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ORIGINAL PAPER

Incidence and impact of prosthesis–patient mismatch following transcatheter aortic valve implantation

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Abstract

Introduction The implications of prosthesis–patient mismatch (PPM) in the context of transcatheter aortic valve implantation (TAVI) are still controversial. The objective of our study was thus to investigate the incidence and prognostic impact of PPM after TAVI.

Methods Our analysis included 613 TAVI patients in whom the indexed effective orifice area (iEOA) after TAVI was obtained in vivo using echocardiography. Prosthesis sizing was guided by pre-procedural ECG-gated computed tomography. Based on VARC-2 established criteria for significant PPM (iEOA ≤ 0.85 cm^2/m^2 in the setting of BMI < 30 kg/m^2 and iEOA ≤ 0.7 cm^2/m^2 in the context of BMI ≥ 30 kg/m^2), patients were attributed to a "No PPM" or a "PPM" group.

Results We observed PPM after TAVI in 192 patients (31.3%) with moderate PPM being present in 150 subjects (24.5%) and severe PPM in 42 patients (6.9%). EuroSCORE, impaired LV function, and male gender were associated with PPM status. The "No PPM" group was characterized by higher rates of self-expandable valves (40.4% vs. 25.5%, $p < 0.001$). In a multivariate analysis age > 81.2 years, chronic obstructive pulmonary disease, peripheral artery disease, impaired LV function, acute kidney failure stage 3 as well as periprocedural myocardial infarction emerged as independent risk predictors for all-cause mortality after TAVI. After a median follow-up of 12.2 months PPM failed to show a significant association with overall survival (79.2% vs. 79.3%, $p = 0.692$).

Conclusions The incidence of PPM after TAVI seems to be substantially lower than after SAVR. PPM was less common using self-expandable valves. In our analysis, patients with PPM following TAVI did not have higher rates of all-cause mortality.

Keywords Transcatheter aortic valve implantation · Aortic stenosis · Valvular heart disease

Abbreviations

AKIN	Acute Kidney Injury Network
AS	Aortic stenosis
AVA	Aortic valve area
BEV	Balloon-expandable valve
BMI	Body mass index
BSA	Body surface area
CAD	Coronary artery disease
CI	Confidence intervals
COPD	Chronic obstructive pulmonary disease
CVD	Cerebrovascular disease
EOA	Effective orifice area
HR	Hazard ratio
hsTnT	High-sensitivity troponin T
iEOA	Indexed effective orifice area
IQR	Interquartile range
LVEF	Left ventricular ejection fraction
PAD	Peripheral artery disease
PAH	Pulmonary arterial hypertension
PPM	Prosthesis–patient mismatch
SAVR	Surgical aortic valve replacement

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SEV	Self-expandable valve
TA	Transapical
TAO	Transaortic
TAVI	Transcatheter aortic valve implantation
TF	Transfemoral
VARC-2	Valve Academic Research Consortium-2

Introduction

Aortic stenosis (AS) is the most frequent type of aortic valve disease in Europe and North America with an age-dependent incidence of approximately 5% in those aged over 65 years [1, 2]. AS constitutes a major challenge for public health care resources, as it is the most common heart valve disease requiring medical intervention [3]. While surgical aortic valve replacement (SAVR) is a well-established therapeutic option for severe AS in low- and intermediate-risk patients, transcatheter aortic valve implantation (TAVI) has emerged as the standard of care in high-risk and selected intermediate-risk patients with severe symptomatic AS [4–6]. Clinical trials investigating the potential role of TAVI even in low-risk patients are currently being conducted based on promising data from observational studies [7, 8].

With the shift towards a lower risk and younger TAVI population, the identification of patients prone to adverse long-term outcome after TAVI becomes increasingly important. In this regard, the Valve Academic Research Consortium-2 (VARC-2) advocates that the evaluation of possible valve dysfunction after TAVI should include the assessment of prosthesis–patient mismatch (PPM) [9].

