


# Reclassification of prosthesis–patient mismatch after transcatheter aortic valve replacement using predicted vs. measured indexed effective orifice area

Julien Ternacle<sup>1,2,3</sup>, Leonardo Guimaraes<sup>1</sup>, Flavien Vincent<sup>1,4</sup>, Nancy Côté<sup>1</sup>,  
Mélanie Côté<sup>1</sup>, Dominique Lachance<sup>1</sup>, Marie-Annick Clavel<sup>1</sup>, Amr E. Abbas<sup>5,6</sup>,  
Philippe Pibarot <sup>1\*</sup>, and Josep Rodés-Cabau<sup>1</sup>

<sup>1</sup>Institut Universitaire de Cardiologie et de Pneumologie de Québec- Université Laval/Québec Heart and Lung Institute, Laval University, 2725 Chemin Sainte-Foy, Québec city, Québec G1V-4G5, Canada; <sup>2</sup>Cardiology Department, Expert Valve Center, Henri Mondor hospital, 51 avenue du Maréchal de Lattre de Tassigny, 94000, Créteil, France; <sup>3</sup>INSERM Unit U955, Team 8, Paris-Est Creteil University, Val-de-Marne, 8 rue du Général Sarraill, 94010, Créteil, France; <sup>4</sup>Département de cardiologie, CHU de Lille, Institut Cœur Poumon, Université de Lille, INSERM U1011, Institut Pasteur de Lille, EGID, Boulevard du Professeur Jules Leclercq, 59000 Lille, France; <sup>5</sup>Oakland University William Beaumont School of Medicine, Auburn Hills, 586 Pioneer Dr, Rochester, MI 48309, USA; and <sup>6</sup>Beaumont Health, 3601 W 13 Mile Rd, Royal Oak, MI 48073, USA

Received 8 April 2020; editorial decision 16 July 2020; online publish-ahead-of-print 30 September 2020

## Aims

The objective was to compare the incidence and impact on outcomes of measured (PPM<sub>M</sub>) vs. predicted (PPM<sub>P</sub>) prosthesis–patient mismatch following transcatheter aortic valve replacement (TAVR).

## Methods and results

All consecutive patients who underwent TAVR between 2007 and 2018 were included. Effective orifice area (EOA) was measured by Doppler-echocardiography using the continuity equation and predicted according to the normal reference for each model and size of valve. PPM was defined using EOA indexed (EOAi) to body surface area as moderate if  $\leq 0.85$  cm<sup>2</sup>/m<sup>2</sup> and severe if  $\leq 0.65$  cm<sup>2</sup>/m<sup>2</sup> (respectively,  $\leq 0.70$  and  $\leq 0.55$  cm<sup>2</sup>/m<sup>2</sup> if body mass index  $\geq 30$  kg/m<sup>2</sup>). The outcome endpoints were high residual gradient ( $\geq 20$  mmHg) and the composite of cardiovascular mortality and hospital readmission for heart failure at 1 year. Overall, 1088 patients underwent a TAVR (55% male, age  $79.1 \pm 8.4$  years, and STS score  $6.6 \pm 4.7\%$ ); balloon-expandable device was used in 83%. Incidence of moderate (10% vs. 27%) and severe (1% vs. 17%) PPM was markedly lower when defined by predicted vs. measured EOAi ( $P < 0.001$ ). Balloon-expandable device implantation (OR: 1.90,  $P = 0.029$ ) and valve-in-valve procedure ( $n = 118$ ; OR: 3.21,  $P < 0.001$ ) were the main factors associated with PPM occurrence. Compared with measured PPM, predicted PPM showed stronger association with high residual gradient. Severe measured or predicted PPM was not associated with clinical outcomes.

## Conclusion

The utilization of the predicted EOAi reclassifies the majority of patients with PPM to no PPM following TAVR. Compared with measured PPM, predicted PPM had stronger association with haemodynamic outcomes, while both methods were not associated with clinical outcomes.

## Keywords

aortic stenosis • transcatheter aortic valve replacement • prosthesis–patient mismatch • measured effective orifice area • predicted effective orifice area • outcomes

\*Corresponding author. Tel: +1 (418) 656 8711; Fax: +1 (418) 656 4715. E-mail: philippe.pibarot@med.ulaval.ca

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2020. For permissions, please email: journals.permissions@oup.com.

## Introduction

Prosthesis–patient mismatch (PPM) consists in a prosthesis with normal function but which effective orifice area (EOA) is too small in relation to patient's body surface area (BSA) thus resulting in the occurrence of elevated transprosthetic pressure gradients. After surgical aortic valve replacement (SAVR), the incidence of overall PPM ranges from 20% to 50% and that of severe PPM from 5% to 25%.<sup>1–3</sup> In SAVR series, severe PPM has been associated with worse post-operative functional status, smaller LV mass regression, and higher risk of mortality and heart failure (HF) rehospitalization.<sup>2,4–6</sup> A significant but weaker association was also reported between moderate PPM and outcomes in SAVR series, particularly in the subset of patients with pre-existing LV systolic dysfunction.<sup>1,4,7</sup> The incidence of overall and severe PPM is generally lower with transcatheter aortic valve replacement (TAVR) vs. SAVR<sup>8–12</sup> but it, nonetheless, remains relatively high (5–36%, for severe PPM).<sup>8,9,13</sup> Furthermore, conflicting results have been reported with regards to the association of severe PPM with outcomes following TAVR. Indeed, several studies found no association<sup>9,13,14</sup> with mortality or re-hospitalization, whereas others found a modest association<sup>15,16</sup> or an association only in specific subsets of patients.<sup>10</sup>

The discrepancies observed between TAVR and SAVR series with regard to the impact of PPM on outcomes may, at least in part, be related to differences in the methods used to define PPM. Indeed, the majority of the SAVR studies have used the predicted indexed EOA (EOAi) to define PPM, which is calculated by dividing the normal reference value of EOA for the model and size of the prosthetic valve by the patient's BSA. On the other hand, all TAVR studies to date have used the EOAI measured by Doppler-echocardiography to identify PPM.

We hypothesized that the predicted EOAI is a more robust parameter to determine the true incidence of PPM. The objective of this study was to compare the incidence and association with haemodynamic and clinical outcomes of PPM defined using the measured vs. predicted EOAI following TAVR.

## Methods

### Study population

All patients with severe aortic stenosis (AS) or failed bioprosthesis who underwent TAVR between May 2007 and December 2018, at the Quebec Heart and Lung Institute (Institut Universitaire de Cardiologie et de Pneumologie de Québec-Université Laval, Québec, QC, Canada) were included in this retrospective study. Severe AS was defined by an aortic valve area  $<1.0$  cm<sup>2</sup>, a mean gradient  $\geq 40$  mmHg, and/or a peak aortic velocity  $\geq 4$  m/s.<sup>17,18</sup> The final decision to perform a TAVR was by the local Heart Team as recommended in the guidelines.<sup>17,18</sup> Only patients who received Edwards Lifesciences (Sapien, Sapien XT, Sapien 3, Irvine, CA, USA) or Medtronic (CoreValve, CoreValve EvolutR, Inc., Minneapolis, MN, USA) were included in the study. We excluded (Supplementary data online, Figure S1): (i) patients ( $n = 43$ , 3.6%) who received other models of valves, (ii) patients with missing echocardiography at discharge and 30-day follow-up ( $n = 25$ , 2.1%), and (iii) patients lost to follow-up ( $n = 24$ , 2.0%). The patients gave their consent for the procedure, and the study protocol was approved by our institution review board and ethics committee. The data, analytic methods, and

materials of this study will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

### Definition of PPM

Two methods were used to define PPM:

- Measured EOAI: The EOA was measured at discharge transthoracic echocardiogram using the continuity equation.<sup>19,20</sup> The diameter of the left ventricular outflow tract was measured just below the left ventricular border of the transcatheter valve stent from outer-to-outer border of the stent.<sup>19</sup> The sample volume of pulse-wave Doppler was positioned just apical to the prosthesis stent at the same level of the measured of the left ventricular outflow tract diameter. The EOA value was then indexed (EOAI) to BSA calculated with the Dubois formula.
- Predicted EOAI: The predicted EOA was obtained from the published normal reference values of EOA for each model and size of transcatheter valve (Supplementary data online, Table S1).<sup>21</sup> The predicted EOA was then indexed to BSA.

