Impact of Prosthesis-Patient Mismatch on Cardiac Events and Midterm Mortality After Aortic Valve Replacement in Patients With Pure Aortic Stenosis

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Background—Prosthesis-patient mismatch (PPM) occurs when the effective orifice area (EOA) of the prosthesis being implanted is too small in relation to body size, thus causing abnormally high transvalvular pressure gradients. The objective of this study was to examine the midterm impact of PPM on overall mortality and cardiac events after aortic valve replacement in patients with pure aortic stenosis.

Methods and Results—The indexed EOA (EOAi) was estimated for each type and size of prosthesis being implanted in 315 consecutive patients with pure aortic stenosis. PPM was defined as an EOAi <0.80 cm²/m² and was correlated with overall mortality and cardiac events. PPM was present in 47% of patients. The 5-year overall survival and cardiac event-free survival were 82±3% and 75±4%, respectively, in patients with PPM compared with 93±3% and 87±4% in patients with no PPM (P=0.01). In multivariate analysis, PPM was associated with a 4.2-fold (95% CI, 1.6 to 11.3) increase in the risk of overall mortality and a 3.2-fold (95% CI, 1.5 to 6.8) increase in the risk of cardiac events. The other independent risk factors were history of heart failure, NYHA class III-IV, severe left ventricular hypertrophy, and absence of normal sinus rhythm before operation.

Conclusions—PPM is an independent predictor of cardiac events and midterm mortality in patients with pure aortic stenosis undergoing aortic valve replacement. As opposed to other risk factors, PPM may be avoided or its severity may be reduced with the use of a preventive strategy at the time of operation. (Circulation. 2006;113:8-.)

Key Words: echocardiography ■ hemodynamics ■ prognosis ■ stenosis ■ valves

Prosthesis-patient mismatch (PPM) occurs when the effective orifice area (EOA) of the prosthesis being implanted is less than that of the normal human valve.1,2 This is a frequent problem in patients undergoing aortic valve replacement (AVR), especially in patients with aortic stenosis (AS), and its main hemodynamic consequence is to generate high transvalvular pressure gradients through normally functioning prosthetic valves.1–7 The issue of PPM still generates much controversy with regard to its clinical relevance and, in particular, with regard to its effect on survival after operation. Whereas some authors have found that the persistence of PPM results in lower postoperative survival,8,9 others have reported that PPM and/or small prostheses have no significant impact on survival,10–13 and on this basis they concluded that PPM is not an important issue. However, the parameter used to define PPM was different from one study to the other, thus making difficult the comparison and interpretation of the results of these previous studies. To this effect, it should be emphasized that the only parameter yet demonstrated as being valid to define PPM is the prosthesis EOA indexed to the patient’s body surface area (EOAi).3–5,14–16 This index has consistently been shown to correlate with postoperative gradients as well as being predictive of adverse outcomes.3–9,14–24

The objective of this study thus was to analyze the impact of PPM, defined on the basis of EOAi, on midterm mortality and cardiac events in patients with pure AS undergoing AVR.

Methods

Patients

Between September 1997 and September 2003, 320 consecutive patients underwent AVR for pure AS. Hospital mortality was 1.6% (5/320), and only the 315 patients who were discharged from the hospital were included in this study. Clinical, echocardiographic, operative, and outcome data were prospectively collected in a
computerized database. The data were collected as part of a larger observational study aiming to identify the independent risk factors for postoperative morbidity and mortality in patients undergoing AVR. All patients had a follow-up visit at the hospital at 3 months. This visit included a physical examination, the determination of NYHA functional class, and an ECG. Thereafter, the patients were interviewed by telephone annually to assess their status. If any fatal or cardiac event occurred, these events were documented by communicating with the patient’s treating physician(s). For the purpose of the present study, we selected the patients who had undergone surgery at least 12 months before the closing date of the study (September 30, 2004), and a final telephone follow-up was conducted within 1 month after this date. The follow-up was complete in 99% (313/315) of the patients, and the mean follow-up time was 3.7 ± 1.7 years.

