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ORIGINAL STUDIES

Prevalence, predictors, and outcomes of patient prosthesis mismatch in women undergoing TAVI for severe aortic stenosis: Insights from the WIN-TAVI registry

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Abbreviations: BMI, body mass index; iEOA, indexed effective orifice area; PPM, patient prosthesis mismatch; TAVI, transcatheter aortic valve intervention.

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Abstract

Objective: To evaluate the incidence, predictors and outcomes of female patients with patient-prosthesis mismatch (PPM) following transcatheter aortic valve intervention (TAVI) for severe aortic stenosis (AS).

Background: Female AS TAVI recipients have a significantly lower mortality than surgical aortic valve replacement (SAVR) recipients, which could be attributed to the potentially lower PPM rates. TAVI has been associated with lower rates of PPM compared to SAVR. PPM in females post TAVI has not been investigated to date.

Methods: The WIN-TAVI (Women's INternational Transcatheter Aortic Valve Implantation) registry is a multicenter registry of women undergoing TAVR for severe symptomatic AS. Two hundred and fifty patients with detailed periprocedural and followup echocardiographic investigations were included in the WIN-TAVI echocardiographic sub-study. PPM was defined as per European guidelines stratified by the presence of obesity.

Results: The incidence of PPM in our population was 32.8%. Patients with PPM had significantly higher BMI (27.4 ± 6.1 vs. 25.2 ± 5.0, p = .002), smaller sized valves implanted (percentage of TAVI ≤23 mm 61% vs. 29.2%, PPM vs. no PPM, p < .001) and were more often treated with balloon expandable valves (48.3 vs. 32.5%, p < .001) rather than self expanding ones (26.3 vs. 52.8%, <.001). BMI (OR = 1.08; 95%CI 1.02–1.14, p = .011) and valve size ≤23 mm (OR = 3.00 95%CI 1.14–7.94, p = .027) were the only independent predictors of PPM. There was no significant interaction between valve size and valve type (p = .203). No significant differences were observed in 1-year mortality or major adverse cardiovascular events.

Conclusions: PPM in females undergoing TAVI occurs in one third of patients. BMI and valve size <23 mm are independent predictors. Larger registries are required to determine the impact of PPM on future clinical outcomes.

KEYWORDS

females, outcomes, patient-prosthesis mismatch, TAVI

1 | INTRODUCTION

The concept of patient prosthesis mismatch (PPM) was first described by Rahimtoola in 1978: "Mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve."¹ This concept was revisited by Pibarot et al² who suggested the process of selecting the appropriate sized prosthesis using the indexed effective orifice area (iEOA), derived from the EOA of the prosthesis and the body surface area of the patient. Pibarot et al proposed avoiding an iEOA less than 0.85 cm²/m² to prevent PPM. This is based on the steep increase in the mean pressure gradient whenever iEOA falls below this cut off. PPM is considered to be haemodynamically insignificant if the iEOA is >0.85 cm²/m², moderate if between 0.65 and 0.85 cm²/m², and severe if <0.65 cm²/m². However, for obese patients (body mass index [BMI] \geq 30 kg/m²) lower criteria may be more appropriate, given the hyperdynamic cardiac output state.³ Indeed new definitions of PPM were introduced in the 2016 European Guidelines for obese patients with BMI over 30.^{4,5}

In a recent meta-analysis⁶ PPM was seen in 35% of patients undergoing transcatheter aortic valve implantation (TAVI), a figure

TABLE 1 Baseline demographics, comorbidities, echocardiographic, and CT parameters in the two groups