For both methods (measured and predicted), PPM was defined as none if EOAI was  $>0.85$  cm<sup>2</sup>/m<sup>2</sup>, moderate if  $>0.65$  and  $\leq 0.85$  cm<sup>2</sup>/m<sup>2</sup>, and severe if  $\leq 0.65$  cm<sup>2</sup>/m<sup>2</sup>. Furthermore, lower cut-off values of EOAI were used in obese patients [body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>] as previously recommended<sup>20</sup>: none if EOAI  $>0.70$  cm<sup>2</sup>/m<sup>2</sup>, moderate if  $>0.55$  and  $\leq 0.70$  cm<sup>2</sup>/m<sup>2</sup>, and severe if  $\leq 0.55$  cm<sup>2</sup>/m<sup>2</sup>.

### Follow-up and outcomes

The primary endpoint was a composite of cardiovascular mortality and hospital readmission for HF at 1 year after TAVR. Secondary endpoints included: 30-day all-cause mortality, 1-year cardiovascular mortality, 1-year all-cause mortality, and the composite of mortality and HF readmission, and long-term (until to 8 years) all-cause mortality. All events were classified according to VARC-2 criteria.<sup>22</sup>

### Statistical analysis

Continuous data were presented as mean  $\pm$  SD, or as median (interquartile range) when distribution was skewed. Categorical data were presented as percentages and fraction of occurrence. Group comparisons were analysed with the  $\chi^2$  test or Fisher's exact test, as appropriate, for categorical variables; the Student's *t*-test or Wilcoxon rank sum for continuous variables. Paired comparisons were performed using paired *t*-test or McNemar's test when appropriate. Logistic regression was used to determine factors associated with measured (PPM<sub>M</sub>) or predicted (PPM<sub>P</sub>) PPM. A non-linear curve regression analysis was used to evaluate the correlation between mean transprosthetic gradient and measured or predicted EOAI. A Cox proportional hazards model was performed to determine factors associated with clinical outcomes. Kaplan–Meier estimates and log-rank test were used to compare incidence of outcomes over 1 year stratified according to presence or absence of PPM and severity of PPM (none, moderate, or severe) using both measured and predicted EOAI. Multivariable analysis was performed with the Cox proportional hazards model and included all variables with a *P*-value  $<0.10$  on univariable analysis. Incidence and association with outcomes of PPM (measured or predicted) were analysed in the total cohort and also separately in the native TAVR and valve-in-valve sub-cohorts. All statistical analyses were performed using SPSS version 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Macintosh, Version 20.0. Armonk, NY, USA) and a *P* value  $<0.05$  was considered statistically significant.

## Results

### Baseline and procedural characteristics

Overall, 1088 patients (55% male and age  $79.1 \pm 8.4$  years) were included in the study (Supplementary data online, Table S2). The mean gradient was  $41 \pm 17$  mmHg, LVEF:  $53\% \pm 13\%$ , and STS score:  $6.6\% \pm 4.7\%$ . Of note, 50% of patients were in low-flow state ( $SV_i \leq 35$  mL/m<sup>2</sup>). Procedural and device characteristics are detailed in Supplementary data online, Tables S1 and S3. The overall procedural success was 96%. The large majority of patients (83%) received balloon-expandable valves. Rate of procedural death and complications was low (Supplementary data online, Table S3): death: 0.8%, coronary obstruction: 0.6%, annulus rupture: 0.4%, and conversion to surgery: 1.5%.

### Incidence of PPM using the measured EOAi (PPM<sub>M</sub>)

Echocardiographic data at discharge are detailed in Supplementary data online, Table S3 and Table 1. The measured EOA was  $1.54 \pm 0.5$  cm<sup>2</sup>, mean gradient  $11 \pm 6$  mmHg, with 9% of patients having high residual gradient ( $\geq 20$  mmHg). Only 4% of the patients had moderate or severe paravalvular regurgitation. According to the measured EOAi, 30% had moderate PPM<sub>M</sub> and 21% severe PPM<sub>M</sub> (overall 51%, Table 1 and Figure 1A). After adjustment for obesity, severe PPM was observed in 17% of patients ( $P < 0.001$  vs. unadjusted cut-off values of EOAi). The incidence of severe PPM<sub>M</sub> was higher in the valve-in-valve (42%) vs. the native TAVR (19%) sub-cohort (Supplementary data online, Tables S4 and S5 and Figure 1B and C).

### Incidence of PPM using the predicted EOAi (PPM<sub>P</sub>)

The predicted EOA ( $1.72 \pm 0.2$  cm<sup>2</sup>) and EOAi ( $0.96 \pm 0.2$  cm<sup>2</sup>/m<sup>2</sup>) were larger than the measured EOA and EOAi, respectively ( $P < 0.001$ , Table 1). According to the predicted EOAi, 18% had moderate PPM<sub>P</sub> and 2% had severe PPM<sub>P</sub> (overall 20%, Table 1 and Figure 1A). After adjustment for obesity, severe PPM<sub>P</sub> was observed in only 1% of patients ( $P < 0.001$  vs. unadjusted cut-off values of EOAi). The incidence of PPM was thus markedly lower with predicted EOAi vs. measured EOAi. Eighty-three percent ( $n = 401/482$ )

of patients with any degree of PPM and 76% ( $n = 140/185$ ) of patients with severe PPM based on measured EOAi were reclassified to no PPM with the use of predicted EOAi. In the native TAVR sub-cohort, the incidence of severe PPM<sub>P</sub> adjusted for obesity was very low: 0.1% vs. 15% for PPM<sub>M</sub> (Supplementary data online, Table S4 and Figure 1B). In the valve-in-valve sub-cohort, the incidence of severe PPM<sub>P</sub> adjusted for obesity was 8% vs. 36% for PPM<sub>M</sub> (Supplementary data online, Table S5 and Figure 1C).

### Risk factors associated with PPM

Factor associated with measured and predicted severe PPM (adjusted for obesity) are presented in Supplementary data online, Table S6. Factors independently associated with severe PPM<sub>M</sub> were: male [odds ratio (OR): 1.86; 95% CI (1.21–2.87);  $P = 0.005$ ], BMI [OR: 1.04; 95% CI (1.01–1.06);  $P = 0.006$ ], valve-in-valve procedure [OR: 3.21; 95% CI (1.95–5.29);  $P < 0.001$ ], device size [OR: 0.90; 95% CI (0.82–0.99);  $P = 0.030$ ], and the implantation of a balloon-expandable device [OR: 1.90; 95% CI (1.07–3.37);  $P = 0.029$ ]. Factors associated with severe PPM<sub>P</sub> were valve-in-valve procedure and prosthesis size in univariable analysis, but the multivariable analysis was not feasible because of the small number of patients ( $n = 11$ ).