### Doppler-Echocardiographic Data

Preoperative echocardiographic data were obtained at our institution 0 to 7 days before operation in 94% (296/315) of patients. The Doppler-echocardiographic measurements were performed as previously described. Briefly, the dimensions of the left ventricle (LV) were assessed with 2-dimensionally guided M-mode tracings, with the measurements being made according to the recommendations of the American Society of Echocardiography. Left ventricular mass (LVM) was calculated with the formula:

\[ \text{LVM} = \frac{1}{2} \times (1.04 \times \text{TWT}^2 + 0.6 \times \text{WT}^2) \]

where TWT is the thickness of the wall of the left ventricle, and WT is the width of the left ventricle. The normal values for each model and size of prosthesis implanted in this cohort were measured 1 year after surgery at least 12 months before the closing date of the study. The projected EOA was then divided by body surface area, and PPM was defined as a projected EOAi ≤ 0.8 cm²/m². The selection of this value was based primarily on the results of previous studies. In addition, we did a preliminary analysis that confirmed that this cutoff value provides the best compromise between sensitivity and specificity to predict the studied end points.

### Statistical Analysis

Continuous variables were expressed as mean ± SD values and compared with a 2-tailed t test. The normality of the distributions in the 2 groups was tested by means of the Kolmogorov-Smirnov test, and, when not normal, the data were log transformed. Categorical variables were expressed as percentage of total and compared with the χ² test. Cumulative probability values of survival and cardiac event-free survival were estimated by the Kaplan-Meier method, reported as mean ± SEM, and compared with the log-rank test. The effect of the preoperative and operative variables on survival and event-free survival was assessed with the Cox proportional hazard model in a stepwise manner. The variables with a probability value < 0.1 were inserted in the final models. The variables tested in the models were as follows: (1) preoperative variables: age, gender, body mass index, NYHA functional class, severity of AS, hypertension, diabetes, coronary artery disease (presence and severity: number of diseased vessels), history of myocardial infarction, LV ejection fraction, history of heart failure, arteriopathy, chronic renal insufficiency, chronic obstructive pulmonary disease, sinus rhythm, left bundle branch block, LVM index, relative wall thickness ratio, presence of severe LV hypertrophy; and (2) operative variables: urgent/emergent operation, way of delivering cardioplegia, aortic cross-clamp time, bicuspid aortic valve, etiology of valve disease, coronary artery bypass graft, type of prosthesis implanted (stenotized bioprosthesis, stented bioprosthesis, mechanical prosthesis), implantation of the prosthesis in supra-annular position, EOAi, PPM, aortic root replacement, isolated replacement of ascending aorta, and septal myectomy. To assess the effect of PPM on outcome variables, we developed a first model with PPM entered as a dichotomous variable (PPM: EOAi ≤ 0.8 cm²/m² versus no PPM) and then a second model with EOAi entered as a continuous variable. The proportional hazards assumption was verified for all models. The data were statistically analyzed with the use of SPSS 13.0 (SPSS Inc).

### Results

#### Preoperative and Operative Data

Forty-seven percent of patients had PPM, and their mean EOAi was 0.71 ± 0.05 cm²/m² versus 0.91 ± 0.09 cm²/m² in the patients with no PPM (P < 0.0001). Five percent of patients had severe PPM (EOAi ≤ 0.6 cm²/m²). Tables 2 and 3 show the preoperative and operative data, respectively. When compared with patients with no PPM, patients with PPM were older and had higher body surface area, body mass index, prevalence of female gender, and proportion of 21-mm

### Definition of PPM

Previous studies have shown that PPM as well as its consequences on morbidity and mortality can be predicted at the time of operation by calculating the projected EOAi. In the present study, the projected EOAi was derived from the published normal in vivo EOA values for each model and size of prosthesis implanted in this cohort except for the Mitroflow prosthesis (Table 1). Indeed, for this prosthesis model, the normal in vivo EOA values have not yet been reported. We thus used the normal EOAI values established in our echocardiography laboratory from the data measured 1 year after operation in the cohort of patients with the Mitroflow prosthesis (Table 1). This information was used in the present study to determine the projected EOA of the patients who received Mitroflow prosthesis.

