODS

2.1 | Study design

This is a retrospective study of registry data collected from consecutive patients who underwent TAVI for severe AS at our institution between January 1, 2015 and December 30, 2018. All subjects were intermediate to high surgical risk. Patients were included if transthoracic echocardiograms (TTEs) pre-TAVI and at 1 year follow-up were available. Exclusion criteria were inadequate acoustic windows, poor endocardial tracking of two adjacent myocardial segments or errors in ECG gating precluding tracking of the R-R interval. Patients who underwent TAVI for severe aortic regurgitation (AR) or aortic valve-in-valve implant were excluded. Study approval was obtained from the IRB.

2.2 | TAVI procedure

TAVI was performed in patients with symptomatic severe AS with a valve area (AVA) ≤1.0 cm^2 and/or mean systolic aortic gradient > 40 mm Hg. Patients were at intermediate to high risk for conventional surgical aortic valve replacement (SAVR) as determined by the heart team. TAVI was performed using the transfemoral, transaortic, trans-subclavian, or transapical approaches as appropriate. Valve sizing was performed by cardiac computed tomography (CCT) in all subjects.

Valve types utilized for TAVI included the balloon expandable Edwards Sapien S3 and XT (Edwards Lifesciences, Irvine, CA, USA) and the self-expanding CoreValve (Medtronic, Minneapolis, MN, USA) (Table 1).

2.3 | Data collection

Demographics, baseline characteristics, medical comorbidities, STS score, NYHA functional class were collected from the TAVI database registry.

2.4 | Echocardiography

TTEs were performed on Philips iE33, Philips Epiq 7, and GE Vivid E95 ultrasound machines using conventional ASE guidelines before and at 1 year follow-up. A multiview approach was used to determine the highest aortic valve gradients before and after TAVI.[12] iEOA post-TAVI was calculated using the left ventricular outflow tract (LVOT) diameter as measured from outer edge to outer edge according to the VARC2 method.[13] The LVOT velocity was measured just underneath the apical margin of the valve stent. In cases where the landing zone of the stent was low in the LVOT, the velocity was measured in the proximal portion of the stent. AT was measured on CW-Doppler from the start of aortic valve ejection to the time peak velocity was noted (Figure 1A, B). ET was measured from CW-Doppler from the start to end of aortic valve ejection (Figure 1C, D). Echo analysis was performed independently by three experienced readers who were blinded to clinical outcomes (A.P.), (F.F.G.), and (M.J.).

2.5 | Definition of PPM

For this study, PPM was not present if the iEOA was > .85 cm^2/m^2, moderate if the iEOA was between .65 and .85 cm^2/m^2, and severe if the iEOA was <.65 cm^2/m^2. For patients with a body mass index ≥30 kg/m^2, lower criteria were used (severe PPM if iEOA < .60 cm^2/m^2 and moderate PPM if iEOA between .60 and .70 cm^2/m^2) as recommended by VARC2.[13]

TABLE 1 Baseline patient characteristics.

	Subjects without PPM (*N* = 194)	Subjects with PPM (*N* = 119)	*p*-value
Age (years)	81 (75,86)	78 (70,82)	<.001
Women (%)	77 (39.7)	63 (53)	.030
Race			.44
Caucasian (%)	170 (87.6)	94 (79)	
Black (%)	6 (3.1)	7 (6)	
Hispanic (%)	6 (3.1)	6 (7.6)	
Asian (%)	4 (2.1)	2 (1.6)	
STS score	5.1 (3.3)	4.6 (3.2)	.22
Body surface area (m^2)	1.87 (.25)	1.96 (.26)	.003
Body mass index (kg/m^2)	27 (4.8)	30 (6.7)	<.001
NYHA class	3 (2,3)		
Hypertension (%)	158 (81.4)	92 (77.3)	.38
Lung disease (%)	24 (12.4)	13 (10.9)	.70
Diabetes (%)	53 (27.3)	48 (40.3)	.017
Cerebrovascular accident (%)	18 (9.3)	18 (15)	.12
Chronic kidney disease (%)	59 (30.4)	30 (25.2)	.32
Coronary artery disease (%)	137 (70.6)	71 (59.6)	.046
Prior cardiac surgery (%)	39 (20.1)	26 (21.8)	.71
Valve type			.38
Edwards Sapien 3 (%)	155 (79.9)	105 (88)	
Edwards Sapien XT (%)	11 (5.7)	2 (1.7)	
Medtronic CoreValve (%)	14 (7.2)	5 (4.2)	
Medtronic evolute R (%)	8 (4.1)	5 (4.2)	
Medtronic Evolute Pro (%)	4 (2.1)	1 (.8)	
Direct flow (%)	2 (1)	1 (.8)	
Prosthesis size			.005
20–23 mm (%)	49 (25.2)	51 (42.8)	
25–27 mm (%)	90 (46.4)	41 (34.4)	
29–34 mm (%)	55 (28.4)	27 (22.6)	

Note: Data are presented as *n* (%), mean $\pm$ SD, or median [interquartile range].
Abbreviations: NYHA, New York Heart Association; STS, Society of Thoracic Surgery.

2.6 | Aortic regurgitation

Paravalvular AR following TAVI was assessed using an integrated approach recommended by the ASE.[14] This was relevant as the presence of AR following TAVI was associated with adverse LV remodeling.[4]

2.7 | Myocardial mechanics

Myocardial strain analysis was performed using speckle tracking echo from apical windows using TOMTEC-Arena 2020 (Philips, USA). Strain analysis was performed retrospectively from DICOMs that were archived across all imaging systems. Reviewers were blinded to outcomes data.