### Association of PPM<sub>M</sub> and PPM<sub>P</sub> with haemodynamic outcomes

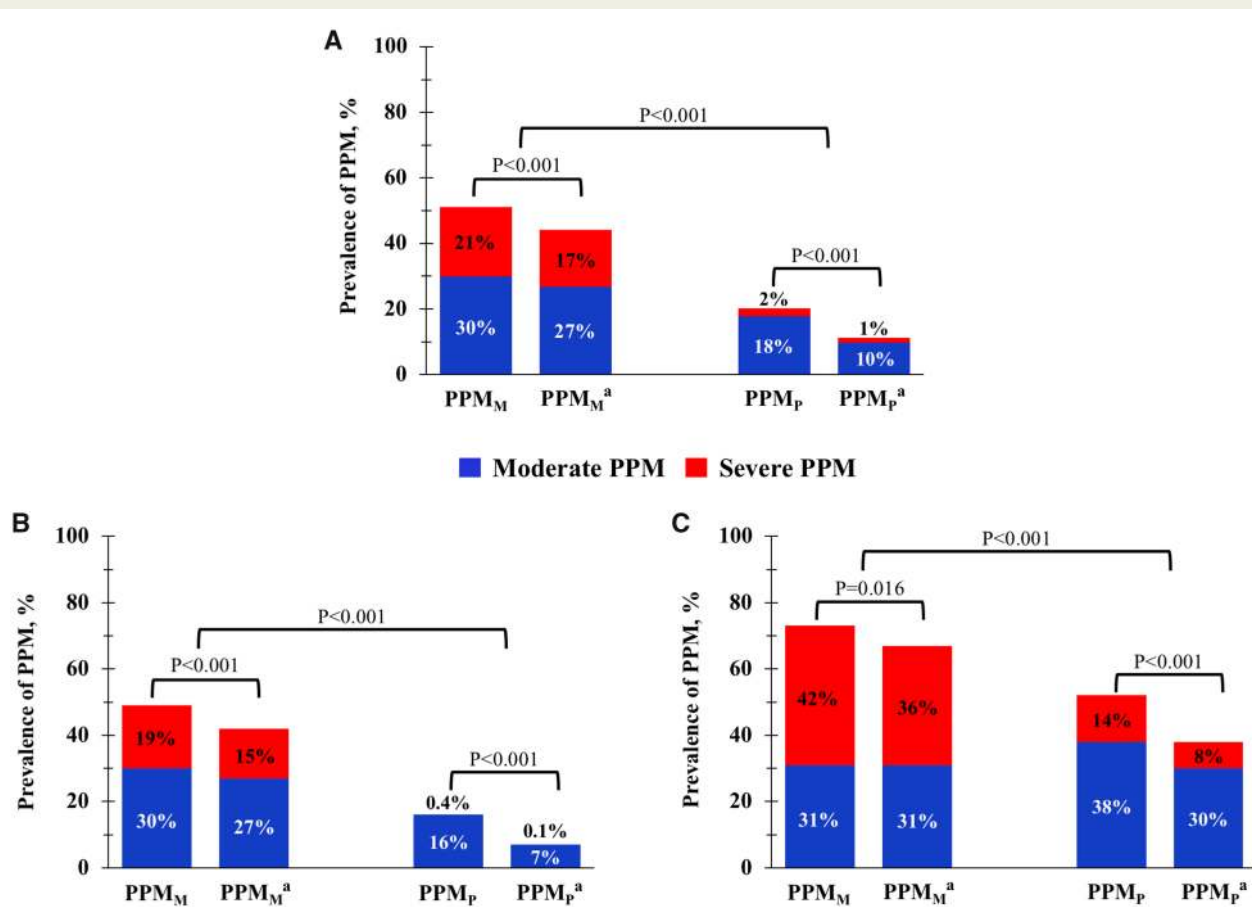
The correlation between EOAi and mean transprosthetic gradient was significantly ( $P < 0.001$ ) stronger when using the predicted EOAi vs. the measured EOAi, both in native and valve-in-valve patients (Supplementary data online, Figure S2). Patients with severe PPM<sub>M</sub> had 1.3-fold higher mean gradient compared with those with no severe PPM<sub>M</sub> ( $14 \pm 8$  vs.  $11 \pm 5$  mmHg,  $P < 0.001$ , Figure 2A), whereas patients with severe PPM<sub>P</sub> had 2.2-fold higher gradient compared with those with no severe PPM<sub>P</sub> ( $23 \pm 7$  vs.  $11 \pm 6$  mmHg,  $P < 0.001$ , Figure 2B). Sixty-four percent of patients with severe PPM<sub>P</sub> had high residual mean gradient vs. 18% of those with severe PPM<sub>M</sub> ( $P < 0.001$ , Figure 2C).

**Table 1** Incidence of PPM at discharge using measured vs. predicted EOA for definition of PPM

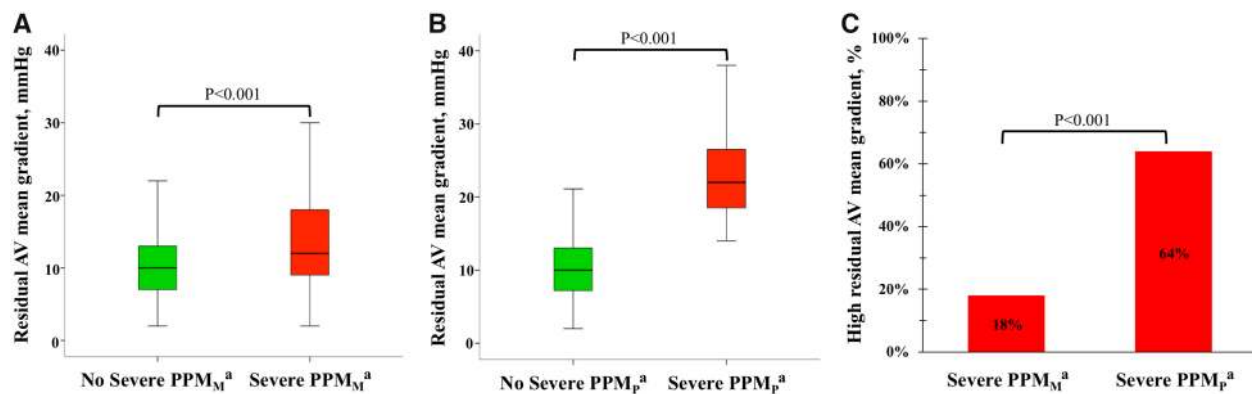
Parameters	Measured PPM ( $n = 1088$ )	Predicted PPM ( $n = 1088$ )	P value
EOA (cm <sup>2</sup> )	$1.54 \pm 0.5$	$1.72 \pm 0.2$	<0.001
EOAi (cm <sup>2</sup> /m <sup>2</sup> )	$0.87 \pm 0.3$	$0.96 \pm 0.2$	<0.001
Any PPM, N (%)	561 (51)	222 (20)	<0.001
Any PPM adjusted for obesity <sup>a</sup> , N (%)	482 (44)	115 (11)	<0.001
Moderate PPM, N (%)	330 (30)	201 (18)	<0.001
Moderate PPM adjusted for obesity <sup>a</sup> , N (%)	297 (27)	104 (10)	<0.001
Severe PPM, N (%)	231 (21)	21 (2)	<0.001
Severe PPM adjusted for obesity <sup>a</sup> , N (%)	185 (17)	11 (1)	<0.001

EOA, effective orifice area; EOAi, effective orifice area indexed to body surface area; PPM, prosthesis–patient mismatch.

<sup>a</sup>Any and moderate PPM defined by an EOAi  $\leq 0.70$  cm<sup>2</sup>/m<sup>2</sup>, and severe PPM defined by an EOAi  $\leq 0.55$  cm<sup>2</sup>/m<sup>2</sup> in patients with a body mass index  $\geq 30$  kg/m<sup>2</sup>.



