



Effects of prosthesis-patient mismatch on cardiac function and clinical outcome after transcatheter aortic valve implantation

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Abstract

Background: Transcatheter aortic valve implantation (TAVI) prostheses have better hemodynamics compared to surgical prostheses, with a lower incidence of prosthesis-patient mismatch (PPM). Nonetheless, the effects of PPM have been controversial regarding clinical impact. This study aims to determine the short-term impact of PPM on cardiac function and the effect of PPM on mid-term outcome in patients undergoing transfemoral TAVI with balloon-expandable valves.

Methods: One hundred sixty consecutive patients (76.5±7.4 years, 85 men) were enrolled and examined before and 30 days after TAVI, by comprehensive echocardiogram (speckle tracking echocardiography and strain analysis). Patients were divided according to measured PPM (PPM_M) into PPM_M group: indexed effective orifice area (EOAi)≤0.85 cm²/m² (n=64), and No-PPM_M group: EOAI>0.85 cm²/m² (n=96). Predictors and predictive value of PPM_M were analyzed based on the primary endpoint, 3-year all-cause mortality.

Results: Impaired LA function was independently associated with PPM_M after TAVI (global LA strain - OR 0.92, p = 0.022). Three-year mortality was higher in the PPM_M group (23.4% vs. 10.4% in the No-PPM_M group, p=0.026).

Conclusions: Our study revealed significantly worse impairment of LA function in patients with PPM_M compared to those without PPM_M on short-term follow-up, which correlated with 3-year mortality.

Keywords

aortic stenosis, TAVI, prosthesis-patient mismatch, LA function, prognosis.

Introduction

Transcatheter aortic valve implantation (TAVI) has gained an important role in the treatment of patients with severe AS, with a rapid extension of its indication from high-risk patients, to intermediate- and low-risk patients with effective and safe results [1-3]. However, long-term transcatheter valve durability remains the main reason for reserved expansion of TAVI in younger patients, due to complications such as structural and nonstructural valve dysfunction [4,5]. Prosthesis-patient mismatch (PPM) is a nonstructural valve dysfunction, defined by an effective orifice area (EOA) of the otherwise functional valve too small in relation to a patient's body surface area [5,6]. Nonetheless, the effects of PPM have been controversial regarding clinical impact [7-12]. Our aim was to determine the short-term impact of PPM on cardiac function and the effect of PPM on mid-term outcomes in patients undergoing transfemoral TAVI with balloon-expandable valves.

Materials and Methods

1. Study population and procedure

Patients with severe symptomatic AS scheduled to undergo transfemoral TAVI in our center were prospectively enrolled

between September 2018 and May 2020. Selection criteria included: age>40, severe AS (aortic valve area, AVA) <1.0 cm², indexed AVA<0.6 cm²/m², peak aortic jet velocity ≥4 m/s, or mean gradient ≥40 mmHg. Exclusion criteria included: hypertrophic cardiomyopathy, prosthetic aortic valve, non-transfemoral TAVI, and poor acoustic window. All patients underwent Heart Team evaluation and were deemed eligible for TAVI based on current guideline recommendations. All procedures were performed in a hybrid operating room with the participation of both an interventional cardiologist and a cardiovascular surgeon.

All patients underwent percutaneous transfemoral TAVI with balloon-expandable valves. Transesophageal echocardiography was used during the procedure for additional guidance and assessment. Clinical, biological, and procedural data were collected. The primary outcome was all-cause mortality (obtained through a query of the National Register of population records), registered three years after TAVI. Informed consent was obtained from each patient. The study protocol, which conforms to the ethical guidelines of the 1975 Declaration of Helsinki, was reviewed and approved by the institutional Ethics Committee.

2. Definitions and data collection – echocardiographic evaluation

All patients underwent a comprehensive echocardiogram performed by experienced echocardiographers both before and 30 days after TAVI using a Vivid E95 ultrasound system (General Electric Healthcare, Horten, Norway), as previously described [13]. Data

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were digitally stored for offline analysis using commercially available software (EchoPac version 203; GE Medical Systems, Horten, Norway), and images were analyzed by a single trained cardiologist according to current guidelines [14]. The evaluation included standard parameters used to assess AS severity: peak aortic jet velocity, peak and mean pressure gradients across the aortic valve (using modified Bernoulli equation), and AVA (using continuity equation). In the parasternal long-axis view, LV dimensions were assessed, and LV mass was calculated using Devereux's formula and indexed to body surface area [14]. LV end-diastolic and end-systolic volumes were measured in the apical 4-chamber and 2-chamber views and indexed to body surface area [14]. LV ejection fraction (EF) was calculated according to the Simpson's biplane method [14]. Left atrial volumes were measured by the biplane method of disks and indexed for body surface area [14]. Transmitral flow was assessed by PW Doppler to measure the peak early (E) and late (A) diastolic velocities, and tissue Doppler imaging of the mitral annulus on the apical 4-chamber view was used to measure the e' velocities at both the lateral and septal sites to calculate the E/e' ratio.

Myocardial deformation analysis using speckle tracking echocardiography (STE) was performed to assess LV and LA function. The evaluation included STE analysis for LV function: LV global longitudinal strain (GLS); LA function: LA global longitudinal strain (LA ϵ , reservoir function), LA systolic strain rate (SSr, reservoir function), LA early diastolic strain rate (ESr, conduit function), LA late diastolic strain rate (ASr, contractile function). Complete myocardial deformation analysis was possible in 132 out of 160 patients. Negative values of strain parameters are used as moduli (positive numbers) for ease of analysis. RV function was assessed by measuring TAPSE, the peak systolic myocardial velocity at the lateral site of the tricuspid annulus (S'RV), RV fractional area change (FAC) and RV longitudinal strain parameters by STE: peak values of global RV strain (RV-GLS), RV free wall longitudinal strain (RV-FWLS) and the interventricular septum longitudinal strain (RV-IVS). The right ventricular systolic pressure was calculated from the peak velocity of the tricuspid regurgitant jet using the Bernoulli equation, and the right atrial pressure (determined by the diameter and inspiratory reduction of the inferior vena cava) was added [15].

3. Patient-prosthesis mismatch definitions

Patient-prosthesis mismatch (PPM) was classified based on EOAI measured at 30 days post-procedure by transthoracic echocardiography using the continuity equation in line with the current guidelines [15]. Additionally, PPM BMI-adjusted was reclassified according to lower EOAI values for obese patients ($\text{BMI} \geq 30 \text{ kg/m}^2$) as stated in the guidelines [15]. Patient-prosthesis mismatch (PPM) was classified as follows: No-PPM – $\text{EOAI} > 0.85 \text{ cm}^2/\text{m}^2$, PPM – $\text{EOAI} \leq 0.85 \text{ cm}^2/\text{m}^2$, further divided in moderate PPM – $\text{EOAI} > 0.65 \text{ cm}^2/\text{m}^2$ and $\leq 0.85 \text{ cm}^2/\text{m}^2$, and severe PPM – $\text{EOAI} \leq 0.65 \text{ cm}^2/\text{m}^2$.

Additionally, PPM BMI-adjusted was reclassified according to lower EOAI values for obese patients ($\text{BMI} \geq 30 \text{ kg/m}^2$) as follows: No-PPM BMI-adjusted – $\text{EOAI} > 0.70 \text{ cm}^2/\text{m}^2$, PPM BMI-adjusted – $\text{EOAI} \leq 0.70 \text{ cm}^2/\text{m}^2$, further divided in moderate PPM BMI-adjusted –

$\text{EOAI} > 0.55 \text{ cm}^2/\text{m}^2$ and $\leq 0.70 \text{ cm}^2/\text{m}^2$, and severe PPM BMI-adjusted – $\text{EOAI} \leq 0.55 \text{ cm}^2/\text{m}^2$.

Patients were grouped according to measured PPM (PPM_M) into PPM_M group: $\text{EOAI} \leq 0.85 \text{ cm}^2/\text{m}^2$ ($n=64$) and No-PPM_M group: $\text{EOAI} > 0.85 \text{ cm}^2/\text{m}^2$ ($n=96$). The PPM_M group was further divided into the predicted PPM_M group ($n=39$) and unpredicted PPM_M group ($n=25$), according to valve-size predicted PPM, using EOAI based on normal reference values of size and model for published data [16]. Predictors and predictive value of PPM_M, predicted PPM_M, and unpredicted PPM_M were analyzed based on the primary endpoint, 3-year all-cause mortality. Analysis of PPM_M adjusted for BMI was also performed revealing the same significant results as in the presented analysis.