2.8 | Intra-and inter-observer variability

Twenty randomly selected studies were reanalyzed for LVOT diameter, AT/ET, and LV GLS by the same observer several months after the initial analysis. A second observer, blinded to previously obtained data, analyzed the same patients and the same loops for inter-observer variability.

2.9 | Statistical analysis

Summary statistics included counts/percentages, means $\pm$ SD or median (interquartile range; IQR) as appropriate. Comparison of temporal trends in echocardiographic parameters among subjects with and

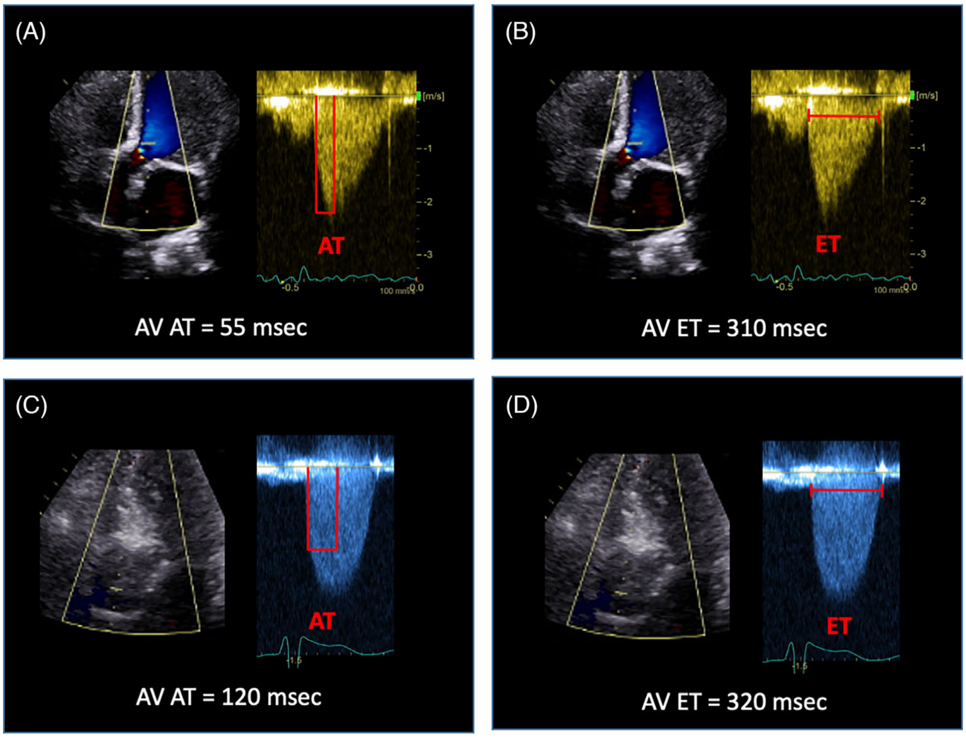

FIGURE 1 Measurement of aortic valve acceleration time (AT) and ejection time (ET). Panels A and B show a normal, early peaking, aortic valve continuous wave Doppler profile post-TAVI with a normal AT (<100 ms) (A) and measurement of ET (B). Panels C and D show an abnormal, rounded, aortic valve continue wave Doppler profile suggestive of prosthesis-patient mismatch with at AT > 100 ms (C) and measurement of ET (D).

without PPM were analyzed to assess relative change from baseline to 1 year post-TAVI.

NYHA functional class was reported pre-TAVI and at 1 year post-procedure. The median (IQR) NYHA class was compared between groups. We tested the differences in mean echocardiographic parameters associated with PPM including DVI, AV mean gradient, AV peak velocity, iEOA, AT/ET, and AV AT 1 year post-TAVI, between subjects with and without improvement in NYHA functional class, using a two-tailed t-test. We also compared differences in mean echocardiographic parameters between males and females.

Overall survival was evaluated using univariable and multivariable predictors, and Cox proportional hazards regression models. PPM and AT/ET variables were forced into the multivariable model, followed by an automated forward selection algorithm (p-value < .05 as entry threshold) from the pool of variables significant univariately, as well as those clinically associated with mortality: age, STS score, LVEF, relative reduction in mean transaortic gradient post-TAVI, post-TAVI AR, and right ventricular systolic pressure (RVSP). The assumption of proportional hazards was assessed using Schoenfeld residual plots and tested by adding time-covariate interaction to the model. We also performed subgroup survival analysis by gender. We chose to use a cutoff of AT/ET > .35 rather than .37 and a DVI of <.3 rather than .25 to ensure adequate sample size for comparison.

Intra- and inter-observer variability was assessed using interclass correlation coefficients. The consistency of measurements was also modeled as a correlation coefficient (R^2). A two-sided level of significance of .05 was used throughout and no adjustments were made for multiplicity. Statistical analyses were conducted using Prism v9 (GraphPad, La Jolla, CA, USA), SPSS v26 (IBM Corp, Armonk, NY, USA) and SAS v 9.4 (SAS Institute, Cary, NC, USA).

3 | RESULTS

3.1 | Baseline characteristics

Out of the 487 patients who underwent TAVI procedure between January 1, 2015 and December 30, 2018, 313 (64.3%) patients constituted the study cohort. Excluded patients consisted of 100 with incomplete echocardiographic data, 26 with poor acoustic windows, 21 with ECG gating abnormalities during strain analysis, two who had TAVI for severe AR, and 25 who underwent aortic valve-in-valve procedure (Figure 2).