| Variable | PPM = 1, N = 82 (32.8%) | PPM = 0, N = 168 (67.2%) | p-value |
|--|-------------------------|--------------------------|---------|
| General demographics | | | |
| Age, years | 82.3 ± 7.3 | 83.1 ± 6.2 | .374 |
| BMI, kg/m ² | 27.4 ± 6.1 | 25.2 ± 5.0 | .002 |
| Height, cm | 161 ± 5.4 | 157 ± 9.7 | <.001 |
| Weight, kg | 71.4 ± 17.0 | 63.6 ± 15.2 | <.001 |
| Caucasian | 76 (95.0%) | 155 (97.5%) | .447 |
| Past medical history | | | |
| Hypertension | 62 (76.5%) | 126 (75.4%) | .850 |
| Diabetes | 24 (29.3%) | 38 (22.6%) | .253 |
| Current smoker | 2 (2.4%) | 9 (5.4%) | .512 |
| Previous MI | 5 (6.1%) | 19 (11.3%) | .189 |
| Previous PCI | 15 (18.3%) | 46 (27.4%) | .116 |
| Previous CABG | 10 (12.3%) | 15 (8.9%) | .401 |
| Previous cardiac surgery | 14 (17.1%) | 26 (15.6%) | .761 |
| Previous stroke | 9 (11.1%) | 19 (11.3%) | .963 |
| Peripheral arterial disease | 11 (13.4%) | 14 (8.4%) | .220 |
| COPD | 17 (20.7%) | 47 (28.0%) | .218 |
| Home O ₂ | 2 (2.5%) | 5 (3.0%) | 1.000 |
| СКD | 24 (29.3%) | 60 (36.1%) | .282 |
| Euroscore I | 18.9 ± 12.8 | 19.2 ± 12.2 | .854 |
| STS score | 8.7 ± 8.2 | 9.6 ± 9.4 | .477 |
| Porcelain aorta | 4 (4.9%) | 18 (10.7%) | .132 |
| High surgical risk | 71 (86.6%) | 143 (85.1%) | .757 |
| Pulmonary hypertension | 21 (25.6%) | 47 (28.1%) | .673 |
| Prior pacemaker | 6 (7.3%) | 13 (7.7%) | .906 |
| Anemia | 26 (31.7%) | 47 (28.3%) | .581 |
| Baseline echocardiography | | | |
| LVEF<30% | 3 (3.8%) | 4 (2.4%) | .685 |
| LVEF | 54.6 ± 11.3 | 56.4 ± 10.5 | .220 |
| Echo annulus size | 21.9 ± 2.2 | 21.7 ± 2.0 | .557 |
| Peak gradient | 78.5 ± 18.3 | 77.1 ± 24.3 | .682 |
| Mean gradient | 47.9 ± 11.5 | 48.6 ± 15.6 | .730 |
| AVA | 0.7 ± 0.4 | 0.6 ± 0.2 | .448 |
| Baseline AR | | | .152 |
| None | 24 (31.2%) | 50 (32.3%) | |
| Mild | 35 (45.5%) | 80 (51.6%) | |
| Moderate | 14 (18.2%) | 24 (15.5%) | |
| Severe | 4 (5.2%) | 1 (0.6%) | |
| Baseline MR | | | .266 |
| None | 12 (15.8%) | 29 (18.1%) | |
| Mild | 44 (57.9%) | 72 (45.0%) | |
| Moderate | 17 (22.4%) | 53 (33.1%) | |
| Severe | 3 (3.9%) | 6 (3.8%) | |
| MSCT parameters (data available on 148 patients) | | | |
| Aortic annulus perimeter (mm) | 64.9 ± 21.5 | 71.6 ± 23.5 | .159 |
| Aortic annular calcification | | | .801 |

(Continues)

TABLE 1 (Continued)

| ١ | Variable | PPM = 1, N = 82 (32.8%) | PPM = 0, N = 168 (67.2%) | p-value |
|---|-------------------------------------|-------------------------|--------------------------|---------|
| | None | 5 (8.1%) | 8 (6.2%) | |
| | Mild | 4 (6.5%) | 12 (9.2%) | |
| | Moderate | 29 (46.8%) | 66 (50.8%) | |
| | Severe | 24 (38.7%) | 44 (33.8%) | |
| | Aortic root calcium score | 711 ± 540 | 720 ± 532 | .933 |
| | Minimal iliofemoral dimesion (mm) | 7.3 ± 2.3 | 8.5 ± 2.9 | .012 |
| (| Coronary angiography | | | |
| | Number of coronary vessels diseased | | | .354 |
| | 0 | 35 (64.8%) | 78 (62.4%) | |
| | 1 | 14 (25.9%) | 23 (18.4%) | |
| | 2 | 2 (3.7%) | 12 (9.6%) | |
| | 3 | 3 (5.6%) | 12 (9.6%) | |
| | LMS disease | 5 (10.6%) | 9 (8.7%) | .765 |
| | | | | |

