Impact of Prosthesis-Patient Mismatch on Long-Term Survival in Patients With Small St Jude Medical Mechanical Prostheses in the Aortic Position

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Background—The impact of aortic prosthesis-patient mismatch (P-PtM) on long-term survival is unclear.

Methods and Results—Between 1985 and 2000, 388 patients at Mayo Clinic in Rochester, Minn, underwent aortic valve replacement (AVR) with 19- or 21-mm St Jude Medical prostheses and had transthoracic echocardiography within 1 year after AVR. Mean age of patients was 62±13 years; 69% were female. Prosthesis effective orifice area (EOA) was derived from the continuity equation. P-PtM was classified as severe (indexed EOA ≤0.60 cm²/m²), moderate (0.60 cm²/m² < indexed EOA ≤0.85 cm²/m²), or not hemodynamically significant (indexed EOA >0.85 cm²/m²). P-PtM was severe in 66 patients (17%), moderate in 168 (43%), and not hemodynamically significant in 154 (40%). Patients with severe P-PtM had a significantly larger body surface area (P<0.0001), higher mean gradient (P<0.0001), lower preoperative (P<0.0001) and postoperative (P<0.0001) ejection fractions, and lower stroke volume (P<0.0001) and more often received a 19-mm prosthesis (P=0.0008) than patients with moderate or no hemodynamically significant mismatch. For patients with severe mismatch, 5-year survival rates (72±6%) and 8-year survival rates (41±8%) were significantly less than for patients with moderate mismatch (80±3% and 65±5%; P=0.026) or no hemodynamically significant mismatch (85±3% and 74±5%; P=0.002). On multivariate analysis after adjustment for other predictors of outcome, severe mismatch was associated with higher mortality (hazard ratio 2.18; 95% confidence interval 1.24 to 3.85; P=0.007) and higher incidence of congestive heart failure (hazard ratio 3.1; 95% confidence interval 1.3 to 7.4; P=0.009) than no hemodynamically significant mismatch.

Conclusions—Severe P-PtM is an independent predictor of higher long-term mortality and congestive heart failure in patients with small St Jude Medical aortic valve prostheses. For patients undergoing AVR who are at risk of severe mismatch, every effort should be made to use a larger prosthesis or to consider a prosthesis with a larger EOA.

Key Words: prosthesis • aorta • survival • valves

Valvular Heart Disease

Prosthesis-patient mismatch (P-PtM) is considered to be present when the effective orifice area (EOA) of the prosthesis is less than that of a normal human valve.1 The main hemodynamic consequence of P-PtM is the generation of high transvalvular gradients through normally functioning prosthetic valves.2 Increased transvalvular gradients after aortic valve replacement (AVR) delay the regression of left ventricular hypertrophy, an important risk factor and predictor of survival.2–6 The problem of P-PtM is most commonly encountered in patients undergoing AVR for severe calcific aortic valve stenosis.7 Because the Western population is aging, with a consequent increased incidence of degenerative aortic valve stenosis, there are concerns about the potential adverse impact of P-PtM on short- and long-term outcomes.2 Nonetheless, several studies have not shown a relation between prosthesis size relative to patient size and intermediate- or long-term survival, and the clinical relevance of P-PtM has been questioned.8–13

In our current practice, mechanical valves account for 36% of all prostheses implanted in the aortic position. Therefore, we sought to evaluate the impact of P-PtM on long-term mortality and morbidity in patients undergoing AVR with a small St Jude Medical (SJM) aortic prosthesis (St Jude Medical, Inc).

