## Clinical Investigation

# Clinical Impact of Patient-Prosthesis Mismatch After Aortic Valve Replacement With a Mechanical or Biological Prosthesis

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### **Abstract**

**Background:** Patient-prosthesis mismatch (PPM) may impair functional capacity and survival after aortic valve replacement. This study aimed to investigate the impact of PPM on long-term survival and quality of life after mechanical and biological aortic valve replacement.

**Methods:** This study included 595 consecutive patients who had undergone isolated aortic valve replacement. Patients were divided into 2 groups according to prosthesis type. The baseline and operative characteristics, survival rates, complications, and quality of life of the groups with and without PPM were compared for up to 6 years. The PPM calculation was performed using the effective orifice area value provided by the manufacturer divided by the patient's body surface area.

**Results:** The moderate to severe PPM rates were 69.8% and 3.7% after biological and mechanical prosthesis implantation, respectively. Mean survival for patients in the biological group who had PPM was statistically significantly shorter (50.2 months [95% CI, 45.2-55.3]) than for patients in the biological group without PPM (60.1 months [95% CI, 55.7-64.4]; P = .04). In the mechanical prosthesis group, there was no difference in mean survival between the subgroup with PPM (66.6 months [95% CI, 58.3-74.9]) and the subgroup without PPM (64.9 months [95% CI, 62.6-67.2]; P = .50). A quality-of-life questionnaire's scores did not differ between the groups.

**Conclusion:** Mismatch is common after biological valve implantation and statistically significantly affects long-term survival and quality of life. If the risk of PPM after implantation of a biological prosthesis is suspected, adopting strategies to avoid PPM at the time of surgery is warranted.

Keywords: Patient outcome assessment; quality of life; heart valve prosthesis implantation; bioprosthesis; aortic valve disease

## Introduction

atient-prosthesis mismatch (PPM) represents the mismatch between the prosthetic valve's effective orifice area (EOA) and the patient's hemodynamic requirements. Given the considerable heterogeneity of the patient population, PPM is most commonly presented as EOA divided by the patient's body surface area, resulting in indexed EOA (iEOA) values. An iEOA between 0.85 cm²/m² and 0.65 cm²/m² is considered moderate PPM, while an iEOA of less than 0.65 cm²/m² is considered severe PPM.² The PPM can furthermore be calculated as measured or predict-

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ed. If it is measured, it is usually done with a transthoracic echocardiography exam before hospital discharge. This echocardiograph-dependent method, however, is subject to diverse findings. It is also flow-dependent and may lead to an overestimation of PPM in hearts with diminished ejection fractions. To avoid these limitations, predicted PPM, which is calculated using EOA values provided by the manufacturer divided by the patient's body surface area, has been introduced.<sup>2,3</sup>

Patient-prosthesis mismatch leads to higher transprosthetic gradients that may impair mass myocardial reduction as well as functional capacity and survival after aortic valve replacement (AVR).<sup>4,5</sup> Several published studies have emphasized the negative impact of PPM on survival.<sup>6-9</sup> Moderate PPM is commonly found after AVR, ranging in frequency from 20% to 70%,<sup>10</sup> depending on the definition and method of calculation. Severity of PPM is the primary determinant of its influence on clinical outcomes. Although severe PPM is responsible for worse long-term survival, it is found in fewer than 2% of all AVRs.<sup>7</sup>

Although mechanical and biological prostheses have a similar rate of valve-related complications, PPM is more frequently observed after biological prosthesis implantation. The impact of structural valve deterioration in a biological prosthesis and stable hemodynamic performance of a mechanical prosthesis on PPM and subsequently on survival has yet to be determined. <sup>10,11</sup> Besides the impact of PPM on survival, the question of a patient's quality of life (QOL) arises. Some authors have claimed that PPM after AVR diminishes patients' physical and mental capacities, especially in patients older than 70 years of age. <sup>9,12</sup> Overall, a mechanical prosthesis tends to have a lower risk of PPM than a biological prosthesis, but the clinical outcomes remain unclear.

This study aimed to investigate the impact of an implanted mechanical or biological prosthesis with PPM on long-term survival and QOL after an isolated AVR procedure.

#### **Patients and Methods**

#### **Ethical Approval**

The clinical studies ethical committee of the University Clinical Centre of Serbia approved the study, and all patients signed the informed consent form (KH151/2020).