Historically, the concept of PPM was first proposed by Rahimtoola [10]. It is defined as an effective orifice area (EOA) of an implanted bioprosthesis being too small in relation to the patient's body surface area (BSA). To characterize PPM, the indexed effective orifice area (iEOA) is calculated by dividing the EOA of the valve prosthesis by the patient's BSA. PPM has been shown to have detrimental effects on hemodynamics, functional status, left ventricular mass regression, and overall survival in patients after SAVR [11, 12]. As the implications of PPM in TAVI patients are still in dispute, we investigated the incidence and prognostic impact of PPM in a single-center study.

Methods

Study design

We conducted a retrospective analysis of 613 patients with in vivo calculated iEOA who underwent TAVI for symptomatic severe AS between July 2012 and November 2017 at our institution. The primary outcome of our study was overall survival.

Prior to TAVI all patients were discussed by our interdisciplinary heart team and precluded from SAVR due to relevant comorbidities. Besides few first-generation CoreValve valves (Medtronic, Fridley, Minnesota), mostly second-generation Sapien XT (Edwards Lifesciences, Irvine, California) and third-generation Sapien 3 and CoreValve Evolut R systems were used. The preferred TAVI access route was transfemoral (TF); otherwise, a transaortic (TAO) or transapical (TA) approach was chosen. Procedures were predominantly performed under conscious sedation with the exception of TAO and TA TAVI. Prosthesis sizing was guided by pre-procedural ECG-gated multislice computed tomography and the use of the 3mensio Structural Heart™ software by Pie Medical Imaging. Calculation of the effective annulus diameter was mainly based on the mean area (measured in systole and diastole) for balloon-expandable valves (BEV) and on the mean perimeter for self-expandable valves (SEV). The choice of the valve type was done at the discretion of the implanting physician.

The data collection was carried out in accordance with the Declaration of Helsinki and was approved by the ethics committee at the University of Kiel. All patients provided informed consent to the procedure and data acquisition.

Data collection

Blood samples and patient data were usually collected 1 day before TAVI. Depending on the date of discharge, postprocedural echocardiography was routinely done 1–3 days after TAVI and included the in vivo calculation of the EOA according to the continuity equation using the velocity time integral. In addition, following data were recorded: age, sex, BMI, BSA, presence of atrial fibrillation/flutter, significant prior coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), diabetes mellitus, dyslipidemia, arterial hypertension, peripheral artery disease (PAD), pulmonary arterial hypertension (PAH), cerebrovascular disease (CVD), chronic kidney disease, hemodynamic variables, logistic EuroSCORE as well as TAVI procedural details. Patient outcomes were analyzed following the VARC-2 system [9]. Follow-up after discharge usually included an in-person visit in our cardiology outpatient clinic 3 months after TAVI. Thereafter, a phone call follow-up was obtained on an annual basis either by calling the patients or their general practitioner/cardiologist. This was done systematically in all patients that had given written consent to participate in our TAVI registry.

Statistical analyses

Based on VARC-2 established criteria for significant PPM (iEOA ≤ 0.85 cm^2/m^2 in the setting of a BMI < 30 kg/m^2 and iEOA ≤ 0.7 cm^2/m^2 in the setting of a BMI ≥ 30 kg/m^2), patients were attributed to either a "No PPM" or a "PPM" group. Moreover, significant PPM was further classified as severe (iEOA < 0.65 cm^2/m^2 in the setting of a BMI < 30 kg/m^2 and iEOA < 0.6 cm^2/m^2 in the setting of a BMI ≥ 30 kg/m^2) and moderate PPM (iEOA 0.65–0.85 cm^2/m^2 in the context of a BMI < 30 kg/m^2 and iEOA 0.6–0.7 cm^2/m^2 in subjects with a BMI ≥ 30 kg/m^2).

All statistical analyses were performed using the statistical software RStudio, version 1.1.453, as well as GraphPad PRISM, version 7. Data are demonstrated using standard statistics. p values ≤ 0.05 were considered to be statistically significant without adjusting for multiple comparisons. Continuous data are presented as median and interquartile range (IQR), whereas categorical data are expressed as counts (percentages). Variables were statistically tested for differences using the χ^2 test as well as the Mann–Whitney U test. Survival data were visualized by Kaplan–Meier plots and assessed using the log-rank test and Cox regression analysis. For the Cox regression model all pre-procedural prognostic factors which were significant in the log-rank test were included. Backward selection was based on the likelihood ratio criteria. Cox regression results are illustrated as adjusted hazard ratios (HR) with 95% confidence intervals (CI).