4. Statistical analysis

Continuous variables are given as mean $\pm$ standard deviation and compared using the Student t-test. Discrete variables were expressed as counts and percentages, and comparisons between groups were done with the χ^2 or Fisher's exact test, when appropriate. For comparisons between subgroups, the Kruskal-Wallis test, Wilcoxon rank sum tests using pairwise comparisons, and the Chi-square test for comparing proportions (of categorical variables), between >2 groups have been used. Bonferroni method was used to adjust p-values for multiple comparisons. Long-term clinical outcomes were estimated using the Kaplan-Meier method, with comparisons made using the log-rank test (overall or pair wise as appropriate). Univariable analysis (linear and binary logistic) was used to identify potential predictors of patient prosthesis-mismatch. After careful selection of variables based on clinical judgment, univariable assessment ($p < 0.05$), exclusion of variables showing collinearity (Pearson's coefficient > 0.6), and multiple testing to ensure stability, a multivariable model has been fitted (by stepwise multivariable regression analysis, linear and binary logistic). Univariable predictors of all-cause mortality were determined using Cox proportional hazards (Enter). Multivariable analysis was also performed in a similar fashion (Forward Wald). A two-sided P-value of 0.05 was considered statistically significant for all tests. All analyses were conducted using SPSS 21.0 (SPSS, Inc., Chicago, IL, USA).

Results

1. Study population and clinical features

According to measured EOAI of 160 patients during the 30-day follow-up post-TAVI, 94 patients did not develop PPM_M (60%), while 47 (29.4%) and 17 (10.6%) patients had moderate and severe PPM_M, respectively, yielding a total of 64 patients with PPM_M (40%). After adjustment for BMI thresholds, only 50 patients had PPM_M (31.3%), of which 34 (21.3%) with moderate and 16 (10.1%) with severe PPM_M.

Except for higher incidence of females (57.8% vs. 39.6%, $p=0.024$) and higher BMI (28.5 ± 5.0 vs. 26.9 ± 4.5 , $p=0.033$) in the PPM_M group, no significant differences in age (76.3 ± 7.8 vs. 76.6 ± 7.1 years, $p=0.8$), body surface area ($p=0.1$), prevalence of obesity

Table 1 - Clinical characteristics according to PPM_M group

Demographic and clinical characteristics	All patients (n=160)	PPM _M group (n=64)	No-PPM _M group (n=96)	p-value
Age (years)	76.5 ± 7.4	76.3±7.8	76.6±7.1	0.818
Sex (female)	75 (46.9%)	37 (57.8%)	38 (39.6%)	0.024
BMI (kg/m ²)	27.5 ± 4.7	28.5±5.0	26.9±4.5	0.033
BSA (m ²)	1.8 ± 0.2	1.9±0.2	1.8±0.2	0.124
Symptoms				
Angina	93 (58.5%)	35 (54.7%)	58 (61.1%)	0.424
Syncope	12 (7.5%)	8 (12.5%)	4 (4.2%)	0.068
Pulmonary oedema	23 (14.5%)	11 (17.2%)	12 (12.6%)	0.423
NYHA functional class	2.8±0.6	2.8±0.5	2.8±0.6	0.466
Class 2	46 (28.9%)	16 (25.0%)	30 (31.6%)	0.659
Class 3	103 (64.8%)	44 (68.8%)	59 (62.1%)	
Class 4	10 (6.3%)	4 (6.3%)	6 (6.3%)	
Comorbidities				
Cardiac				
Atrial fibrillation	50 (31.4%)	22 (34.4%)	28 (29.5%)	0.514
CAD	87 (54.7%)	30 (46.9%)	57 (60.0%)	0.103
Prior MI	22(13.8%)	7 (10.9%)	15 (15.8%)	0.385
Prior CABG	8 (5.0%)	1 (1.6%)	7 (7.4%)	0.145
Prior PCI	38 (23.9%)	15 (23.4%)	23 (24.2%)	0.911
Other				
Obesity	37 (23.1%)	18 (28.1%)	19 (19.8%)	0.221
Type 2 DM	45 (28.3%)	18 (28.1%)	27 (28.4%)	0.968
Systemic hypertension	142 (88.8%)	59 (92.2%)	83 (86.5%)	0.261
COPD	18 (11.3%)	7 (10.9%)	11 (11.5%)	0.919
Cirrhosis	16 (10.1%)	6 (9.4%)	10 (10.5%)	0.813
PAD	19 (11.9%)	6 (9.4%)	13 (13.7%)	0.411
CKD (≥3)	32 (20.1%)	16 (25.0%)	16 (16.8%)	0.208
Frailty	63 (39.5%)	26 (40.6%)	37 (38.9%)	0.832

Values are mean ±SD, n (%), or median (interquartile range)

(p=0.2), nor in the presence of cardiovascular risk factors (p>0.2 for all) were observed between groups (Table 1).

Based on preoperative echocardiographic evaluation, the patients in the PPM group had smaller AVA and AVAi, with no difference in mean gradient or LVOT diameter between groups. Impaired LA function (LA-GLS, SSr, ASr) was more frequent in the PPM group, despite similar LAVI between groups (Appendix 1). According to preoperative angio-CT evaluation, the patients in the PPM group had smaller aortic roots (smaller aortic annulus, smaller LVOT, lower LCA and RCA origin with smaller sinuses), but no differences in calcium load or calcium disposition, nor in the presence of bicuspid valve (Appendix 2). There were no differences between groups regarding intraprocedural features, except for a higher rate use of 20/23 valves in the PPM group (Appendix 3).

2. Echocardiographic changes after TAVI

All echocardiographic parameters describing AS severity, LA reservoir, contractile function, LV systolic and diastolic function improved significantly after the procedure as previously presented[13], but also in PPM_M and No-PPM_M groups, respectively (Table 2).

At 1 month after TAVI, there were no significant differences in terms of indexed LV mass, LV volumes, LVEF, and LV global

longitudinal strain (p=NS) between patients with or without PPM (Table 3). Post-TAVI prevalence of paravalvular aortic regurgitation or mitral regurgitation was also not different between the two groups (p=0.96, p=0.12, respectively). Although LA indexed area and volume were similar between groups, in the PPM_M group we found a significantly worse systolic global LA strain (13.7±6.1 vs. 16.9±7.4%, p=0.005) and LA contractile function (ASr: -1.0±0.6 vs. -1.3±0.6 in the No-PPM_M group, p=0.013).

Subgroup analysis of patients with PPM according to predicted vs. unpredicted PPM_M revealed larger LV volumes, significant mitral regurgitation, and larger aortic root in the unpredicted PPM_M group (Appendix 4). Complete data regarding preoperative CT evaluation and procedural characteristics are available in the appendix (Appendix 5 and 6). After TAVI, unpredicted PPM_M was associated with worse subclinical LV dysfunction and larger LV volumes (Appendix 7).

3. Predictors of PPM and PPM effects on cardiac function

Two separate analyses were performed: one based on preoperative characteristics to determine factors associated with the occurrence of PPM_M, and one based on postoperative characteristics, to analyze the relationship between PPM_M and cardiac function after TAVI. In the multivariable regression model (Table 4), higher BMI

Table 2 - Echocardiographic changes after TAVI according to PPM_M group

Echocardiographic parameters	PPM _M group (n=64)			No- PPM _M group (n=96)		
	Baseline	1m post-TAVI	p-value	Baseline	1m post TAVI	p-value
Aortic stenosis severity						
Vmax, m/s	4.6±0.8	2.4±0.6	<0.001	4.6±0.7	2.1±0.3	<0.001
Mean gradient, mmHg	57.4±19.4	14.05.8	<0.001	56.3±18.6	10.4±3.1	<0.001
AVA, cm ²	0.67±0.3	1.3±0.3	<0.001	0.77±0.3	2.0±0.6	<0.001
AVAi, cm ² /m ²	0.37±0.2	0.7±0.1	<0.001	0.44±0.2	1.1±0.3	<0.001
Aortic regurgitation	1.2±0.6	0.8±0.6	0.001	1.3±0.7	0.8±0.6	<0.001
Left ventricle						
LVEF, %	51.5±12.6	53.9±10.0	0.242	52.0±11.2	54.3±9.2	0.132
LV-GLS, %	-11.9±4.0	-13.9±4.3	0.008	-12.6±4.3	-14.2±3.6	0.009
LVMi, g/m ²	174.7±46	149.7±42	0.002	181.4±50	159.7±40	0.001
LVESVi, ml/m ²	27.2±18.2	23.0±13.6	0.147	28.3±15.3	23.7±13.6	0.028
LVEDVi, ml/m ²	54.7±20.0	49.6±21.5	0.174	57.4±19.5	50.9±18.0	0.018
LVSVi, ml/m ²	27.0±8.7	26.1±10.9	0.606	28.4±8.6	26.7±8.4	0.172
E/A	1.3±0.8	1.0±0.4	0.024	1.1±0.8	0.8±0.5	0.003
E/e' septal	23.2±13.1	20.5±9.7	0.203	21.6±10.7	18.2±7.1	0.012
E/e' lateral	17.0±11.3	13.8±6.6	0.062	15.0±8.1	13.8±7.4	0.277
E/e' average	18.1±9.2	16.0±6.7	0.157	16.6±7.4	15.3±6.7	0.231
Mitral regurgitation	1.3±0.6	1.2±0.5	0.326	1.3±0.6	1.0±0.4	<0.001
Left Atrium						
LAAi, cm ² /m ²	14.8±2.4	13.9±2.3	0.036	15.0±3.7	14.0±3.5	0.052
LAVi, ml/m ²	53.0±13.1	47.5±12.3	0.015	54.4±21.2	48.6±19.7	0.052
LA-GLS, % (LAε)	-10.2±5.5	-13.7±6.1	0.001	-13.8±7.1	-16.9±7.4	0.004
SSr, s ⁻¹	0.50±0.5	1.0±2.1	0.080	0.76±0.6	0.8±0.4	0.476
ESr, s ⁻¹	-0.31±0.5	-0.6±0.5	0.001	-0.38±0.5	-0.5±0.6	0.168
ASr, s ⁻¹	-0.71±0.6	-1.0±0.6	0.024	-0.97±0.6	-1.3±0.6	0.004
Right ventricle						
TAPSE, cm/s	2.0±0.4	21.3±3.7	0.122	2.0±0.4	20.5±3.9	0.712
S'RV, cm/s	10.4±2.9	11.8±2.5	0.004	10.5±3.1	12.4±7.8	0.031
PASP, mmHg	42.0±16.3	34.9±12.4	0.017	37.8±14.3	31.5±11.1	<0.001
FAC, %	40.7±8.1	42.8±8.2	0.211	40.5±8.0	43.0±6.8	0.023
RV-GLS, %	-16.1±5.7	-18.2±5.9	0.039	-17.0±6.3	-18.6±5.6	0.162
RV-FWLS, %	-20.4±7.6	-22.5±8.0	0.111	-22.0±7.5	-23.4±7.4	0.450
RV-IVS, %	-9.2±6.8	-12.8±5.3	0.003	-12.1±5.3	-12.9±4.6	0.393
RA, mm	38.5±8.5	36.8±6.5	0.276	36.9±8.5	35.5±8.3	0.248
RV, mm	35.4±5.6	34.5±6.0	0.613	34.1±6.4	33.2±5.9	0.283