#### **Key Points**

- Aortic valve replacement with a mechanical prosthesis had a lower rate of PPM than AVR with a biological prosthesis in the present study's population.
- Patients who received biological prostheses and had PPM had worse rates of long-term survival.
- Patients who received biological prostheses and had PPM had worse QOL physical component scores after long-term follow-up.

## **Abbreviations and Acronyms**

AVR	aortic valve replacement
EOA	effective orifice area
iEOA	indexed effective orifice area
PPM	patient-prosthesis mismatch
QOL	quality of life

SF-12 12-Item Short Form Health Survey

#### **Study Design**

Between January 2015 and December 2020, 652 consecutive patients underwent an isolated AVR procedure at the University Clinical Centre of Serbia in Belgrade. This observational analysis included elective, urgent, and emergent cases performed for any pathology. Combined surgery was the exclusion criterion. Of the 641 patients who survived the index procedure, 35 refused to participate in research, and 11 were lost to follow-up (Fig. 1).

The remaining 595 patients were divided into 2 groups according to whether they had received a biological or mechanical prosthesis and were evaluated for the presence or absence of PPM. The groups with and without PPM were compared with regard to baseline characteristics, operative characteristics, survival, complications, freedom from angina, and QOL for up to 6 years of follow-up. The data were obtained from medical records and through telephone surveys during the follow-up period.

#### **Surgical Procedure**

The surgical procedures were performed using cardiopulmonary bypass, and cardioplegic arrest was achieved using a cold, crystalloid cardioplegic solution. Standard median sternotomy, upper ministernotomy through the fourth intercostal space, or anterior minithoracotomy was used for the surgical approach. The following mechanical prostheses were used: St Jude

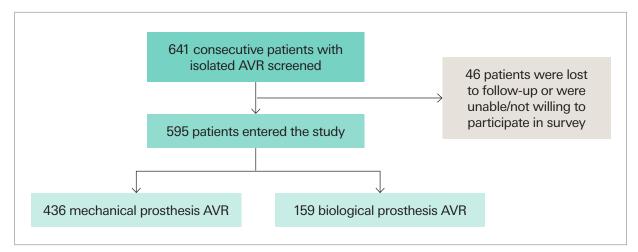


Fig. 1 Flowchart of patient enrollment in the present study.

AVR, aortic valve replacement.

Regent, St Jude Master (Abbott Laboratories); ATS Open Pivot (Medtronic); On-X Heart Valve (CryoLife Inc); and Carbomedics (LivaNova). The biological prostheses used in the study were Hancock (Medtronic); Epic, Trifecta (Abbott Laboratories); CROWN PRT, SoloSmart; and the sutureless Perceval S valve (LivaNova). The choice of the implant procedure was made according to the current guidelines and the surgeon's discretion as well as with the input of the fully informed patient.

#### **Definitions and Study End Points**

The data were extracted from the University Clinical Centre of Serbia's Aortic Valve Registry, a prospectively maintained clinical registry of all patients undergoing AVR or repair at the institution, and double-checked for accuracy (M.M. and A.M.). All operative survivors were followed regularly, and follow-up was completed in 641 of 652 patients (98.3%). All clinically gathered data, including adverse events during follow-up and cause of death, were registered and reported according to the standardized institutional protocol.

#### **Patient-Prosthesis Mismatch**

Patient-prosthesis mismatch was defined as having an iEOA less than 0.85 cm²/m². An iEOA between 0.85 cm²/m² and 0.65 cm²/m² was considered moderate, and an iEOA less than 0.65 cm²/m² was considered severe. The PPM calculations were performed using the EOA value provided by the prothesis manufacturer divided by the patient's body surface area. Patients with mechanical

and biological prostheses were compared according to the presence (iEOA  $<0.85~cm^2/m^2$ ) or absence (iEOA  $>0.85~cm^2/m^2$ ) of PPM.

#### **QOL Survey**

Quality of life was estimated using the 12-Item Short Form Health Survey (SF-12), which is derived from the 36-Item Short Form Health Survey and scored the mental and physical components of the study. The SF-12's physical component investigates physical function, pain levels, and role physical; the cognitive component surveys mental health and social and emotional functioning. The results of these 2 components were scored from 0 to 100, with higher scores representing better mental and physical health.