Results

Baseline patient characteristics

Patient characteristics at baseline are presented in Table 1 illustrating a typical real-world TAVI population comparable to the data from the German Aortic Valve Registry [13]. A total of 613 patients with a median age of 81.2 years were available for analysis with 54.5% of these subjects being female. In accordance with the VARC-2 criteria for relevant

Table 1 Baseline characteristics in patients undergoing TAVI

	All (n = 613)	No PPM (n = 421)	PPM (n = 192)	p value
Age (years)	81.2 (78.0–85.0)	82.0 (78.0–85.5)	80.5 (77.0–85.0)	0.080
BSA (m^2)	1.9 (1.7–2.0)	1.8 (1.7–2.0)	1.9 (1.8–2.0)	< 0.001
BMI (kg/m^2)	26.1 (23.7–29.4)	26.3 (23.4–30.4)	25.8 (24.1–28.0)	0.441
hsTnT (ng/l)	25.4 (15.9–46.3)	25.6 (15.8–47.0)	24.8 (16.3–5.9)	0.889
Creatinine (mg/dl)	99.1 (79.7)	98.2 (79.7–126.5)	101.8 (79.2–131.0)	0.562
Log. EuroScore (%)	15.4 (9.5–24.5)	14.5 (9.5–24)	18.1 (10.4–28.0)	0.019
AVA (cm^2)	0.8 (0.6–0.9)	0.8 (0.6–0.9)	0.7 (0.6–0.9)	0.435
iEOA (cm^2/m^2)	0.9 (0.8–1.1)	1.0 (0.9–1.2)	0.7 (0.6–0.8)	< 0.001
Female, n (%)	334 (54.5)	247 (58.7)	87 (45.3)	0.002
Atrial fibrillation, n (%)	252 (41.1)	163 (38.7)	89 (46.4)	0.075
CAD, n (%)	412 (67.2)	269 (63.9)	143 (74.5)	0.010
COPD, n (%)	87 (14.2)	62 (14.7)	25 (13.0)	0.575
Diabetes mellitus, n (%)	186 (30.3)	122 (29.0)	64 (33.3)	0.278
Dyslipidemia, n (%)	310 (50.6)	208 (49.4)	102 (53.1)	0.393
Hypertension, n (%)	553 (90.2)	377 (89.6)	176 (91.7)	0.413
PAD, n (%)	93 (15.2)	59 (14.0)	34 (17.7)	0.237
CVD, n (%)	127 (20.7)	90 (21.4)	37 (19.3)	0.551
PAH, n (%)	113 (18.4)	76 (18.1)	37 (19.3)	0.718
LVEF				
> 55%, n (%)	362 (59.1)	274 (65.1)	88 (45.8)	< 0.001
< 55%, n (%)	251 (41.0)	147 (34.9)	104 (54.2)	< 0.001
45–55%, n (%)	128 (20.9)	87 (20.7)	41 (21.4)	0.856
35–45%, n (%)	70 (11.4)	31 (7.4)	39 (20.3)	< 0.001
< 35%, n (%)	53 (8.6)	29 (6.9)	24 (12.5)	0.022

Values are presented as counts (percentages) or median (IQR)

BSA body surface area, *BMI* body mass index, *hsTnT* high-sensitivity troponin T, *AVA* aortic valve area, *iEOA* indexed effective orifice area, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *PAD* peripheral artery disease, *CVD* cerebrovascular disease, *PAH* pulmonary arterial hypertension, *LVEF* left ventricular ejection fraction

PPM, a total of 421 patients were assigned to the "No PPM" group, while the "PPM" group comprised 192 patients.