Values are mean ±SD, n (%), or median (interquartile range)

(per unit increase OR 1.01, $p=0.012$) and smaller valve number (OR 0.79, $p=0.001$) were independent predictors for PPM_M before the procedure, while LA-GLS (OR 0.92, $p=0.022$) was independently associated with PPMM after the procedure. There was no significant association between PPM_M and age, BSA, obesity, aortic valve calcium score, LV mass index, oversizing, or post-dilatation. After TAVI, LA-GLS (OR 0.93, $p=0.014$) was independently associated with unpredicted PPM_M, while LV-GLS (OR 0.81, $p=0.015$) was independently associated with predicted PPM_M.

4. Clinical outcomes

3-year mortality was higher in the PPM_M group (23.4% vs. 10.4% in the No-PPM_M group, $p=0.026$), even after BMI-adjustment (25.5% vs. 11.2%, $p=0.019$). Reclassification of PPM_M group into No-PPM_M, moderate PPM_M, and severe PPM_M showed a trend for higher mortality in both moderate and severe PPM_M as compared to No-PPM_M but no overall significant difference (23.4% and 23.5%

vs. 10.4%, $p=0.104$). Valve-predicted PPM underestimates the incidence of measured PPM_M (27.5% vs. 40.0% PPM_M, $p=0.011$) and is not predictive for mortality (HR=0.67, $p=0.42$; AUC=477, $p=0.71$). Reclassification of PPM_M group into predicted PPM_M and unpredicted PPM_M, according to valve-size predicted PPM, demonstrated a progressively unfavorable prognosis from No-PPM_M, to predicted and unpredicted PPM_M in terms of all-cause mortality at 3 years follow-up (10.4%, 16.0% and 28.2%, respectively; $p=0.036$). Kaplan-Meier survival analysis depicts event-free survival during follow-up, with differences between groups becoming apparent after 1-year follow-up and achieving statistical significance at 3-year follow-up (Figure 1).

None of the baseline characteristics were predictive for mortality in the univariate analysis, therefore were not included. Procedural and post-TAVI echocardiographic parameters were further analyzed, together with various definitions of PPM. While increased transvalvular aortic mean gradient, impaired LA-GLS, and LV

Table 3 - Echocardiographic differences between groups 1-month after TAVI (short-term effects of PPM_M on cardiac function)

Echocardiographic parameters	PPM _M group (n=64)	No-PPM _M group (n=96)	p-value
Aortic stenosis severity			
Vmax, m/s	2.4±0.6	2.1±0.3	0.001
Mean gradient, mmHg	14.05.8	10.4±3.1	<0.001
AVA, cm ²	1.3±0.3	2.0±0.6	<0.001
AVAi, cm ² /m ²	0.7±0.1	1.1±0.3	<0.001
DVI	0.42±0.1	0.57±0.1	<0.001
Aortic regurgitation	0.8±0.6	0.8±0.6	0.956
Left ventricle			
LVEF, %	53.9±10.0	54.3±9.2	0.810
LV-GLS, %	-13.9±4.3	-14.2±3.6	0.674
LVMi, g/m ²	149.7±42	159.7±40	0.132
LVESVi, ml/m ²	23.0±13.6	23.7±13.6	0.768
LVEDVi, ml/m ²	49.6±21.5	50.9±18.0	0.689
LVSVi, ml/m ²	26.1±10.9	26.7±8.4	0.723
E/A	1.0±0.4	0.8±0.5	0.019
E/e' septal	20.5±9.7	18.2±7.1	0.084
E/e' lateral	13.8±6.6	13.8±7.4	0.987
E/e' average	16.0±6.7	15.3±6.7	0.504
Mitral regurgitation	1.2±0.5	1.0±0.4	0.118
Left Atrium			
LAAi, cm ² /m ²	13.9±2.3	14.0±3.5	0.980
LAVi, ml/m ²	47.5±12.3	48.6±19.7	0.682
LA-GLS, % (LAε)	13.7±6.1	16.9±7.4	0.005
SSr, s ⁻¹	1.0±2.1	0.8±0.4	0.459
ESr, s ⁻¹	-0.6±0.5	-0.5±0.6	0.214
ASr, s ⁻¹	-1.0±0.6	-1.3±0.6	0.013
Right ventricle			
TAPSE, cm/s	21.3±3.7	20.5±3.9	0.179
S' RV, cm/s	11.8±2.5	12.4±7.8	0.517
SPAP, mmHg	34.9±12.4	31.5±11.1	0.075
FAC, %	42.8±8.2	43.0±6.8	0.881
RV-GLS, %	-18.2±5.9	-18.6±5.6	0.648
RV-FWLS, %	-22.5±8.0	-23.4±7.4	0.497
RV-IVS, %	-12.8±5.3	-12.9±4.6	0.946
RA, mm	36.8±6.5	35.5±8.3	0.270
RV, mm	34.5±6.0	33.2±5.9	0.161

Values are mean ±SD, n (%), or median (interquartile range)

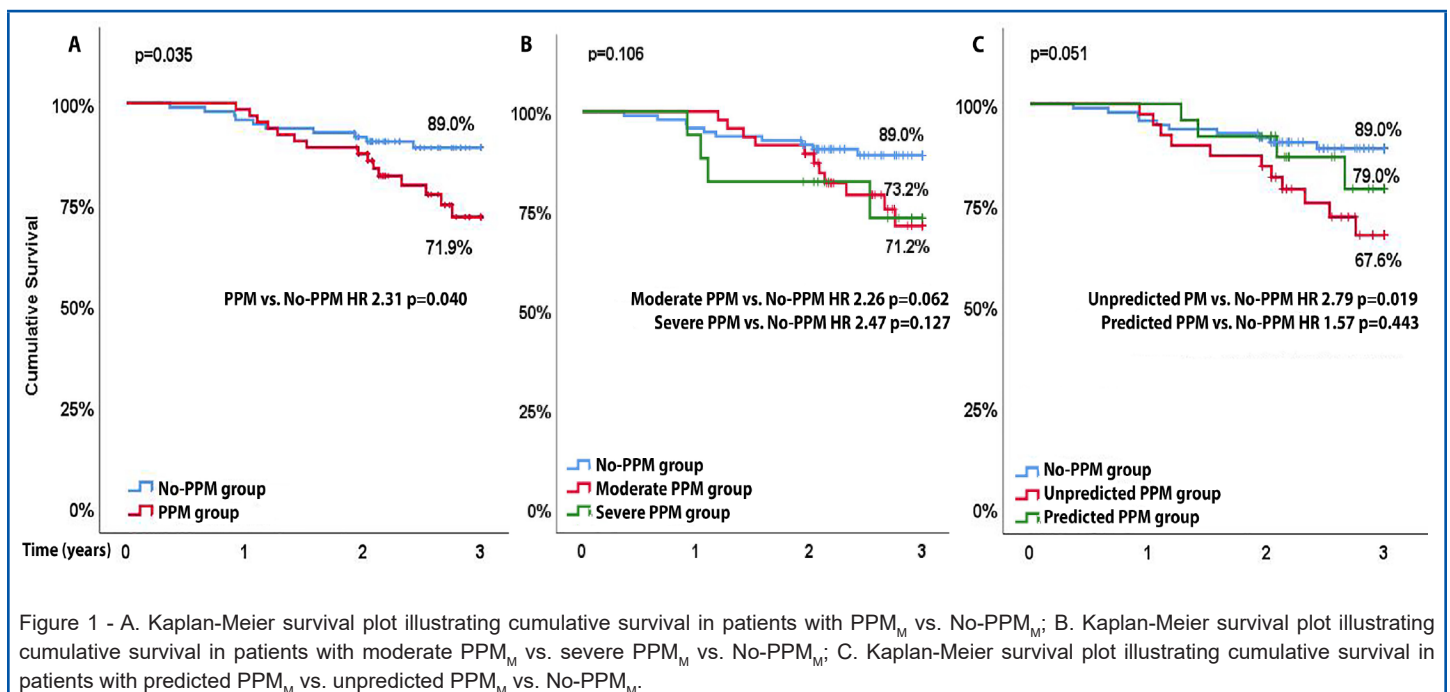


Table 4 - Univariable and multivariable predictors of PPM_M (binary logistic regression)