Abbreviations: AR, aortic regurgitation; AVA, aortic valve area; BMI, body mass index; CABG, coronary artery bypass surgery; CKD, chronic kindey disease; COPD, chronic obstructive pulmonary artery disease; iEOA, indexed estimated orifice area; LMS, left main stem; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MSCT, mutlislice computed tomography; PCI, percutaneous coronary intervention; PPM, patientprosthesis mismatch.

| Variable | PPM = 1, N = 82 (32.8%) | PPM = 0, N = 168 (67.2%) | p-value | TABLE 2 Female specif |
|---------------------------|-------------------------|--------------------------|---------|-----------------------|
| Hx of pregnancy | 63 (76.8%) | 111 (66.1%) | .083 | characteristics |
| Gestational diabetes | 1 (1.7%) | 0 (0.0%) | .365 | |
| Gestational hypertension | 2 (3.4%) | 2 (2.0%) | .623 | |
| Age at menopause | 49.2 ± 5.6 | 50.0 ± 4.4 | .289 | |
| History of HRT use | 5 (7.1%) | 4 (2.7%) | .150 | |
| Hx of gynecolofical Ca | 1 (1.3%) | 6 (3.7%) | .432 | |
| Hx of gynecologic surgery | 9 (11.3%) | 28 (17.0%) | .241 | |
| Hx of breast Ca | 6 (8.1%) | 14 (8.9%) | .838 | |
| Hx of osteoporosis | 17 (23.3%) | 23 (15.2%) | .140 | |

Abbreviations: Ca, cancer; HRT, hormonal replacement therapy; Hx, history; iEOA, indexed estimated orifice area; PPM, patient prosthesis mismatch.

significantly lower to the one seen in patients undergoing surgical aortic valve replacement (SAVR) (OR 0.23;95%CI 0.07-0.79). This finding may be related to differences in TAVI valve design, such as the absence of a sewing ring and the supra-annular location of the neo valve in some of the TAVI valves. Although the annulus is not prepared by excising calcium, as is done in surgery, transcatheter valves are associated with a larger EOA and iEOA, and lower peak as well as mean transprosthetic gradients.⁷⁻¹⁷

Large surgical registries and a recent meta-analysis have demonstrated an association between PPM and decreased long-term survival.¹⁸⁻²⁰ Female gender was found to be a predictor of PPM in a recent literature review.²¹ A predisposition of female patients to PPM was demonstrated. This effect of PPM on survival, however, was not shown in a recent meta-analysis of TAVI trials.⁶ This finding, however, needs to be interpreted cautiously given the much shorter follow up times. Of interest, recent reports²² point toward an association between severe PPM with subclinical valve thrombosis.

In a meta-analysis of patients with aortic stenosis (AS),²³ among females, TAVI recipients had a significantly lower mortality than SAVR recipients, at 1 year (OR 0.68; 95%CI 0.50-0.94) and at 2 years (OR 0.74; 95%CI 0.58-0.95). One of the suggested mechanisms for the increased survival amongst females treated with TAVI was the lower PPM rates which could facilitate greater recovery in left ventricular systolic function.9,16,24

In the current study we aim to investigate the prevalence of PPM, its predictors and associated outcomes in females undergoing TAVI included in the WIN-TAVI (Women's INternational Transcatheter Aortic Valve Implantation) registry.

2 **METHODS**

The WIN-TAVI registry (NCT01819181) is an international, multicenter, prospective, observational registry of women undergoing TAVR at

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19 European and North American centers treated with commercially available and approved TAVR devices and delivery systems for the treatment of severe symptomatic AS. Details of the registry and eligibility criteria have been described in previous publications.²⁵ Out of the total of 1,019 patients, 250 patients who had detailed periprocedural and follow-up echocardiographic investigations were included in the WIN TAVI echocardiographic sub-study. PPM was defined^{4,5} as

- moderate if iEOA 0.85–0.66 and severe if iEOA ≤0.65 in patients with BMI <30 kg/m²
- moderate if iEOA 0.70–0.56 and severe if iEOA ${\leq}0.55$ in patients with BMI ${\geq}30~\text{kg/m}^2$

TABLE 3Procedural parameters inpatients with and without patientprosthesis mismatch

All patients underwent multislice computed tomography (MSCT) in their participating centre. Reporting of echocardiographic and MSCT parameters was performed at each participating centre.