**Figure 1** Prevalence of severe and moderate PPM using both measured and predicted methods with further adjustment for obesity in the global population (A), in native TAVR (B) and in valve-in-valve TAVR (C). PPM, prosthesis–patient mismatch; PPM<sub>M</sub>, measured PPM; PPM<sub>P</sub>, predicted PPM; TAVR, transcatheter aortic valve replacement. <sup>a</sup>Adjusted for obesity (body mass index  $\geq 30$  kg/m<sup>2</sup>).



**Figure 2** Haemodynamic outcomes associated with the presence of severe PPM with further adjustment for obesity. Residual transprosthetic aortic valve mean gradient in patients without and with severe PPM<sub>M</sub> (A) and PPM<sub>P</sub> (B). Percentage of patients with a high residual transprosthetic mean gradient ( $\geq 20$  mmHg) according to the presence of severe PPM<sub>M</sub> or PPM<sub>P</sub> (C). AV, aortic valve; PPM, prosthesis–patient mismatch; PPM<sub>M</sub>, measured PPM; PPM<sub>P</sub>, predicted PPM. <sup>a</sup>Adjusted for obesity (body mass index  $\geq 30$  kg/m<sup>2</sup>).

**Table 2** Post-procedural outcomes by adjusted PPM using measured and predicted EOAI

Parameters	Total	Severe PPM <sub>M</sub> <sup>a</sup>	No severe PPM <sub>M</sub> <sup>a</sup>	P value	Severe PPM <sub>P</sub> <sup>a</sup>	No severe PPM <sub>P</sub> <sup>a</sup>	P value
All-cause mortality at 30 days, N (%) (n = 1059)	48 (4)	9 (5)	39 (4)	0.741	0 (0)	48 (5)	0.489
HF readmission at 1 year, N (%) (n = 680)	107 (16)	20 (16)	87 (16)	0.962	0 (0)	107 (16)	0.219
Cardiovascular mortality at 1 year, N (%) (n = 773)	69 (9)	9 (6)	60 (9)	0.263	0 (0)	69 (9)	0.373
Cardiovascular mortality or HF readmission at 1 year, N (%) (n = 787)	167 (21)	27 (19)	140 (22)	0.507	0 (0)	167 (21)	0.140
All-cause mortality at 1 year, N (%) (n = 773)	121 (16)	19 (14)	102 (16)	0.477	0 (0)	121 (16)	0.221
All-cause mortality or HF readmission at 1 year, N (%) (n = 787)	214 (27)	35 (25)	179 (28)	0.485	0 (0)	214 (27)	0.082

EOAi, effective orifice area indexed to body surface area; HF, heart failure; PPM<sub>M</sub>, measured prosthesis–patient mismatch; PPM<sub>P</sub>, predicted prosthesis–patient mismatch.  
<sup>a</sup>Any and moderate PPM defined by an EOAI  $\leq 0.70$  cm<sup>2</sup>/m<sup>2</sup>, and severe PPM defined by an EOAI  $\leq 0.55$  cm<sup>2</sup>/m<sup>2</sup> in patients with a body mass index  $\geq 30$  kg/m<sup>2</sup>.

## Association of PPM<sub>M</sub> and PPM<sub>P</sub> with clinical outcomes

One-year rates of all-cause and cardiovascular mortality were 16% and 9%, respectively (Table 2). Mortality or HF readmission rates at 1 year were 27% and 21% for all-cause and cardiovascular deaths, respectively. On univariable analysis, neither severe PPM<sub>M</sub> nor severe PPM<sub>P</sub> were associated with outcomes (Figures 3 and 4). On multivariable analysis, factors independently associated with higher risk of 1-year cardiovascular death or HF readmission were history of atrial fibrillation, stroke, COPD, low baseline LVEF and low baseline mean transprosthetic gradient, a non-transfemoral approach, and TAVR for native AS (Table 3). In addition, moderate paravalvular AR was not associated with increased risk of adverse outcomes [HR: 0.96; 95% CI (0.30–3.04);  $P=0.946$ ], regardless of the presence of PPM. When analysed separately, severe PPM<sub>M</sub> and PPM<sub>P</sub> were not associated with outcomes in both TAVR populations (native TAVR, Supplementary data online, Tables S7 and S9, and Supplementary data online, Figure S3; valve-in-valve TAVR, Supplementary data online, Tables S8 and S10, and Supplementary data online, Figure S4). On long-term (until 8 years) follow-up, severe PPM<sub>M</sub> and PPM<sub>P</sub> were not associated with all-cause mortality on uni- and multivariable analyses (Supplementary data online, Figure S5).

## Discussion

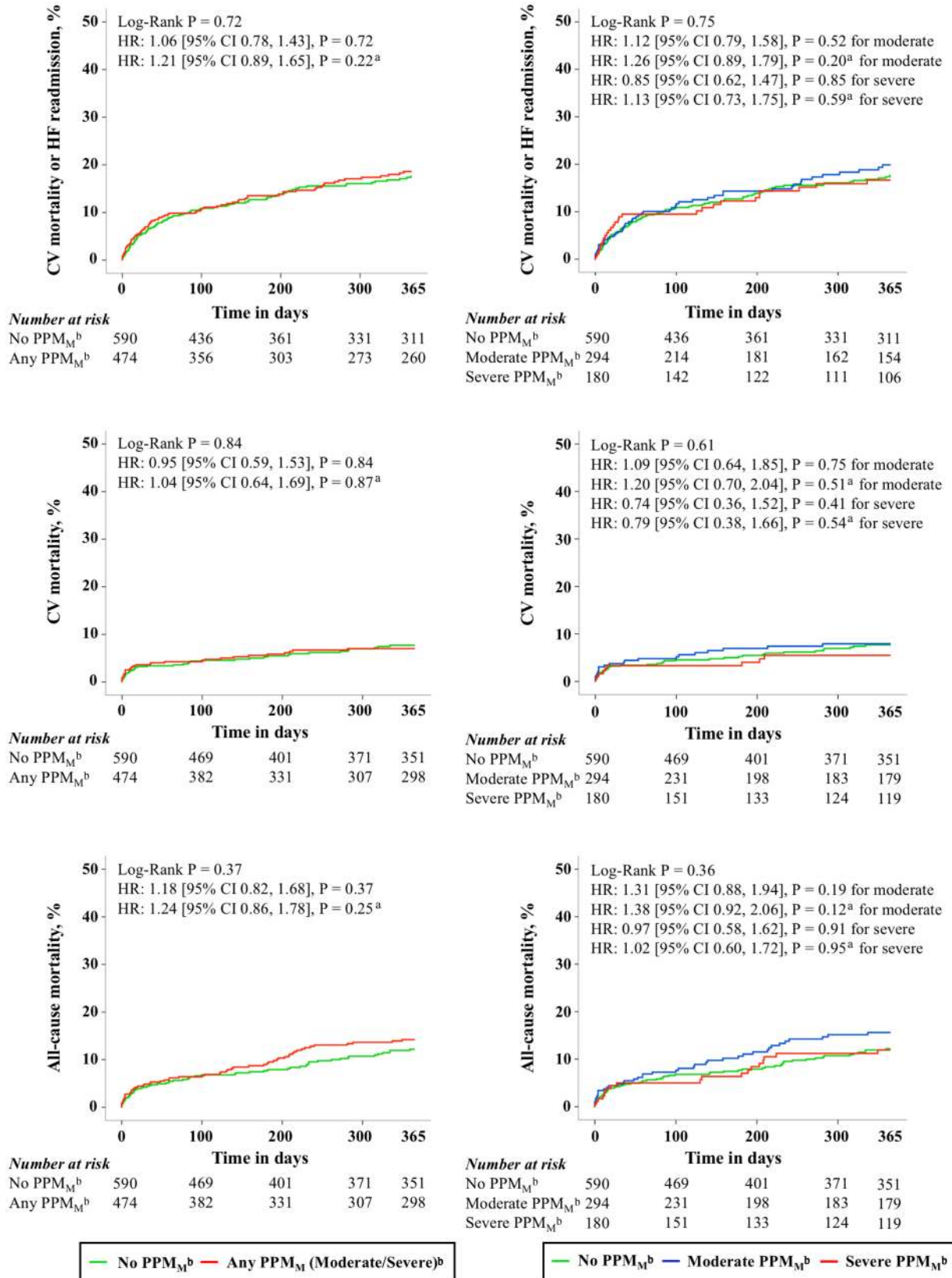
The main findings of this study are (i) the incidence of overall and severe PPM following TAVR was, respectively, 2- and 10-fold lower when using the predicted vs. the measured EOAI; (ii) the incidence of severe PPM<sub>P</sub> based on predicted EOAI was 0.1% vs. 15% with measured EOAI following native TAVR and 8% vs. 36% following valve-in-valve TAVR; (iii) PPM<sub>P</sub> had stronger association with transprosthetic gradients and occurrence of high residual gradient, compared with PPM<sub>M</sub>; (iv) neither PPM<sub>P</sub> or PPM<sub>M</sub> were associated with clinical outcomes; (v) the main factors associated with the occurrence of PPM were utilization of balloon vs. self-expanding device and valve-in-valve TAVR.