Methods

Eligibility Criteria

The patients considered for the present study were all patients who had AVR with a 19- or 21-mm standard or Hemodynamic Plus (HP)
SJM bileaflet mechanical prosthesis at Mayo Clinic in Rochester, Minn, between January 1, 1985, and December 31, 2000. Patients were excluded if they were younger than 18 years at AVR, if they died perioperatively, or if a postoperative transthoracic echocardiogram was not performed at Mayo Clinic within 1 year after AVR. Patients were not excluded from the study if they had prior cardiac surgery, including coronary artery bypass graft (CABG) surgery or aortic, mitral, or tricuspid valve surgery, or any combination thereof, or if they had concomitant procedures such as CABG, aortic root enlargement, and mitral or tricuspid surgery. During this period, 5378 patients underwent AVR. The prostheses were mechanical valves in 2401 patients (45%); the size was 19 or 21 mm in 673 patients, of whom 518 (77%) received SJM prostheses. Excluded were patients who died within 30 days of operation (n = 31), patients who did not have a postoperative echocardiogram within 1 year at our institution (n = 82), and patients whose echocardiogram did not allow measurement of the EOA (n = 17). The study was approved by the Mayo Foundation Institutional Review Board, and all participating patients provided informed consent.

Data Collection
The baseline clinical variables were obtained from review of medical records. Follow-up clinical information was received from mailed questionnaires, review of medical records, or death certificates and scripted telephone interviews with the patients or their local physicians. To avoid misclassification of causes of death, all-cause mortality was selected as an objective end point.14

EOA of the Prosthesis
Data from the first postoperative transthoracic echocardiographic study performed at our institution were transferred electronically without alteration from the prospective echocardiography database. As is routine practice in our echocardiography laboratory, the EOA was derived from the continuity equation, using the area of the left ventricular outflow tract (LVOT) and the time-velocity integral (TVI) of the LVOT and the prosthesis, as follows: EOA = (LVOT area × LVOT TVI)/aortic prosthesis TVI. The mean gradient was measured by use of continuous-wave Doppler echocardiography and the simplified Bernoulli equation. The Doppler velocity profile for the LVOT TVI was obtained by positioning the pulsed-wave sample volume 0.5 to 1 cm below the sewing ring, so as to avoid the zone of flow convergence just below the aortic prosthesis. Continuous-wave Doppler echocardiography was performed with a nonimaging probe from apical, right parasternal, right supraclavicular, and suprasternal positions. The prosthesis TVI and mean gradient were obtained by measuring spectra from the position that yielded the highest velocity. The sewing ring diameter was used for the LVOT diameter in all patients.15 P-PtM was classified as severe (indexed EOA ≤ 0.60 cm²/m²), moderate (0.60 cm²/m² ≤ EOA < 0.85 cm²/m²), or not hemodynamically significant (IEOA > 0.85 cm²/m²).2

Prosthesis Geometric Orifice Area
For each prosthesis type, the geometric orifice area (GOA) was calculated from the prosthesis internal orifice diameter, as provided by the manufacturer, assuming a circular orifice (1.7 cm² for the 19-mm standard valve, 2.19 cm² for the 19-mm HP and 21-mm standard valves, and 2.69 cm² for the 21-mm HP valve),13 and was expressed relative to patient size (body surface area) as indexed GOA (GOA).

Statistical Methods
Patients were divided into 3 P-PtM groups according to severity: severe, moderate, and not hemodynamically significant. Continuous variables were reported as mean ± SD, and the groups were compared with 1-way ANOVA. Reported probability values are based on the overall comparisons. Categorical variables were reported as a percentage of the total, and the groups were compared with the Pearson χ² test. The primary end point was survival from the time of surgery; secondary end points were congestive heart failure, reoperation, and hemorrhage or embolism. The cumulative probability of an event for each end point was estimated by the Kaplan-Meier method and compared with the log-rank test; results are presented at 5 and 8 years postoperatively. Log-rank tests were used to test for significance in survival between each of the P-PtM groups.