### Table 1. Reference EOA for Each Size and Model of Prosthesis

<table>
<thead>
<tr>
<th>Prosthesis Size, mm</th>
<th>No. of Patients (%)</th>
<th>19</th>
<th>21</th>
<th>23</th>
<th>25</th>
<th>27</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.7</td>
<td>3 (10)</td>
<td>1.0</td>
<td>1.5</td>
<td>2.0</td>
<td>2.3</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>21 (72)</td>
<td>1.3</td>
<td>1.5</td>
<td>1.7</td>
<td>1.8</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>4 (13)</td>
<td>1.4</td>
<td>1.6</td>
<td>1.7</td>
<td>1.8</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>1.2</td>
<td>3 (10)</td>
<td>1.5</td>
<td>1.7</td>
<td>1.8</td>
<td>1.9</td>
<td>21</td>
<td></td>
</tr>
</tbody>
</table>

*Data obtained from our echocardiography laboratory.
Tasca et al. Impact of Prosthesis-Patient Mismatch on Outcomes

### TABLE 2. Preoperative Data

<table>
<thead>
<tr>
<th>Mismatch (n=149)</th>
<th>No Mismatch (n=166)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>74±8</td>
<td>68±11</td>
</tr>
<tr>
<td>Age &gt;75 y</td>
<td>90 (60)</td>
<td>42 (25)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>88 (59)</td>
<td>70 (42)</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.85±0.21</td>
<td>1.76±0.19</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27±5</td>
<td>25±4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22 (15)</td>
<td>31 (19)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>81 (54)</td>
<td>116 (70)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>71 (48)</td>
<td>56 (37)</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>134 (90)</td>
<td>150 (90)</td>
</tr>
<tr>
<td>Arteriopathy</td>
<td>22 (15)</td>
<td>40 (24)</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>4 (3)</td>
<td>15 (9)</td>
</tr>
<tr>
<td>COPD</td>
<td>13 (9)</td>
<td>10 (6)</td>
</tr>
<tr>
<td>Preoperative NYHA class III-IV</td>
<td>55 (37)</td>
<td>46 (28)</td>
</tr>
<tr>
<td>Myocardial infection</td>
<td>9 (6)</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Preoperative heart failure*</td>
<td>46 (31)</td>
<td>38 (23)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>59±11</td>
<td>56±12</td>
</tr>
<tr>
<td>LVEF &lt;=40%</td>
<td>13 (9)</td>
<td>22 (14)</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>50±7</td>
<td>52±8</td>
</tr>
<tr>
<td>IVS, mm</td>
<td>14±2</td>
<td>14±2</td>
</tr>
<tr>
<td>LVPW, mm</td>
<td>12.9±1.5</td>
<td>12.6±1.6</td>
</tr>
<tr>
<td>LVM, g</td>
<td>281±65</td>
<td>298±78</td>
</tr>
<tr>
<td>LVMi, g/m²²</td>
<td>74±17</td>
<td>77±19</td>
</tr>
<tr>
<td>Preoperative LV hypertrophy</td>
<td>135 (96)</td>
<td>152 (97)</td>
</tr>
<tr>
<td>Preoperative severe LV hypertrophy</td>
<td>8 (6)</td>
<td>22 (14)</td>
</tr>
<tr>
<td>RLWT</td>
<td>0.52±0.11</td>
<td>0.49±0.09</td>
</tr>
<tr>
<td>Aortic valve EOAi, cm²</td>
<td>0.86±0.18</td>
<td>0.83±0.17</td>
</tr>
<tr>
<td>Aortic valve EOAi, cm²/m²</td>
<td>0.48±0.09</td>
<td>0.46±0.08</td>
</tr>
<tr>
<td>Mean aortic valve gradient, mm Hg</td>
<td>50±14</td>
<td>48±13</td>
</tr>
</tbody>
</table>

*History of preoperative hospital admission for heart failure.

