Prosthesis–patient mismatch in high-risk patients with severe aortic stenosis: A randomized trial of a self-expanding prosthesis

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ABSTRACT

Objectives: We compared the incidence of prosthesis–patient mismatch (PPM) between transcatheter aortic valve replacement (TAVR) using a self-expanding bioprosthesis and surgical aortic valve replacement (SAVR) in the CoreValve US High Risk Pivotal Trial. We sought to determine the influence of PPM on clinical outcomes.

Methods: Patients with severe aortic stenosis and at increased risk for surgery were randomized 1:1 to TAVR or SAVR. Postoperative PPM was defined by the effective orifice area index (EOAi) as severe PPM ($\text{EOAi} \leq 0.65 \text{ cm}^2/\text{m}^2$) and no severe PPM ($\text{EOAi} > 0.65 \text{ cm}^2/\text{m}^2$); clinical outcomes were analyzed in the TAVR arm ($n = 389$) and SAVR arm ($n = 353$). Left ventricular mass index and regression were analyzed at baseline and 1 year.

Results: The incidence of severe PPM in the SAVR group at 1 year was 25.7% versus 6.2% in the TAVR group ($P < .0001$). Left ventricular mass index regression at 1 year was 6.8% for TAVR and 15.1% for SAVR in patients with severe PPM. At 1 year the rate of all-cause mortality and acute kidney injury were significantly greater in all patients (TAVR + SAVR) with severe PPM compared with no severe PPM (20.6% vs 12.0% [$P = .0145$] for death and 19.2% vs 8.5% [$P = .0008$] for acute kidney injury).

Conclusions: In patients with high surgical risk and severe aortic stenosis, severe PPM is more common in patients treated with SAVR than those treated with TAVR. Patients with severe PPM are a greater risk for death and acute kidney injury than patients without severe PPM. (J Thorac Cardiovasc Surg 2016;151:1014-23)

Cumulative incidence of all-cause mortality at 1 year for patients undergoing surgical aortic valve replacement plus transcatheter aortic valve replacement with and without severe prosthesis–patient mismatch (PPM).

Central Message

Patients with severe PPM are at greater risk for death and acute kidney injury than patients without severe PPM.

Perspective

Severe prosthesis–patient mismatch (PPM) is significantly more common after surgical aortic valve replacement than after transcatheter aortic valve replacement in patients at high risk with symptomatic severe aortic stenosis. Patients with severe PPM are at a greater risk for death and acute kidney injury than patients without severe PPM.

See Editorial Commentary page 1024.

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The clinical effects of prosthesis–patient mismatch (PPM) after surgical aortic valve replacement (SAVR) has been debated for the past 3 decades.^{1,2} When a normally functioning prosthetic valve is too small to meet the flow requirements of a specific patient, then a condition of mismatch has occurred. A commonly accepted indicator

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Abbreviations and Acronyms

EOAi	= effective orifice area index
LV	= left ventricular
LVEDD	= left ventricular end-diastolic dimension
LVM	= left ventricular mass
LVMI	= left ventricular mass index
NYHA	= New York Heart Association
PARTNER	= Placement of Aortic Transcatheter Valve Trial
PPM	= prosthesis–patient mismatch
SAVR	= surgical aortic valve replacement
TAVR	= transcatheter aortic valve replacement
VARC	= Valve Academic Research Consortium-1

of PPM severity is the effective orifice area calculated by the continuity equation using echocardiography. When divided by the patient's body surface area, an effective orifice area index (EOAi) provides a threshold to define whether severe PPM is present ($\text{EOAi} \leq 0.65 \text{ cm}^2/\text{m}^2$) or absent ($\text{EOAi} > 0.65 \text{ cm}^2/\text{m}^2$). Severe PPM has been associated with higher early³⁻⁶ and late mortality^{5,7-11} after surgical valve replacement; the association of moderate PPM and late clinical outcomes has been less clear.² The effect of PPM on late mortality may be influenced by the presence of obesity, older age, left ventricular (LV) dysfunction, New York Heart Association (NYHA) functional class III or IV symptoms, and concomitant coronary artery bypass grafting.¹²⁻¹⁴

Transcatheter aortic valve replacement (TAVR) has provided another option for reducing PPM in patients undergoing aortic valve replacement due to the lower profile of the transcatheter valve without a sewing ring.¹⁵ The influence of PPM on late outcomes was examined in 699 patients at high risk for surgery who were randomized to surgery or TAVR in the Placement of Aortic Transcatheter Valve Trial (PARTNER) A trial.¹⁴ The frequencies of moderate and severe PPM were lower after TAVR than after SAVR in the PARTNER A trial, and these differences were accentuated in those patients with echocardiographic-determined annular diameters $< 20 \text{ mm}$.¹⁴ This study also identified an important relationship between PPM after surgery and 2-year mortality and left ventricular mass regression.¹⁴

The design of the CoreValve transcatheter bioprosthesis (Medtronic, Minneapolis, Minn) includes a supraannular porcine pericardial aortic valve that provides durable hemodynamic parameters after implantation.^{16,17} The objectives of this study were to compare the incidence and prognosis of PPM between TAVR

using a self-expanding prosthesis and SAVR in the CoreValve US High Risk Pivotal Trial ([ClinicalTrials.gov](https://clinicaltrials.gov/registration/identifier/NCT01240902) registration identifier: NCT01240902).

METHODS**Patient Flow and Demographics**

We performed a prospective, randomized multicenter investigation at 45 US clinical sites that enrolled 790 patients who were randomly assigned to treatment with self-expanding TAVR or SAVR.¹⁶ Inclusion and exclusion criteria have been reported in detail elsewhere; patients at increased surgical risk were considered to have a $>15\%$ surgical mortality rate at 30 days by 2 clinical site cardiac surgeons.¹⁶ Severe aortic stenosis was defined as an aortic valve area $\leq 0.8 \text{ cm}^2$ or aortic valve index $\leq 0.5 \text{ cm}^2/\text{m}^2$ and either a mean aortic valve gradient $>40 \text{ mm Hg}$ or a peak aortic valve velocity $>4.0 \text{ meters per second}$, at rest or with dobutamine.¹⁶ Anatomic exclusion criteria included an aortic annular diameter $<18 \text{ mm}$ or $>29 \text{ mm}$.

Patient randomization was stratified by femoral or alternative (subclavian or direct aortic) access for device placement. All patients who were implanted with a CoreValve transcatheter bioprosthesis are included in this analysis. Clinical outcomes and echocardiographic results were collected for >1 year. All clinical events were adjudicated by an independent clinical events committee using standardized Valvular Academic Research Consortium-1 (VARC-1) criteria.¹⁸

Clinical and Echocardiographic Outcomes

Criteria for major adverse cardiovascular and cerebrovascular events comprising all-cause death; myocardial infarction; all stroke; and reintervention to alter, adjust, or replace a previously implanted valve were adjudicated by an independent clinical events committee using VARC-1 criteria.¹⁸ Symptom status was assessed using the NYHA functional classification system.