No significant differences between both groups were observed with respect to age (median 81.2 years), pre-procedural creatinine (median 99.1 mg/dl), pre-procedural aortic valve area (median 0.8 cm^2) as well as chronic atrial fibrillation (41.1%), COPD (14.2%), diabetes mellitus (30.3%), dyslipidemia (50.6%), arterial hypertension (90.2%), peripheral artery disease (15.2%), cerebrovascular disease (20.7%), and pulmonary hypertension (18.4%). Pre-procedural high-sensitivity Troponin T (hsTnT) levels were also quite similar (25.6 ng/l vs. 24.8 pg/ml, $p=0.889$).

Both groups differed, however, regarding BSA (1.8 vs. 1.9 m^2, $p<0.001$), logistic EuroSCORE (14.5% vs. 18.1%, $p=0.019$), female gender (58.7% vs. 45.3%, $p=0.002$) as well as coronary artery disease (63.9% vs. 74.5%, $p=0.010$). Notably, in the "PPM" group a higher prevalence of impaired LV function, defined as a systolic left ventricular ejection fraction (LVEF) < 55%, was found compared to the "No PPM" group (54.2% vs. 34.9%, $p<0.001$). In particular, the "PPM" group included more patients with severely impaired LVEF < 35% (12.5% vs. 6.9%, $p=0.022$).

Procedural outcomes and their association with PPM

Procedural data and outcomes are summarized in Table 2. Notably, in the "No PPM" group patients were treated more often with self-expandable valves (SEV) compared to the "PPM" group (40.4% vs. 25.5%, $p<0.001$), as illustrated in Fig. 1. Patients without PPM also had higher rates of TF access (69.1% vs. 59.9%, $p=0.025$). The number of implanted BEV and SEV for both groups is provided in Fig. 2.

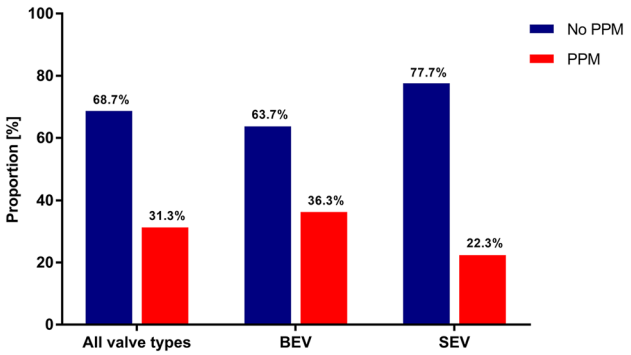

Fig. 1 Valve type and PPM. Proportion of PPM shown for all, balloon-expandable and self-expandable valves

Procedural duration (65 min vs. 73.5 min, $p=0.103$) also showed a trend in favor of the "No PPM" group, yet this did not reach statistical significance. Regarding VARC-2 outcomes, patients in the "PPM" group had higher incidences of life-threatening bleeding (5.7% vs. 2.1%, $p=0.020$) and major vascular access complications (3.1% vs. 0.7%, $p=0.021$). Median follow-up was 12.2 months (2.1–24.4 months). Kaplan–Meier curves for the "No PPM" and "PPM" group are shown in Fig. 3, demonstrating no statistically significant difference in overall survival.

Independent risk predictors of outcome after TAVI

Table 3 summarizes variables which were significantly associated with survival after TAVI using log-rank tests. These included age > median (81.2 years), chronic atrial

Table 2 Procedural variables and outcomes

	All ($n=613$)	No PPM ($n=421$)	PPM ($n=192$)	p value
TF access, n (%)	406 (66.2)	291 (69.1)	115 (59.9)	0.025
Self-expandable valve, n (%)	219 (35.7)	170 (40.4)	49 (25.5)	< 0.001
Procedural duration (min)	66 (50–91)	65 (48–88)	73.5 (50–95)	0.103
Contrast medium (ml)	80 (65–101)	80 (65–100)	80 (60–103)	0.368
VARC-2				
Conversion (%)	2 (0.3)	2 (0.5)	0 (0)	–
New pacemaker, n (%)	53 (8.6)	39 (9.3)	14 (7.3)	0.420
Myocardial infarction, n (%)	4 (0.7)	3 (0.7)	1 (0.5)	0.784
AKIN stage 3, n (%)	13 (2.1)	10 (2.4)	3 (1.6)	0.517
Life-threatening bleeding, n (%)	20 (3.3)	9 (2.1)	11 (5.7)	0.020
Disabling stroke, n (%)	5 (0.8)	3 (0.7)	2 (1.0)	0.674
Major vascular access complication, n (%)	9 (1.5)	3 (0.7)	6 (3.1)	0.021
iEOA (cm^2/m^2)	0.93 (0.77–1.09)	1.01 (0.91–1.17)	0.72 (0.65–0.78)	< 0.001