Regression analysis	PPM _M (Model 1)				Unpredicted PPM _M (Model 2)				Predicted PPM _M (Model 3)			
	Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR	p-value
Perioperative characteristics												
Age	0.99	0.590			0.97	0.279			1.04	0.292		
Sex (f)	2.09	0.024			0.96	0.917			4.47	0.003		
BMI	1.08	0.032	1.10	0.012	0.96	0.337			1.24	<0.001	1.26	<0.001
BSA	3.51	0.108			0.59	0.547			23.7	0.005		
Obesity	1.59	0.223			0.66	0.380			3.29	0.009		
AAo	0.99	0.018			1.00	0.601			0.99	<0.001		
dLVOT	0.87	0.035			1.06	0.459			0.69	<0.001		
Ca score	1.000	0.328			1.000	0.780			1.000	0.325		
Valve no.	0.809	0.003	0.79	0.001	1.009	0.900			0.639	<0.001	0.584	<0.001
Valve 20/23	2.720	0.003			1.270	0.537			9.500	<0.001		
Oversizing	0.981	0.213			0.964	0.043			1.014	0.476		
Postdilation	1.327	0.474			0.253	0.031	0.174	0.021	5.011	0.001	3.165	0.040
Postoperative characteristics (30-day follow-up)												
LA-GLS	0.935	0.006	0.921	0.022	0.937	0.019	0.931	0.014	0.972	0.357		
LAVI	0.999	0.980			1.004	0.704			0.984	0.317		
E/A	3.113	0.034			1.812	0.212			2.243	0.120	2.789	0.074
LVEF	0.996	0.809			0.975	0.178			1.036	0.205		
LV-GLS	1.019	0.672			1.124	0.024			0.867	0.028	0.809	0.015
LVMi	0.995	0.133			0.998	0.627			0.991	0.146		
PAPS	1.025	0.081			1.022	0.140			1.011	0.529		

Table 5 - Predictors of mortality (Cox regression analysis)

Mortality	Univariable analysis			Multivariable analysis		
Clinical parameters	HR	95% CI	p-value	HR	95% CI	p-value
PPM _M (measured EOAi)	0.56	0.15-2.09	0.384			
PPM _M ≤0.85	2.31	1.04-5.15	0.040	5.92	1.92-18.2	0.002
PPM _M BMI adjusted ≤0.85/0.70	2.45	1.12-5.37	0.025			
Valve predicted PPM (prosthesis predicted EOAi)	0.99	0.03-35.8	0.993			
Predicted PPM _M	1.05	0.36-3.05	0.936			
Unpredicted PPM _M	2.50	1.13-5.50	0.023			
Transvalvular mean gradient	1.07	1.00-1.15	0.054			
Post-dilation	1.80	0.75-4.32	0.189			
LAVi	1.01	1.00-1.03	0.118			
LA-GLS	0.94	0.89-1.00	0.050			
LA-GLS<19	3.11	1.06-9.12	0.038			
E/A	1.95	1.02-3.73	0.044	2.07	0.90-4.77	0.088
LVEF	1.04	0.99-1.04	0.170			

diastolic dysfunction were associated with mortality in the univariate analysis, only the presence of PPM_M was independently associated with mortality (Table 5).

Discussion

The main findings of our study can be summarized as follows:

- PPM_M is independently associated with impaired LA function after TAVI
- measured PPM_M is associated with increased mortality, even after BMI-adjustment

- valve-predicted PPM is less frequent than measured PPM_M and does not correlate with mortality
- reclassification of PPM_M into predicted PPM_M and unpredicted PPM_M, reveals higher mortality in unpredicted PPM_M and association with LA function impairment

1. Definition and Incidence of PPM

In the present study, we found an incidence of PPM_M of 40%, of which 47 (29.4%) and 17 (10.6%) patients had moderate and severe PPM_M, respectively. Adjustment for BMI thresholds decreased the incidence of PPM_M to 31.3%, with a similar proportion of severe PPM_M (10.1%). The reported incidence of PPM after TAVI varies

between 6 - 46% for moderate PPM and 1- 15% for severe PPM [12,17-19], according to the definition used [8,20,21], the type of valve [22-24] and positioning [25,26]. The relatively high incidence of PPM_M in our study may be related to the exclusive use of balloon-expandable valves, which have higher rates of PPM compared to self-expandable valves, especially in small valves [25,27]. Moreover, use of newer balloon-expandable valves has been associated with lower paraprosthesis leak rate, but higher PPM rate compared to prior generation, due to flared inflow stent-frame morphology [28,29]. Concerns about accurate EOA measurement have led to comprehensive research using multimodality imaging and different parametric approaches to efficiently establish PPM [17,30,31]. Studies have shown a lower rate of predicted PPM based on implanted valve size or CT-measured LVOT area, which was consistent with our results and led to separate analyses of predicted and unpredicted PPM_M [8,20]. A potential cause of PPM_M overestimation may be the pressure recovery phenomenon, which can be responsible for this EOA discrepancy in relation to the patient's anatomy, especially in a small aortic root [21,30,32]. A recent study suggests that this effect may be more important in TAVI than in SAVR and with balloon-expandable valves than with self-expandable valves [31].

2. Predictors and impact of PPM

Previous studies have shown that preoperative prediction of PPM in TAVI patients based on valve type, annular size, and BSA varies from measured PPM_M, rendering EOA charts utility to predict actual PPM_M rather limited [8]. Our results are consistent with previously published data and add information regarding patients with unpredicted PPM_M.

Based on perioperative characteristics, PPM_M was predicted by BMI (higher risk per unit increase in BMI) and valve size (larger valve size protective for PPM_M). While predicted PPM_M was independently associated with BMI and valve size in a similar fashion, unpredicted PPM_M was independently associated with post-dilation (protective effect). Previous studies have shown reduced rates of moderate or severe prosthesis-patient mismatch after post-dilation, with no evidence for short-term structural deterioration of the balloon-expandable transcatheter valve [33]. Although post-dilation was associated with higher rates of early stroke, there was no significant association between post-dilation and mortality [33]. Oversizing also had a protective effect for unpredicted PPM_M but failed to be significant in the multivariate analysis. This may suggest a certain degree of under expansion, despite larger aortic root and valve size in the unpredicted PPM_M group vs. predicted PPM_M group.

In-depth analysis of postprocedural parameters revealed that significant PPM_M is associated with impaired LA function, specifically impaired left atrial reservoir function. Previous published studies suggest that LA strain was associated with a significant stepwise decrease in all stages of diastolic dysfunction, supporting LA dysfunction as a potential marker of diastolic dysfunction [34]. Furthermore, LA strain has been proven useful in the non-invasive assessment of left ventricular filling pressures [35]. In the subgroup analysis, unpredicted PPM_M was associated

with impaired LA reservoir function (lower LA-GLS values in the presence of PPM_M), while predicted PPM_M was associated with impaired LV global longitudinal strain (lower LV-GLS values in the presence of PPM_M). In other words, unpredicted PPM_M correlates with LA function impairment, while predicted PPM_M correlates with subclinical LV dysfunction. LA and LV reverse remodeling were not correlated with either of the PPM_M groups, based on 30-days echocardiography.

3. Clinical implications

Despite being a controversial parameter [8,36-38], measured PPM_M assessed by echocardiography 30 days after the procedure, crude or BMI-adjusted, appears to select a population with higher mortality risk in our study. The excess mortality associated with unpredicted PPM_M may be accounted to some extent to LA impairment, as LA reservoir dysfunction (LA-GLS) is known to be related to increased LV filling pressures [35], which are higher in the presence of PPM [39]. As previously shown in the literature, reverse LA remodeling and improvement in LA reservoir function occur post-TAVI and are independently associated with major adverse cardiac events [40]. Lack of correlation between LA and LV reverse remodeling with either of the PPM_M groups could be related to early post-procedural echocardiography, without additional echocardiographic follow-up. Furthermore, LA strain is a marker of LV diastolic dysfunction and has been proven to be a useful tool for diastolic dysfunction assessment [41], but also a measure for the non-invasive assessment of LV filling pressures [35].