#### **Statistical Analyses**

Descriptive statistics were calculated for baseline demographic and clinical features as well as for treatment outcomes. Graphical and mathematical methods tested the normality of distribution. As appropriate, continuous variables were presented as mean (SD) or median (IQR). Categorical variables were presented as numbers and percentages. Differences between groups were analyzed using the t test or the Mann-Whitney test for continuous variables and the Pearson  $\chi^2$  test for categorical variables.

A propensity score was developed based on differences in patient age and sex in the PPM and no-PPM groups. Logistic regression analysis with the propensity score as a covariate was performed. Differences in QOL in the PPM and no-PPM groups were analyzed with analysis of covariance, with adjustments made for age and sex. Survival analysis was performed using the Kaplan-Meier method, and the groups were compared using the log-rank test. In addition, Kaplan-Meier survival curves were truncated at a point during follow-up when at least 10% of patients were still at risk to avoid visual misinterpretation. Cox proportional hazards regression was performed with propensity score adjustment. P < .05 was considered statistically significant, and all testing was 2-sided. Statistical analysis was performed using SPSS Statistics for Windows, version 21.0 (IBM Corp).

## **Results**

Of the 595 patients enrolled in the present study, 159 (26.7%) received a biological prosthesis, and 436 (73.3%) received a mechanical prosthesis. The baseline characteristics of patients with biological and mechanical valves are presented in Table I. Patients with biological valves were statistically significantly older than

patients with mechanical valves (mean [SD] age, 69.9 [7.7] years vs 62.6 [12.1] years, P<.001). A mechanical prosthesis was more frequently implanted in men than a biological prosthesis (60.4% vs 49.1%, P=.01). In the mechanical prosthesis group, 5.5% of patients had native valve endocarditis compared with 0.6% of patients in the biological prosthesis group (P=.009). There was no statistically significant difference in the other preoperative characteristics and demographics. After applying logistic regression and controlling for propensity score, the mechanical prosthesis still had a lower risk of PPM (odds ratio, 0.02 [95% CI, 0.01-0.03]; P<.001).

The patients' operative characteristics are presented in Table II. There was no statistically significant difference between the groups in European System for Cardiac Operative Risk Evaluation II, cardiopulmonary bypass, or aortic cross-clamp times. Ejection fraction and mean intensive care unit stays were similar between the groups, as well. Moderate and severe PPM (iEOA <0.85 cm²/m²) were present in 69.8% of patients in the biological prosthesis group compared with 3.7% in the mechanical prosthesis group (*P*<.001) (Table III). Se-

TABLE I. Baseline Characteristics of Patients With a Biological or Mechanical Prosthesis

Characteristic	Biological (n = 159)	Mechanical (n = 436)	<i>P</i> value <sup>a</sup>
Age, mean (SD), y	69.9 (7.7)	62.6 (12.1)	.001
Male sex, No. (%)	78 (49.1)	262 (60.4)	.01
Female sex, No. (%)	81 (50.9)	172 (39.6)	
Body surface area, mean (SD), m <sup>2</sup>	1.9 (0.3)	2.3 (7.4)	.45
Body mass index, mean (SD)	27.7 (11.7)	27.9 (12.8)	.81
Aortic stenosis, No. (%)	137 (86.1)	78 (83.5)	.71
Aortic insufficiency, No. (%)	22 (13.9)	72 (16.5)	.63
Arterial hypertension, No. (%)	131 (82.4)	364 (83.5)	.75
Hyperlipidemia, No. (%)	76 (47.8)	222 (50.9)	.50
Chronic obstructive pulmonary disease, No (%)	22 (13.8)	56 (12.8)	.75
Chronic kidney disease, No. (%)	16 (10.1)	58 (13.3)	.29
Diabetes No. (%)	39 (24.5)	94 (21.6)	.44
Previous stroke, No. (%)	5 (3.1)	18 (4.1)	.58
Endocarditis, No. (%)	1 (0.6)	24 (5.5)	.009

<sup>&</sup>lt;sup>a</sup>P<.05 was considered statistically significant.

vere PPM (iEOA <0.65 cm²/m²) was present in 5.1% of patients in the biological group and 1.3% of patients in the mechanical prosthesis group, with a statistically significant difference (P<.001). There was no difference in the number of redo surgeries or the frequency of postoperative endocarditis in the follow-up period between the mechanical and biological prosthesis groups. Freedom from angina at the time of the latest follow-up was also similar between the groups (85.1% vs 88.8%, P=.28).