Values are presented as counts (percentages) or median (IQR)

TF transfemoral, *VARC-2* Valve Academic Research Consortium-2, *AKIN* Acute Kidney Injury Network, *iEOA* indexed effective orifice area

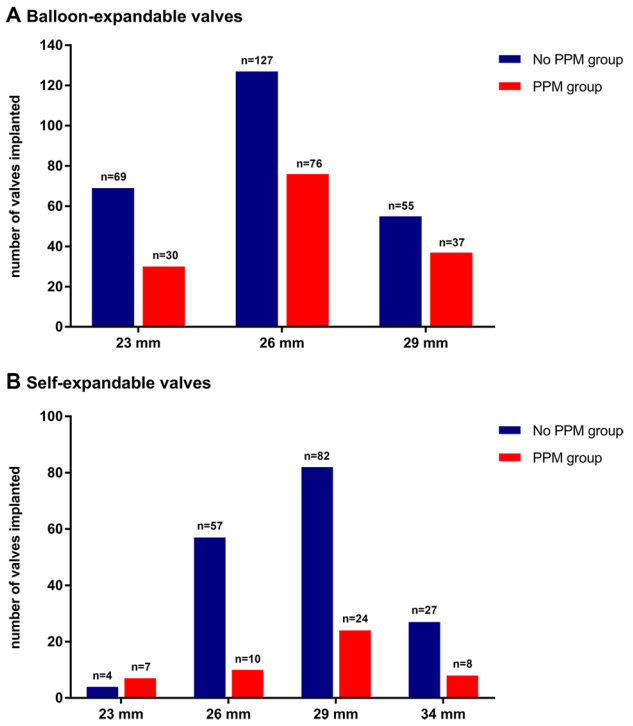

Fig. 2 Number of valves implanted. Number and sizes of implanted balloon-expandable **a** and self-expandable valves **b** for both the "No PPM" and the "PPM" group

fibrillation, COPD, PAD, PAH as well as impaired LVEF, especially severely impaired LV function (LVEF < 35%). The amount of contrast medium used and the procedural duration were also significant factors. Regarding VARC-2 defined outcomes, acute kidney failure stage 3 (AKIN stage 3), periprocedural myocardial infarction, major vascular access complication, disabling stroke, and conversion to open heart surgery were significantly linked to all-cause mortality after TAVI.

Multivariate Cox regression analysis was then employed including backward selection based on the likelihood criteria to determine independent risk factors for TAVI outcome (Table 4). From all potential risk predictors, age > 81.2 years, COPD, PAD, LVEF, AKIN stage 3 as well as myocardial infarction emerged as independent prognostic parameters for all-cause mortality after TAVI. As mentioned before, PPM failed to show a significant association with overall survival in our cohort, as shown by Kaplan–Meier curves (Fig. 3).

Discussion

We retrospectively analyzed 613 patients undergoing TAVI at our institution. In our study, PPM was not associated with overall survival after TAVI. In comparison with published SAVR data, our results suggest that relevant PPM is less common after TAVI than after SAVR.

Incidence and variables associated with PPM

In our study, relevant PPM according to VARC-2 defined criteria was observed in 192 subjects (31.3%) after TAVI, with moderate PPM being found in 150 patients (24.5%) and severe PPM being present in 42 patients (6.9%).