## Incidence of measured vs. predicted PPM after AVR

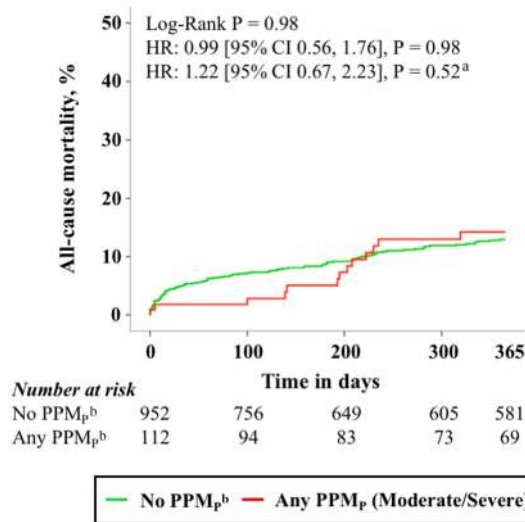
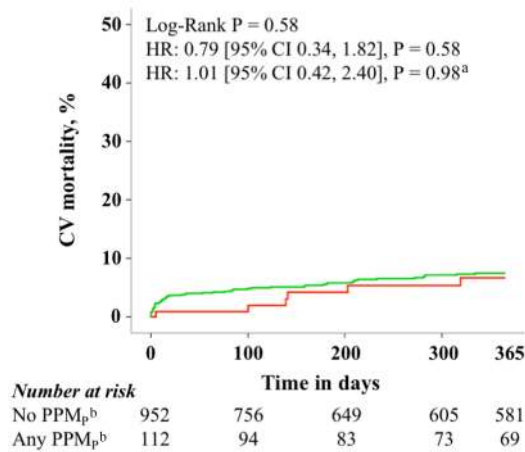
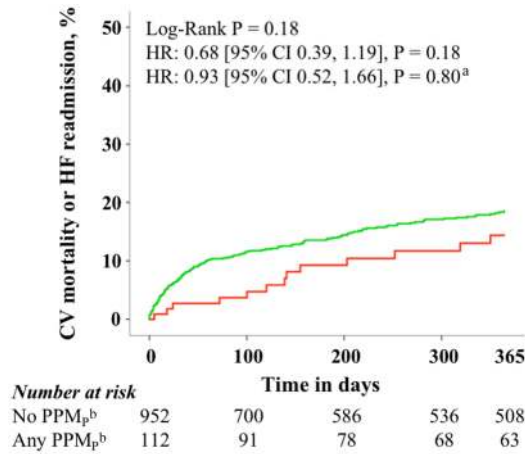
Several factors may lead to overestimation of the presence and severity of PPM. First, the use of the body surface area may cause an over-indexation of the EOA and thus an overestimation of the presence and severity of PPM in obese patients. Several studies reported that severe PPM is associated with worse outcomes following SAVR in patients with BMI  $<30$  kg/m<sup>2</sup> but not in those with larger BMI.<sup>1,7</sup> To overcome this limitation, VARC 2 and EACVI recommendations suggested using lower cut-off values of EOAI to define PPM in obese vs. non-obese patients.<sup>20,23</sup> We applied this adjustment in this study. The reduction in the incidence of PPM when adjusting the EOAI cut-off values in obese patients was significant but minimal because of the low prevalence of obesity in this cohort.

Second, a large proportion (up to 45%) of patients undergoing TAVR are in a low-flow state (i.e. stroke volume index  $<35$  mL/m<sup>2</sup>).<sup>24,25</sup> In low-flow conditions, the prosthetic valve leaflets may not be fully opened and the EOA measured by Doppler echocardiography may thus be smaller than the normal reference value of EOA obtained at normal flow. Consequently, the measured EOAI may be  $<0.65$  cm<sup>2</sup>/m<sup>2</sup> and lead to the erroneous conclusion that the patient has severe PPM whereas the patient, in fact, has pseudo-severe PPM.<sup>3</sup> There is an analogy between this phenomenon and the concept of pseudo-severe AS in low-flow low-gradient native AS.<sup>20</sup> The utilization of the predicted EOAI rather than of the measured EOAI allows, in part, to overcome this limitation (Supplementary data online, Table S11). Furthermore, in contrast to the measured EOAI, the predicted EOAI is not subject to technical pitfalls or inter/intra-observer measurement variability. As shown in the present study, the use of the predicted EOAI identified a much smaller proportion of patients with severe PPM compared with the measured EOAI and these patients appear to have true haemodynamically significant PPM. Indeed, the predicted EOAI showed stronger correlation with residual transprosthetic gradients than the measured EOAI. The main reason for this important difference in the incidence of PPM is likely that the measured EOAI classifies as severe PPM a large number of patients with erroneous PPM due to technical pitfalls and measurement errors or with pseudo-PPM due to low-flow state. The predicted EOA is more specific to the intrinsic haemodynamic





**Figure 3** Unadjusted and adjusted event curves of 1-year outcomes according to presence and severity of PPM<sub>M</sub> with further adjustment for obesity. CV, cardiovascular; HF, heart failure; HR, hazard ratio; PPM, prosthesis–patient mismatch; PPM<sub>M</sub>, measured PPM. <sup>a</sup>Adjusted for age, sex, AF or Flutter, stroke, COPD, baseline creatinine, baseline LVEF, baseline AV mean gradient, non-transfemoral approach, and valve-in-valve. <sup>b</sup>Adjusted for obesity (body mass index ≥30 kg/m<sup>2</sup>).



**Figure 4** Unadjusted and adjusted event curves of 1-year outcomes according to Presence of any PPM<sub>p</sub> with further adjustment for obesity. CV, cardiovascular; HF, heart failure; HR, hazard ratio; PPM, prosthesis–patient mismatch; PPM<sub>p</sub>, predicted PPM. <sup>a</sup>Adjusted for age, sex, AF or Flutter, stroke, COPD, baseline creatinine, baseline LVEF, baseline AV mean gradient, non-transfemoral approach, and valve-in-valve. <sup>b</sup>Adjusted for obesity (body mass index  $\geq 30$  kg/m<sup>2</sup>).

performance of the prosthetic valve, and is not influenced by the patient’s haemodynamic conditions or the variability and errors measurements. Our results based on the predicted EOA<sub>i</sub> suggest that true severe PPM is uncommon following native TAVR.