Separate analysis of PPM with various prosthesis manufacturers and models was conducted in both the mechanical and biological prosthesis groups. In the mechanical valve group, 16 patients had PPM; there was no difference in the frequency of PPM among the different prosthesis models. In the biological valve group, 111 patients had PPM; the prostheses most common found with PPM were the Trifecta (28 [25.2%], *P*<.001) and Epic valves (25 [22.5%], *P*<.001) (Table IV).

The median (IQR) follow-up was 31.8 (1-74) months. When the mechanical and biological prostheses were analyzed overall, mean survival was statistically significantly shorter in the PPM group (57.0 months [95% CI, 51.9-62.2]) than in the no-PPM group (65.2 months [95% CI, 63.1-67.4]; log-rank test P=.008) (Fig. 2). When data were analyzed separately for the biological prosthesis group, mean survival was statistically significantly shorter in patients with PPM (50.2 months [95% CI, 45.2-55.3]) than in patients without PPM (60.1 months [95% CI, 55.7-64.4]; log-rank test P=.04) (Fig. 3). After applying Cox regression with propensity score adjustments, the difference was still statistically significant (hazard ratio, 3.27 [95% CI, 1.00-10.91]; *P*=.046). Analysis of survival in patients who had received a mechanical prosthesis did not show a difference in mean survival between the PPM group (66.6 months [95% CI, 58.3-74.9]) and the no-PPM group (64.9 months [95% CI, 62.6-67.2]; log-rank test *P*=.50) (Fig. 4). After

TABLE II. Operative Characteristics of Patients With a Biological or Mechanical Prosthesis

Characteristic	Biological (n = 159)	Mechanical (n = 436)	P value <sup>a</sup>
EuroSCORE II, mean (SD)	1.9 (1.4)	1.6 (1.3)	.54
Cardiopulmonary bypass time, mean (SD), min	85.9 (23.3)	89.6 (32.2)	.18
Aortic cross-clamp time, mean (SD), min	61.6 (18.4)	62.4 (24.2)	.16
Ejection fraction, mean (SD), %	58.9 (13.4)	58.5 (12.2)	.42
Intensive care unit time, mean (SD), d	3.5 (2.9)	3.1 (2.5)	.12

EuroSCORE II, European System for Cardiac Operative Risk Evaluation II.

TABLE III. Occurrence of Patient-Prosthesis Mismatch, by Type of Prosthesis, and Associated Clinical Outcomes for up to 6 Years of Follow-Up

	Biological	Mechanical	
Clinical outcome	(n = 159)	(n = 436)	P value <sup>a</sup>
PPM, moderate to severe	111 (69.8)	16 (3.7)	<.001
Survival	133 (83.7)	381 (87.3)	.24
Endocarditis	4 (2.5)	2 (0.5)	.07
Redo surgery	3 (1.8)	5 (1.2)	.53
Freedom from angina	114 (85.1)	340 (88.8)	.28

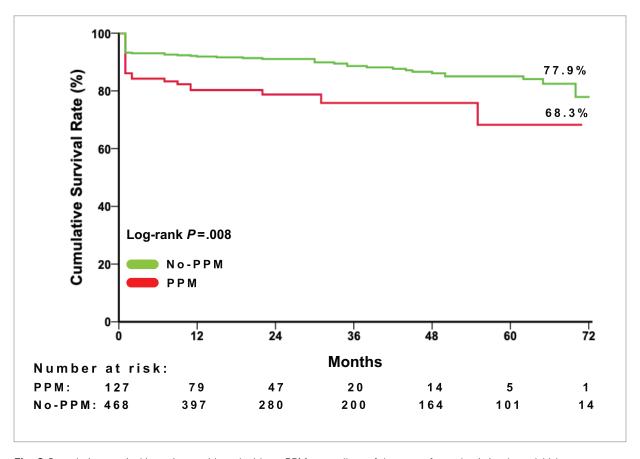
PPM, patient-prosthesis mismatch.

<sup>&</sup>lt;sup>a</sup>P<.05 was considered statistically significant.