Values are expressed as mean±SD or number (%). COPD indicates chronic obstructive pulmonary disease, LVEF, LV ejection fraction; LVEDD, LV end-diastolic diameter; IVS, interventricular septum; LVPW, LV posterior wall; RLWT, relative LV wall thickness; and LVMi, LVM index.

### TABLE 3. Operative Data

<table>
<thead>
<tr>
<th>Mismatch (n=149)</th>
<th>No Mismatch (n=166)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent/emergent</td>
<td>10 (7)</td>
<td>12 (7)</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>16 (11)</td>
<td>43 (26)</td>
</tr>
<tr>
<td>Stented bioprosthetic valve</td>
<td>109 (74)</td>
<td>71 (43)</td>
</tr>
<tr>
<td>Stentless bioprosthetic valve</td>
<td>23 (15)</td>
<td>25 (15)</td>
</tr>
<tr>
<td>Full-root implantation</td>
<td>8 (5)</td>
<td>14 (8)</td>
</tr>
<tr>
<td>Valve replacement implantation</td>
<td>15 (65)</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Mechanical valve</td>
<td>17 (11)</td>
<td>70 (42)</td>
</tr>
<tr>
<td>Prosthesis size ≥21 mm</td>
<td>119 (80)</td>
<td>53 (32)</td>
</tr>
<tr>
<td>Projected EOAi, cm²/m²</td>
<td>0.71±0.05</td>
<td>0.91±0.09</td>
</tr>
<tr>
<td>CABG</td>
<td>62 (42)</td>
<td>52 (31)</td>
</tr>
<tr>
<td>CABG =2 grafts</td>
<td>26 (17)</td>
<td>14 (8)</td>
</tr>
<tr>
<td>Supra-annular prosthesis implantation</td>
<td>21 (14)</td>
<td>32 (19)</td>
</tr>
<tr>
<td>Aortic root replacement</td>
<td>8 (5)</td>
<td>19 (11)</td>
</tr>
<tr>
<td>Aortic root enlargement</td>
<td>0 (0)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Isolated ascending aorta replacement</td>
<td>4 (3)</td>
<td>11 (7)</td>
</tr>
<tr>
<td>CPB time, min</td>
<td>120±34</td>
<td>119±32</td>
</tr>
<tr>
<td>Aortic cross-clamp time, min</td>
<td>82±24</td>
<td>84±26</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD or number (%). CABG indicates coronary artery bypass graft; CPB, cardiopulmonary bypass.

Follow-up Data

The mean follow-up time was similar in both groups (PPM: 3.9±1.7 years versus no PPM: 3.4±1.7 years; P=NS). During follow-up, 23 patients died in the PPM group versus 6 patients in the no PPM group (P<0.001). The causes of death are reported in Table 4. The 5-year cumulative survival was 75±4% in the PPM group and 87±4% in the no-PPM group (P=0.005) (Figure 2). In multivariate analysis, PPM was a strong independent predictor of both overall mortality (Table 5) and cardiac events (Table 6). PPM was associated with a 4.2-fold (95% CI, 1.6 to 11.3) increase in the risk of mortality and 3.2-fold (95% CI, 1.5 to 6.8) increase in the risk of cardiac events. PPM remained a strong independent predictor of mortality (hazard