With regard to the incidence of PPM after TAVI, our results are in line with previously published data. In a meta-analysis, Takagaki et al. found a statistically significant reduction in moderate, severe, and overall PPM incidence after TAVI compared to SAVR [14]. Whether these differences in PPM relate to procedural aspects or to the specific patient population treated is still unclear. One important explanation may be the different hemodynamic profiles of TAVI prostheses which have thinner stent frames and do not have a sewing ring. Another significant contributing factor in our study may be the supra-annular positioning of the

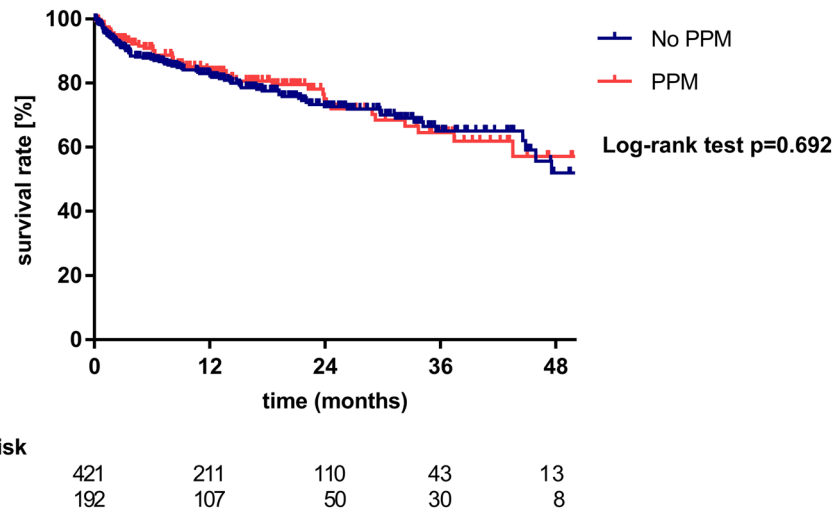

Fig. 3 Clinical outcomes and follow-up. Kaplan–Meier survival curves for overall survival comparing the "No PPM" and the "PPM" group

Table 3 Mortality-associated factors (log-rank test)

	p value
Age > median (81.2 years)	0.002
Chronic atrial fibrillation	0.005
COPD	0.014
PAD	0.006
PAH	0.017
LVEF	0.047
LVEF < 35%	0.031
Contrast medium	< 0.001
AKIN stage 3	< 0.001
Major vascular access complication	0.022
Myocardial infarction	0.001
Procedural duration	< 0.001
Disabling stroke	< 0.001
Conversion	0.018

COPD chronic obstructive pulmonary disease, *PAD* peripheral artery disease, *PAH* pulmonary arterial hypertension, *LVEF* left ventricular ejection fraction, *AKIN* Acute Kidney Injury Network

Table 4 Cox regression analysis

Variable	Adjusted HR (95% CI)	*p* value
Age > median (81.2 years)	2.16 (1.45–3.21)	< 0.001
COPD	1.92 (1.23–3.00)	0.004
PAD	1.84 (1.13–2.99)	0.014
LVEF	0.74 (0.62–0.89)	0.001
AKIN stage 3	9.81 (4.70–20.49)	< 0.001
Myocardial infarction	4.12 (1.13–15.01)	0.032

Results are presented as adjusted hazard ratios (HR) with 95% confidence intervals (CI)

COPD chronic obstructive pulmonary disease, *PAD* peripheral artery disease, *LVEF* left ventricular ejection fraction, *AKIN* Acute Kidney Injury Network

Medtronic CoreValve platform which may exert favorable effects regarding the iEOA [15].

In summary, TAVI prostheses seem to be able to achieve an adequate iEOA in most cases and anatomies despite the fact that catheter-based procedures do not allow for aortic root enlargement especially in patients with small aortic annuli. With respect to large aortic roots, we have recently reported our experience with the self-expanding Medtronic Corevalve Evolut R, 34 mm, device in a multi-center registry [16]. This largest SEV currently available provides a useful option to avoid PPM in patients with large aortic annuli.

In our cohort, predisposing factors for PPM included ischemic cardiomyopathy with reduced LVEF. This seems intuitive as patients with an impaired left ventricular function might have a tendency towards a low-flow state resulting in incomplete opening of the valve orifice after TAVI and, therefore, lower iEOA. This observation is supported by a surgical study published by Fallon et al. [17]. In their analysis of 59,779 SAVR patients, impaired LVEF also showed a highly significant association with PPM. In our opinion, this is an interesting finding, as it suggests that impaired LV might be a risk factor for PPM. Moreover, patients with an impaired LVEF constitute an important subgroup of patients, as they seem to be particularly prone to the adverse effects of PPM and show worse outcomes than patients with a normal LVEF, both after TAVI and after SAVR [18, 19]. To account for that possible confounder, we have also analyzed the subgroup of only patients with normal LVEF (Supplemental Figure 1). Acknowledging the smaller sample size and shorter follow-up, this analysis also did not show a statistically significant survival difference regarding the "No PPM" and "PPM" group.