For the primary end point of survival from the time of surgery, the objective was to assess the effect of P-PtM severity as measured by the IEOA on survival; additionally, we considered the IGOA and valve size. Both the IEOA and the IGOA were evaluated as continuous variables. To assess how the results were attenuated with the inclusion of relevant covariates, we fit a series of Cox proportional hazards models. First, we fit the P-PtM severity, IGOA, and valve size univariately. Next, we fit each of the models after adjusting for age and sex. Finally, we fit each of these models after adjusting for all variables that were deemed clinically relevant (age, sex, ejection fraction [EF], New York Heart Association class, prior cardiac surgery, prior aortic valve surgery, concomitant mitral surgery, concomitant CABG, aortic root enlargement, and modified Charlson index of comorbidity).16 In addition, after evaluating the results, we also fit the model with all the clinically relevant variables and the interaction of severe P-PtM and valve size. The proportionality assumption was verified for all models with use of the Schoenfeld residuals. Results were reported as hazard ratios (HRs) with corresponding probability values. Because a patient was not at risk until after echocardiography was performed to determine IEOA, we also calculated the HRs from the time of echocardiography. These results were nearly identical to the results presented and are not included in the Results section.

Results
The study population consisted of 388 patients who had a postoperative echocardiogram performed at Mayo Clinic within 1 year after AVR (median 6 days; 353 patients [91%] within the first 30 days) and who received a 19- or 21-mm SJM bileaflet mechanical valve. Surgical procedures performed included AVR with or without aortic root enlargement or CABG.

Baseline Characteristics
Among the 388 patients, 266 were women (69%), and the mean age was 62 ± 13 years (Table 1). Mean body surface area was 1.76 ± 0.2 m², and mean left ventricular EF was 59 ± 13%. Forty-one patients (11%) received a 19-mm standard SJM prosthesis, and 98 patients (25%) received a 19-mm HP SJM prosthesis; 112 patients (29%) received a 21-mm standard SJM prosthesis, and 137 (35%) received a 21-mm HP SJM prosthesis. The main indication for AVR was aortic valve stenosis in 59% of the patients, mixed aortic disease in 15%, reoperation for aortic prosthesis dysfunction in 15%, and isolated aortic regurgitation in 10%. The cause of aortic valve disease was degenerative in 34%, rheumatic in 30%, congenital bicuspid in 26%, endocarditis in 2%, radiation-induced in 3%, unicuspid in 1%, and unknown or other causes in 5%. Prior cardiac surgery had been performed in 147 patients (38%; CABG in 144 patients and aortic valve surgery in 73 patients). Concomitant CABG was performed in 29% of patients, concomitant mitral repair or replacement in 27%, and concomitant aortic root enlargement with peri-cardial patch in 18%. AVR was performed emergently in 57 patients (15%).

Table 1 and Table 2 compare the baseline clinical characteristics of patients divided into 3 groups according to the severity of P-PtM. Patients with severe P-PtM had a significantly larger body surface area (P < 0.0001), a lower preop-
TABLE 1. Baseline Demographic Data

<table>
<thead>
<tr>
<th>Feature</th>
<th>Prosthesis-Patient Mismatch*†</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe (n=66)</td>
<td>Moderate (n=168)</td>
<td>NHS (n=154)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>61±13</td>
<td>63±13</td>
<td>62±13</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>62 (41)</td>
<td>68 (114)</td>
<td>72 (111)</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.91±0.22</td>
<td>1.77±0.18</td>
<td>1.69±0.18</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>NYHA class I or II</td>
<td>44 (29)</td>
<td>49 (75)</td>
<td>49 (75)</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>History of CHF</td>
<td>48 (32)</td>
<td>48 (81)</td>
<td>38 (58)</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>History of MI</td>
<td>20 (13)</td>
<td>15 (25)</td>
<td>7 (11)</td>
<td>0.02</td>
<td></td>
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<tr>
<td>Preoperative LVEF, %</td>
<td>55±16</td>
<td>57±13</td>
<td>63±10</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Preoperative LVEF&lt;40%</td>
<td>16 (10)</td>
<td>13 (20)</td>
<td>4 (6)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>53 (35)</td>
<td>54 (91)</td>
<td>52 (80)</td>
<td>0.92</td>
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<td>Serum creatinine, μmol/L</td>
<td>102±59</td>
<td>112±107</td>
<td>95±44</td>
<td>0.16</td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>30 (20)</td>
<td>21 (35)</td>
<td>11 (17)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>56 (37)</td>
<td>56 (95)</td>
<td>62 (96)</td>
<td>0.51</td>
<td></td>
</tr>
</tbody>
</table>

BSA indicates body surface area; CHF, congestive heart failure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NHS, not hemodynamically significant; and NYHA, New York Heart Association.