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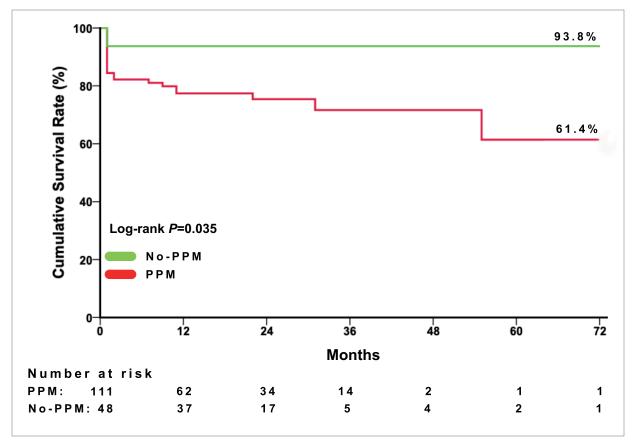
TABLE IV. Distribution of Prosthesis Manufacturers and Models in Groups

Mechanical prosthesis	Patients, No. (%) (n = 436)		
St Jude Master (Abbott Laboratories)	54 (12.4)		
St Jude Regent (Abbott Laboratories)	263 (60.3)		
ATS Open Pivot (Medtronic)	102 (23.4)		
On-X Heart Valve (CryoLife Inc)	8 (1.8)		
Carbomedics (LivaNova)	9 (2.1)		
Biological prosthesis	Patients, No. (%) (n = 159)		
Hancock II (Medtronic)	11 (6.9)		
Epic (Abbott Laboratories)	30 (18.9)		
Trifecta GT (Abbott Laboratories)	64 (40.4)		
CROWN PRT (LivaNova)	19 (11.9)		
SoloSmart (LivaNova)	1 (0.6)		
Perceval S (LivaNova)	34 (21.3)		



**Fig. 2** Cumulative survival in patients with and without PPM, regardless of the type of prosthesis implanted. Values are Kaplan-Meier event rates, with P values from the log-rank test. P < .05 was considered statistically significant.

PPM, patient-prosthesis mismatch.



**Fig. 3** Cumulative survival in patients with and without PPM who had received a biological prosthesis. Values are Kaplan-Meier event rates, with P values from the log-rank test. P < .05 was considered statistically significant.

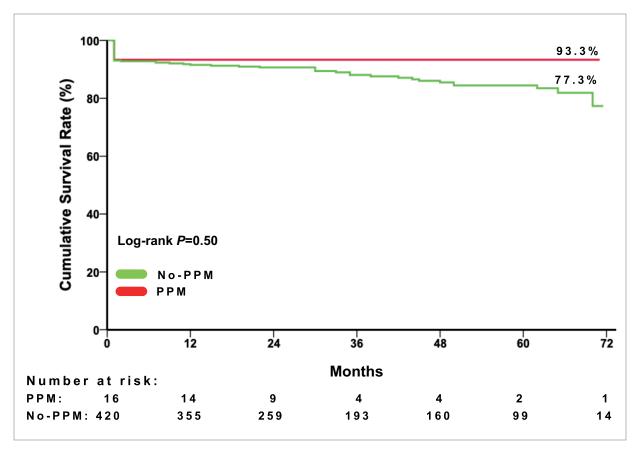
PPM, patient-prosthesis mismatch.

TABLE V. Quality-of-Life 12-Item Short Form Health Survey Questionnaire Among Patients With a Biological or Mechanical Prosthesis

Prosthesis type	Score	PPM group, mean (SD))	No-PPM group, mean (SD)	P valueª
Mechanical	Physical	43.9 (9.4)	46.9 (8.3)	.34
	Mental	54.8 (4.4)	53.5 (5.9)	.16
Biological	Physical	39.4 (8.4)	45.7 (10.1)	.29
	Mental	53.9 (6.1)	53.1 (8.1)	.43
All	Physical	44.4 (8.7)	46.5 (8.6)	.82
	Mental	54.2 (5.9)	53.5 (6.2)	.26

PPM, patient-prosthesis mismatch.

<sup>&</sup>lt;sup>a</sup>P<.05 was considered statistically significant.



**Fig. 4** Cumulative survival in patients with and without PPM who had received a mechanical prosthesis. Values are Kaplan-Meier event rates, with *P* values from the log-rank test. *P* < .05 was considered statistically significant.

PPM, patient-prosthesis mismatch.

applying Cox regression with propensity score adjustments, the difference was not statistically significant (hazard ratio, 0.53 [95% CI, 0.07-3.83]; P=.53).