### TABLE 4. Cause of Death and Types of Cardiac Events

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Mismatch (n=149)</th>
<th>No Mismatch (n=164)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>11 (7.4)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Sudden death</td>
<td>1 (0.7)</td>
<td>2 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>1 (0.7)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>6 (4.0)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>2 (1.3)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.7)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Overall mortality</td>
<td>23 (15)</td>
<td>6 (3.6)</td>
<td>0.003</td>
</tr>
<tr>
<td>Cardiac events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>11 (7.4)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Sudden death</td>
<td>1 (0.7)</td>
<td>2 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>13 (8.7)</td>
<td>5 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Syncope/lipothymia</td>
<td>4 (2.7)</td>
<td>3 (1.8)</td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Total cardiac events</td>
<td>30 (20.2)</td>
<td>11 (6.6)</td>
<td>0.006</td>
</tr>
<tr>
<td>Follow-up time interval, y</td>
<td>3.9±1.7</td>
<td>3.4±1.7</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD or number of patients (%).
ratio, 4.01; 95% CI, 1.5 to 11.2) and cardiac events (hazard ratio, 2.9; 95% CI, 1.3 to 6.5) when age and gender were forced into the models. A second model was developed by incorporating into the multivariate model EOAi as a continuous variable instead of PPM (Tables 5 and 6). In this model, higher EOAi (ie, lower degree of PPM) was independently associated with a reduction in the risk of overall mortality (hazard ratio, 0.67; 95% CI, 0.46 to 0.97 for 0.1 cm²/m² increase in EOAi) and cardiac events (hazard ratio, 0.63; 95% CI, 0.47 to 0.84). EOAi also remained an independent predictor of mortality (hazard ratio, 0.65; 95% CI, 0.43 to 0.98) and cardiac events (hazard ratio, 0.66; 95% CI, 0.48 to 0.90) when age and gender were forced into the models. The other independent risk factors were history of heart failure and absence of normal sinus rhythm for overall mortality and severe LV hypertrophy, NYHA class III-IV, and absence of normal sinus rhythm for cardiac events.

Discussion

The major finding of this study is that PPM is a strong and independent risk factor for cardiac events and midterm mortality in patients undergoing AVR for pure AS. Indeed, the risk of cardiac events and mortality was increased ~3- to 4-fold in patients with PPM as opposed to those with no PPM.

The issue of PPM still generates controversy concerning its effects on postoperative morbidity and mortality. Whereas some authors have found that the persistence of PPM results in a higher incidence of cardiac events and lower survival rates,8,9,17,18,21,23 others have reported that PPM and/or small prosthesis size has no or minimal impact on morbidity and mortality.10–13

Definition of PPM

The discrepancies between these previous studies are likely due to the fact that they did not use the same parameter to define PPM. Some authors have indeed attempted to characterize PPM using the internal geometric orifice area (GOA) of the prosthesis rather than the EOA because it is more reproducible.10,11,13,28,29 The GOA is a static manufacturing specification based on the ex vivo measurement of the diameter of the prosthesis. The criteria used for its measurement unfortunately differ from one type of prosthesis to the other so that, for instance, the IGA grossly overestimates the EOA but to a much larger extent in the case of a bioprosthesis than in the case of a mechanical prosthesis (Figure 3).6 In the present study the indexed GOA varied from 1.1 to 1.9 cm²/m² for an EOAi of 0.80 cm²/m². Hence, the relation between GOA and EOA varies extensively depending on the type and size of prosthesis, and it has been shown that the indexed GOA cannot be used to predict postoperative gradients.16,28 Most studies using the indexed GOA have failed to find any significant relation between this parameter and adverse clinical outcomes.10,11,13,28,29 This should, however, come as no surprise because, as mentioned, the indexed GOA does not bear any relationship whatsoever to postoperative hemodynamics. In contrast, the indexed EOA has consistently been shown to correlate with postoperative gradients as well as being highly predictive of adverse outcomes.3,5,8,9,16,21–24,30

Impact of PPM on Cardiac Events

Our results are consistent with previous studies reporting that PPM is independently associated with a higher occurrence of cardiac events.17,18,21,23 Milano et al21 reported that the free-
dom of late cardiac events (new episodes of angina, congestive heart failure, or myocardial infarction) was 56±15% in patients with severe PPM (EOAi ≤0.60 cm²/m²), 80±5% in patients with moderate PPM (EOAi ≤0.60 cm²/m² and >0.60 cm²/m²), and 94±4% in patients with no PPM (EOAi >0.90 cm²/m²). Moreover, in a recent study including 1681 patients, Ruel et al reported that PPM defined as an EOAi ≤0.80 cm²/m² is associated with a 60% increase in the risk of congestive heart failure after AVR.