2.1 | Endpoints

The primary endpoint was Valve Academic Research Consortium (VARC)-2 early safety (at 30 days); this is a composite of all-cause mortality, stroke, life-threatening bleeding, acute kidney injury (Stages 2 and 3), coronary artery obstruction, major vascular complication, and valve-related dysfunction requiring repeat procedure

| Variable | PPM = 1, N = 82 (32.8%) | PPM = 0, N = 168 (67.2%) | p-value |
|------------------------------|-------------------------|--------------------------|---------|
| Type of valve inserted | | | <.001 |
| Edwards S3 | 22 (27.5%) | 26 (16.0%) | |
| Edwards XT | 17 (21.3%) | 28 (17.2%) | |
| Evolut R | 6 (7.5%) | 16 (9.8%) | |
| Corevalve | 15 (18.8%) | 70 (42.9%) | |
| Direct flow | 10 (12.5%) | 5 (3.1%) | |
| Portico | 0 (0.0%) | 2 (1.2%) | |
| Lotus | 9 (11.3%) | 16 (9.8%) | |
| ACURATE neo | 1 (1.3%) | 0 (0.0%) | |
| Valve type | | | <.001 |
| Balloon expandable | 39 (48.8%) | 54 (33.1%) | |
| Self-expanding | 21 (26.3%) | 86 (52.8%) | |
| Others | 20 (25.0%) | 23 (14.1%) | |
| Valve size | | | <.001 |
| 20 mm | 1 (1.2%) | 0 (0.0%) | |
| 23 mm | 49 (59.8%) | 49 (29.2%) | |
| 25 mm | 7 (8.5%) | 13 (7.7%) | |
| 26 mm | 19 (23.2%) | 67 (39.9%) | |
| 27 mm | 2 (2.4%) | 2 (1.2%) | |
| 29 mm | 4 (4.9%) | 36 (21.4%) | |
| 31 mm | 0 (0.0%) | 1 (0.6%) | |
| Valve ≤23 mm | 50 (61.0%) | 49 (29.2%) | <.001 |
| Paravalvular AR post TAVI | | | .898 |
| None | 29 (55.8%) | 37 (51.4%) | |
| Mild | 21 (40.4%) | 32 (44.4%) | |
| Moderate | 2 (3.8%) | 3 (4.2%) | |
| Paravalvular AR at 6/12 | | | 1.000 |
| None | 13 (46.4%) | 24 (49.0%) | |
| Mild | 14 (50.0%) | 23 (46.9%) | |
| Moderate | 1 (3.6%) | 2 (4.1%) | |
| New pacemaker | 11 (13.4%) | 18 (10.7%) | .531 |
| Major vascular complications | 9 (11.0%) | 15 (8.9%) | .606 |
| Life threatening bleeding | 2 (2.4%) | 12 (7.1%) | .154 |

Abbreviations: AR, aortic regurgitation; iEOA, indexed estimated orifice area; PPM, patient prosthesis mismatch.

(BAV, TAVI, or SAVR).²⁶ Secondary endpoints included 1-year all cause mortality, cardiovascular mortality, stroke and the composites death or stroke, and major adverse cardiovascular events (death, MI, or stroke).

2.1.1 | Statistical analysis

All continuous variables were tested for normality using the Kolmogorov–Smirnov test. Categorical data are presented as frequencies and percentages and were compared using the chi-square or Fisher exact test. Continuous variables are presented as mean \pm *SD* or medians and interquartile range and were compared using Student's t test or Wilcoxon signed rank test. Time-to-event curves were repre-



FIGURE 1 Incidence of patient prosthesis mismatch in various groups. Balloon expandable transcatheter heart valves (THV) include all the Edwards valves (S3, XT) and self-expanding THV all the Medtronic iterations (CoreValve and Evolut R) [Color figure can be viewed at wileyonlinelibrary.com]

| sented | using | Kaplan-Meie | er methods. | Using | logistic | regression |
|----------|----------|----------------|----------------|-----------|-----------|-------------|
| method | s, we g | enerated a m | ultivariable m | odel for | predicto | ors of PPM. |
| Variable | es that | were significa | ntly different | in the | two PPN | 1 groups in |
| the univ | variable | analysis (Tab | oles 1-3) were | e include | ed in the | regression |
| model | (p < .05 |). Computed | tomography | (CT) pa | rameters | were not |
| included | d in the | model due to | large number | s of mis | sing data | that would |
| weaken | the mo | del. | | | | |

3 | RESULTS

Incidence of PPM in our population was 32.8% (82/250 patients). Severe PPM was seen in 18 (7.2%) patients. Baseline demographic, echocardiographic, CT, and procedural characteristics in patients with and without PPM are shown in Table 1.