Echocardiograms were evaluated by an independent echocardiographic core lab (Mayo Clinic, Rochester, Minn). Echocardiography measurement methods by the echocardiography core lab have been published.¹⁹ Specifically, LV stroke volume was calculated by both Doppler (LV outflow track area $\times$ velocity time integral) and 2-dimensional volumetric methods whenever feasible. LV outflow track area was calculated from its diameter at baseline and outer to outer measurement of the bioprosthesis after its implantation. Valvular regurgitation was determined using VARC-1 criteria.¹⁸

LV mass (LVM) is determined by the formula $\text{LVM} = 0.83 \times [(\text{LVEDD} + \text{LVPW} + \text{IVS})^3 - (\text{LVEDD})^3] + 0.6$, where LVEDD = LV end-diastolic dimension, LVPW = LV posterior wall thickness, and IVS = interventricular septal thickness.

Definition of PPM

PPM was defined as moderate when the EOAI was $\leq 0.85 \text{ cm}^2/\text{m}^2$ but $> 0.65 \text{ cm}^2/\text{m}^2$ and severe when the EOAI was $\leq 0.65 \text{ cm}^2/\text{m}^2$. All patients were assessed for either the presence or absence of severe PPM. The first available EOAI at discharge or after was used to define PPM for this analysis.

Statistical Analysis

Categorical variables were compared with the use of the χ^2 or Fisher exact test. Continuous variables were presented as mean $\pm$ standard deviation and compared with the use of the Student *t* test for independent samples and a paired *t* test for matched samples. Kaplan-Meier estimates were used to construct the survival curves based on all available follow-up for the time-to-event analysis. The log-rank test was used to compare the time to events. All testing used a 2-sided alpha level of 0.05. For selected safety outcomes, the Cox proportional hazard model was used

TABLE 1. Prosthesis–patient mismatch*

EOAi† (cm ² /m ²)	TAVR (n = 389)	SAVR (n = 353)	P value
1 mo	n = 344	n = 280	
Severe PPM	24 (7.0)	58 (20.7)	<.0001
Not severe PPM	320 (93.0)	222 (79.3)	
Moderate PPM	66 (19.2)	88 (31.4)	
None to mild PPM	254 (73.8)	134 (47.9)	
12 mo	n = 274	n = 206	
Severe PPM	17 (6.2)	53 (25.7)	<.0001
Not severe PPM	257 (93.8)	153 (74.3)	
Moderate PPM	57 (20.8)	63 (30.6)	
None to mild	200 (73.0)	90 (43.7)	

Values are presented as n (%). EOAi, Effective orifice area index; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch. *Prosthesis–patient mismatch was defined by the first available EOAi at discharge or 1 month. †Severe PPM defined as EOAi ≤ 0.65, not severe PPM defined as EOAi > 0.65, moderate PPM defined as 0.65 < EOAi ≤ 0.85, and none to mild PPM defined as PPM EOAi > 0.85.

to compare the difference between severe PPM and no severe PPM in the combined cohort, where treatment (SAVR and TAVR) was included as a covariate. All statistical analyses were performed with the use of SAS software, version 9.2 (SAS Institute, Cary, NC).

RESULTS

Frequency of PPM and Patient Characteristics

The incidence of severe PPM in the SAVR group at 1 month was 20.7% versus 7.0% in the TAVR group and at 1 year was 25.7% versus 6.2% ($P < .0001$ for both time points) (Table 1). At 1 year, moderate PPM was present in 20.8% of TAVR and 30.6% of SAVR patients, and no/mild PPM was present in 73.0% of TAVR patients and 43.7% of SAVR patients.

Patients with severe PPM at 1 month had a significantly higher body mass index in both the TAVR and SAVR groups. The TAVR patients with severe PPM had more severe chronic lung disease and home oxygen use than those without severe PPM (Table E1).

Echocardiographic Findings

Baseline echocardiographic findings are found in Table E2. The EOAi was significantly lower in the severe PPM compared with the no severe PPM patients from both the TAVR (0.32 ± 0.07 vs 0.40 ± 0.12 cm²/m²; $P = .0005$) and the SAVR (0.36 ± 0.14 vs 0.41 ± 0.12 cm²/m²; $P = .0109$) groups. The aortic annulus diameter was significantly less in the severe PPM patients treated by TAVR (2.07 ± 0.16 vs 2.23 ± 0.21 cm; $P = .0006$) but was only marginally less in the SAVR group with severe PPM (2.14 ± 0.22 vs 2.19 ± 0.21 ; $P = .0676$).

At baseline, LVM was significantly greater in the patients with severe PPM than in the patients with no severe PPM treated with SAVR (243.18 vs 224.68 g; $P = .0434$). This difference was not observed in the TAVR patients (severe PPM 226.45 vs no severe PPM 225.95 g; $P = .9781$).

The deceleration time of the early diastolic mitral valve Doppler inflow (ie, the E wave) was significantly shorter in SAVR patients with PPM than in those with no severe PPM (204.86 vs 236.27 ms; $P = .0020$) but was not different in TAVR patients with or without severe PPM (231.40 vs 226.60 ms; $P = .7812$).

Changes in echocardiographic parameters during the 12 months after valve replacement for paired patients are found in Table 2. Both TAVR and SAVR were successful in significantly reducing mean gradient and peak velocity; however, patients with severe PPM in both groups had significantly higher mean gradients (11.18 vs 8.92 mm Hg [$P = .0060$] for TAVR and 16.41 vs 11.32 mm Hg [$P < .0001$] for SAVR) and peak velocities (2.25 vs 2.01 m/s [$P = .0082$] for TAVR and 2.68 vs 2.22 m/s [$P < .0001$] for SAVR) compared with the nonsevere PPM patients at 1 year.

LVEDD as measured at 1 year showed a significant difference in the SAVR group between severe PPM and no severe PPM patients (4.97 vs 4.75 cm; $P = .0320$). This difference was not observed in the TAVR group (4.89 vs 4.98 cm; $P = .6516$). All SAVR patients had a significant change from baseline in LVEDD at 1 year (-0.28 cm; $P = .0091$ in severe PPM and -0.27 cm; $P < .0001$ in no severe PPM SAVR patients) that was not observed in the TAVR patients.

The EOAi was significantly greater at 12 months for all TAVR and SAVR patients, but the improvement was significantly greater in the no PPM group compared with the severe PPM group for TAVR (0.67 ± 0.29 vs 0.44 ± 0.24 ; $P = .0064$) and for SAVR (0.47 ± 0.26 vs 0.31 ± 0.29 ; $P = .0006$).

At 1 year LVM index was significantly reduced in severe PPM patients in the SAVR (-22.67 ± 38.47 g; $P = .0019$) but not the TAVR group (-11.88 ± 34.26 g; $P = .3288$). Both the TAVR and the SAVR no severe PPM patients had significant reductions in LV mass index ($P < .0001$ for both) at 1 year. In the patients with severe PPM, LVM index regression at 1 year was 6.8% for TAVR and 15.1% for SAVR (Table 2 and Figure 1).