The median age at the time of TAVI was 80 (73–85) years, and 139 (44.4%) were women. Using iEOA, a total of 194 (62%) subjects did not have PPM, 82 (26%) had moderate PPM, and 37 (12%) had severe PPM. Baseline characteristics of those with any degree of PPM (N = 119) and without PPM (N = 194) are reported in Table 1. Two hundred and seventy-six (88%) received a balloon expandable valve. Patients with PPM were younger and more likely to be women. The BSA and BMI were greater in the PPM group. There was a greater percentage of patients with diabetes in the PPM group. Finally, there was a larger

Echocardiography WILEY

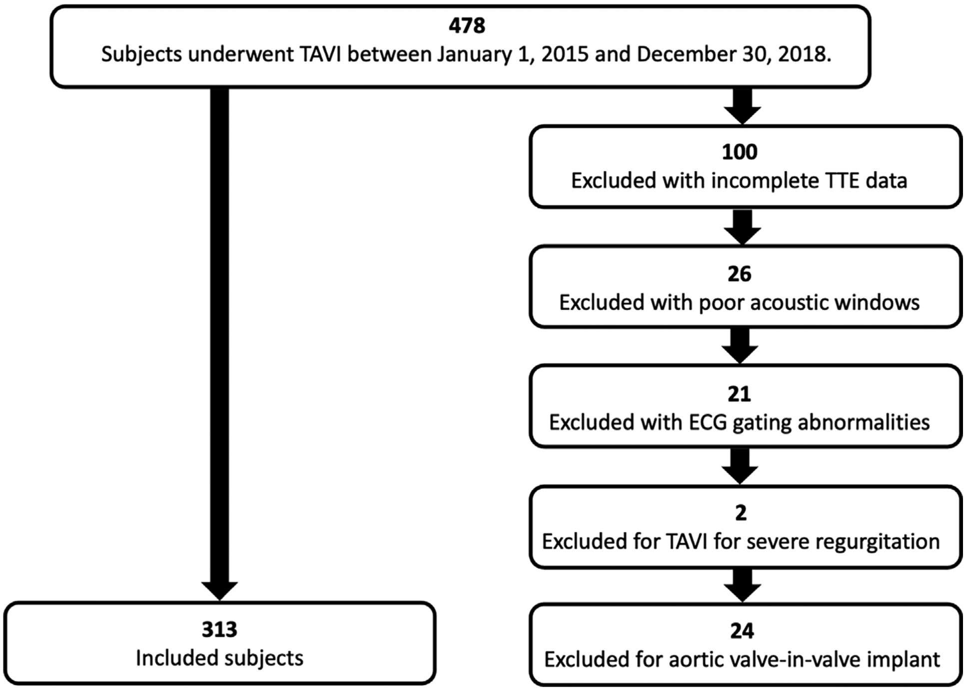

FIGURE 2 Flow diagram including the number of included and excluded patients.

portion of patients with smaller valves (20–23 mm) in the PPM group (Table 1).

3.2 | Echo characteristics

The relative change in TTE parameters was compared between subjects with PPM and those without PPM. There was less relative improvement in LVEF for those with PPM (1.9 ± 21.3% vs. 8.2 + 30.1%, p = .045) (Table 2). There was no statistically significant difference in change in LVEF by gender (Tables S1 and S2). LV GLS also exhibited less relative improvement in those with PPM (13.4 ± 34.1% vs. 30.9 ± 73.3%, p = .012). Males with and without PPM had improvement in LV GLS post-TAVI, but there was no significant difference in percentage change between groups (Table S1). Females exhibited less relative change in those with PPM vs. no PPM (13.6 ± 31.1% vs. 22.1 ± 28.8%, p = .007) (Table S2). The change in LV volume and mass was not significantly different between groups (Table 2). All aortic valve indices including velocity, gradients, acceleration time, AT/ET, and valve area improved more in subjects without PPM. There was no difference between the change in LV diastolic parameters including medial and lateral mitral valve E′, E/E′, left atrial volume index, or right ventricular systolic pressure (Table 2).

3.3 | Heart failure functional class

NYHA functional class improved in 84.3% (N = 264) of subjects by one grade or more. Figure 3 shows the distribution of improvement based on initial NYHA functional class. Comparisons of mean echo parameters associated with PPM were made at 1 year between subjects with and without improvement in NYHA class. DVI was statistically less (.46 vs. .51, p = .021) in those without improvement in NYHA class. iEOA was also less (.8 cm/m^2 vs. .9 cm/m^2, p = .025) in those without improvement in NYHA class. AT/ET was also greater in those without improvement in NYHA class (.29 vs. .27, p = .05). AV mean gradient, peak velocity, and AT were not different between groups (Table 3).

3.4 | Survival

During the study there were 53 deaths; 43 occurred in subjects without PPM (22%); four deaths occurred in those with PPM (15%). Concerns about selection bias were alleviated by the fact that overall survival since TAVI was not significantly different between individuals included and excluded (Figure S1, p = .63, 79.9% vs 79.4% at 3-years). Overall survival measured 1-year post TAVI was not significantly associated with AT/ET > .35 (Figure 4A, p = .81), the presence of PPM versus no PPM by iEOA (Figure 4B, p = .24), AV AT > 100 ms (Figure 4C, p = .13), or DVI < .3 (Figure 4D, p = .83). There was no significant difference in survival seen with subgroup analysis was performed by gender (Figures S2 and S3).