3.1 | Baseline characteristics

3.1.1 | Demographics, risk factors, and past medical history

Female patients with PPM had a significantly higher BMI (27.4 \pm 6.1 vs. 25.2 \pm 5, *p* = .002). Hypertension, diabetes, smoking status, previous stroke, peripheral arterial disease, chronic kindey disease, previous cardiac surgery, or CABG did not differ between the two groups (Table 1). Both groups had similar Euroscore I and STS scores.

| | | <i>,</i> , | | | | |
|--|-------|------------|------------------|---------|---------|--|
| | OR | 95% co | onfidence interv | al | p-value | |
| BMI | 1.077 | 1.02 | 1. | .14 | .009 | |
| Valve type | | | | | | |
| Balloon expandable | Ref | | | | | |
| Self-expanding | 0.669 | 0.32 | 1. | .39 | .281 | |
| Others | 1.552 | 0.70 | 3. | .42 | .276 | |
| Valve ≤23 mm | 3.385 | 1.77 | 6 | .46 | <.001 | |
| Model including interaction between valve type and valve size ≤23 mm | | | | | | |
| | OR | 95% confid | ence interval | p-value | | |
| BMI | 1.075 | 1.02 | 1.14 | .011 | | |
| Valve type | | | | | | |
| Balloon expandable | Ref | | | | | |
| Self-expanding | 0.498 | 0.18 | 1.40 | .185 | | |
| Others | 1.994 | 0.62 | 6.40 | .246 | | |
| | | | 7.04 | 007 | | |
| Valve ≤23 mm | 3.003 | 1.14 | 7.94 | .027 | | |

TABLE 4 Multivariable regression model identifying independent predictors for patient-prosthesis mismatch

Abbreviations: BMI, body mass index; OR, odds ratio.

3.1.2 | Echocardiographic data

Baseline echocardiographic data pre-TAVI were similar in the two groups (Table 1). Baseline left ventricular ejection fraction was 54.6 ± 11.3 and 56.4 ± 10.5 in the PPM and no PPM groups, respectively (p = .220). Peak and mean gradients alongside aortic valve area were all similar in the two groups.

3.1.3 | CT parameters

TABLE 5 One year follow-up echocardiographic parameters

CT measured aortic annulus perimeter (64.9 ± 21.5 PPM vs. 71.6 \pm 23.5 mm no PPM, *p* = .159) and aortic annular calcification were similar in the two groups. There was a smaller minimal

iliofemoral dimension in patients with PPM $(7.3 \pm 2.3 \text{ vs. } 8.5 \pm 2.9 \text{ mm}, p = .012)$ (Table 1).

No significant differences were seen in terms of coronary artery disease severity.

3.2 | Female specific characteristics

With regards to female specific characteristics, there was a small trend for increase in history of pregnancy amongst patients with PPM post TAVI (Table 2). Gestational diabetes and hypertension, age at menopause, history of HRT use, history of gynecological or breast Ca and osteoporosis did not differ between the two groups.

| | PPM = 1, N = 82 (32.8%) | PPM = 0, N = 168 (67.2%) | p- value |
|-----------------------------------|----------------------------|-----------------------------|-------------|
| LVEF | 57.8 ± 9.1 | 58.5 ± 8.6 | .650 |
| Peak AV gradient (mmHg) | 24.5 ± 13.0 | 19.8 ± 10.5 | .040 |
| Mean AV gradient (mmHg) | 14.0 ± 5.9 | 10.7 ± 5.4 | .001 |
| Aortic paravalvular regurgitation | | | .898 |
| None | 29 (55.8%) | 37 (51.4%) | |
| Mild | 21 (40.4%) | 32 (44.4%) | |
| Moderate | 2 (3.8%) | 3 (4.2%) | |

Abbreviations: AV, aortic valve; LVEF, left ventricular ejection fraction; PPM, patient prosthesis mismatch.