These findings may also help to explain some of the discrepancies observed in the literature regarding the incidence of PPM in TAVR vs. SAVR. Although head-to-head comparisons generally show that TAVR is associated with lower incidence of severe PPM compared with SAVR,<sup>8–12</sup> the incidence of severe PPM reported in the STS registry<sup>2</sup> following SAVR (11%) was similar than that reported in the TVT registry<sup>15</sup> following TAVR (12%). However, the STS registry used the predicted EOA<sub>i</sub>, whereas the TVT registry used the measured EOA<sub>i</sub>.

Another factor that may lead to overestimation of PPM following TAVR is the pressure recovery phenomenon. Indeed, a proportion of the transprosthetic pressure gradient that is initially lost at the level of the vena contracta is recovered downstream to the prosthetic valve. Doppler-echocardiography relies on the maximum transvalvular flow velocities measured at the level of the vena contracta by continuous-wave Doppler to estimate the pressure gradient, and this measure thus does not account for the pressure recovery. Pressure recovery may occur with any type of aortic valve, native or prosthetic. However, it has been suggested that the magnitude (in %) of pressure recovery may be more important in normal prosthetic aortic vs. native stenotic aortic valves, in TAVR vs. SAVR bioprosthetic valves, and in valve-in-valve vs. native TAVR.<sup>26,27</sup> In this study, all the severe PPM cases based on predicted EOA<sub>i</sub> were in the valve-in-valve sub-cohort and these patients had good clinical outcomes despite high residual transprosthetic gradients. Hence, it is likely that a substantial proportion of the patients undergoing valve-in-valve TAVR and classified as severe PPM with the predicted EOA<sub>i</sub> in fact have significant pressure recovery and thus did not exhibit true severe PPM. The predicted EOA<sub>i</sub> does not permit to account for the pressure recovery phenomenon because (i) the normal reference values of EOA used to define PPM were derived from native TAVR cohorts and not from valve-in-valve and (ii) the extent of pressure recovery is determined by the valve EOA but also by the diameter of the ascending aorta and the flow patterns within the aorta portion of the valve stent.

### Association of PPM with haemodynamic and clinical outcomes

The vast majority of SAVR studies report significant association between severe PPM and clinical outcomes,<sup>2,4–6</sup> whereas most TAVR studies report no or modest association with outcomes.<sup>9,10,13–16</sup> One of the main reasons explaining this results is likely related to the difference in the methods used for the definition of PPM. Indeed, the vast majority of SAVR studies used the predicted EOA<sub>i</sub> to define PPM,<sup>28</sup> whereas all previous TAVR studies used the measured EOA<sub>i</sub>. In the largest TAVR study from the STS/ACC TVT registry, Herrmann *et al.*<sup>15</sup> reported a significant but modest association between severe PPM<sub>M</sub> and outcomes [HR: 1.13, 95% CI (1.06–1.22);  $P < 0.001$ ], which appeared to be stronger in patients with valve-in-valve procedure. However, this previous study did not examine the incidence and impact of PPM defined based on the predicted EOA<sub>i</sub>, and did not perform separate analyses in native vs. valve-in-valve TAVR. Furthermore, the indexed EOAs used for defining PPM<sub>M</sub>

**Table 3** Univariable and multivariable analysis of factors associated with cardiovascular mortality or heart failure re-admission at 1 year

Parameters	Univariable analysis		Multivariable analysis					
	Hazard ratios (95% CI)	P value	Hazard ratios (95% CI)	P value	Hazard ratios (95% CI)	P value	Hazard ratios (95% CI)	P value
Sex: male	1.12 (0.83–1.52)	0.468	0.91 (0.66–1.27)	0.585	0.94 (0.67–1.30)	0.686	0.94 (0.68–1.30)	0.689
Age (years)	1.00 (0.98–1.02)	0.814	1.01 (0.99–1.03)	0.398	1.01 (0.99–1.03)	0.430	1.01 (0.99–1.03)	0.438
Stroke	1.89 (1.33–2.69)	<b>&lt;0.001</b>	1.68 (1.18–2.41)	<b>0.004</b>	1.66 (1.16–2.38)	<b>0.005</b>	1.66 (1.16–2.37)	<b>0.006</b>
AF or flutter	2.27 (1.67–3.07)	<b>&lt;0.001</b>	2.15 (1.58–2.93)	<b>&lt;0.001</b>	2.13 (1.57–2.90)	<b>&lt;0.001</b>	2.13 (1.57–2.90)	<b>&lt;0.001</b>
COPD	1.53 (1.12–2.09)	<b>0.008</b>	1.45 (1.05–2.02)	<b>0.026</b>	1.45 (1.04–2.02)	<b>0.027</b>	1.45 (1.05–2.02)	<b>0.026</b>
Baseline creatinine	1.01 (1.00–1.01)	<b>0.004</b>	1.00 (1.00–1.01)	0.098	1.00 (1.00–1.01)	0.104	1.00 (1.00–1.01)	0.103
Baseline LVEF	0.98 (0.97–0.99)	<b>&lt;0.001</b>	0.99 (0.98–1.00)	<b>0.047</b>	0.99 (0.98–1.00)	<b>0.046</b>	0.99 (0.98–1.00)	<b>0.049</b>
Baseline AV mean gradient	0.98 (0.97–0.99)	<b>&lt;0.001</b>	0.98 (0.97–0.99)	<b>0.007</b>	0.98 (0.97–0.99)	<b>0.008</b>	0.98 (0.97–0.99)	<b>0.008</b>
Non-transfemoral approach	1.86 (1.37–2.53)	<b>&lt;0.001</b>	1.71 (1.24–2.36)	<b>0.001</b>	1.70 (1.23–2.34)	<b>0.001</b>	1.69 (1.22–2.34)	<b>0.001</b>
Valve-in-valve	0.34 (0.16–0.72)	<b>0.005</b>	0.34 (0.16–0.73)	<b>0.005</b>	0.35 (0.16–0.75)	<b>0.008</b>	0.36 (0.16–0.78)	<b>0.010</b>
Any PPM <sub>M</sub> <sup>a</sup>	1.06 (0.78–1.43)	0.719	1.21 (0.89–1.65)	0.226				
Severe PPM <sub>M</sub> <sup>a</sup>	0.92 (0.61–1.39)	0.699			1.04 (0.68–1.58)	0.687		
Any PPM <sub>P</sub> <sup>a</sup>	0.68 (0.39–1.19)	0.178					0.93 (0.52–1.66)	0.798
Severe PPM <sub>P</sub> <sup>a</sup>								

AF, atrial fibrillation; AR, aortic regurgitation; AV, aortic valve; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; PPM<sub>M</sub>, measured prosthesis–patient mismatch; PPM<sub>P</sub>, predicted prosthesis–patient mismatch. P values in bold indicate those that are statistically significant (<0.05).

<sup>a</sup>Any and moderate PPM defined by an EOAI ≤0.70 cm<sup>2</sup>/m<sup>2</sup>, and severe PPM defined by an EOAI ≤0.55 cm<sup>2</sup>/m<sup>2</sup> in patients with a body mass index ≥30 kg/m<sup>2</sup>.

were reported by the sites and not measured centrally in an echocardiography core laboratory. The results of this study suggest that the measured EOAI may lead to overestimation of the presence and severity of PPM. A large proportion of TAVR patients are in low-flow state and may thus have a pseudo-PPM, which is misclassified as severe PPM with the use of the measured EOAI. These findings may explain the low rate of high residual gradient and the lack of association with clinical outcomes in patients with severe PPM<sub>M</sub>. Another advantage of the predicted EOAI is that it can be estimated in all patients and it thus allows the assessment of effect of PPM on periprocedural outcomes, whereas with the measured EOAI, the patients who die in the peri-procedural period (i.e. prior the discharge echo) are excluded, thus introducing a survivorship bias.