3.5 | Inter-and intra-observer variability

Analysis of intra-and inter-observer variability was performed on 20 subjects. The inter- and intra-class correlation coefficient (ICC) was .94 (.58–.98) and .95 (.72–.98) for LV GLS (Table S3). The R^2 was .88 and .9, respectively, indicating agreement between

TABLE 2 Comparison of temporal trends in echocardiographic parameters among subjects with and without PPM.

	Subjects without PPM (*N* = 194)			Subjects with PPM (*N* = 119)			
	Baseline	1 year	Relative change (%)	Baseline	1 year	Relative change (%)	*p*-value for% change:
Parameter	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	No PPM versus PPM
LVEF (%)	59 (12.6)	61 (11.2)	8.2% (30.1%)	60 (13.5)	59 (11.2)	1.9% (21.3%)	.045
LVEDVi (mL/m^2)	52 (22.4)	45 (16.7)	−5.6% (39.6%)	52 (20.1)	47 (17.9)	−1.5% (37.2%)	.18
LVESVi (mL/m^2)	23 (16.7)	19 (12.1)	−1.2% (61.4%)	22 (16.6)	20 (12.9)	7.1% (58.1%)	.12
LV mass (g)	208 (71.5)	183 (68.6)	−9.6% (26.2%)	214 (60.8)	186 (64.5)	−7.8% (30.1%)	.37
LV mass index (g/m^2)	111 (34.7)	97 (32.5)	−9.6% (26.2%)	109 (28.8)	95 (31.3)	−7.8% (30.1%)	.37
LV GLS (%)	−13.6 (4.1)	−16.3 (3.7)	30.9% (73.3%)	−14.1 (4.2)	−15.9 (3.7)	13.4% (34.1%)	.012
AV max velocity (m/s)	4.3 (.7)	2.2 (.4)	−48.1% (11.9%)	4.3 (.6)	2.6 (.5)	−38.2% (15.0%)	<.001
AV mean gradient (mm Hg)	44 (14.3)	10 (4)	−75.2% (10.9%)	44 (13)	15 (5.9)	−62.0% (22.4%)	<.001
AV acceleration time (ms)	118 (19)	81 (13.9)	−29.4% (16.4%)	121.1 (19.9)	83 (16.4)	−22.8% (23.7%)	<.001
AV ejection time (ms)	322 (34.2)	308 (35.4)	−.3% (12.6%)	328 (35.5)	311 (38.6)	−4.6% (12.5%)	.76
AV AT/ET	.37 (.05)	.26 (.04)	−26.5% (15.3%)	.47 (.06)	.27 (.04)	−18.8% (22.1%)	<.001
Dimensionless index	.23 (.06)	.57 (.1)	161.7% (85.2%)	.23 (.05)	.39 (.06)	75.5% (52.8%)	<.001
AVA (VTI) (cm^2)	.77 (.2)	1.9 (.4)	165.5% (82.4%)	.75 (.19)	1.4 (.28)	82.9% (62.2%)	<.001
AVAi (cm^2/m^2)	.41 (12)	1 (.2)	165.5% (82.4%)	.39 (.1)	.69 (.1)	82.9% (62.2%)	<.001
Stroke volume index (VTI) (mL/m^2)	41.3 (12)	43.5 (12.6)	10.0% (32.9%)	39.9 (10.7)	36.6 (9.9)	−4.3% (35.2%)	<.001
MV peak E velocity (cm/s)	100 (35.7)	100 (35.8)	4.0% (28.0%)	112 (39)	105.5 (36.8)	.4% (30.0%)	.39
Medial E′ (cm/s)	4.9 (1.7)	5.1 (1.7)	14.0% (46.7%)	5.3 (2)	5.4 (2.2)	9.2% (46.2%)	.91
Lateral E′ (cm/s)	6.3 (2.3)	6.5 (2.2)	13.5% (45.3%)	6.6 (2.3)	7.1 (2.9)	18.0% (61.4%)	.11
E/E′	19.5 (9.5)	18.8 (9.6)	−.04% (32.9%)	21.8 (13.5)	18.1 (6.8)	4.0% (49.1%)	.46
LAVI (mL/m^2)	42 (16.4)	40 (15.3)	−1.9% (30.5%)	41 (13.8)	40 (16.8)	−2.4% (40.0%)	.61
RVSP (mm Hg)	40 (13.6)	36 (10.8)	−2.1% (31.2%)	41 (13.4)	36 (10.7)	−6.6% (24.5%)	.43

Note: Data are presented as mean (SD). *p*-values are based on relative (%) change in regression models adjusted for age, sex, BSA, hypertension, and STS score. $p < .05$ is statistically significant.
Abbreviations: AT/ET, ratio of acceleration time to ejection time; AV, aortic valve; AVA, aortic valve area; LAVI, left atrial volume index; LVEDVi, indexed left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESVi, indexed left ventricular end systolic volume; LV GLS, left ventricular global longitudinal strain; MV, mitral valve; RVSP, right ventricular systolic pressure.