Total aortic regurgitation at 1 month and 1 year is shown in Table E3. Moderate or greater aortic regurgitation was not found in any severe PPM patients at 1 year and was not significantly different between the severe PPM and no severe PPM groups for TAVR or SAVR (Table 2). The presence or absence of aortic regurgitation did not appear to influence the magnitude of LVM regression experienced by patients with severe PPM after SAVR or TAVR (Table E4).

Clinical Outcomes

Clinical outcomes at 1 year for the SAVR, TAVR, and combined SAVR + TAVR groups in patients with and without severe PPM are found in Table 3. In the combined group the patients with severe PPM had a higher rate of

TABLE 2. Change in echocardiographic findings from baseline to 12 month follow-up on paired patients

Characteristic	TAVR			SAVR		
	Severe PPM (n = 24)	No severe PPM (n = 343)	P value	Severe PPM (n = 75)	No severe PPM (n = 259)	P value
Aortic valve peak velocity (m/s)	n = 19	n = 270		n = 47	n = 174	
Baseline	4.64 (0.63)	4.38 (0.56)	.0532	4.47 (0.55)	4.34 (0.58)	.1787
1 y	2.25 (0.38)	2.01 (0.38)	.0082	2.68 (0.60)	2.22 (0.55)	<.0001
Change	−2.39 (0.49)	−2.37 (0.64)	.8696	−1.79 (0.76)	−2.12 (0.73)	.0060
P value for change from baseline to 1 y	<.0001	<.0001		<.0001	<.0001	
Mean gradient (mm Hg)	n = 19	n = 270		n = 47	n = 174	
Baseline	52.63 (15.84)	47.74 (13.50)	.1332	50.13 (16.41)	47.19 (13.69)	.2119
1 y	11.18 (3.92)	8.92 (3.41)	.0060	16.41 (7.74)	11.32 (6.93)	<.0001
Change	−41.45 (14.12)	−38.83 (13.62)	.4193	−33.72 (18.10)	−35.87 (14.68)	.3994
P value for change from baseline to 1 y	<.0001	<.0001		<.0001	<.0001	
Aortic valve EOA or valve area (cm ²)	n = 13	n = 240		n = 30	n = 142	
Baseline	0.61 (0.14)	0.72 (0.22)	.0757	0.75 (0.33)	0.76 (0.21)	.8439
1 y	1.45 (0.47)	1.94 (0.50)	.0007	1.36 (0.54)	1.63 (0.46)	.0020
Change	0.84 (0.45)	1.22 (0.53)	.0126	0.61 (0.59)	0.87 (0.46)	.0136
P value for change from baseline to 1 y	<.0001	<.0001		<.0001	<.0001	
EOAi (cm ² /m ²)	n = 13	n = 240		n = 40	n = 142	
Baseline	0.32 (0.08)	0.39 (0.11)	.0242	0.38 (0.16)	0.42 (0.12)	.1684
1 y	0.76 (0.26)	1.06 (0.28)	.0002	0.69 (0.25)	0.89 (0.27)	<.0001
Change	0.44 (0.24)	0.67 (0.29)	.0064	0.31 (0.29)	0.47 (0.26)	.0006
P value for change from baseline to 1 y	<.0001	<.0001		<.0001	<.0001	
LVEDD (cm)	n = 12	n = 226		n = 37	n = 137	
Baseline	5.03 (0.50)	4.98 (0.57)	.7697	5.25 (0.60)	5.02 (0.52)	.0260
1 y	4.89 (0.74)	4.98 (0.65)	.6516	4.97 (0.63)	4.75 (0.53)	.0320
Change	−0.13 (0.82)	0.00 (0.56)	.5806	−0.28 (0.61)	−0.27 (0.64)	.9695
P value for change from baseline to 1 y	.5863	.9248		.0091	<.0001	
LVESD (cm)	n = 7	n = 184		n = 29	n = 109	
Baseline	3.26 (0.54)	3.15 (0.76)	.7216	3.57 (0.78)	3.34 (0.67)	.1049
1 y	3.03 (0.62)	3.21 (0.80)	.5440	3.28 (0.70)	2.99 (0.56)	.0212
Change	−0.23 (0.72)	0.06 (0.71)	.2934	−0.29 (0.65)	−0.34 (0.68)	.7224
P value for change from baseline to 1 y	.4306	.2519		.0212	<.0001	
LVM (g)	n = 9	n = 210		n = 33	n = 133	
Baseline	230.12 (41.88)	226.59 (65.45)	.8730	260.33 (59.36)	230.93 (57.56)	.0099
1 y	209.35 (62.98)	207.64 (62.82)	.9366	216.50 (74.23)	188.76 (52.35)	.0495
Change	−20.77 (66.20)	−18.95 (57.86)	.9268	−43.83 (76.01)	−42.17 (59.90)	.8928
P value for change from baseline to 1 y	.3742	<.0001		.0023	<.0001	
LVM index (g/m ²)	n = 9	n = 210		n = 33	n = 133	
Baseline	117.68 (20.90)	122.89 (32.78)	.6370	134.47 (32.35)	126.00 (30.97)	.1652
1 y	105.80 (25.82)	111.95 (29.86)	.5440	111.80 (38.58)	102.18 (24.53)	.1801
Change	−11.88 (34.26)	−10.94 (31.13)	.9302	−22.67 (38.47)	−23.82 (32.79)	.8622
P value for change from baseline to 1 y	.3288	<.0001		.0019	<.0001	
LVM index regression at 1 y (%)	6.76 (31.98)	5.41 (27.25)	.8849	15.08 (32.01)	15.72 (23.27)	.9150
Ejection fraction (%)	n = 19	n = 276		n = 47	n = 175	
Baseline	56.84 (11.08)	58.72 (11.23)	.4815	54.57 (14.02)	57.71 (11.80)	.1216
1 y	61.05 (8.09)	59.37 (9.90)	.4687	58.51 (8.90)	59.92 (8.48)	.3178
Change	4.21 (10.04)	0.65 (9.92)	.1313	3.94 (11.56)	2.21 (10.04)	.3113
P value for change from baseline to 1 y	.0841	.2782		.0240	.0041	
Doppler stroke volume (mL)	n = 13	n = 244		n = 40	n = 142	
Baseline	69.71 (20.47)	76.69 (21.49)	.2538	73.51 (16.65)	79.98 (21.62)	.0820
1 y	68.03 (23.27)	80.15 (22.38)	.0588	76.76 (25.15)	74.98 (20.03)	.6404
Change	−1.68 (23.34)	3.46 (26.13)	.4884	3.25 (26.50)	−4.99 (22.60)	.0516
P value for change from baseline to 1 y	.7997	.0399		.4426	.0094	
≥Moderate total AR (%)	n = 19	n = 273		n = 46	n = 171	
Baseline	1 (5.3)	15 (5.5)	>.9999	2 (4.3)	12 (7.0)	.7391

(Continued)