While TAVI reduces afterload and improves LV remodeling recovery, myocardial fibrosis may not completely reverse after the procedure, resulting in persistent diastolic dysfunction [42]. Moderate to severe diastolic dysfunction can still be observed up to 10 years after AVR, despite significant reductions in LV mass [39]. Studies investigating the impact of mismatch on heart failure concluded that diastolic dysfunction was a predictor of mortality, independent of PPM [43]. These results are inconsistent with our findings, which prove PPM_M a predictor of adverse outcomes, irrespective of diastolic dysfunction [39,43]. Another study analyzing the effect of PPM on long-term outcomes in a large cohort of patients undergoing SAVR found no significant impact [44]. However, the definition of PPM was based only on predicted PPM, as no echocardiographic was available. Our analysis is consistent with these results; as predicted, PPM was not associated with increased all-cause mortality at 3 years. However, our study provided evidence that PPM cannot simply be prevented in the clinical setting just by relying on determining valve predicted EOA and that predicted PPM underestimated measured PPM_M. Technical adjustments such as avoidance of underexpansion, higher depth of implantation, balloon postdilation, or use of self-expandable valves could improve these results but associate additional risks and are not always anatomically feasible [45].

Nonetheless, this controversial parameter, PPM_M determined by echocardiography at 30 days post-TAVI identifies a population with higher all-cause mortality at 3 years follow-up. Although extensive echocardiographic data in our study indicate that significant PPM_M does not hinder the immediate effects of intervention, it appears to

influence the preexisting cardiac damage and contribute to other comorbid conditions that may lead to increased medium-term and potentially long-term mortality. The relatively low incidence of mortality in our study group (25 events, 15.6% at 3-year follow-up) is encouraging but limits extensive analysis. The causal relationship between PPM, left atrial function, and mortality remains yet to be determined.

4. Limitations

This is a prospective study conducted on consecutive AS patients who underwent TAVI, resulting in a heterogeneous population in terms of cardiac damage and associated comorbidities. Despite that, all patients underwent TAVI with balloon-expandable valves. One limitation of the study consisted in lack of repeat echocardiographic evaluation after the initial 1-month follow-up visit. While 3-year mortality, obtained through queries of the National Register of population records, is a robust endpoint, no information regarding cause of death was available. The findings outlined throughout our study must be interpreted in the context of a relatively small number of patients but with comprehensive advanced echocardiographic assessment and require confirmation in larger studies.

Conclusions

Our study revealed significantly worse impairment of LA function in patients with PPM_M compared to those without PPM_M on short-term follow-up, which correlated with 3-year mortality. To our knowledge, this is the first report about the effect of PPM on the LA reservoir function that impacts clinical outcomes.

Author Contributions

CAP, AC, and BAP contributed to the conception and design of the study. AC, MR, SB, RE, and CB organized the database. CAP and AC performed the statistical analysis. CAP and AC wrote the first draft of the manuscript. DC, MR, SB, RE, and CB wrote sections of the manuscript; DD, OC, SBT, VAI, and BAP made critical revisions to the paper. All authors contributed to the manuscript revision and read and approved the submitted version.

Conflicts of Interest

Nothing to declare.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Emergency Hospital of Cardiovascular Diseases “Prof. Dr. C.C. Iliescu”, Bucharest, Romania (protocol code 236/2019)

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

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Abbreviations

Aao – CT-derived aortic annulus area
 AVA – aortic valve area
 AVAi – aortic valve area index
 ASr – late diastolic strain rate
 BMI – body mass index
 BSA – body surface area
 Ca score – CT derived Calcium score
 CABG =coronary artery bypass grafting
 CAD - Coronary artery disease
 CaAd – carotid artery disease
 CKD - Chronic kidney disease
 COPD – Chronic obstructive pulmonary disease
 DM – Diabetes mellitus
 dLVOT – CT derived mean diameter LVOT
 ESr – early diastolic strain rate
 FAC – right ventricle fractional area change
 LVEF – left ventricle ejection fraction
 LV-GLS – left ventricle global longitudinal strain
 LA – left atrium
 LAAi – LA area index
 LAVi – LA volume index
 LVmi – LV mass index
 LVESVi – indexed LV end-systolic volume
 LVEDVi – indexed LV end-diastolic volume
 LA-GLS – LA global longitudinal strain
 NYHA – New York Hear Association Class
 PAD - Peripheral arterial disease
 PCI =percutaneous coronary intervention
 RA-right atrium
 RV – right ventricle
 RV-GLS – RV global longitudinal strain

RV-FWLS - RV free wall longitudinal strain

RV-IVS - RV interventricular septum strain

SSr - systolic strain rate

S`RV - peak systolic myocardial velocity at the lateral site of the tricuspid annulus

SPAP - systolic pulmonary artery pressure

TAPSE – tricuspid annular plane systolic excursion

Vmax – maximum aortic velocity

REFERENCES

1. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019; 380:1706-1715. doi:10.1056/NEJMoa1816885.
2. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019; 380:1695-1705. doi:10.1056/NEJMoa1814052.
3. Braghiroli J, Kapoor K, Thielhelm TP, Ferreira T, Cohen MG. Transcatheter aortic valve replacement in low risk patients: A review of PARTNER 3 and Evolut low risk trials. *Cardiovascular Diagnosis and Therapy* 2020. doi:10.21037/cdt.2019.09.12.
4. Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL, Takkenberg JJ, David TE, Butchart EG, Adams DH, et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. *J Thorac Cardiovasc Surg* 2008; 135:732-738. doi:10.1016/j.jtcvs.2007.12.002.
5. Capodanno D, Petronio AS, Prendergast B, Elchaninoff H, Vahanian A, Modine T, Lancellotti P, Sondergaard L, Ludman PF, Tamburino C, et al. Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: A consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J Cardiovasc Imaging* 2017; 38:3382-3390. doi:10.1093/eurheartj/ehx303.
6. Pibarot P, Magne J, Leipsic J, Côté N, Blanke P, Thourani VH, Hahn R. Imaging for predicting and assessing prosthesis-patient mismatch after aortic valve replacement. *JACC: Cardiovascular Imaging* 2019; 12. doi:10.1016/j.jcmg.2018.10.020.
7. Ternacle J, Pibarot P, Herrmann HC, Kodali S, Leipsic J, Blanke P, Jaber W, Mack MJ, Clavel MA, Salaun E, et al. Prosthesis-patient mismatch after aortic valve replacement in the PARTNER 2 trial and registry. *JACC Cardiovasc Interv* 2021; 14:1466-1477. doi:10.1016/j.jcin.2021.03.069.
8. Catalano MA, Rutkin B, Koss E, Maurer G, Berg J, Hartman A, Yu PJ. Accuracy of predicted effective orifice area in determining incidence of patient-prosthesis mismatch after transcatheter aortic valve replacement. *J Card Surg* 2021; 36:191-196. doi:10.1111/jocs.15148.
9. Bleiziffer S, Rudolph TK. Patient prosthesis mismatch after SAVR and TAVR. *Frontiers in Cardiovascular Medicine* 2022; 9. doi:10.3389/fcvm.2022.761917.
10. Herrmann HC, Daneshvar SA, Fonarow GC, Stebbins A, Vemulapalli S, Desai ND, Malenka DJ, Thourani VH, Rymer J, Kosinski AS. Prosthesis-patient mismatch in patients undergoing transcatheter aortic valve replacement: From the STS/ACC TVT Registry. *J Am Coll Cardiol* 2018; 72:2701-2711. doi:10.1016/j.jacc.2018.09.001.
11. Van Linden A, Kempfert J, Blumenstein J, Rastan A, Holzhey D, Lehmann S, Mohr FW, Walther T. Prosthesis-patient mismatch after transcatheter aortic valve implantation using the Edwards SAPIEN prosthesis. *Thorac Cardiovasc Surg* 2013; 61:414-420. doi:10.1055/s-0032-1311534.
12. Pibarot P, Weissman NJ, Stewart WJ, Hahn RT, Lindman BR, McAndrew T, Kodali SK, Mack MJ, Thourani VH, Miller DC, 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 analysis. *J Am Coll Cardiol* 2014; 64:1323-1334. doi:10.1016/j.jacc.2014.06.1195.
13. Parasca CA, Calin A, Cadil D, Mateescu A, Rosca M, Botezatu SB, Enache R, Beladan C, Ginghina C, Deleanu D, et al. Right ventricle to pulmonary artery coupling after transcatheter aortic valve implantation - determinant factors and prognostic impact. *Front Cardiovasc Med* 2023; 10:1150039. doi:10.3389/fcvm.2023.1150039.
14. Lang RM, Badano LP, Mor-Avi V, Afalalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015; 16:233-270. doi:10.1093/ehjci/jev014.
15. Lancellotti P, Pibarot P, Chambers J, Edvardsen T, Delgado V, Dulgheru R, Pepi M, Cosyns B, Dweck MR, Garbi M, 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; 17:589-590. doi:10.1093/ehjci/jev025.
16. Hahn RT, Leipsic J, Douglas PS, Jaber WA, Weissman NJ, Pibarot P, Blanke P, Oh JK. Comprehensive echocardiographic assessment of normal transcatheter valve function. *JACC Cardiovasc Imaging* 2019; 12:25-34. doi:10.1016/j.jcmg.2018.04.010.
17. Leone PP, Fazzari F, Cannata F, Sanz-Sanchez J, Mangieri A, Monti L, Cozzi O, Stefanini GG, Bragato R, Colombo A, et al. Clinical and technical challenges of prosthesis-patient mismatch after transcatheter aortic valve implantation. *Front Cardiovasc Med* 2021; 8:670457. doi:10.3389/fcvm.2021.670457.
18. Schofer N, Deuschl F, Rubsamen N, Skibowski J, Seiffert M, Voigtlander L, Schaefer A, Schneeberger Y, Schirmer J, Reichenspurner H, et al. Prosthesis-patient mismatch after transcatheter aortic valve implantation: Prevalence and prognostic impact with respect to baseline left ventricular function. *EuroIntervention* 2019; 14:1648-1655. doi:10.4244/EIJ-D-18-00827.
19. Miyasaka M, Tada N, Taguri M, Kato S, Enta Y, Otomo T, Hata M, Watanabe Y, Naganuma T, Araki M, et al. Incidence, predictors, and clinical impact of prosthesis-patient mismatch following transcatheter aortic valve replacement in Asian patients: The OCEAN-TAVI registry. *JACC Cardiovasc Interv* 2018; 11:771-780. doi:10.1016/j.jcin.2018.01.273.
20. Head SJ, Reardon MJ, Deeb GM, Van Mieghem NM, Popma JJ, Gleason TG, Williams MR, Radhakrishnan S, Fremes S, Oh JK, et al. Computed tomography-based indexed aortic annulus size to predict prosthesis-patient mismatch. *Circ Cardiovasc Interv* 2019; 12. doi:10.1161/CIRCINTERVENTIONS.118.007396.
21. Ternacle J, Guimaraes L, Vincent F, Cote N, Cote M, Lachance D, Clavel MA, Abbas AE, Pibarot P, Rodes-Cabau J. Reclassification of prosthesis-patient mismatch after transcatheter aortic valve replacement using predicted vs. measured indexed effective orifice area. *Eur Heart J Cardiovasc Imaging* 2021; 22:11-20. doi:10.1093/ehjci/jeaa235.
22. Hase H, Yoshijima N, Yanagisawa R, Tanaka M, Tsuruta H, Shimizu H, Fukuda K, Naganuma T, Mizutani K, Yamawaki M, et al. Transcatheter aortic valve replacement with Evolut R versus Sapien 3 in Japanese patients with a small aortic annulus: The OCEAN-TAVI registry. *Catheter Cardiovasc Interv* 2021; 97. doi:10.1002/ccd.29259.
23. Bleiziffer S, Hettich I, Hutter A, Wagner A, Deutsch MA, Piazza N, Lange R. Incidence and impact of prosthesis-patient mismatch after transcatheter aortic valve implantation. *J Heart Valve Dis* 2013; 22:309-316.