With respect to procedural data, the "No PPM" group included more patients treated with a transfemoral access. Notably, SEV were associated with lower rates of PPM than BEV. This may be explained by the aforementioned supra-annular positioning of the Medtronic CoreValve system compared to the intra-annular design of the Edwards Sapien platform potentially resulting in beneficial hemodynamics and larger iEOA especially in patients with small aortic annuli [20]. In fact, this assumption is supported by an analysis of Kim et al. who in a study of 587 SAVR patients compared the outcomes of patients receiving supra-annular and intra-annular bioprostheses [21]. The authors concluded that the implantation of supra-annular prostheses resulted in better hemodynamics, while there was no difference between both groups regarding long-term mortality. Nevertheless, as shown in Fig. 2b, even with the 23 mm self-expandable Medtronic heart valve, an adequate iEOA may not be achievable in a subgroup of TAVI patients with small aortic annuli. One should also bear in mind that BEV seem to offer advantages over SEV regarding other procedural outcomes, for example, in patients with severe calcifications of the device landing zone, as was pointed out by Kim et al. [22].

Impact of PPM after SAVR and TAVI

Although there have been conflicting data in the past, there is now widespread consensus that PPM following SAVR has significant implications and is an important risk factor for adverse outcome.

In a study of 2154 patients who underwent SAVR, Rao et al. showed that 30-day mortality was significantly higher in patients with PPM than in patients without PPM (7.9% vs. 4.6%, $p = 0.027$) [23]. Investigating the impact of PPM on 30-day mortality in 1266 SAVR patients, Blais et al. reported that the relative risk of mortality was increased 2.1-fold in patients with moderate PPM and 11.4-fold in patients with severe PPM [24]. Finally, in a meta-analysis

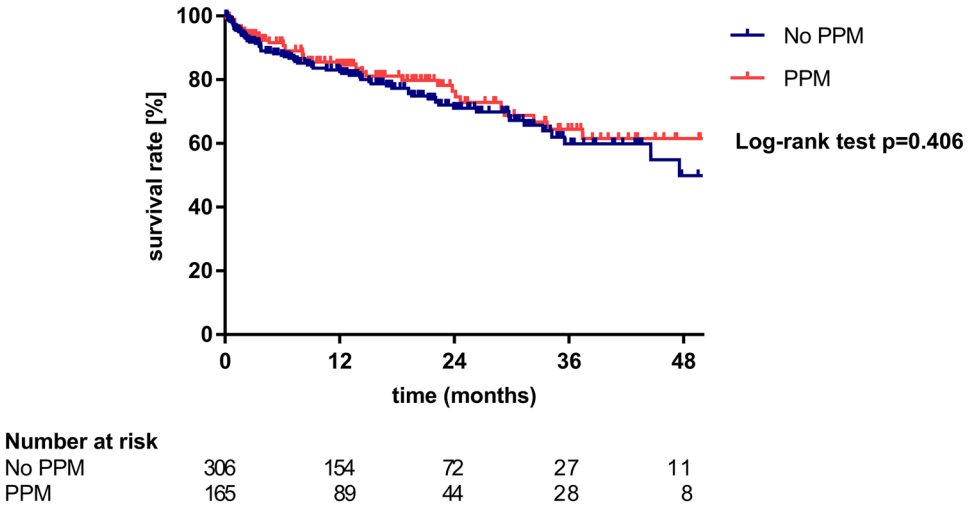

Fig. 4 Clinical outcomes and follow-up in non-obese patients. Kaplan–Meier survival curves for overall survival in non-obese patients (BMI < 30 kg/m^2) comparing the "No PPM" and the "PPM" group