TABLE 2. Continued

Characteristic	TAVR			SAVR		
	Severe PPM (n = 24)	No severe PPM (n = 343)	P value	Severe PPM (n = 75)	No severe PPM (n = 259)	P value
1 y	0 (0.0)	20 (7.3)	.2216	0 (0.0)	3 (1.8)	>.9999
Change no to yes	0 (0.0)	15 (5.5)	.2942	0 (0.0)	3 (1.8)	>.9999
Change yes to no	1 (5.3)	10 (3.7)	.5293	2 (4.3)	12 (7.0)	.7391
E/e' ratio	n = 11	n = 158		n = 29	n = 106	
Baseline	27.50 (13.35)	24.79 (12.77)	.4978	25.34 (12.26)	23.14 (10.13)	.3258
1 y	25.03 (15.82)	26.09 (12.75)	.7945	23.83 (9.56)	22.03 (9.95)	.3839
Change	−2.46 (12.75)	1.30 (11.35)	.2927	−1.50 (11.24)	−1.12 (10.09)	.8585
P value for change from baseline to 1 y	.5362	.1511		.4773	.2573	
Mitral E/A ratio	14	195		27	107	
Baseline	1.06 (0.44)	1.13 (0.74)	.6357	1.34 (0.96)	1.01 (0.55)	.1041
1 y	0.87 (0.33)	1.03 (0.61)	.1008	1.10 (0.45)	0.91 (0.33)	.0557
Change	−0.20 (0.24)	−0.09 (0.85)	.2454	−0.24 (0.86)	−0.10 (0.48)	.4241
P value for change from baseline to 1 y	.0090	.1269		.1623	.0344	
Deceleration time of E (ms)	13	190		36	125	
Baseline	236.08 (79.21)	233.91 (74.57)	.9197	197.92 (59.40)	234.22 (81.80)	.0042
1 y	249.46 (91.02)	255.05 (83.96)	.8177	214.61 (76.88)	240.70 (76.29)	.0730
Change	13.38 (73.60)	21.14 (83.50)	.7448	16.69 (68.91)	6.48 (73.23)	.4561
P value for change from baseline to 1 y	.5244	.0006		.1550	.3246	
Septal thickness (mm)	n = 10	n = 222		n = 33	n = 137	
Baseline	12.00 (1.70)	11.91 (2.20)	.9035	12.79 (2.01)	12.28 (1.89)	.1707
1 y	11.60 (2.01)	11.32 (2.14)	.6846	12.09 (2.35)	11.39 (2.29)	.1164
Change	−0.40 (1.90)	−0.59 (2.47)	.8065	−0.70 (2.02)	−0.89 (2.40)	.6690
P value for change from baseline to 1 y	.5217	.0004		.0565	<.0001	
Posterior wall thickness (mm)	n = 10	n = 217		n = 37	n = 136	
Baseline	11.50 (1.35)	11.18 (1.91)	.6015	11.51 (1.77)	11.27 (1.94)	.4833
1 y	10.40 (1.65)	10.47 (1.90)	.9027	10.57 (2.38)	10.23 (1.73)	.4203
Change	−1.10 (1.73)	−0.71 (2.21)	.5782	−0.95 (2.58)	−1.04 (2.22)	.8305
P value for change from baseline to 1 y	.0751	<.0001		.0321	<.0001	
Relative wall thickness	n = 10	n = 216		n = 37	n = 135	
Baseline	0.46 (0.07)	0.45 (0.10)	.7599	0.45 (0.09)	0.46 (0.09)	.6311
1 y	0.43 (0.09)	0.43 (0.10)	.9835	0.43 (0.12)	0.44 (0.09)	.8801
Change	−0.03 (0.11)	−0.03 (0.12)	.8171	−0.01 (0.12)	−0.02 (0.12)	.8168
P value for change from baseline to 1 y	.3533	.0018		.5505	.0887	

Categorical variables are presented as n (%); continuous variables are mean (SD). TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch; EOA, effective orifice area; EOA_i, effective orifice area index; LVEDD, left ventricular end diastolic dimension; LVESD, left diastolic end systolic dimension; LVM, left ventricular mass; AR, aortic regurgitation; E/e', early mitral inflow velocity/mitral annulus early diastolic velocity; E/A, early mitral inflow velocity/late mitral inflow velocity.

FIGURE 1. Percent left ventricular mass regression at 1 year. TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch.

all-cause mortality (20.6% vs 12.0%; $P = .0145$) (Figure 2). When adjusted for treatment differences between TAVR and SAVR overall, the P value was .0666 for the difference in all-cause mortality between severe and no severe PPM.

Acute kidney injury was more commonly seen with severe PPM in the SAVR patients (21.3% vs 12.4%; $P = .0476$). In the TAVR group, severe PPM was increasingly involved with acute kidney injury, but this did not achieve statistical significance (12.5% vs 5.5%; $P = .1633$).

NYHA functional class III or IV improved similarly regardless of PPM status in the TAVR and the SAVR groups (Table 4). The severe PPM TAVR group was 91.7% at baseline and improved to 5.3% at 1 year, whereas the severe PPM SAVR patients were 81.1% at baseline and 10.4% NYHA functional class III or IV at 1 year.

TABLE 3. Cumulative incidence of clinical outcomes to 1 year

Characteristic	Overall			TAVR			SAVR		
	Severe PPM* (n = 99)	No severe PPM* (n = 602)	P value	Severe PPM* (n = 24)	No severe PPM* (n = 343)	P value	Severe PPM* (n = 75)	No severe PPM* (n = 259)	P value
All-cause mortality	20.6	12.0	.0145†	16.9	10.0	.2436	21.8	14.5	.1358
Cardiovascular mortality	11.7	8.2	.2326	9.1	7.4	.7696	12.5	9.2	.3882
All stroke	8.4	10.1	.6756	0.0	8.3	.1623	11.1	12.6	.8184
Myocardial infarction	0.0	1.7	.2068	0.0	1.8	.5237	0.0	1.6	.2849
Reintervention	0.0	0.9	.3863	0.0	1.5	.5706	0.0	0.0	NA
Life-threatening or disabling bleeding	33.6	24.3	.0521	26.5	13.5	.1128	35.8	38.5	.6817
Major vascular complication	3.0	4.2	.6004	4.2	6.1	.6993	2.7	1.5	.5184
Valve thrombosis	0.0	0.0	NA	0.0	0.0	NA	0.0	0.0	NA
Aortic valve hospitalization	17.8	14.0	.3515	22.0	15.6	.4169	16.3	11.7	.3141
Acute kidney injury	19.2	8.5	.0008†	12.5	5.5	.1633	21.3	12.4	.0476

Values are presented as %. TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch; NA, not applicable. *PPM was defined as severe PPM when the external orifice area index was $\leq 0.65 \text{ cm}^2/\text{m}^2$; no severe PPM was defined as external orifice area index $> 0.65 \text{ cm}^2/\text{m}^2$. †Adjusted $P = .0860$ for all-cause mortality or major stroke; adjusted $P = .0666$ for all-cause mortality; and adjusted $P = .0230$ for acute kidney injury.