*Severe: indexed effective orifice area (EOA)≤0.60 cm²/m²; moderate: 0.60 cm²/m²<indexed EOA≤0.85 cm²/m²; NHS: indexed EOA>0.85 cm²/m².

†Continuous data are presented as mean±SD; categorical data as percent-age of sample (No. of patients in sample).

TABLE 2. Surgical Data

<table>
<thead>
<tr>
<th>Patients With Prosthesis-Patient Mismatch*</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Prior surgery</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Cardiac</td>
<td>39</td>
<td>26</td>
<td>39</td>
<td>66</td>
<td>36</td>
</tr>
<tr>
<td>Aortic valve</td>
<td>26</td>
<td>17</td>
<td>18</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>Elective surgery</td>
<td>82</td>
<td>54</td>
<td>82</td>
<td>138</td>
<td>90</td>
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<tr>
<td>Concomitant surgery</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>30</td>
<td>20</td>
<td>27</td>
<td>45</td>
<td>31</td>
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<tr>
<td>Mitral valve</td>
<td>24</td>
<td>16</td>
<td>28</td>
<td>47</td>
<td>26</td>
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<tr>
<td>Aortic root enlargement</td>
<td>20</td>
<td>13</td>
<td>13</td>
<td>22</td>
<td>21</td>
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<tr>
<td>SJM aortic prosthesis</td>
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</tr>
<tr>
<td>19 mm</td>
<td>47</td>
<td>31</td>
<td>42</td>
<td>70</td>
<td>25</td>
</tr>
<tr>
<td>21 mm</td>
<td>53</td>
<td>35</td>
<td>58</td>
<td>98</td>
<td>75</td>
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<tr>
<td>Standard</td>
<td>45</td>
<td>30</td>
<td>44</td>
<td>74</td>
<td>32</td>
</tr>
<tr>
<td>Hemodynamic Plus</td>
<td>55</td>
<td>36</td>
<td>56</td>
<td>94</td>
<td>68</td>
</tr>
</tbody>
</table>

NHS indicates not hemodynamically significant. Other abbreviations as in text.

*Severe: indexed effective orifice area (EOA)≤0.60 cm²/m²; moderate: 0.60 cm²/m²<indexed EOA≤0.85 cm²/m²; NHS: indexed EOA>0.85 cm²/m².

Postoperative Hemodynamics

Patients with severe P-PtM had higher mean gradients (P<0.0001), lower stroke volume (P<0.0001), and slightly lower postoperative EF (P<0.0001) than patients with moderate or no hemodynamically significant P-PtM (Table 3). By definition, the in vivo EOA was significantly smaller for patients with severe P-PtM. The mean prosthesis performance index (EOA/GOA) was 0.62±0.15 (median 0.60), analogous to the findings in a previous report.15

Long-Term Outcome

Follow-up data were available for all patients. The mean follow-up was 5.3±3.3 years (median 4.8 years; maximum 21 years). There were 103 deaths. Overall survival was 95%, 81%, and 62% at 1, 5, and 8 years, respectively.

Effect of In Vivo Prosthesis EOA

The long-term survival rates (excluding operative mortality) at 5 and 8 years, respectively, for patients with severe P-PtM (72±6% and 41±8%) were significantly lower than those for patients with moderate P-PtM (80±3% and 65±5%; P=0.026) or no hemodynamically significant P-PtM (85±3% and 74±5%; P=0.002; Figure 1). The survival rates for patients with moderate P-PtM were not significantly different from those for patients with no hemodynamically significant P-PtM (P=0.17). There was a significant association between P-PtM severity and the 5- and 8-year rates for congestive heart failure but not for reoperation (Table 4). Severe P-PtM was an independent predictor of congestive heart failure after adjustment for all the clinically relevant covariates (HR 3.1; 95% confidence interval [CI] 1.3 to 7.4; P=0.009). The rates of other valve-related complications, such as embolism, hemorrhage, and endocarditis, were low in the present study cohort.