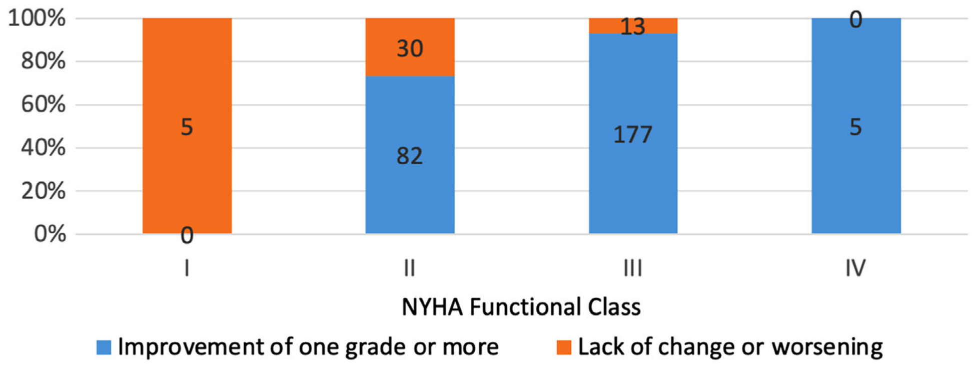

FIGURE 3 Graph of the change in NYHA functional class after transcatheter aortic valve implant (TAVI) based on initial NYHA functional class. Blue indicates improvement in NYHA class by one grade or more. Orange indicates no improvement or worsening in NYHA class.

TABLE 3 Comparison of mean echo parameters in those with and without improvement in NYHA functional class.

	Change in NYHA class at 1 year			
Variable (at 1 year)	Improvement of one grade or more ($N = 264$)	Lack of change/worsening ($N = 48$)	Difference	*p*-value
DVI	.51	.46	.05	.021
AV mean gradient	11.78	13.96	−2.18	.076
AV peak velocity	2.33	2.43	−.10	.27
Indexed EOA	.90	.82	.80	.025
AT/ET	.27	.29	−.02	.05
AV AT	84.15	86.82	−2.67	.39

Note: Values are reported as means between the two groups. The absolute difference between the two groups is reported (Difference). *p*-value reflects two-tailed *t*-test between groups. $p \leq .05$ is significant.
Abbreviations: AT/ET, ratio of acceleration time to ejection time; AV, aortic valve; DVI, dimensionless valve index; EOA, Effective orifice area; MV, mitral valve.

measurements (Figure S4A). For LVOT diameter, the ICC was .81 (.47–.93) and .91 (.78–.97), respectively (Table S3). R^2 revealed more modest agreement with a value of .55 and .75, respectively (Figure S4B). The inter- and intra-reader ICC for AT/ET was .85 (.64–.94) and .83 (.54–.93) (Table S3), respectively. R^2 was .54 and .54, respectively (Figure S4C).

4 | DISCUSSION

In this single center series, we identified PPM in 38% of patients, 26% with moderate and 12% with severe. These results are congruent with current literature,[4,6,15,16] which is less when compared to SAVR.[17–19] The occurrence of PPM remains frequent following TAVI despite improvements in valve sizing using cardiac CT.[20] Despite this, there is controversy over how PPM should be defined and its clinical significance. Ternacle et al. recently published using the predicted EOA based on reference values for transcatheter valves compared to the iEOA. They found that the incidence of moderate PPM declined from 27% to 10% and severe from 17% to 1% using predicted EOA.[21] They found better correlation between predicated EOA than iEOA with elevated aortic valve gradients; however, PPM was not associated with adverse clinical events.[21] A study by Watson et al. suggests that calculation of the TAVI iEOA by the continuity method may systematically underestimate valve area compared to that assessed by three-dimensional planimetry.[22] For this study, we were interested in the association of other echocardiographic parameters associated with PPM and lack of LV reverse remodeling.

4.1 | Ventricular remodeling post-TAVI

In addition to traditional metrics of LV remodeling including LV ejection fraction, mass, and volume, we utilized myocardial mechanics as a marker of reverse LV remodeling since abnormal GLS is a strong predictor of mortality in severe AS.[23,24] Also, improvement in GLS post-TAVI is tied to increased survival[25] and improved NYHA functional class.[26] LV GLS has been shown to better predict survival[27–29] and is more reproducible than LVEF.[30,31] Numerous studies have shown improvement in LV GLS post-TAVI,[32–35] but fewer studies have looked at the effect of PPM on LV GLS.[4,36] We found that there was an association with less improvement of LV GLS in those with PPM. These findings are congruent with prior studies. Poulin et al. showed that patients with