DISCUSSION

There are 3 principal findings from this study. First, PPM is more common with SAVR than TAVR in this randomized trial of a self-expanding prosthesis in the treatment of aortic stenosis in high-risk patients. Second, LVM regression is

less robust in the treatment group receiving TAVR compared with SAVR. Third, we observed that patients with severe PPM have a higher rate of all-cause mortality and acute kidney injury compared with patients without severe PPM.

FIGURE 2. Cumulative incidence of all-cause mortality at 1 year for A, surgical aortic valve replacement, B, transcatheter aortic valve replacement, and C, patients undergoing combined transcatheter aortic valve replacement plus surgical aortic valve replacement. PPM, Prosthesis–patient mismatch.

TABLE 4. New York Heart Association functional classification III or IV over time

Time	TAVR			SAVR		
	Severe PPM (n = 24)	No severe PPM (n = 343)	<i>P</i> value	Severe PPM (n = 75)	No severe PPM (n = 259)	<i>P</i> value
Baseline	91.7 (22/24)	82.5 (283/343)	.2470	81.1 (60/74)	81.8 (207/253)	.8854
1 mo	21.7 (5/23)	12.7 (42/331)	.2161	27.7 (18/65)	21.7 (52/240)	.3055
6 mo	10.5 (2/19)	6.6 (20/305)	.5046	6.9 (4/58)	5.5 (11/200)	.6890
1 y	5.3 (1/19)	5.3 (15/282)	.9916	10.4 (5/48)	5.5 (10/183)	.2152

Values are presented as % (n/N). TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch.

Comparative Incidence of PPM

TAVR has provided another option for reducing PPM in patients undergoing aortic valve replacement due to the lower profile of the transcatheter valve without a sewing ring.¹⁵ A matched analysis of patients with aortic stenosis compared 50 patients treated using a balloon-expandable transcatheter valve with two groups of 50 patients who underwent surgery with a stented valve (Perimount Magna; Edwards Lifesciences, Irvine, Calif) or a stentless valve (Freestyle; Medtronic).¹⁵ The incidence of severe PPM was significantly lower in the TAVR group (6%) than in the stented (28%) or stentless (20%) surgical groups, albeit with a higher rate of moderate paravalvular regurgitation with TAVR (8%) than surgery (0%).¹⁵ Pibarot and colleagues¹⁴ evaluated the influence of PPM on late outcomes in 699 patients at “high-risk” for surgery who were randomized to surgery or TAVR in the PARTNER A trial.¹⁴ Patients in the TAVR group were exclusively treated with the balloon-expandable Sapien (Edwards Lifesciences) bioprosthesis. Similar to ours and other studies, the frequency of severe PPM was lower after TAVR (19.7%) than after SAVR (28.1%), although the severe PPM rates were higher than our experience in the current randomized CoreValve trial.¹

LVM Regression

At baseline both treatment groups were similar with no significant difference in LVEDD, LVESD, LV end diastolic volume, or LV end systolic volume. Patients with severe PPM after SAVR had larger baseline LVM compared with those patients without severe PPM after SAVR and compared with TAVR-treated patients with or without severe PPM.

Comparing patients with severe PPM with those without severe PPM in the TAVR treatment arm, there was no significant difference in LVM index at baseline, LVM index at 1 year, or in the magnitude of LVM index regression at 1 year. Within the SAVR treatment group, the comparison of patients with severe PPM to those without severe PPM demonstrated a similar lack of difference in LVM index at baseline, LVM index at 1 year, or in the magnitude of LVM index regression at 1 year.

Although severe PPM or no severe PPM did not appear to influence LVM index within each treatment group, there

were notable differences in LVM index regression between the TAVR and SAVR treatment arms, irrespective of the finding of severe PPM. Within the TAVR group the LVM index regression was 6.8% with severe PPM and 5.4% without severe PPM. Within the SAVR group the LVM index regression was 15.1% with severe PPM and 15.7% without severe PPM. We hypothesized that the higher incidence of aortic valve regurgitation in the TAVR treatment group may have adversely influenced LVM index regression at 1 year. However, within both the TAVR and SAVR treatment groups the finding of moderate or greater aortic valve regurgitation was not associated with reduced LVM index regression. It is important to note the importance of LVEDD and wall thickness measures in the calculation of LVM. The change in wall thickness was not different between SAVR and TAVR groups, and only LVEDD was relatively smaller after SAVR. Because LVEDD can be profoundly affected by LV preload, which could be reduced on the basis of acute right ventricular dysfunction after SAVR, it is possible that the calculated LVM may not be the most representative measure of myocardial remodeling. This question is the subject of ongoing studies that use cardiac magnetic resonance imaging to provide a more robust measure of LVM before and after aortic stenosis intervention. Although the apparent influence of severe PPM on LV remodeling at 1 year was unremarkable within each treatment group, the echocardiographic diagnosis of severe PPM was nonetheless associated with an increased risk of mortality at 1-year follow-up.

Severe PPM Outcomes

PPM has been associated with higher early³⁻⁶ and late mortality^{5,7-11} after aortic valve surgery. In a meta-analysis comprising 34 studies that included 27,186 patients and 133,141 patient-years, both moderate and severe PPM increased all-cause mortality (hazard ratio, 1.19 and 1.84, respectively) and cardiac-related mortality (hazard ratio, 1.32 and 6.46, respectively); these relationships were consistent over long-term follow-up out to 12 years.²⁰

Our TAVR patients with severe PPM did not demonstrate a significant difference in all-cause mortality at 1 year (16.9% vs 10.0%; *P* = .2436). Similarly, mortality in SAVR patients with and without severe PPM trended but did not achieve statistical significance (21.8% vs 14.5%;

$P = .1358$). Grouping our TAVR and SAVR patients together demonstrated a significant mortality increase in severe PPM compared with no severe PPM ($P = .0145$). We believe these results are consistent with previous studies concluding that severe PPM matters. It is just a matter of having adequate patient numbers.

Study Limitations

This study included data from a large, multi-institutional, randomized trial comparing TAVR with contemporary open surgical results. Our study is a post hoc analysis of 12-month data and thus is not powered for these subgroup analyses. The comparison between severe PPM and no severe PPM groups was not adjusted for differences in other patient variables. Although the demographic characteristics of the severe PPM and no severe PPM patients were essentially the same between the groups, there were a couple of differences in baseline echocardiographic parameters (Tables E1 and E2). Subsequent evaluations will benefit from the long-term follow-up of the CoreValve trial.

Although this represents the largest randomized trial of a self-expanding valve in the treatment of aortic stenosis, our analysis remains limited by patient numbers. There were too few patients with severe PPM in the TAVR treatment group to allow meaningful comparisons of some clinical and echocardiographic outcomes.

Clinical Implications

Patients with severe PPM have increased all-cause mortality and acute kidney injury. TAVR using a self-expanding valve decreases the incidence of PPM in high-risk patients with severe aortic stenosis. Longer-term studies are necessary to better understand LV mass regression for patients with severe PPM.