IEOA Versus IGOA

Larger IEOA as a continuous variable was predictive of better survival, and the HR remained relatively unaffected whether analysis was conducted univariately (HR 0.27; 95% CI 0.10 to 0.72; P=0.009), after adjustment for age and sex (HR 0.28; 95% CI 0.10 to 0.75; P=0.01), or after adjustment for the clinically relevant covariates (HR 0.32; 95% CI 0.11 to 0.94; P=0.04). Similar results were observed when P-PtM was...
expressed categorically (Table 5). In contrast, larger IGOA, expressed as a continuous variable, showed only a trend of association with better survival (HR 0.37; 95% CI 0.13 to 1.06 for 1-cm² increase; \( P=0.06 \)) but showed a weaker association with survival, after adjustment for all the clinically relevant variables, that was not significant (HR 0.47; 95% CI 0.14 to 1.54 for 1-cm² increase; \( P=0.21 \)). None of the patients in the present study had an IGOA < 0.85 cm²/m².

Effect of Prosthesis Size

All-cause mortality was higher for patients with a 19-mm valve than for those with a 21-mm valve (HR 2.20; 95% CI 1.34 to 3.61; \( P=0.002 \)), whether standard (HR 2.16; \( P=0.02 \)) or HP (HR 2.22; \( P=0.005 \)). Adjusted all-cause mortality was not significantly different between patients with a 21-mm HP SJM valve and those with a 21-mm standard SJM valve (HR 0.93; \( P=0.82 \)).

The mean ± SD EOA for the different valve sizes was as follows: 19-mm standard, 1.14 ± 0.22 cm²; 19-mm HP, 1.29 ± 0.30 cm²; 21-mm standard, 1.41 ± 0.37 cm²; and 21-mm HP, 1.62 ± 0.35 cm². Severe P-PtM was present in 22% of patients with a 19-mm valve and in 14% of patients with a 21-mm valve (\( P=0.0008 \)).

Because of this confounder, we examined the interaction between P-PtM and valve size (Figure 2). Patients with 21-mm valves and severe P-PtM had worse long-term survival than patients with 21-mm valves and no hemodynamically significant P-PtM or moderate P-PtM (adjusted HR 1.8; \( P=0.07 \)). There was a trend of worse long-term survival among patients with a 19-mm valve and severe P-PtM compared with patients with a lesser degree of P-PtM (adjusted HR 1.8; \( P=0.10 \)).

Association Between Mean Gradient and In Vivo IEOA

As expected, and analogous to the findings in the report by Pibarot and Dumesnil on bioprosthesis, there was a curvilinear correlation between transvalvular gradients and IEOA. There was a marked increase in gradient when the IEOA was 0.6 cm²/m² or less (24.9 ± 9.2 versus 16.8 ± 6.4 mm Hg; \( P<0.001 \)). The correlation between log mean gradient and IEOA was of low strength (\( R^2=0.29 \)) because the gradient may vary with cardiac output. In contrast, the correlation between log mean gradient and IGOA was poor (\( R^2=0.06 \)).

Discussion

Impact of P-PtM on Long-Term Survival

In this study of patients with small SJM aortic prostheses, severe P-PtM, as assessed by in vivo IEOA, was an independent predictor of long-term survival, with significantly lower 5- and 8-year survival rates for patients with severe P-PtM than for patients with a lesser degree of P-PtM. Although there was no significant difference in long-term survival of patients with moderate P-PtM compared with patients with no hemodynamically significant P-PtM, the survival curve was intermediate between the curves for patients with severe P-PtM and patients with no hemodynamically significant P-PtM. Patients with 19-mm valves fared worse than patients with 21-mm valves but had a significantly higher prevalence of severe P-PtM. Severe P-PtM was associated with worse long-term survival for patients with 21-mm valves and with a trend toward worse long-term survival for patients with 19-mm valves than for patients with the same valve size but a lesser degree of P-PtM. In the present study, there was no significant association between P-PtM as assessed by the IGOA and long-term survival, analogous to the findings of prior studies. Previous reports showed increased operative mortality associated with AVR when there was severe or moderate