TABLE 6Clinical outcomes in thetwo groups at 30-days and 1-year

| | PPM = 1, N = 82 (32.8%) | PPM = 0, N = 168 (67.2%) | p-value |
|--------------------------------------|----------------------------|-----------------------------|---------|
| 30-day outcomes | No. of events (%) | | |
| All-cause death | 0 (0.0%) | 3 (1.8%) | .225 |
| All stroke | 0 (0.0%) | 2 (1.2%) | .322 |
| Life-threatening bleeding | 9 (11.0%) | 19 (11.3%) | .948 |
| Acute kidney injury | 2 (2.4%) | 3 (1.8%) | .728 |
| Coronary artery obstruction | 1 (1.2%) | 2 (1.2%) | .984 |
| Major vascular complication | 9 (11.0%) | 14 (8.3%) | .494 |
| Valve-related dysfunction | 0 (0.0%) | 0 (0.0%) | n.a |
| VARC2 early safety | 21 (25.6%) | 43 (25.6%) | .888 |
| 1-year outcomes | | | |
| Death | 4 (4.9%) | 14 (8.5%) | .296 |
| Cardiovascular death | 2 (2.5%) | 12 (7.4%) | .122 |
| Stroke | 4 (4.9%) | 5 (3.0%) | .480 |
| MACE (death, MI, stroke) | 6 (7.3%) | 19 (11.5%) | .289 |
| Death or stroke | 6 (7.3%) | 19 (11.5%) | .289 |
| Arrhythmia or conduction disturbance | 16 (19.5%) | 36 (21.4%) | .717 |

Abbreviations: MACE, major adverse cardiovascular endpoints; MI, myocardial infarction.

3.3 | Procedural parameters

PPM was associated with significantly higher rates of balloon expandable valve implantation (48.8 vs. 33.1%) and significantly lower rates of self-expanding valve implantation (26.3 vs. 52.8%, p < .001) (Table 3). Patients in the PPM group were more frequently implanted smaller sized valves (61 vs. 29.2% had valve size ≤ 23 mm, p < .001) (Table 3, Figure 1 and Supplementary Table). There were no significant differences in rates of new pacemaker, moderate paravalvular leak, major vascular or bleeding complications.

3.4 | Predictors of PPM

In the multivariable regression model independent predictors of PPM included raised BMI (per unit increase OR 1.08, (95%CI: 1.02–1.14) and valve size equal to or under 23 mm (\leq 23 vs. >23, OR 3, 95%CI 1.14–7.94, *p* = .027). There was no significant interaction between valve type and valve size *p* = .203. (Table 4).

3.5 | Follow-up

At 1-year echocardiographic follow-up there were significantly increased peak and mean gradients across the aortic valve in the PPM group (Table 5).

No significant differences were seen in VARC-2 early safety endpoint at 30-days (25.6% PPM group vs. 25.6% no PPM group, p = .888) or in any of the clinical outcomes at 1 year (Table 6).

4 | DISCUSSION

In the current study, prevalence of PPM in this all-female TAVI cohort was 32.8%. Independent predictors of PPM included larger BMI and valve size ≤23 mm, whereas there was no interaction between valve size and valve type. There does not appear to be any significant difference in 1-year clinical outcomes in the two groups; however, these results should be interpreted cautiously given the small sample size of our study and relatively short-term follow-up.

Despite several studies demonstrating that PPM incidence is reduced when patients are treated with TAVI compared to SAVR,^{6,9} in the current cohort nearly one third of females treated with TAVI appear to have at least moderate PPM. This finding is important as PPM has the potential implication of reduced LV hypertrophy regression and persistence of residual LV afterload^{11,27,28} which impacts on coronary flow reserve.⁹ PPM post-TAVI has been associated with less regression of LV hypertrophy, LV diastolic dysfunction, LV filling pressure (measured by E/e'), less improvement in LV systolic function (LVEF and myocardial strain), and less reduction of left atrial volume.^{11,28,29}

Interestingly, however, there may be a differential impact of PPM on mortality in patients treated with TAVI and those with

SAVR.^{6,9,13,27,29} In the study by Pibarot et al⁹ an increased mortality was seen in surgical patients with PPM but not in TAVI patients. In that particular study, as in the current study, TAVI PPM patients had significantly higher BMI, a previous shown independent predictor of PPM.⁶ Body surface area greater than 1.88 m² independently predicted severe PPM with satisfactory sensitivity (0.71) and specificity (0.70).³⁰ A higher BMI has been shown to be a powerful independent predictor of improved 2-year survival post TAVI in the PARTNER-A TRIAL.³¹ Such a higher BMI was not seen in PPM patients post surgery.⁹ Furthermore, indexing the EOA to the patient's BSA may overestimate PPM severity in obese individuals.³² The higher than expected valve gradient can be due, at least in part, to patient's supranormal cardiac output and high flow state due to morbid obesity.³³ In the current study we did not identify any survival benefit in females with no PPM, concurring with the study from Pibarot et al⁹; however, the small patient numbers and reduced power limit our ability to answer this question with certainty.