Conflict of Interest Statement

George L. Zorn, III, reports receiving consulting fees from Medtronic and Edwards Lifesciences (Irvine, Calif). Stephen Little has received lecture fees from St Jude Medical (St Paul, Minn) and grant support from Seimens Healthcare (Erlangen, Germany) and St Jude Medical. Peter Tadros has received consulting fees from Medtronic and St Jude Medical. G. Michael Deeb serves as an advisor and consultant to Medtronic. Thomas G. Gleason has received institutional research grant support from Medtronic. Neal S. Kleiman has received grant support from Medtronic. Jae K. Oh reports research support for the echocardiographic core laboratory from Medtronic. Jeffrey J. Popma has received institutional research grants from Boston Scientific (Natick, Mass), Direct Flow Medical (Santa Rosa, Calif), and Medtronic. David Adams has royalty agreements through Mount Sinai School of Medicine with Edwards Lifesciences and Medtronic and has received institutional grant support

from Medtronic. Jian Huang is an employee and shareholder of Medtronic. Michael Reardon reports receiving consulting fees from Medtronic. John Heiser has nothing to disclose with regard to commercial support.

You can watch a Webcast of this AATS meeting presentation by going to: http://webcast.aats.org/2015/Video/Monday/04-27-15_4E_1420_Zorn.mp4.

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Key Words: aortic stenosis, transcatheter aortic valve replacement, prosthesis-patient mismatch

Discussion

Dr Craig Smith (New York, NY). I have 1 disclosure. As the surgical principal investigator of the Placement of Aortic Transcatheter Valve (PARTNER) trial, I receive reimbursement from the sponsor for travel and other expenses related to trial management.

That was a very nice subset analysis on patient-prosthesis mismatch (PPM). If nothing else, this adds to the accumulating evidence that transcatheter aortic valve replacement (TAVR) offers advantages in orifice area in small roots regardless of risk profile. But I have a cautionary observation and 3 questions.

One of the 3 major conclusions is that PPM is about fourfold more common following surgical aortic valve replacement than TAVR at 1 year: 25.7 versus 6.2. It is not surprising that the authors could not resist a direct comparison to results from the PARTNER trial, which I appreciate you sharing in advance. Although the surgical arms in the 2 trials had very similar frequency of severe PPM, about 26% versus 28%, severe PPM was lower in the CoreValve TAVR group than PARTNER, at 6.2% versus 19.7%.

I can certainly understand the desire to emphasize this seeming competitive advantage of 1 platform over another, but it is important to remember that PARTNER treated higher-risk patients with average risk scores and 1-year all-cause mortality that was about 50% higher than the somewhat lower-risk patients in the CoreValve trial. So they are just different populations.

They were also not contemporaneous. The nonrandomized continuous access cohort of the PARTNER trial was somewhat more contemporaneous, and also a little bit lower risk; the Society of Thoracic Surgeons score was a little closer to 10. In that cohort, the severe PPM incidence fell to about 13.6%.

Even more importantly, the 2 trials used different core labs, which leads to my first question: At what level was

the orifice measured? Specifically, was it measured at the inflow end of the valve, or right below the visible valve hinges, closer to the annulus?

Dr Zorn. I can't answer that question directly about the PARTNER trial.

Dr Smith. There is debate about this, and I gather the 2 core labs differ on this point. If it is measured at the inflow level, the orifice will be larger than if it is measured right below the leaflets, and I believe the 2 trials differ on this point, so it is a potential source of ostensibly larger orifice areas in the CoreValve trial. That is something we can let the echocardiographers settle.

Dr Zorn. Let me comment on that briefly. They were both core lab-reviewed trials and I agree with you. I do not want to make any strong comparisons across trials here.

Dr Smith. I understand.

Dr Zorn. We were concerned about the issue of measuring and inconsistencies in a calculated number.

Dr Smith. Understood. The authors also show that PPM correlated with late mortality. Totally unsurprising; it is what would be expected. And it was only significant when the surgical and TAVR arms were combined.

Another unique feature of the CoreValve trial that you touched on is that the surgical aortic valve replacement (SAVR) mortality at 1 year was significantly higher than the TAVR mortality. Is it possible that whatever accounts for that mortality imbalance is also distorting the PPM correlation with mortality? Acknowledging that sample size might be a big problem here, was a Cox regression analysis considered or done to test for interaction between PPM and procedure type?

Dr Zorn. It was. In fact, we did a Cox regression analysis accounting for the different therapies that had a *P* value of .086.

Dr Smith. So close, but not.

Dr Zorn. Correct, when comparing for those.

Dr Smith. Okay. Thank you. Finally, Table 1 shows that there were 24 patients in the TAVR group who had severe PPM at 1 month that decreased to 17 at 12 months, which is a departure of 7 patients, or about 29% of the group. I hope I am reading that correctly. Were these mortalities? It does not appear that they were downgraded, because the moderate group does not change, and it would be surprising if it did. In contrast, the severe PPM SAVR group decreased by a relatively modest 5 patients, from 58 to 53, which is about 9%.

Is the higher proportional loss from the TAVR group in the severe PPM category accentuating the differences between the groups? And if the departures were all mortalities, as I assume they were, what accounts for what appears to be a differential influence of PPM in the TAVR group?

Dr Zorn. They were not all mortalities. The difference in numbers—and I would have to look specifically at the chart

that we are talking about in the manuscript—a number of those, if we did not have paired analysis at both 1 month and 1 year, those patients were not used in certain analyses. So if patients were not available for both studies, we did not use their data for the paired analysis but we did for some of the mean variables.

Dr Smith. That probably was there and I missed it, but those patients are still subtractions from the total.

Dr Michael Reardon (*Houston, Tex*). Also, we did not measure effective orifice area because it is a calculated value. We measured at the inflow for the left ventricular outflow tract.

Two things, Craig. First of all, we should not compare these trials; they are not meant to be compared at all. The CoreValve trial was just to look at CoreValve versus surgery, not to compare CoreValve to PARTNER. They are 2 separate and completely different things.

When you look at these, you are better off looking at mean gradients because we actually measure those, whereas effective orifice area is a calculated value, much like left ventricular mass is a calculated value that is greatly influenced by a cube of left ventricular end diastolic dimension.

Dr Niv Ad (*Falls Church, Va*). Excellent presentation. I wonder if in lieu of the inability to show the differences with PPM you really made the right analysis. In other words, the role of diastolic dysfunction, especially in patients with residual aortic insufficiency, should be emphasized more than it is, because this might put some light on why patients in the TAVR group are not doing as well as we expected when they do not have PPM.

To be able to fully answer the question you need to look at diastolic dysfunction as well.

Dr Zorn. I agree with you. To that end, Steve Little is working on a manuscript that I believe has been submitted where he spends a lot of time looking at that exact issue. It was not the focus of our study, but Little's work is going to look a lot at diastolic dysfunction and its results.