**TABLE 4. Five-Year and 8-Year Complication Rates**

<table>
<thead>
<tr>
<th>Prosthesis-Patient Mismatch†</th>
<th>Congestive Heart Failure, % (( P=0.02 ))</th>
<th>Reoperation, % (( P=0.56 ))</th>
<th>Hemorrhage or Embolism, % (( P=0.34 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5-Year</td>
<td>8-Year</td>
<td>5-Year</td>
</tr>
<tr>
<td>Severe</td>
<td>21±6</td>
<td>29±8</td>
<td>1.8±1.8</td>
</tr>
<tr>
<td>Moderate</td>
<td>12±3</td>
<td>14±3</td>
<td>0.7±0.7</td>
</tr>
<tr>
<td>NHS</td>
<td>8±3</td>
<td>13±4</td>
<td>1.6±1.2</td>
</tr>
</tbody>
</table>

NHS indicates not hemodynamically significant.

†Values are mean rate ± SE.

‡Severe: indexed effective orifice area (EOA) ≤ 0.60 cm²/m²; moderate: 0.60 cm²/m² < indexed EOA < 0.85 cm²/m²; NHS: indexed EOA ≥ 0.85 cm²/m².

§\( P \) values were calculated using the log-rank test.
P-PtM, as defined in the present study,\textsuperscript{18} or when the IGOA derived from the manufacturer was \(<1.2\, \text{cm}^2\).\textsuperscript{11} However, with the exception of 1 study,\textsuperscript{19} prosthesis size relative to patient size was not shown to adversely influence long-term survival after AVR.\textsuperscript{8–10,12,13} Milano et al\textsuperscript{12} did not find a negative impact of P-PtM on long-term survival among patients with small SJM aortic prostheses, but only 8 patients had severe P-PtM in that study. Ismeno et al\textsuperscript{11} found no survival advantage for the 19-mm HP valve over the 19-mm standard valve, despite a significantly lower mean gradient with the HP prosthesis. None of the patients in that study had an in vivo IEOA \(<0.9\, \text{cm}^2/\text{m}^2\), however. Blackstone et al\textsuperscript{13} did not demonstrate an effect of prosthesis size or IGOA, regardless of the type of prosthesis, on long-term outcome. In contrast, in a study of patients who received stented aortic bioprostheses, Rao et al\textsuperscript{19} found that severe P-PtM was a statistically significant predictor of long-term mortality, but a survival difference was not detected until postoperative year 7. A major limitation of that study was the lack of long-term follow-up echocardiograms. Therefore, it is unclear whether the observed findings were from true P-PtM or bioprosthesis degeneration over time with a secondary decrease in the IEOA. Because all patients in the present study received mechanical aortic prostheses, degeneration was not an issue relative to long-term hemodynamics.

\textbf{Impact of P-PtM on Long-Term Morbidity}

Previous studies that investigated the clinical impact of P-PtM on postoperative morbidity,\textsuperscript{8,20,21} exercise tolerance, and New York Heart Association class\textsuperscript{20,22–24} have been inconclusive. Our finding of a significant association between P-PtM severity and long-term risk of congestive heart failure is in agreement with the reports by Milano et al,\textsuperscript{12} Pibarot et al,\textsuperscript{27} and Ruel et al.\textsuperscript{25} This may relate to decreased regression of left ventricular hypertrophy, because of the persistence of a significantly higher mean systolic aortic gradient in patients with severe P-PtM. Our finding of a significantly lower stroke volume in patients with severe P-PtM is similar to the findings by Pibarot et al,\textsuperscript{20,21} Nearly 10% of the patients in the present study had a preoperative EF \(<40\%\), which was similar to the findings of Blais et al.\textsuperscript{18} The prevalence of left ventricular systolic dysfunction was significantly higher among patients with severe and moderate P-PtM than among patients with no hemodynamically significant P-PtM. Nonetheless, preoperative left ventricular systolic dysfunction was not associated with a risk of long-term congestive heart failure.