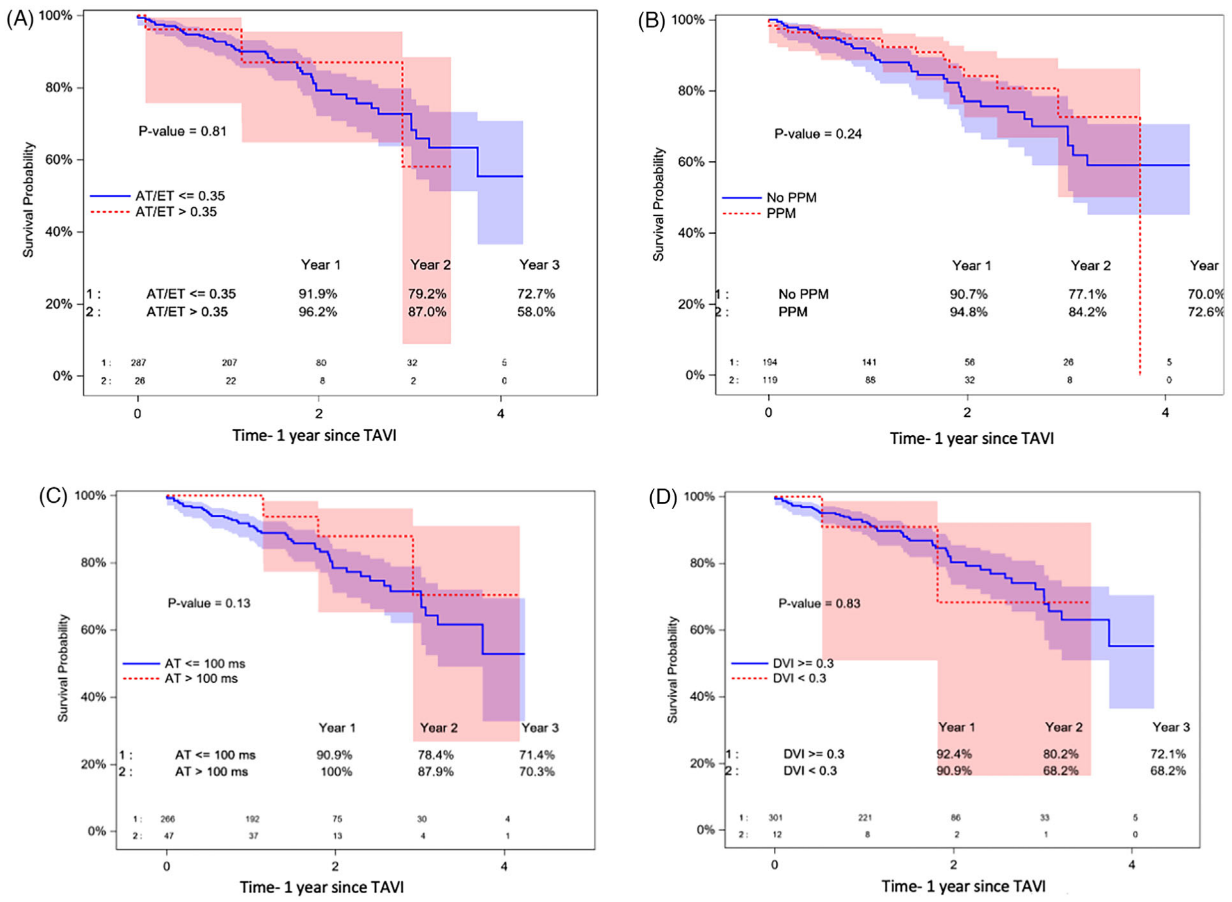

FIGURE 4 Kaplan–Meier survival estimates 1-year post-TAVI on the influence of echocardiographic evidence of PPM: (A) AT/ET > .35 versus AT/ET < .35, (B) No PPM versus PPM, (C) AT < 100 ms versus AT > 100 ms, (D) DVI < .3 versus DVI > .3.

moderate to severe PPM defined by an iEOA of <.85 cm^2/m^2 had lack of improvement in LV GLS compared to those without PPM.[4] Zhang et al. examined LV GLS in patients with PPM by subdividing them into those with significant regression in LVMI and those without regression. Those without regression in LVMI had a decline in LV GLS and had increased risk of cardiac death and major adverse valve-related events.[36]

In addition to the controversy about how to define PPM post-TAVI, there is also discordance in the literature over the clinical significance. Hermann et al. reported higher mortality and heart failure hospitalization at 1 year in those with severe PPM using an unadjusted iEOA of <.65 cm^2/m^2,[6] while Tang et al. found no association with clinical outcomes in patients undergoing supra-annular TAVI using an iEOA of <.65 cm^2/m^2 in those with a BMI < 30 kg/m^2 and <.55 cm^2/m^2 in those with a BMI > 30 kg/m^2.[37] A meta-analysis on clinical outcomes and PPM recently showed that severe PPM defined by an iEOA < .65 cm^2/m^2 was associated with an increased risk of mortality in the first 30 months post-TAVI but not beyond that.[38] We found that echocardiographic parameters associated with PPM including iEOA, AT/ET, and DVI were worse in those without improvement in NYHA functional class. There was no association in our cohort with PPM and mortality.

4.2 | Clinical context

The use of iEOA to define PPM may result in an excess number of patients classified as having PPM. This may be harmful, particularly, in the moderate PPM group as this could lead to unnecessary testing or interventions since moderate PPM has not been found to be associated with adverse clinical outcomes. Using lower thresholds for iEOA to define PPM in those with a BMI > 30 kg/m^2 may help reduce the over diagnosis of PPM. Using AT/ET and DVI in addition to iEOA may offer incremental value to identify subjects at risk for adverse outcomes. An elevated AT/ET ratio may identify a ventricle with worse performance that is less able to compensate for PPM. While aortic valve mean gradient and peak velocity are useful, they were not associated with lack of improvement in NYHA class, while AT/ET and DVI were. This may reflect physiologically that a heart with performance reserve is able to generate a higher gradient in response to PPM, to some degree, while those with greater AT/ET may have less performance reserve. Patients with an abnormal AT/ET (possibly > .35–.36, and >.37) may benefit from more intensive monitoring post-TAVI.

While, echocardiography is indispensable for the assessment of aortic stenosis pre-TAVI and for long-term monitoring of prosthetic valve function post-procedure, cardiac CT is the modality of choice for pre-procedural planning and device sizing. Severe calcification of the LVOT identified on CT are associated with increased risk of paravalvular leak, device failure, and short-term mortality post-TAVI.[39,40] The impact of LVOT calcification on the development of PPM has not been well studied. This is an important direction for future study.