In this study, PPM<sub>P</sub> showed stronger association with haemodynamic outcomes compared with PPM<sub>M</sub>. Nonetheless, PPM<sub>P</sub> did not associate with clinical outcomes. This finding is explained by the fact that severe PPM<sub>P</sub> was quasi-absent (0.1%) following native TAVR in this series. Interestingly, PPM<sub>P</sub> tended to be associated with clinical outcomes in the subset of patients undergoing valve-in-valve TAVR [HR: 3.13; 95% CI (0.50–19.62); P = 0.223] but the sample size was too small to detect a difference. Other factors that are unaccounted for with the echo-derived gradient following valve-in-valve TAVR, such as flow patterns, multiple flow convergence points (below valve, below leaflets, and at the exit of the TAVR) may increase the discordance between echo and catheterization measures.

### Clinical implications

The use of the measured EOAI yields to a gross overestimation of the incidence of PPM following AVR, in large because of the high prevalence of low-flow state and ensuing pseudo-PPM. The utilization

of the predicted EOAI allows overcoming this limitation and provides a more accurate estimation of the true incidence of PPM. This study suggests that true severe PPM defined with the use of the predicted EOAI is very rare following TAVR or contemporary SAVR. The predicted EOAI method can easily be applied to every patient and does not require performing an echocardiogram. Furthermore, this method better correlates with haemodynamic and clinical outcomes. Further studies are needed to examine the association between PPM<sub>P</sub> and longer-term outcomes, especially in patients undergoing valve-in-valve.

### Limitations

This is a single-centre retrospective study. Post-TAVR echocardiograms were not analysed by a Core Laboratory; the single-centre nature of the study, however, contributed to reduce measurement variability in EOA and gradients. In this study, we examined the impact of PPM on 30-day and 1-year outcomes as well as on long-term (until 8 years) all-cause mortality. We however did not report the long-term rates of HF readmission because an important proportion of these events were not recorded and/or adjudicated.

Catheterization data at the time of the TAVR procedure were not available in this study and we were thus not able to estimate the extent of pressure recovery following native or valve-in-valve TAVR.

In this study, we used the EOAs predicted according to prosthetic valve model and label size to define PPM<sub>P</sub>. The implantation of a given valve model and size in aortic annuli of different size may yield somewhat different EOAs. Hence, it would have been useful to use the EOAs predicted from the aortic annulus area or perimeter measured by CT prior to the procedure in order to obtain a more precise definition of PPM<sub>P</sub>. However, the aortic annulus size data were missing



in a substantial proportion of the patients. Furthermore, for a given aortic annulus size, the final valve deployment may vary from one patient to the other. A post-procedural CT would have been useful to assess the extent of valve deployment but was not included in the protocol of this study.

The small number of events in the valve-in-valve population may have contributed to the absence of significant association between PPM<sub>P</sub> and the primary endpoint.

Finally, >80% of our patients received a balloon-expandable device, which limit the generalization of these results to other types of device.

## Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

## Conclusions

The utilization of the predicted EOAI reclassifies the majority of PPM based on measured EOAI to no-PPM and reveals that the incidence of true severe PPM is very low (<2%) following TAVR. Compared with PPM<sub>M</sub>, PPM<sub>P</sub> had stronger association with transprosthetic gradients and occurrence of high residual gradient and thus appears more relevant from a haemodynamic standpoint. Neither severe PPM<sub>M</sub> nor PPM<sub>P</sub> did associate with mortality or HF readmission.

**Conflict of interest:** P.P. has echo Core Lab contracts with Edwards Lifesciences, for which he receives no direct compensation. A.E.A. is on the speaker bureau and has received research grants from Edwards Lifesciences. M.A.C. has CT Core Lab contracts with Edwards Lifesciences, for which he receives no direct compensation. J.R.-C. has received institutional research grants from Edwards Lifesciences, Medtronic and Boston Scientific. All other authors have no conflicts of interest.

## References

- Dayan V, Vignolo G, Soca G, Paganini JJ, Brusich D, Pibarot P. Predictors and outcomes of prosthesis patient mismatch after aortic valve replacement. *JACC Cardiovasc Imaging* 2016;**9**:924–33.
- Fallon JM, DeSimone JP, Brennan JM, O'Brien S, Thibault DP, DiScipio AW et al. The incidence and consequence of prosthesis-patient mismatch after surgical aortic valve replacement. *Ann Thorac Surg* 2018;**106**:14–22.
- Pibarot P, Clavel MA. Prosthesis-patient mismatch after transcatheter aortic valve replacement: it is neither rare nor benign. *J Am Coll Cardiol* 2018;**72**:2712–6.
- Head S, Mokhes M, Osnabrugge R, Pibarot P, Mack MJ, Takkenberg J et al. The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27,186 patients with 133,141 patient-years. *Eur Heart J* 2012;**33**:1518–29.
- Popma JJ, Khabbaz K. Prosthesis-patient mismatch after “high-risk” aortic valve replacement. *J Am Coll Cardiol* 2014;**64**:1335–8.
- Sa M, de Carvalho MMB, Sobral Filho DC, Cavalcanti LRP, Rayol SDC, Diniz RGS et al. Surgical aortic valve replacement and patient-prosthesis mismatch: a meta-analysis of 108 182 patients. *Eur J Cardiothorac Surg* 2019;**56**:44–54.
- Mohty D, Dumesnil JG, Echahidi N, Mathieu P, Dagenais F, Voisine P et al. Impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: influence of age, obesity, and left ventricular dysfunction. *J Am Coll Cardiol* 2009;**53**:39–47.
- Clavel MA, Webb JG, Pibarot P, Altwegg L, Dumont É, Thompson C et al. Comparison of the hemodynamic performance of percutaneous and surgical bioprostheses for the treatment of severe aortic stenosis. *J Am Coll Cardiol* 2009;**53**:1883–91.
- Thyregod HG, Steinbruchel DA, Ihlemann N, Ngo TA, Nissen H, Kjeldsen BJ et al. No clinical effect of prosthesis-patient mismatch after transcatheter versus surgical aortic valve replacement in intermediate- and low-risk patients with severe aortic valve stenosis at mid-term follow-up: an analysis from the NOTION trial. *Eur J Cardiothorac Surg* 2016;**50**:721–8.
- Pibarot P, Weissman NJ, Stewart WJ, Hahn RT, Lindman BR, McAndrew T et al. Incidence and sequelae of prosthesis-patient mismatch in transcatheter versus surgical valve replacement in high-risk patients with severe aortic stenosis- A PARTNER trial cohort A analysis. *J Am Coll Cardiol* 2014;**64**:1323–34.
- Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019;**380**:1706–15.
- Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;**380**:1695–705.
- Tzikas A, Piazza N, Geleijnse ML, Van Mieghem N, Nuis RJ, Schultz C et al. Prosthesis-patient mismatch after transcatheter aortic valve implantation with the medtronic CoreValve system in patients with aortic stenosis. *Am J Cardiol* 2010;**106**:255–60.
- Miyasaka M, Tada N, Taguri M, Kato S, Enta Y, Otomo T 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**:771–80.
- Herrmann HC, Daneshvar SA, Fonarow GC, Stebbins A, Vemulapalli S, Desai ND et al. Prosthesis-patient mismatch in patients undergoing transcatheter aortic valve replacement: from the STS/ACC TVT registry. *J Am Coll Cardiol* 2018;**72**:2701–11.
- Ewe SH, Muratori M, Delgado V, Pepi M, Tamborini G, Fusini L et al. Hemodynamic and clinical impact of prosthesis-patient mismatch after transcatheter aortic valve implantation. *J Am Coll Cardiol* 2011;**58**:1910–8.
- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ et al. ESC/EACTS guidelines for the management of valvular heart disease: the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2017;**38**:2739–91.
- Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, Guyton RA et al. AHA/ACC Guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American heart association task force on practice guidelines. *Circulation* 2014;**129**:e521–643.
- Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA et al. Recommendations for evaluation of prosthetic valves with echocardiography and Doppler ultrasound: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2009;**22**:975–1014.
- Lancellotti P, Pibarot P, Chambers J, Edvardsen T, Delgado V, Dulgheru R 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 Interamerican Society of Echocardiography and the Brazilian Department of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016;**17**:589–90.
- Hahn RT, Leipsic J, Douglas PS, Jaber WA, Weissman NJ, Pibarot P et al. Comprehensive echocardiographic assessment of normal transcatheter valve function. *JACC Cardiovasc Imaging* 2019;**12**:25–34.
- Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol* 2012;**60**:1438–54.
- Kappetein AP, Head SJ, Genereux P, Piazza N, Van Mieghem NM, Blackstone EH et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur J Cardiothorac Surg* 2012;**42**:S45–60.
- Le Ven F, Thébault C, Dahou A, Ribeiro HB, Capoulade R, Mahjoub H et al. Evolution and prognostic impact of low flow after transcatheter aortic valve replacement. *Heart* 2015;**101**:1196–203.