24. Unbehaun A, Pasic M, Drews T, Buz S, Dreyse S, Kukucka M, Mladenow A, Ivanitskaja-Kuhn E, Hetzer R. New 29-mm balloon-expandable prosthesis for transcatheter aortic valve implantation in large annuli. *Ann Thorac Surg* 2013; 95:1982-1990. doi:10.1016/j.athoracsur.2013.02.038.
25. Okuno T, Khan F, Asami M, Praz F, Heg D, Winkel MG, Lanz J, Huber A, Grani C, Raber L, et al. Prosthesis-patient mismatch following transcatheter aortic valve replacement with supra-annular and intra-annular prostheses. *JACC Cardiovasc Interv* 2019; 12:2173-2182. doi:10.1016/j.jcin.2019.07.027.
26. Voigtlander L, Kim WK, Mauri V, Gossling A, Renker M, Sugiura A, Linder M, Schmidt T, Schofer N, Westermann D, et al. Transcatheter aortic valve implantation in patients with a small aortic annulus: Performance of supra-, intra- and infra-annular transcatheter heart valves. *Clin Res Cardiol* 2021; 110:1957-1966. doi:10.1007/s00392-021-01918-8.
27. Abbas AE, Mando R, Kadri A, Khalili H, Hanzel G, Shannon F, Al-Azizi K, Waggoner T, Kassas S, Pilgrim T, 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. doi:10.1161/JAHA.120.021014.
28. Miyasaka M, Tada N, Taguri M, Kato S, Enta Y, Hata M, Watanabe Y, Naganuma T, Yamawaki M, Yamanaka F, et al. Incidence and predictors of prosthesis-patient mismatch after TAVI using SAPIEN 3 in Asian: Differences between the newer and older balloon-expandable valve. *Open Heart* 2021; 8. doi:10.1136/openhrt-2020-001531.
29. Kazuno Y, Maeno Y, Kawamori H, Takahashi N, Abramowitz Y, Babak H, Kashif M, Chakravarty T, Nakamura M, Cheng W, et al. Comparison of SAPIEN 3 and SAPIEN XT transcatheter heart valve stent-frame expansion: Evaluation using multi-slice computed tomography. *Eur Heart J Cardiovasc Imaging* 2016; 17:1054-1062. doi:10.1093/ehjci/jew032.
30. Niederberger J, Schima H, Maurer G, Baumgartner H. Importance of pressure recovery for the assessment of aortic stenosis by Doppler ultrasound. Role of aortic size, aortic valve area, and direction of the stenotic jet in vitro. *Circulation* 1996; 94:1934-1940. doi:10.1161/01.cir.94.8.1934.
31. Hatoum H, Hahn RT, Lilly S, Dasi LP. Differences in pressure recovery between balloon-expandable and self-expandable transcatheter aortic valves. *Ann Biomed Eng* 2020; 48:860-867. doi:10.1007/s10439-019-02425-8.
32. Hite A, Karabon P, Mando R, Hanzel G, Shannon F, Abbas AE. The impact of energy loss index and body mass index on prosthesis patient mismatch. *Structural Heart* 2021; 5:376-381. doi:10.1080/24748706.2021.1912444.
33. Hahn RT, Pibarot P, Webb J, Rodes-Cabau J, Herrmann HC, Williams M, Makkar R, Szeto WY, Main ML, Thourani VH, et al. Outcomes with post-dilation following transcatheter aortic valve replacement: The PARTNER I trial (placement of aortic transcatheter valve). *JACC Cardiovasc Interv* 2014; 7:781-789. doi:10.1016/j.jcin.2014.02.013.
34. Thomas L, Marwick TH, Popescu BA, Donal E, Badano LP. Left atrial structure and function, and left ventricular diastolic dysfunction: JACC state-of-the-art review. *Journal of the American College of Cardiology* 2019; 73. doi:10.1016/j.jacc.2019.01.059.
35. Singh A, Medvedofsky D, Mediratta A, Balaney B, Kruse E, Cizek B, Shah AP, Blair JE, Maffessanti F, Addetia K, et al. Peak left atrial strain as a single measure for the non-invasive assessment of left ventricular filling pressures. *Int J Cardiovasc Imaging* 2019; 35:23-32. doi:10.1007/s10554-018-1425-y.
36. Amorim PA, Diab M, Walther M, Farber G, Hagendorff A, Bonow RO, Doenst T. Limitations in the assessment of prosthesis-patient mismatch. *Thorac Cardiovasc Surg* 2020; 68:550-556. doi:10.1055/s-0038-1676814.
37. Vriesendorp MD, Deeb GM, Reardon MJ, Kiaii B, Bapat V, Labrousse L, Rao V, Sabik JF, Gearhart E, Klautz RJM. Why the categorization of indexed effective orifice area is not justified for the classification of prosthesis-patient mismatch. *J Thorac Cardiovasc Surg* 2022; 164:822-829 e826. doi:10.1016/j.jtcvs.2020.10.123.
38. Coisne A, Ninni S, Edmé JL, Modine T, Mouton S, Pilato R, Ridon H, Richardson M, Klein C, Ortmans S, et al. Obesity paradox in the clinical significance of effective prosthetic orifice area after aortic valve replacement. *JACC: Cardiovascular Imaging* 2019; 12. doi:10.1016/j.jcmg.2018.04.018.
39. Brown J, Shah P, Stanton T, Marwick TH. Interaction and prognostic effects of left ventricular diastolic dysfunction and patient-prosthesis mismatch as determinants of outcome after isolated aortic valve replacement. *Am J Cardiol* 2009; 104:707-712. doi:10.1016/j.amjcard.2009.04.035.
40. Weber J, Bond K, Flanagan J, Passick M, Petillo F, Pollack S, Robinson N, Petrossian G, Cao JJ, Barasch E. The prognostic value of left atrial global longitudinal strain and left atrial phasic volumes in patients undergoing transcatheter valve implantation for severe aortic stenosis. *Cardiology* 2021; 146:489-500. doi:10.1159/000514665.
41. Singh A, Addetia K, Maffessanti F, Mor-Avi V, Lang RM. LA strain for categorization of LV diastolic dysfunction. *JACC Cardiovasc Imaging* 2017; 10:735-743. doi:10.1016/j.jcmg.2016.08.014.
42. Aalaei-Andabili SH, Bavry AA. Left ventricular diastolic dysfunction and transcatheter aortic valve replacement outcomes: A review. *Cardiology and Therapy* 2019; 8. doi:10.1007/s40119-019-0134-5.
43. Nozohoor S, Nilsson J, Luhrs C, Roijer A, Sjogren J. Influence of prosthesis-patient mismatch on diastolic heart failure after aortic valve replacement. *Ann Thorac Surg* 2008; 85:1310-1317. doi:10.1016/j.athoracsur.2007.12.069.
44. Dismorr M, Glaser N, Franco-Cereceda A, Sartipy U. Effect of prosthesis-patient mismatch on long-term clinical outcomes after bioprosthetic aortic valve replacement. *J Am Coll Cardiol* 2023; 81:964-975. doi:10.1016/j.jacc.2022.12.023.
45. Pibarot P, Magne J, Leipsic J, Côté N, Blanke P, Thourani VH, Hahn R. Imaging for predicting and assessing prosthesis-patient mismatch after aortic valve replacement. *JACC: Cardiovascular Imaging* 2019; 12:149-162. doi:10.1016/j.jcmg.2018.10.020.