of 34 studies comprising 27,186 patients, Head et al. evaluated the prognostic implications of PPM on long-term survival after SAVR [11]. PPM, both moderate and severe, was associated with a statistically significant reduction in overall and cardiac-related long-term survival in patients after SAVR. PPM has also been linked to other endpoints: In a study of 1103 patients, Del Rizzo et al. showed that PPM after SAVR is associated with decreased left ventricular mass regression compared to patients without PPM [25]. Pibarot et al. demonstrated that PPM leads to impaired hemodynamics including reduced cardiac index, less symptomatic improvement, and higher transvalvular gradients which may ultimately be associated with accelerated valve degeneration [26, 27].

In our study, PPM failed to show a significant association with overall survival after TAVI. This is also in line with the aforementioned meta-analysis by Takagi et al. demonstrating that neither severe nor moderate PPM influenced mortality after TAVI [14]. As to the reasons, there are several possible explanations, some of which we would like to present: first of all, there are substantial procedural differences between SAVR and TAVI including conceptual aspects like valve design and hemodynamic profile. In addition, most TAVI patients are still high-risk individuals with advanced age. It is, therefore, reasonable to assume that the majority of TAVI patients treated today will not experience potential long-term implications of PPM which may manifest after a period of 10 years, as reported in various SAVR studies. However, with the continuing shift of TAVI towards a younger population with lower risk and higher life expectancy, the prognostic implications of PPM may become more clinically evident. Finally, with growing evidence specific TAVI subgroups who are overly affected by severe PPM may be identified. In the PARTNER trial cohort-A analysis severe PPM was associated with higher mortality in a subset of patients with no postprocedural aortic regurgitation which makes this the only randomized trial showing an impact of PPM on survival in TAVI patients [28].

Another possible explanation is the potential overestimation of PPM in obese patients who seem to have a better long-term outcome after TAVI—a phenomenon commonly being referred to as the "obesity paradoxon" [29, 30]. To account for that potential interaction, we also analyzed the impact of PPM in patients who are not obese (BMI < 30 kg/m^2). In this subgroup analysis, PPM also did not have any significant impact on survival after TAVI (Fig. 4).

In summary, the prognostic relevance of PPM after TAVI remains controversial. Although it seems obvious to extrapolate the implications of PPM after SAVR to TAVI patients, both differences in procedural aspects as well as the patient population should be taken into consideration. Future studies are thus necessary to better determine the role of PPM in patients undergoing TAVI.

Limitations

Our study is mainly limited by its retrospective single-center design with the focus on overall survival and the inherent uncertainty including residual measured and unmeasured confounding factors. Endpoints such as heart failure symptoms, accelerated valve degeneration, physical capacity, cardiac-related rehospitalization, and quality of life are thus not accounted for. In addition, mortality in certain subgroups may have been underestimated. Moreover, we acknowledge that our follow-up might not be long enough to adequately evaluate long-term implications of PPM in TAVI patients, especially considering the fact that effects of PPM in SAVR patients were mostly observed after 5–10 years. However, our study cohort is highly representative of an unselected real-world TAVI population. In comparison with other published single-center reports on PPM following TAVI, our sample size is large and follow-up period relatively longer.

In addition, the iEOA data used in our study were derived from in vivo obtained echocardiography measurements.

Conclusions

In our retrospective analysis, PPM after TAVI was not associated with increased mortality, yet due to the limitations of our study, this has to be confirmed in large randomized studies. The incidence of PPM after TAVI seems to be lower than after SAVR and PPM was less common using SEV compared to BEV. Furthermore, impaired LVEF seems to be associated with higher rates of PPM.

Future studies are needed to determine the long-term prognostic relevance of PPM, including secondary endpoints such as quality of life and accelerated valve degeneration. They should also address the question whether or not SEV should be preferred to BEV in patients at risk for PPM.

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Compliance with ethical standards

Conflict of interest C. Kuhn received speaker's honoraria from Medtronic. D. Frank works as a proctor for and has received speaker's honoraria as well as travel support from Medtronic and Edwards. The other authors have no conflicts of interest to declare.

Ethical statement All participants gave informed consent. This study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee at the Kiel University.

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