Impact of PPM on Survival

Several studies reported that PPM has a significant impact on in-hospital mortality. This finding may be related to the fact that patients’ LV function and hemodynamic status are more vulnerable during the early postoperative period and that an increase in afterload due to PPM may contribute to the development of irreversible LV failure, especially in patients already having depressed LV function before operation. In the present study the number of perioperative deaths was, however, too small to allow meaningful analysis of the impact of PPM on in-hospital mortality.

In a study of 2516 patients who underwent AVR with a stented bioprosthetic valve, Rao and colleagues reported that freedom from valve-related mortality at 12 years was significantly lower in patients with an indexed EOA of ≤0.75 cm²/m² compared with those with a larger indexed EOA (75.5% versus 84.2%; P=0.004). However, other studies with shorter follow-up failed to demonstrate any significant impact on midterm mortality. The present study is thus the first study to report that PPM is an independent risk factor for midterm mortality. The absence of significant association between PPM and midterm mortality reported in previous studies may be due to the fact that, as opposed to the present study, these previous studies were performed in heterogeneous populations of patients including patients with pure AS, pure aortic insufficiency, and mixed aortic valve disease. Patients with aortic insufficiency are more likely to receive a larger valve with lower probability of having PPM, but their postoperative survival is generally lower than that of patients with AS probably because they have eccentric rather than concentric LV hypertrophy.

Potential Mechanisms Responsible for the Adverse Effects of PPM

Mehta et al reported that LV hypertrophy is a strong risk factor for in-hospital mortality after AVR. In the present study the presence of severe LV hypertrophy before operation was also found to be an independent risk factor for cardiac events after AVR. Previous studies have suggested that the residual pressure overload due to PPM may hamper the regression of LV hypertrophy after AVR, and this may have contributed to the higher occurrence of cardiac events and deaths in the PPM group. Beyond the persistence of LV hypertrophy after AVR, other mechanisms may explain the worse outcome of patients with PPM. In this regard, Rajappan et al demonstrated that, in patients with AS and angiographically normal coronary arteries, the improvement of coronary flow reserve after AVR is directly dependent on the improvement of valve EOA that is achieved with AVR. Hence, the increased LV systolic pressure associated with PPM may compromise the normalization of coronary flow reserve after AVR and may thus predispose to the
development of LV dysfunction and the occurrence of ad-
verse events.