Appendix 1. Echocardiographic characteristics before TAVI according to PPM_M group

Echocardiographic characteristics	All patients (n=160)	PPM _M group (n=64)	No-PPM _M group (n=96)	p-value
Aortic stenosis severity				
Vmax, m/s	4.6±0.8	4.6±0.8	4.6±0.7	0.704
Mean gradient, mmHg	56.7 ±18.9	57.4±19.4	56.3±18.6	0.708
AVA, cm ²	0.73±0.3	0.67±0.3	0.77±0.3	0.039
AVAi, cm ² /m ²	0.41±0.2	0.37±0.2	0.44±0.2	0.015
dLVOT, mm		21.8±2.5	22.3±2.3	0.244
Bicuspid valve AS	30 (20.0%)	11 (19.3%)	19 (20.4%)	0.866
Aortic regurgitation	1.2±0.7	1.2±0.6	1.3±0.7	0.486
Left ventricle				
LVEF, %	51.8±11.8	51.5±12.6	52.0±11.2	0.781
LVESVi, ml/m ²	27.9±16.5	27.2±18.2	28.3±15.3	0.677
LVEDVi, ml/m ²	56.3±20.0	54.7±20.0	57.4±19.5	0.416
LVSVi, ml/m ²	27.8±8.6	27.0±8.7	28.4±8.6	0.330
LV-GLS, %	-12.3±4.2	-11.9±4.0	-12.6±4.3	0.276
LVMi, g/m ²	178.7±48.9	174.7±46	181.4±50	0.396
E/A	1.2±0.8	1.3±0.8	1.1±0.8	0.227
E/e' septal	22.3±11.7	23.2±13.1	21.6±10.7	0.420
E/e' lateral	15.9±9.6	17.0±11.3	15.0±8.1	0.217
E/e' average	17.2±8.3	18.1±9.2	16.6±7.4	0.250
Mitral regurgitation	1.3±0.6	1.3±0.6	1.3±0.6	0.735
Left atrium				
LAAi, cm ² /m ²	14.9±3.2	14.8±2.4	15.0±3.7	0.783
LAVi, ml/m ²	53.8±18.4	53.0±13.1	54.4±21.2	0.607
LA-GLS, % (LA _g)	12.3±6.7	10.2±5.5	13.8±7.1	0.001
SSr, s ⁻¹	0.66±0.6	0.50±0.5	0.76±0.6	0.007
ESr, s ⁻¹	-0.35±0.5	-0.31±0.5	-0.38±0.5	0.385
ASr, s ⁻¹	-0.88±0.6	-0.71±0.6	-0.97±0.6	0.033
Right ventricle				
TAPSE, cm	2.0±0.4	2.0±0.4	2.0±0.4	0.968
S'RV, cm/s	10.5±3.0	10.4±2.9	10.5±3.1	0.745
SPAP, mmHg	40.5±15	42.0±16.3	37.8±14.3	0.244
FAC, %	40.7±8.1	40.7±8.1	40.5±8.0	0.740
RV-GLS, %	-16.8±6.1	-16.1±5.7	-17.0±6.3	0.185
RV-FWLS, %	-21.5±7.6	-20.4±7.6	-22.0±7.5	0.071
RV-IVS, %	-11.0±6.1	-9.2±6.8	-12.1±5.3	0.006
RA, mm	37.5±8.5	38.5±8.5	36.9±8.5	0.306
RV, mm	34.5±6.1	35.4±5.6	34.1±6.4	0.352

Values are mean ±SD, n (%), or median (interquartile range).

Vmax – maximum aortic velocity, AVA – aortic valve area, AVAi – aortic valve area index, dLVOT – diameter of left ventricle outflow tract, LVEF – left ventricle ejection fraction, LV-GLS – left ventricle global longitudinal strain, LA – left atrium, LAAi – LA area index, LAVi – LA volume index, LVMi – LV mass index, LA-GLS – LA global longitudinal strain, SSr - systolic strain rate, ESr – early diastolic strain rate, ASr – late diastolic strain rate, TAPSE – tricuspid annular plane systolic excursion, S'RV - peak systolic myocardial velocity at the lateral site of the tricuspid annulus, SPAP - systolic pulmonary artery pressure, FAC – right ventricle fractional area change, RA-right atrium, RV – right ventricle RV-GLS – RV global longitudinal strain, RV-FWLS - RV free wall longitudinal strain, RV-IVS - RV interventricular septum strain.

Appendix 2. Computed tomography characteristics before TAVI according to PPM_M group

Angio-CT characteristics	All patients (n=160)	PPM _M group (n=64)	No-PPM _M group (n=96)	p-value
A _{Ao} , mm ²	473.7±90	452.4±95	487.8±84	0.018
d A _{Ao} , mm	24.4±2.4	23.9±2.5	24.8±2.2	0.012
Annular eccentricity	0.23±0.06	0.23±0.05	0.23±0.07	0.367
A _{LVOT} , mm ²	468.9±101	450.1±105	481.4±97	0.061
d A _{LVOT} , mm	24.3±2.6	23.8±2.8	24.6±2.5	0.048
Ca score	1112.5±618	1051.8±523	1152.5±673	0.329
LCC Ca score	335.5±226	294±182	362±248	0.067
RCC Ca score	321.1±214	323±220	319±211	0.922
NCC Ca score	457.7±302	426±265	478±324	0.302
Severe leaflet calcification	22 (14.6%)	7 (11.7%)	15 (16.5%)	0.412
Severe annular calcification	20 (13.2%)	7 (11.7%)	13 (14.3%)	0.642
Severe LVOT calcification	17 (11.3%)	7 (11.7%)	10 (11.1%)	0.916
hLCA	14.3±3.7	13.5±3.5	14.9±3.8	0.032
hRCA	18.0±2.9	17.3±2.9	18.5±2.9	0.017
hSTJ	23.1±3.6	22.9±2.9	23.3±3.9	0.494
NCC sinus	32.8±4.1	31.9±4.1	33.3±3.9	0.285
LCC sinus	32.6±4.1	32.3±4.1	32.9±4.2	0.038
RCC sinus	30.5±3.9	29.6±3.8	31.0±4.0	0.030
Bicuspid valve	30 (19.9%)	12 (20%)	18 (19.8%)	0.974
STJ	28.4±4.0	27.8±3.8	28.7±4.1	0.185
AscAo	35.5±5.1	35.1±4.4	35.8±5.5	0.403

A_{Ao} - Aortic annular area, dA_{Ao} – Aortic annular area-derived diameter, Ca score – CT derived Calcium score, LCC – left coronary cusp, NCC – non-coronary cusp, RCC – right coronary cusp.

Appendix 3. Procedural characteristics according to PPM_M group

Periprocedural characteristics	All patients (n=160)	PPM _M group (n=64)	No-PPM _M group (n=96)	p-value
Valve no.	25.4±2.5	24.7±2.6	25.9±2.3	0.004
20/23	60 (37.6%)	33 (51.6%)	27 (28.1%)	0.010
26	65 (40.6%)	21 (32.8%)	44 (45.8%)	
29	35 (21.9%)	10 (15.6%)	25 (26.0%)	
Oversizing (%)	9.0±11.2	7.6±10.1	10.0±11.9	0.213
Oversizing ≥15%	45 (29.8%)	16 (26.7%)	29 (31.9%)	0.494
Oversizing <0%	28 (18.5%)	12 (20.0%)	16 (17.6%)	0.708
Pre-dilation	20 (13.2%)	7 (11.7%)	13 (14.3%)	0.642
Post-dilation	33 (20.6%)	15 (23.4%)	18 (18.8%)	0.476

Appendix 4. Echocardiographic characteristics before TAVI according to **predicted vs. unpredicted PPM_M**