25. Anjan VY, Herrmann HC, Pibarot P, Stewart WJ, Kapadia S, Tuzcu EM et al. Evaluation of flow after transcatheter aortic valve replacement in patients with low-flow aortic stenosis. A secondary analysis of the PARTNER randomized clinical trial. *JAMA Cardiol* 2016;**1**:584–92.
26. Abbas AE, Hanzel G, Shannon F, Gallagher M, Mando R, Chaddha A et al. Post-TAVR trans-aortic valve gradients: echocardiographic versus invasive measurements: the role of pressure recovery. *Struct Heart* 2019;**3**:348–50.
27. Abbas AE, Mando R, Hanzel G, Gallagher M, Safian R, Hanson I et al. Invasive versus echocardiographic evaluation of transvalvular gradients immediately post-transcatheter aortic valve replacement. *Circ Cardiovasc Interv* 2019;**12**:e007973.
28. Chacko SJ, Ansari AH, McCarthy PM, Malaisrie SC, Andrei AC, Li Z et al. Prosthesis-patient mismatch in bovine pericardial aortic valves: evaluation using 3 different modalities and associated medium-term outcomes. *Circ Cardiovasc Imaging* 2013;**6**:776–83.

## IMAGE FOCUS

doi:10.1093/ehjci/jeaa145

Online publish-ahead-of-print 20 May 2020

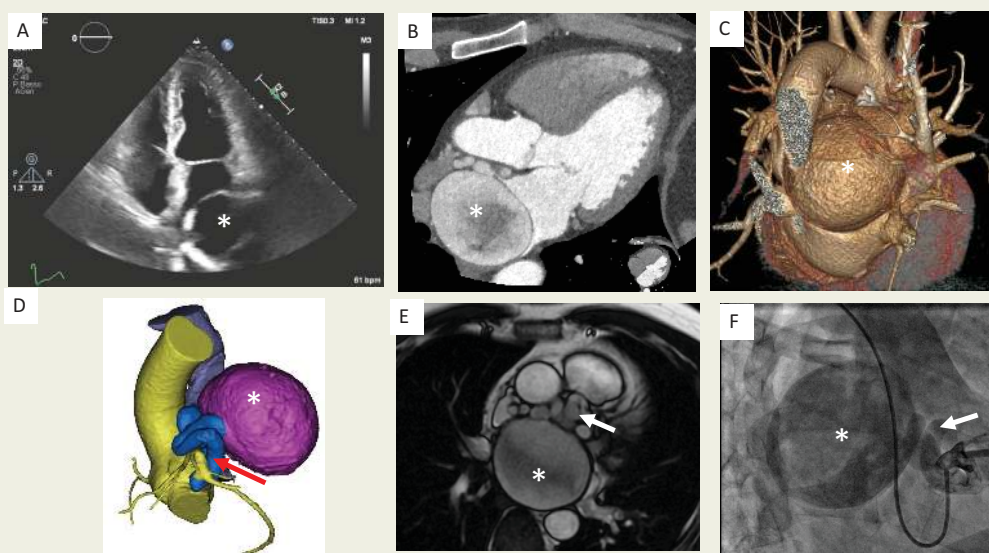
# Multimodality imaging of a left circumflex artery to right atrium coronary artery fistula associated with giant aneurysm

Marco Guglielmo, Alberico Del Torto, Giuseppe Muscogiuri, Giulia Mostardini, and Gianluca Pontone  \*

Centro Cardiologico Monzino, IRCCS, Via Carlo Parea, 4, 20138 Milan, Italy

\*Corresponding author. Tel: +39 02 58002574. E-mail: gianluca.pontone@ccfm.it

A 46-year-old man, with a history of palpitations and a 24-h Holter monitoring demonstrating only mild supraventricular ectopic beats, underwent a transthoracic echocardiogram showing a large anechoic chamber with slow flow inside, compressing the left atrial roof (Panel A, [Supplementary data](#) online, [Video S1](#)). A coronary computed tomography angiography (CCTA) showed a proximal left circumflex artery giving rise to a dilated and tortuous coronary artery fistula (CAF) draining into a giant aneurysm ( $62 \times 66 \times 74$  mm) compressing the left atrium; the aneurysm itself drained into a kinked vessel coursing posteriorly to the aorta and the pulmonary artery, winding laterally around the superior vena cava and eventually terminating into the right atrium (Panels B–D, [Supplementary data](#) online, [Videos S2](#) and [S3](#)).



The mid and distal left circumflex artery had a normal calibre. No significant coronary artery disease was noted. The patient underwent a cardiac magnetic resonance (CMR) with phase-contrast flow quantification and 4D flow imaging ([Supplementary data](#) online, [Video S4](#)), confirming the presence of the CAF, demonstrating a normal biventricular cavity size and systolic function, normal biatrial size, and normal pulmonary to systemic flow ratio, ruling out aneurysm thrombosis (Panel E, [Supplementary data](#) online, [Figure S1](#)). A coronary angiogram was also performed (Panel F, [Supplementary data](#) online, [Video S5](#)). After Heart Team discussion, surgical treatment with ligation of the proximal and distal openings of the fistula was planned due to the large size of the CAF aneurysm. The patient eventually decided to refuse the intervention for personal reasons. Giant coronary aneurysms (diameter exceeding 20 mm) have been described in 5.9% of patients with a CAF. The complications of coronary artery aneurysm include thrombosis, embolization and rupture. Management of these patients is controversial. Treatment options include follow-up, surgical repair or catheter embolization. However, in presence of large aneurysm, surgical procedures are usually preferred.

(Panel A) Transthoracic echocardiography four-chamber view: large round anechoic chamber compressing the left atrium (asterisk). Three-chamber view (Panel B) and volume rendering (Panels C and D) CCTA, (Panel E) CMR and invasive coronary angiography (Panel F) showing dilated and tortuous CAF (arrow) draining into a giant aneurysm (asterisk).

[Supplementary data](#) are available at *European Heart Journal - Cardiovascular Imaging* online.