Smaller valve size (≤23 mm) was associated with PPM in our cohort. Given that the CT annulus perimeter was not significantly different in the two groups, and assuming optimal sizing, this can be explained by valve choice (balloon expandable vs. self expanding). This highlights the importance of optimal valve sizing based on CT parameters³⁴ and raises the question of a potential benefit in implantation of supra-annular self-expanding valves in female patients with small aortic annuli. In the randomized CHOICE study,³⁵ implantation of balloon-expandable valves was associated with significantly reduced oversizing percent and significantly higher mean transvalvular gradients (8.9 mmHg; 95% CI, 8.3-9.7 vs. 6.6 mmHg; 95%Cl, 6.0-7.3; p < .001). In the same study, despite having a significantly larger MSCT calculated aortic annulus perimeter, the balloon-expandable group ended up with a significantly higher % of 23 mm valves (9.9 vs 1.7%, p < .001). Our results agreed with the large retrospective TVT registry from Herrman et al on 62,125 TAVI patients which confirmed small valve size (≤23 mm) to be a significant predictor of severe PPM.³⁶

Previous studies have shown a hemodynamic benefit of TAVR over SAVR in the subset of patients with small aortic annulus.⁹ In high-risk patients with severe AS and a small aortic annulus (diameter < 20 mm), TAVI compares favorably with currently available surgical options, and may provide a reasonable alternative to conventional AVR in elderly patients with a small aortic annulus.³⁷ In a recent meta-analysis,²³ female AS patients treated with TAVI had improved survival to those treated with SAVR and one of the potential explanations was the presence of a larger iEOA post procedure. Therefore, TAVI valve size and type selection becomes more important in females who are known to have smaller size aortic annuli than their male counterparts.^{38,39}

In the current study no differences were observed in new pacemaker rates, paravalvular leak, or major adverse cardiovascular events in the PPM versus no PPM groups, probably secondary to improvements in valve design and increasing operator experience. This is in line with other studies which have shown no significant differences in terms of major adverse cardiovascular, cerebrovascular and valverelated events, cardiac-related hospitalizations, improvement in functional status, NYHA class, and self-assessed health state between patients with PPM and those without PPM after TAVI.^{11,13,27,28,40,41}

4.1 | Study limitations

One of the main limitations of the current study is the small sample size. However, this represents the largest echocardiographic study on PPM in female patients undergoing TAVI implantation. Another limitation is the solely echocardiographic definition of PPM and absence of a central echocardiographic core-lab. A recent study by Mooney et al,⁴² however, showed that even though the incidence of PPM was reduced when EOA was estimated using left ventricular outflow tract measured from CT (iEOA_{CT}), this did not associate with outcomes. Furthermore, in that study it was the echo $-iEOA_{TTE}$ and not the CT $-iEOA_{CT}$ that correlated with LV mass regression, posing questions on the clinical value of the need for iEOA_{CT}. The small proportion of patients with severe PPM (7.2%) may be the reason for the lack of differences in clinical outcomes at 1-year. In the large TVT registry it was only the severe PPM mismatch group that exhibited increased mortality at 1 year.³⁶ However, even in patients with moderate PPM, differences in clinical outcomes may only become evident at a later time (>5 years), due to faster valve degeneration, as shown in surgical bioprosthetic valve PPM registries.⁹ Detailed longitudinal data on LV mass, diastolic dysfunction, LV filling pressures, and LA size were lacking in the current study. PPM may have a particular impact on these variables and should be the focus of future longitudinal echocardiographic studies.

4.2 | Conclusions

PPM in female patients with AS undergoing TAVI is seen in almost one third of cases. Main predictors include raised BMI and small valve size. Appropriate sizing, and potentially use of self-expanding valves, which allows for the use of larger valves in smaller anatomies, may contribute to reduce the incidence of PPM. Even though in our study at least moderate PPM was not associated with clinical endpoints, results should be validated in larger, adequately powered cohorts.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

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

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