Dr Pasquale Totaro (*Palermo, Italy*). Congratulations for your presentation. I am a little bit surprised by the relatively high incidence of severe and moderate PPM in the surgical group. Can you tell us something more about the choice of the prosthesis—if anything was done intraoperatively to prevent this? And also just another comment: You showed us a significant reduction in left ventricular mass regression in the surgical group, but especially in patients with severe PPM. Do you have any idea or comments about that?

Dr Zorn. Let me answer the first question. There was no restriction on use of surgical valves in the trial. So surgeons were free to choose their valves. The majority of valves used were 21 and 23; there was a relatively small use of

25 and 27 valves for the trial. They were encouraged not to enroll patients who would require annular enlarging procedures, but they were not strictly prohibited. Surgeons could do what they needed to do to treat the patient at the time of the procedure.

Your second question is whether there was only left ventricular mass regression in the PPM surgical group?

Dr Totaro. No. I question if it was higher in the surgical group and, more precisely, if left ventricular mass regression was higher in the patients with severe PPM than in the patients without.

Dr Zorn. We saw mass regression with everything, so with TAVR, SAVR, and all subsets with PPM and without PPM, we saw mass regression.

Part of the issue with this trial is we have so few TAVR patients with severe PPM; we do not have enough numbers. There were only 9.

Dr Totaro. I am just talking about the surgical group.

Dr Zorn. We do not see an influence of PPM on mass regression. We see, as a percentage, it is almost identical in the SAVR groups between those with and without PPM.

Dr Totaro. That is a little bit strange. Do you have any idea why patients with severe PPM experienced such an important left ventricular mass regression compared with patients without severe PPM? We could imagine that a patient with severe PPM should not have an important left ventricular mass regression.

Dr Zorn. My only comment is I have been delving into this issue of PPM after SAVR, and it is a morass—there is so much data out there—I do not have the definitive answer as to why we do not see a difference between these groups.

Dr Vinayak Bapat (*London, United Kingdom*). I am just going to go a bit further on PPM. In TAVR we do not excise the leaflets and in SAVR we excise the leaflets, and your data show very clearly now that despite excising the leaflets we are tending to undersize the valve. Do you think in the future, especially in small adults, we should be looking at newer designs where you can excise the leaflet and you can actually put a bigger valve but that is like a TAVR valve? Do you think that will cause probably less PPM because we are still using the same valves with not much design change for the past 60 years?

Dr Zorn. Agreed, and some of the data presented earlier today would certainly lend some credence to that; they are some interesting data. In truth, an instance of severe PPM of 6% is relatively low. We can anticipate with further technologic advances that that may even get lower.

One of the thrusts of our study was to find out exactly how important that is. So we do know that severe PPM matters. Any opportunities we have to decrease that are worth exploring. I am not sure we are going to get back to the point where we are going to have to in high-risk patients take out aortic valve leaflets to put a device in.

TABLE E1. Clinical demographic characteristics for patients with severe prosthesis–patient mismatch (PPM) versus no severe PPM

Characteristic	TAVR			SAVR		
	Severe PPM (n = 24)	No severe PPM (n = 343)	P value	Severe PPM (n = 75)	No severe PPM (n = 259)	P value
Age (y)*	81.5 (8.4)	83.1 (7.0)	.2756	82.1 (7.0)	83.7 (6.1)	.0531
Male sex	11 (45.8)	186 (54.2)	.4253	34 (45.3)	140 (54.1)	.1831
Society of Thoracic Surgeons score (%)*	7.3 (2.9)	7.2 (2.9)	.8368	7.6 (2.9)	7.5 (3.4)	.7779
Body mass index (kg/m ²)*	31.9 (7.5)	27.8 (6.0)	.0016	30.4 (7.9)	28.0 (5.8)	.0134
Logistic European System for Cardiac Operative Risk Evaluation score (%)*	17.6 (14.5)	17.2 (12.5)	.8946	20.5 (15.2)	17.8 (11.9)	.1615
New York Heart Association functional class III or IV	22 (91.7)	292 (85.1)	.5517	67 (89.3)	223 (86.1)	.4660
Hypertension	24 (100.0)	326 (95.0)	.2641	72 (96.0)	250 (96.5)	.7356
Diabetes mellitus	11 (45.8)	121 (35.3)	.2975	43 (57.3)	111 (42.9)	.0268
Insulin controlled	3 (12.5)	39 (11.4)	.7462	8 (10.7)	36 (13.9)	.4660
Prior stroke	2 (8.3)	43 (12.5)	.7524	10 (13.3)	39 (15.1)	.7012
Coronary artery disease	17 (70.8)	262 (76.4)	.5380	58 (77.3)	195 (75.3)	.7161
Prior coronary artery bypass grafting	6 (25.0)	105 (30.6)	.5628	26 (34.7)	76 (29.3)	.3781
Prior percutaneous coronary intervention	6 (25.0)	118 (34.4)	.3465	32 (42.7)	97 (37.5)	.4140
Severe chronic lung disease	6 (25.0)	43 (12.5)	.0827	8 (10.7)	22 (8.5)	.5623
Home oxygen	7 (29.2)	40 (11.7)	.0134	9 (12.0)	28 (10.8)	.7726
Anemia with prior transfusion	7 (30.4)	57 (17.1)	.1059	8 (10.8)	46 (18.5)	.1209
Albumin < 3.3 g/dL	5 (21.7)	51 (15.0)	.3865	6 (8.6)	42 (16.5)	.0968
5-m Walk test > 6 s	17 (81.0)	242 (78.8)	>.9999	55 (85.9)	183 (79.9)	.2752
Assisted living	5 (20.8)	32 (9.3)	.0704	6 (8.0)	31 (12.0)	.3348
≥2 Katz Index of Independence Activities of Daily Living deficits	2 (8.3)	19 (5.5)	.6383	5 (6.7)	19 (7.3)	.8433
Wheelchair bound	1 (4.2)	13 (3.8)	>.9999	7 (9.3)	16 (6.2)	.3419

TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch. *Values are presented as mean (SD); all other values are number of patients (%).