\textbf{In Vivo Prosthesis EOA}

The EOA is a measure of the physiological area occupied by blood flow and not of the larger true anatomic area of the prosthesis, ie, the GOA.\textsuperscript{26} Importantly, the caveats and pitfalls associated with in vivo EOA measurements notwithstanding,\textsuperscript{26} EOA—not GOA—determines the residual pressure gradient after AVR.\textsuperscript{2} Pibarot et al\textsuperscript{27} showed that the IEOA estimated at the time of AVR correlated well with both

\begin{table}[h]
\centering
\caption{Multivariate Cox Proportional Hazards Models Assessing the Effect of P-PtM on Mortality}
\begin{tabular}{lccc}
\hline
 & Univariate Models & Adjusted for Age and Sex & Adjusted for All Clinically Relevant Covariables \\
 P-PtM* & HR† (95% CI) & P & HR† (95% CI) & P & HR† (95% CI) & P \\
 Moderate & 1.37 (0.86–2.20) & 0.19 & 1.27 (0.79–2.04) & 0.32 & 1.21 (0.72–2.03) & 0.48 \\
 Severe & 2.31 (1.38–3.87) & 0.002 & 2.15 (1.27–3.64) & 0.004 & 2.18 (1.24–3.85) & 0.007 \\
\hline
\end{tabular}
\end{table}

\textsuperscript{*}Severe P-PtM: indexed effective orifice area (IEOA) \(<0.60\, \text{cm}^2/\text{m}^2\); moderate P-PtM: \(0.60\, \text{cm}^2/\text{m}^2\)

\textsuperscript{†}HRs are relative to not hemodynamically significant P-PtM (IEOA \(>0.85\, \text{cm}^2/\text{m}^2\)).

\begin{figure}[h]
\centering
\includegraphics{figure2}
\caption{Long-term survival after AVR with a bileaflet mechanical prosthesis according to valve size and severity of P-PtM (severe mismatch: IEOA \(<0.60\, \text{cm}^2/\text{m}^2\); moderate or no hemodynamically significant [NHS] mismatch: IEOA \(>0.60\, \text{cm}^2/\text{m}^2\)). A, Patients with 19-mm valves. B, Patients with 21-mm valves.}
\end{figure}
resting and exercise gradients measured 1 year after operation. In contrast, in the same subset of patients, there was a very poor correlation between the IGOA and postoperative gradients. The prosthesis IEOA was derived from in vitro measurements provided by the manufacturer in the study by Rao et al.\textsuperscript{18} and from reference in vivo values in the study by Blais et al.\textsuperscript{16} Although both studies showed the clinical impact of P-PtM, we thought it was clinically more relevant to measure the in vivo IEOAs for the study patients using the full form of the continuity equation. The measured in vivo IEOA was then used to classify patients as having severe, moderate, or no hemodynamically significant P-PtM. On the basis of the findings of this report, we believe that in vivo IEOA itself, rather than geometric surrogates, should be used to define P-PtM for future investigations.

Clinical Implications

Because long-term survival among patients with severe P-PtM after AVR is significantly decreased compared with survival among patients with moderate or no hemodynamically significant P-PtM, reoperation may need to be considered for this group of patients. We previously published a study of 21 patients who underwent surgery to replace aortic prostheses that resulted in severe P-PtM.\textsuperscript{28} Five of 9 patients who required concomitant major cardiac surgical procedures died in-hospital. However, there were no in-hospital deaths for the 12 patients who had reoperations for isolated, severe P-PtM. To fully define risk for this group of patients, larger studies are required.