**Clinical Implications**

The practical implications of these findings are important
given that PPM is a frequent occurrence with a prevalence of
47% in the present study, which is consistent with the results
generally reported in the literature (19% to 70%).3,6,8,16 More
importantly, as opposed to other risk factors for cardiac
events and mortality, PPM is a modifiable risk factor that can,
in large part, be avoided with the use of a prospective strategy
at the time of operation.5,9,16,37 As proposed by Pibarot and
Dumesnil,3 this strategy consists of the systematic calculation
of the projected EOAi before the implantation of the pros-
thesis. If the projected EOAi is lower than the recommended
value (0.8 to 0.9 cm²/m²), the surgeon may either use another
type of prosthesis with a better hemodynamic profile and
hence a larger EOa (eg, bileaflet mechanical valves of new
generation or stentless bioprostheses)16,38,39 or perform an
aortic root enlargement procedure to accommodate a larger
prosthesis.37 Castro et al37 have demonstrated that this pro-
spective strategy to avoid PPM can be applied with success.
Nonetheless, it is also possible that, given the operative
circumstances (eg, comorbidities, anatomy of the aortic root),
the surgeon may have to accept the PPM, and if such is the
case, the calculation of the projected EOAi is useful to
forecast how the selected prosthesis will perform thereafter in
the patient. Particular attention should be given to completely
avoid PPM, ie, provide a minimum EOAi of ≥0.8 to 0.9
cm²/m², in young, physically active patients as well as in
patients with depressed LV function since they are the most
vulnerable to PPM.9 However, lesser values of EOAi are
probably acceptable in older sedentary patients with pre-
served LV function. This underscores the importance of
individualizing the PPM preventive strategy according to the
patient’s age, level of physical activity, and status of LV
function. If PPM cannot be completely avoided, however,
every effort should be made to implant a prosthesis that
would provide the largest possible EOa because it has been
suggested that the postoperative regression of LV mass as
well as the improvement of coronary flow reserve is directly
related to the magnitude of valve EOa improvement
achieved with AVR.30,34

**Study Limitations**

The number of patients with severe PPM was not sufficient to
allow for separate analysis in these patients and determine
whether severe PPM was associated with significantly more
adverse outcomes compared with mild/moderate/no PPM.
Nevertheless, the fact that the EOa emerged as an indepen-
dent predictor of adverse outcomes when entered as a
continuous variable in multivariate analysis (Tables 5 and 6)
supports the notion that the adverse effects of PPM increase
with its degree of severity, as suggested in previous studies.9,18,21

The body surface area may overestimate the cardiac output
requirement in obese patients, and, consequently, the utiliza-
ation of the EOa indexed to body surface area would then
overestimate the degree of PPM in these patients. Hence, the
difference between the PPM and non-PPM groups may have
been overstated because of the significantly greater propor-
tion of obese patients (49% versus 27%) in the PPM group.
Finally, this study was not of randomized design, and it is
possible that unrecognized biases may have influenced the
results.

**Conclusion**

PPM is a strong and independent predictor of cardiac events
and midterm mortality in patients with pure AS undergoing
AVR. As opposed to most other risk factors for postoperative
morbidity and mortality, PPM is a modifiable risk factor that
can be avoided, or its severity may be reduced with the use of
a preventive strategy at the time of operation.

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Prosthesis-patient mismatch (PPM), defined as a projected indexed valve effective orifice area (EOA) \( \leq 0.8 \text{ cm}^2/\text{m}^2 \), was present in 47% of the patients. The major finding of this study is that PPM is a strong and independent risk factor for cardiac events and midterm mortality in patients undergoing aortic valve replacement for pure aortic stenosis. Indeed, the risk of cardiac events and mortality was increased \( \approx 3 \) - to 4-fold in patients with PPM as opposed to those with no PPM. In contrast, values derived from geometric measurements of the prosthesis (eg, label size, internal diameter, or geometric area) were not found to be independent predictors of postoperative outcomes. The clinical implications of these results are important given that PPM is a frequent and modifiable risk factor. As opposed to other risk factors, PPM may be avoided or its severity may be reduced with the use of a preventive strategy at the time of operation. To achieve this goal, the projected indexed EOA should be systematically calculated before prosthesis implantation to estimate the risk of PPM and, if PPM is anticipated, alternative options should be considered including (1) the implantation of another type of prosthesis with a larger EOA or (2) the enlargement of the aortic root to accommodate a larger prosthesis. These alternative options should always be considered in light of the patient’s overall clinical conditions and risk-benefit ratio.
Impact of Prosthesis-Patient Mismatch on Cardiac Events and Midterm Mortality After Aortic Valve Replacement in Patients With Pure Aortic Stenosis
Giordano Tasca, Zen Mhagna, Silvano Perotti, Pietro Berra Centurini, Tony Sabatini, Andrea Amaducci, Federico Brunelli, Giovanni Troise and Philippe Pibarot

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