5 | LIMITATIONS

We acknowledge that there are several limitations to our study, the first being the retrospective nature. Additionally, we excluded patients who had a pre- or post-procedure echos done at outside institutions and technically inadequate studies. Another limitation is the fact that we assessed PPM at 1 year post-TAVI. We disregarded the periprocedural echocardiograms performed after TAVI as they are fraught with poor acoustic windows, abnormal hemodynamics due to vasoactive agents, or acute hemodynamic changes post valve replacement. However, this may have introduced the possibility that abnormal flow-dynamics suggestive of PPM could be related to prosthesis degeneration. During our analysis, we were careful to exclude patients with evidence of structural valve degeneration. We acknowledge in Table 2 the relative differences are small with wide standard deviations. The wide standard deviation is reflective of the fact that many subjects had a change of near zero, thus resulting in wider confidence intervals. Another limitation is the sample size. This study was underpowered to look at clinical events. Finally, we were unable to report clinical events such as heart failure hospitalization after TAVI as many patients were referred from other regions.

6 | CONCLUSIONS

PPM is associated with lack of LV reverse remodeling seen by less improvement in LVEF and LV GLS. The definition of PPM is primarily based on iEOA but worse DVI and AT/ET were associated with lack of functional improvement but not survival. Further work should focus on the assessment of hemodynamic parameters associated with PPM.

ACKNOWLEDGMENT

No external funding was used for this study.

CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

Data are available by request.

ORCID

Andrew C. Peters MD https://orcid.org/0000-0001-9833-9069
Fei Fei Gong MD https://orcid.org/0000-0003-0730-2928

REFERENCES

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363(17):1597-1607.
2. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2016;374(17):1609-1620.
3. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med*. 2019;380(18):1695-1705.
4. Poulin F, Yingchoncharoen T, Wilson WM, et al. Impact of prosthesis-patient mismatch on left ventricular myocardial mechanics after transcatheter aortic valve replacement. *J Am Heart Assoc*. 2016;5(2):e002866. doi:10.1161/JAHA.115.002866
5. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J*. 2012;33(19):2403-2418.
6. Herrmann HC, Daneshvar SA, Fonarow GC, et al. Prosthesis-patient mismatch in patients undergoing transcatheter aortic valve replacement: from the STS/ACC TVT registry. *J Am Coll Cardiol*. 2018;72(22):2701-2711.
7. Lancellotti P, Pibarot P, Chambers J, et al. Recommendations for the imaging assessment of prosthetic heart valves: a report from the European Association of Cardiovascular Imaging endorsed by the Chinese Society of Echocardiography, the Inter-American Society of Echocardiography, and the Brazilian Department of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2016;17(6):589-590.
8. Zoghbi WA, Chambers JB, Dumesnil JG, et al. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2009;22(9):975-1014.
9. Gamaza-Chulian S, Diaz-Retamino E, Camacho-Freire S, Ruiz-Fernandez D, Gutierrez-Barrios A, Oneto-Otero J. Acceleration time and ratio of acceleration time to ejection time in aortic stenosis: new echocardiographic diagnostic parameters. *J Am Soc Echocardiogr*. 2017;30(10):947-955.
10. Ringle Griguer A, Tribouilloy C, Truffier A, et al. Clinical significance of ejection dynamics parameters in patients with aortic stenosis: an outcome study. *J Am Soc Echocardiogr*. 2018;31(5):551-560. e2.
11. Ben Zekry S, Saad RM, Ozkan M, et al. Flow acceleration time and ratio of acceleration time to ejection time for prosthetic aortic valve function. *JACC Cardiovasc Imaging*. 2011;4(11):1161-1170.
12. Benfari G, Nistri S, Cerrito LF, et al. Usefulness of the right parasternal echocardiographic view to improve the hemodynamic assessment after valve replacement for aortic stenosis. *Am J Cardiol*. 2021;142:103-108.
13. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). *Eur J Cardiothorac Surg*. 2012;42(5):S45-60.
14. Zoghbi WA, Asch FM, Bruce C, et al. Guidelines for the evaluation of valvular regurgitation after percutaneous valve repair or replacement: a report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Angiography and Interventions, Japanese Society of Echocardiography, and Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr*. 2019;32(4):431-475.