Rather than having to consider reoperation for patients with severe P-PtM, it is best to avoid this problem altogether. Pibarot and Dum ensni\textsuperscript{2} have detailed a preventive strategy that involves use of reference EOAs and patient body surface area to determine preoperatively whether the type and size of prosthesis being considered are sufficient to avoid hemodynamically significant P-PtM. Castro et al.\textsuperscript{29} used this strategy and, as a result, performed aortic root enlargement in 114 of 657 patients undergoing AVR. Operative mortality in that study cohort was not increased, and the incidence of moderate or severe P-PtM was decreased to 2.5% compared with 17% if preventive aortic root enlargement had not been performed. Other investigators,\textsuperscript{3,30–32} have also recommended aortic root enlargement for patients with a small aortic annulus. Alternatively, a prosthesis that provides a larger EOA in relation to body size (eg, newer-generation prostheses) should be implanted. On the basis of the present data, severe P-PtM may be avoided in the majority of patients being considered for a small SJM aortic prosthesis if the body surface area does not exceed 1.53, 1.65, 1.73, and 2.10 m\textsuperscript{2} for the 19-mm standard, 19-mm HP, 21-mm standard, and 21-mm HP valve sizes, respectively. Because severe P-PtM has been shown to independently decrease both short- and long-term mortality after AVR, careful consideration of such preventative strategies is certainly warranted.

Potential Limitations

This was a retrospective study. Although the Doppler echocardiographic data were obtained from review of the official echocardiogram reports, all studies were performed in the same center and according to a well-established and standardized protocol. Our study inclusion criteria were broad and reflected normal practice. We specifically excluded patients who died within 30 days of prosthesis implantation to eliminate any confounding factor not related to P-PtM that may have affected operative but not necessarily long-term mortality\textsuperscript{2} and, therefore, to better determine the impact of P-PtM on late survival. There are pitfalls that need to be avoided when using Doppler echocardiography to calculate prosthesis EOA. Although EOA is not a perfect technique for assessing prosthesis performance, the predictive value of IEOA demonstrated in the present study lends further support to the utility of EOA in the assessment of prosthetic valve function.

Conclusions

Severe P-PtM mismatch is an independent predictor of long-term mortality and congestive heart failure among patients with a small SJM aortic valve prosthesis. In vivo EOA measurements derived from Doppler ultrasonography, rather than geometric surrogates, should be used to determine the severity of P-PtM. Preventive strategies, such as aortic root enlargement or implantation of a prosthesis with a larger EOA, should be considered in patients who have an increased risk of severe P-PtM developing at the time of AVR.

References


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**CLINICAL PERSPECTIVE**

The clinical significance of prosthesis-patient mismatch (P-PtM) has been the subject of recent research and considerable debate among cardiologists and cardiac surgeons. Prior reports showed an association between prosthesis effective orifice area (EOA), a measure of the physiological area occupied by blood flow, hence the residual pressure gradient and severity of P-PtM, and short-term outcome after aortic valve replacement (AVR) with a small aortic prosthesis. EOA indexed to the patient’s body surface area has been shown to correlate well with perioperative mortality, with postoperative resting and exercise gradients, and with clinical morbidity end points in the immediate follow-up of AVR. The present study, for the first time, shows an association between indexed EOA derived in vivo from Doppler ultrasonography and long-term outcome. Indexed EOA ≤0.60 cm²/m² was an independent predictor of higher long-term mortality and congestive heart failure among patients with a small St Jude Medical aortic valve prosthesis. In contrast, there was no significant association between P-PtM as assessed by the indexed geometric orifice area, a measure of the maximum potential area of flow through a prosthesis, and long-term survival, analogous to the findings of prior studies. Moreover, the correlation between the mean aortic gradient and indexed EOA was superior to that with the indexed geometric orifice area. Until a better measure of prosthesis performance becomes available, we believe that EOA is a valid method for assessing prosthetic valve performance in vivo and for predicting outcome.
Impact of Prosthesis-Patient Mismatch on Long-Term Survival in Patients With Small St Jude Medical Mechanical Prostheses in the Aortic Position
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In the article, “Impact of Prosthesis-Patient Mismatch on Long-Term Survival in Patients With Small St Jude Medical Mechanical Prostheses in the Aortic Position,” which appeared in the January 26, 2006, issue of the journal (Circulation. 2006;113:420–426), the first author’s name was listed incorrectly. Dania Mohty-Echahidi, MD, should have been listed as Dania Mohty, MD. The corrected version of the article appears online.

The authors regret this error.

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