TABLE E2. Baseline echocardiographic findings for patients with subsequent severe prosthesis–patient mismatch (PPM) versus no severe PPM

Characteristic	TAVR			SAVR		
	Severe PPM (n = 24)	No severe PPM (n = 343)	P value	Severe PPM (n = 75)	No severe PPM (n = 259)	P value
Aortic valve						
Aortic valve peak velocity (m/s)	4.60 (0.64)	4.35 (0.60)	.0512	4.37 (0.56)	4.38 (0.58)	.9236
Peak gradient (mm Hg)	86.20 (23.66)	77.16 (21.75)	.0511	77.69 (19.73)	78.04 (20.74)	.8967
Mean gradient (mm Hg)	51.13 (15.48)	47.30 (14.36)	.2094	47.79 (14.98)	47.79 (13.66)	.9997
Aortic valve effective orifice area or valve area (cm ²)	0.62 (0.12)	0.73 (0.23)	.0010	0.69 (0.28)	0.75 (0.22)	.1664
Effective orifice area index (cm ² /m ²)	0.32 (0.07)	0.40 (0.12)	.0005	0.36 (0.14)	0.41 (0.12)	.0109
Aortic annulus diameter (cm)	2.07 (0.16)	2.23 (0.21)	.0006	2.14 (0.22)	2.19 (0.21)	.0676
Left ventricle						
End diastolic dimension (cm)	5.09 (0.68)	4.97 (0.62)	.4292	5.12 (0.72)	4.98 (0.61)	.1179
End systolic dimension (cm)	3.35 (0.78)	3.20 (0.79)	.4668	3.42 (0.76)	3.23 (0.72)	.0702
End diastolic volume (mL)	121.49 (45.67)	132.76 (50.04)	.5093	141.15 (56.26)	135.06 (53.03)	.5368
End systolic volume (mL)	58.37 (34.56)	61.90 (34.15)	.7628	73.77 (46.78)	60.38 (35.23)	.1050
Stroke volume 2DE (mL) calculated	63.12 (19.67)	70.86 (27.65)	.4088	67.38 (23.65)	74.67 (28.24)	.1455
Doppler stroke volume (mL)	69.60 (16.92)	76.50 (23.93)	.2050	69.16 (18.06)	77.45 (20.39)	.0025
Left ventricular mass (g)	226.45 (60.41)	225.95 (71.69)	.9781	243.18 (67.42)	224.68 (63.52)	.0434
Left ventricular mass index (g/m ²)	119.70 (30.64)	122.29 (35.50)	.7744	127.29 (33.99)	123.10 (33.43)	.3790
Ejection fraction (%)	56.04 (12.25)	58.17 (11.25)	.3737	55.07 (13.04)	58.30 (11.44)	.0380
≥ Moderate mitral regurgitation (%)	5 (20.8)	31 (9.2)	.0661	10 (13.5)	26 (10.4)	.4541
≥ Moderate total aortic regurgitation (%)	1 (4.2)	17 (5.0)	>.9999	2 (2.7)	18 (7.1)	.2675
Mitral E velocity (m/s)	1.10 (0.35)	1.06 (0.32)	.5793	1.08 (0.30)	1.01 (0.34)	.1576
Mitral E/A ratio	1.24 (0.65)	1.22 (0.86)	.8890	1.28 (0.89)	1.07 (0.66)	.1265
Deceleration time of E (ms)	231.40 (81.50)	226.60 (74.07)	.7812	204.86 (64.78)	236.27 (80.60)	.0020
E/e' ratio	28.06 (12.46)	24.49 (11.87)	.2329	24.51 (10.27)	23.20 (10.47)	.3989

Categorical variables are presented as n (%); continuous variables are mean (SD). TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch; 2DE, 2-dimensional echocardiography; E/A, early mitral inflow velocity/late mitral inflow velocity; E/e', early mitral inflow velocity/mitral annulus early diastolic velocity.

TABLE E3. Total aortic regurgitation over time according to prosthesis–patient mismatch (PPM) status

Time and status	TAVR		SAVR	
	Severe PPM	No severe PPM	Severe PPM	No severe PPM
1 mo				
None	17.4 (4/23)	12.1 (40/330)	74.2 (46/62)	62.3 (149/239)
Trace	43.5 (10/23)	41.5 (137/330)	19.4 (12/62)	23.8 (57/239)
Mild	30.4 (7/23)	36.1 (119/330)	6.5 (4/62)	12.1 (29/239)
Moderate	8.7 (2/23)	8.2 (27/330)	0.0 (0/62)	1.7 (4/239)
Severe	0.0 (0/23)	2.1 (7/330)	0.0 (0/62)	0.0 (0/239)
1 y				
None	36.8 (7/19)	28.2 (78/277)	72.3 (34/47)	66.7 (116/174)
Trace	31.6 (6/19)	35.7 (99/277)	21.3 (10/47)	21.8 (38/174)
Mild	31.6 (6/19)	28.9 (80/277)	6.4 (3/47)	9.8 (17/174)
Moderate	0.0 (0/19)	6.9 (19/277)	0.0 (0/47)	1.1 (2/174)
Severe	0.0 (0/19)	0.4 (1/277)	0.0 (0/47)	0.6 (1/174)

Values are presented as % (n/N). TAVR, Transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; PPM, prosthesis–patient mismatch.

TABLE E4. Change in left ventricular (LV) mass and LV mass index

Characteristic	PPM + AR	PPM no AR	No PPM + AR	No PPM no AR
SAVR	n = 0	n = 71	n = 3	n = 232
LV mass (g)				
Baseline	0	243.87 (67.18) (n = 61)	228.72 (26.28) (n = 3)	223.93 (61.20) (n = 202)
1 y	0	215.28 (73.28) (n = 36)	178.27 (12.48) (n = 2)	188.34 (54.17) (n = 132)
Change	0	-44.04 (77.21) (n = 32)	-65.39 (18.96) (n = 2)	-41.15 (58.15) (n = 119)
P value for change from baseline to 1 y	NA	.0030	.1288	<.0001
LV mass index (g/m ²)				
Baseline	0	128.10 (34.55) (n = 61)	125.82 (16.10) (n = 3)	122.25 (32.13) (n = 202)
1 y	0	109.66 (38.36) (n = 36)	98.44 (4.59) (n = 2)	101.42 (25.10) (n = 132)
Change	0	-22.72 (39.08) (n = 32)	-36.26 (11.33) (n = 2)	-23.44 (32.33) (n = 119)
P value for change from baseline to 1 y	NA	.0025	.1384	<.0001
TAVR	n = 3	n = 13	n = 29	n = 193
LV mass (g)				
Baseline	0	205.21 (48.65) (n = 10)	271.68 (87.16) (n = 26)	216.36 (66.54) (n = 170)
1 y	205.71 (136.17) (n = 2)	216.85 (65.74) (n = 8)	228.58 (86.84) (n = 19)	198.96 (62.49) (n = 135)
Change	0	-17.54 (83.02) (n = 6)	-36.91 (59.88) (n = 17)	-17.37 (59.72) (n = 122)
P value for change from baseline to 1 y	NA	.6269	.0218	.0017
LV mass index (g/m ²)				
Baseline	0	111.26 (25.69) (n = 10)	146.84 (47.58) (n = 26)	117.29 (32.39) (n = 170)
1 y	106.09 (49.54) (n = 2)	105.58 (24.82) (n = 8)	123.87 (41.97) (n = 19)	108.03 (29.34) (n = 135)
Change	0	-11.04 (43.09) (n = 6)	-21.69 (31.93) (n = 17)	-10.15 (32.29) (n = 122)
P value for change from baseline to 1 y	NA	.5579	.0128	.0007

Values are presented as mean (SD). PPM, Prosthesis–patient mismatch; AR, aortic regurgitation; SAVR, surgical aortic valve replacement; LV, left ventricular; NA, not applicable; TAVR, transcatheter aortic valve replacement.