Echocardiographic characteristics	Unpredicted PPM _M group (n=39)	Predicted PPM _M group (n=25)	p-value
Aortic stenosis severity			
Vmax, m/s	4.5±0.8	4.8±0.8	0.104
Mean gradient, mmHg	55.0±18.9	61.3±19.9	0.203
AVA, cm ²	0.69±0.3	0.65±0.2	0.618
AVAi, cm ² /m ²	0.38±0.2	0.35±0.1	0.305
Aortic regurgitation	1.2±0.6	1.2±0.8	0.785
Left ventricle			
LVEF, %	49.1±13.3	55.3±10.7	0.055
LVESVi, ml/m ²	31.3±20.6	20.7±11.2	0.010
LVEDVi, ml/m ²	59.9±23.0	46.7±12.8	0.005
LVSVi, ml/m ²	28.1±8.6	25.4±8.8	0.221
LV-GLS, %	-11.6±4.3	-12.3±3.4	0.482
LVMi, g/m ²	178.4±42	169.0±52	0.432
E/A	1.5±0.9	1.1±0.5	0.103
E/e' septal	24.0±12.9	19.3±13.6	0.525
E/e' average	19.3±10.3	16.2±6.9	0.186
Mitral regurgitation	1.4±0.7	1.1±0.4	0.041
Left atrium			
LAAi, cm ² /m ²	15.4±2.5	14.0±2.0	0.027
LAVi, ml/m ²	55.2±13.7	49.6±11.6	0.093
LA-GLS, % (LA _g)	-9.6±4.8	-11.2±6.4	0.236
SSr, s ⁻¹	0.45±0.5	0.58±0.5	0.305
ESr, s ⁻¹	-0.32±0.5	-0.30±0.5	0.927
ASr, s ⁻¹	-0.67±0.6	-0.76±0.7	0.614
Right ventricle			
TAPSE, cm	2.0±0.4	2.1±0.4	0.711
S'RV, cm/s	10.0±2.6	11.0±3.0	0.134
PASP, mmHg	42.3±16.7	39.2±15.2	0.459
FAC, %	40.5±8.4	41.7±8.4	0.581
RV-GLS, %	-15.6±5.5	-16.5±5.8	0.555
RV-FWLS, %	-20.3±7.4	-20.0±7.3	0.876
RV-IVS, %	-10.2±5.3	-8.0±8.1	0.221
RA, mm	39.1±9.8	37.1±6.5	0.373
RV, mm	35.0±6.0	35.2±6.7	0.916

Values are mean ±SD, n (%), or median (interquartile range).

Vmax – maximum aortic velocity, AVA – aortic valve area, AVAi – aortic valve area index, LVEF – left ventricle ejection fraction, LV-GLS – left ventricle global longitudinal strain, LA – left atrium, LAAi – LA area index, LAVi – LA volume index, LVMi – LV mass index, LA-GLS – LA global longitudinal strain, SSr – systolic strain rate, ESr – early diastolic strain rate, ASr – late diastolic strain rate, TAPSE – tricuspid annular plane systolic excursion, S'RV – peak systolic myocardial velocity at the lateral site of the tricuspid annulus, PASP – systolic pulmonary artery pressure, FAC – right ventricle fractional area change, RA – right atrium, RV – right ventricle RV-GLS – RV global longitudinal strain, RV-FWLS – RV free wall longitudinal strain, RV-IVS – RV interventricular septum strain.

Appendix 5. Computed tomography characteristics before TAVI according to **predicted vs. unpredicted PPM_M**

Angio-CT characteristics	PPM _M group (n=39)	No-PPM _M group (n=25)	p-value
A _{Ao} , mm ²	480.3±93	408.5±86	0.004
d A _{Ao} , mm	24.6±2.4	22.7±2.3	0.003
Annular eccentricity	0.23±0.05	0.23±0.07	0.886
A _{LVOT} , mm ²	479.8±101	404.4±96	0.005
d A _{LVOT}	24.6±2.6	22.5±2.5	0.004
Ca score	1087.4±491	998.4±574	0.523
LCC Ca score	309±174	271±195	0.440
RCC Ca score	352±219	280±219	0.218
NCC Ca score	426±251	426±291	0.994
Severe leaflet calcification	5 (13.9%)	2 (8.3%)	0.691
Severe annular calcification	4 (11.1%)	3 (12.5%)	1.000
Severe LVOT calcification	4 (11.1%)	3 (12.5%)	1.000
hLCA	13.5±3.7	13.6±3.4	0.945
hRCA	17.5±2.5	17.1±3.4	0.551
hSTJ	23.2±2.8	22.4±3.1	0.270
NCC sinus	32.8±3.9	30.5±4.1	0.033
LCC sinus	33.1±3.9	30.9±3.9	0.037
RCC sinus	30.3±3.7	28.6±3.8	0.099
Bicuspid valve	9 (25.0%)	3 (12.5%)	0.329
STJ	28.3±4.1	27.1±3.3	0.230
AscAo	35.4±4.5	34.7±4.2	0.569

A_{Ao} - Aortic annular area, dA_{Ao} – Aortic annular area-derived diameter, Ca score – CT derived Calcium score, LCC – left coronary cusp, NCC – non-coronary cusp, RCC – right coronary cusp.

Appendix 6. Procedural characteristics according to **predicted vs. unpredicted PPM_M**

Periprocedural characteristics	Unpredicted PPM _M group (n=39)	Predicted PPM _M group (n=25)	p-value
Valve no.	25.5±2.3	23.5±2.6	0.003
20/23	13 (33.4%)	20 (80.0%)	0.001
26	19 (48.7%)	2 (8.0%)	
29	7 (17.9%)	7 (12.0%)	
Oversizing (%)	5.7±10.0	10.5±9.8	0.069
Oversizing ≥15%	8 (33.3%)	8 (22.2%)	0.383
Oversizing <0%	3 (12.5%)	9 (25.0%)	0.329
Predilatation	4 (10.3%)	3 (10.3%)	1.000
Postdilatation	12 (48.0%)	3 (7.7%)	<0.001

Appendix 7. Echocardiographic differences after TAVI according to **predicted vs. unpredicted PPM_M**

Echocardiographic parameters	Unpredicted PPM _M group (n=39)	Predicted PPM _M group (n=25)	p-value
Aortic stenosis severity			
Vmax, m/s	2.3±0.6	2.5±0.3	0.223
Mean gradient, mmHg	13.6±6.8	14.4±4.1	0.616
AVA, cm ²	1.3±0.3	1.4±0.6	0.265
AVAi, cm ² /m ²	0.7±0.2	0.7±0.1	0.871
Aortic regurgitation	0.7±0.6	1.0±0.8	0.165
Left ventricle			
LVEF, %	52.3±9.6	56.4±10.3	0.116
LV-GLS, %	-12.8±4.0	-15.8±4.2	0.009
LVMi, g/m ²	152.9±44	144.7±40	0.451
LVESVi, ml/m ²	26.2±15.1	18.2±9.3	0.012
LVEDVi, ml/m ²	54.7±23.7	41.9±15.1	0.011
LVSVi, ml/m ²	28.1±11.8	23.1±8.9	0.072
E/A	1.0±0.4	1.1±0.3	0.578
E/e' septal	21.2±9.1	19.4±10.7	0.490
E/e' average	17.3±7.1	13.9±5.7	0.061
Mitral regurgitation	1.2±0.5	1.0±0.4	0.066
Left Atrium			
LAAi, cm ² /m ²	14.4±2.4	13.3±2.1	0.077
LAVi, ml/m ²	49.1±12.9	45.1±11.2	0.204
LA-GLS, % (LA _g)	-13.2±5.2	-14.4±7.4	0.456
SSr, s ⁻¹	1.1±2.7	0.8±0.4	0.496
ESr, s ⁻¹	-0.7±0.5	-0.5±0.6	0.311
ASr, s ⁻¹	-1.0±0.6	-0.9±0.6	0.569
Right ventricle			
TAPSE, cm/s	21.2±3.8	21.5±3.7	0.801
S'RV, cm/s	11.5±2.5	12.2±2.6	0.257
PASP, mmHg	35.3±10.5	34.2±15.2	0.734
FAC, %	43.0±8.1	42.5±8.4	0.822
RV-GLS, %	-18.3±6.0	-18.0±5.9	0.842
RV-FWLS, %	-22.7±8.5	-22.1±7.3	0.789
RV-IVS, %	-12.5±5.5	-13.4±5.1	0.595
RA, mm	36.7±6.3	37.9±6.9	0.882
RV, mm	34.3±5.8	34.9±6.4	0.713

Values are mean ±SD, n (%), or median (interquartile range).

Vmax – maximum aortic velocity, AVA – aortic valve area, AVAi – aortic valve area index, LVEF – left ventricle ejection fraction, LV-GLS – left ventricle global longitudinal strain, LA – left atrium, LAAi – LA area index, LAVi – LA volume index, LVMi – LV mass index, LA-GLS – LA global longitudinal strain, SSr – systolic strain rate, ESr – early diastolic strain rate, ASr – late diastolic strain rate, TAPSE – tricuspid annular plane systolic excursion, S'RV – peak systolic myocardial velocity at the lateral site of the tricuspid annulus, PASP – systolic pulmonary artery pressure, FAC – right ventricle fractional area change, RA – right atrium, RV – right ventricle RV-GLS – RV global longitudinal strain, RV-FWLS – RV free wall longitudinal strain, RV-IVS – RV interventricular septum strain.