15. Schofer N, Deuschl F, Rübsamen N, et al. Prosthesis-patient mismatch after transcatheter aortic valve implantation: prevalence and prognostic impact with respect to baseline left ventricular function. *EuroIntervention*. 2019;14(16):1648-1655.
16. Okuno T, Khan F, Asami M, et al. Prosthesis-patient mismatch following transcatheter aortic valve replacement with supra-annular and intra-annular prostheses. *JACC: Cardiovascular Interventions*. 2019;12(21):2173.
17. Finkelstein A, Schwartz AL, Uretzky G, et al. Hemodynamic performance and outcome of percutaneous versus surgical stentless bioprostheses for aortic stenosis with anticipated patient-prosthesis mismatch. *J Thorac Cardiovasc Surg*. 2014;147(6):1892-1899.
18. Zorn GL 3rd, Little SH, Tadros P, et al. Prosthesis-patient mismatch in high-risk patients with severe aortic stenosis: a randomized trial of a self-expanding prosthesis. *J Thorac Cardiovasc Surg*. 2016;151(4):1014-1022. 23.e1-3.
19. Pibarot P, Weissman NJ, Stewart WJ, et al. Incidence and sequelae of prosthesis-patient mismatch in transcatheter versus surgical valve replacement in high-risk patients with severe aortic stenosis: a PARTNER trial cohort–a analysis. *J Am Coll Cardiol*. 2014;64(13):1323-1334.
20. Jilaihawi H, Kashif M, Fontana G, et al. Cross-sectional computed tomographic assessment improves accuracy of aortic annular sizing for transcatheter aortic valve replacement and reduces the incidence of paravalvular aortic regurgitation. *J Am Coll Cardiol*. 2012;59(14):1275-1286.
21. Ternacle J, Guimaraes L, Vincent F, et al. Reclassification of prosthesis–patient mismatch after transcatheter aortic valve replacement using predicted vs. measured indexed effective orifice area. *Eur Heart J Cardiovasc Imaging*. 2021;22(1):11-20.
22. Watson RA, Vishnevsky A, Dikdan S, et al. Orifice areas of balloon-expandable transcatheter heart valves: a three-dimensional transesophageal echocardiographic study. *J Am Soc Echocardiogr*. 2022;35(5):460-468.
23. Kearney LG, Lu K, Ord M, et al. Global longitudinal strain is a strong independent predictor of all-cause mortality in patients with aortic stenosis. *Eur Heart J Cardiovasc Imaging*. 2012;13(10):827-833.
24. Kusunose K, Goodman A, Parikh R, et al. Incremental prognostic value of left ventricular global longitudinal strain in patients with aortic stenosis and preserved ejection fraction. *Circ Cardiovasc Imaging*. 2014;7(6):938-945.
25. Logstrup BB, Andersen HR, Thuesen L, et al. Left ventricular global systolic longitudinal deformation and prognosis 1 year after femoral and apical transcatheter aortic valve implantation. *J Am Soc Echocardiogr*. 2013;26(3):246-254.
26. Kempny A, Diller GP, Kaleschke G, et al. Longitudinal left ventricular 2D strain is superior to ejection fraction in predicting myocardial recovery and symptomatic improvement after aortic valve implantation. *Int J Cardiol*. 2013;167(5):2239-2243.
27. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. *Heart*. 2014;100(21):1673-1680.
28. Stanton T, Leano R, Marwick TH. Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. *Circ Cardiovasc Imaging*. 2009;2(5):356-364.
29. Park JJ, Park JB, Park JH, Cho GY. Global longitudinal strain to predict mortality in patients with acute heart failure. *J Am Coll Cardiol*. 2018;71(18):1947-1957.
30. Negishi T, Negishi K, Thavendiranathan P, et al. Effect of experience and training on the concordance and precision of strain measurements. *JACC Cardiovasc Imaging*. 2017;10(5):518-522.
31. Karlsen S, Dahlslett T, Grenne B, et al. Global longitudinal strain is a more reproducible measure of left ventricular function than ejection fraction regardless of echocardiographic training. *Cardiovasc Ultrasound*. 2019;17(1):18.
32. D'Ascenzi F, Cameli M, Iadanza A, et al. Improvement of left ventricular longitudinal systolic function after transcatheter aortic valve implantation: a speckle-tracking prospective study. *Int J Cardiovasc Imaging*. 2013;29(5):1007-1015.
33. Shiino K, Yamada A, Scalia GM, et al. Early changes of myocardial function after transcatheter aortic valve implantation using multilayer strain speckle tracking echocardiography. *Am J Cardiol*. 2019;123(6):956-960.
34. Delgado M, Ruiz M, Mesa D, et al. Early improvement of the regional and global ventricle function estimated by two-dimensional speckle tracking echocardiography after percutaneous aortic valve implantation speckle tracking after corevalve implantation. *Echocardiography*. 2013;30(1):37-44.
35. Schattke S, Baldenhofer G, Prauka I, et al. Acute regional improvement of myocardial function after interventional transfemoral aortic valve replacement in aortic stenosis: a speckle tracking echocardiography study. *Cardiovasc Ultrasound*. 2012;10(1):15.
36. Zhang HW, Gu J, Xiao ZH, et al. Global longitudinal strain in prosthesis-patient mismatch: relation to left ventricular mass regression and outcomes. *J Cardiovasc Med (Hagerstown)*. 2019;20(7):434-441.
37. Tang GHL, Sengupta A, Alexis SL, et al. Outcomes of prosthesis-patient mismatch following supra-annular transcatheter aortic valve replacement: from the STS/ACC TVT registry. *JACC Cardiovasc Interv*. 2021;14(9):964-976.
38. Sá MP, Jacquemyn X, Van den Eynde J, et al. Impact of prosthesis-patient mismatch after transcatheter aortic valve replacement: meta-analysis of Kaplan-Meier-derived individual patient data. *JACC: Cardiovasc Imag*. 2023;16(3):298-310.
39. Jochheim D, Deseive S, Gschwendtner S, et al. Impact of severe left ventricular outflow tract calcification on device failure and short-term mortality in patients undergoing TAVI. *J Cardiovasc Comput Tomogr*. 2020;14(1):36-41.
40. Kofler M, Meyer A, Schwartz J, et al. A new calcium score to predict paravalvular leak in transcatheter aortic valve implantation. *Eur J Cardiothoracic Surg*. 2021;59(4):894-900.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Peters AC, Gong FF, Ramesh A, et al. Echocardiographic parameters associated with less reverse left ventricular remodeling after transcatheter aortic valve implant in subjects with prosthesis patient mismatch. *Echocardiography*. 2024;41:e15698. https://doi.org/10.1111/echo.15698