In total, 87.6% of patients responded to the QOL survey. The SF-12 questionnaires were analyzed separately for patients with mechanical and biological prostheses (Table V). After adjusting for age and sex, there was no statistically significant difference between the mean [SD] physical and mental scores in patients with and without PPM who had received a mechanical prosthesis (physical: 43.9 [9.4] vs 46.9 [8.3], P=.34; mental: 54.8 [4.4] vs 53.5 [5.9], P=.16). Similarly, there was no statistically significant difference between the mean (SD) physical and mental scores in patients with and without PPM who had received a biological prosthesis (physical: 39.4 [8.4] vs 45.7 [10.1], P=.29; mental: 53.9 [6.1] vs 53.1 [8.1], P = .43). Although there was a difference in physical scores in patients with biological valves with and without PPM, the difference was nonsignificant after adjusting for age and sex. There was no statistically significant difference between the mental scores of patients with and without PPM regardless of the type of prosthesis implanted (Table V).

## **Discussion**

The present study analyzed the impact of PPM with a mechanical or biological prosthesis on survival and QOL after AVR. Substantial findings included the following: (1) AVR with a mechanical prosthesis had a markedly lower risk of PPM than AVR with a biological prosthesis, (2) patients with moderate to severe PPM and an implanted biological prosthesis were at the highest risk of long-term mortality, and (3) there was no difference in QOL for patients with biological or mechanical prostheses for up to 6 years of follow-up.

Patient-prosthesis mismatch is associated with a higher risk of poor outcomes after AVR, and its prevention is of paramount importance when selecting a surgical heart valve for implantation.<sup>14</sup> Valve manufacturers provide iEOA values as the most appropriate measurement for predicting PPM after implantation.<sup>15</sup> A cutoff level of iEOA less than 0.85 cm<sup>2</sup>/m<sup>2</sup> has been introduced to define moderate to severe PPM. In the present study population, PPM was found in 21.5% of all patients who underwent AVR. When analyzed separately, however, 69.8% of patients with biological valves implanted had PPM, while just 3.7% of patients with mechanical valves implanted had PPM (*P*<.001).

The Quebec group brought PPM into the spotlight, publishing several studies that showed statistically significantly reduced long-term survival in patients with PPM.<sup>15,16</sup> The Toronto group confirmed their findings.<sup>17</sup> In a large study that enrolled 1,856 patients with mechanical prostheses and 2,275 patients with biological prostheses implanted after AVR, the presence of PPM statistically significantly reduced both short-term and long-term survival. The present study supports these findings, showing lower rates of survival in patients with PPM than in patients without PPM. Although none of the previous studies distinguished outcomes by the presence of a biological or a mechanical prosthesis, the present study revealed lower survival rates with PPM for patients with biological prostheses, while PPM with mechanical prostheses did not affect survival or the physical component of a patient's QOL.

Hoffmann et al<sup>12</sup> analyzed 632 consecutive patients who underwent AVR procedures with only Hancock II biological prostheses. Patient-prosthesis mismatch was present in 93.8% of patients; 71% of patients had moderate PPM, and 22.8% of patients had severe PPM. The authors found no difference in 5-year survival for the groups with and without PPM. The present study found a similar distribution of moderate PPM in the biological prosthesis group, but severe PPM was found in only 5.1% of patients. Patients with biological prostheses and PPM had statistically significantly lower survival rates after 6 years of follow-up than patients without PPM. One potential explanation for the observed differences is that the present study included several biological prosthesis types and complete follow-up. Sportelli et al<sup>4</sup> conducted an observational study that included 152 patients with both mechanical and biological prostheses implanted after AVR. The overall PPM rate was 53%, and 11.7% of patients had severe PPM. The authors reported that PPM had no influence on survival after long-term follow-up, but no separate analyses for biological and mechanical prostheses were reported. In another study, Weber et al<sup>11</sup> revealed more frequent PPM in the biological prosthesis group than in the mechanical prosthesis group, but they did not perform a survival analysis for these groups. Severe PPM was rare in the present study, so it was not suitable for the subanalysis of this population. It should be mentioned that none of the listed studies included patients with sutureless biological prostheses, as appeared in the present study.

It should also be mentioned that nearly 37% of the biological valves implanted in the present study's population were Trifecta valves, whose frequent structural valve disease issues have been raised in a few previously published studies. The prosthesis used in these studies, however, was an earlier Trifecta model; the present study used the new Trifecta GT model. The clinical importance of this fact has yet to be determined. Analysis in the present study revealed a higher frequency of Trifecta and Epic valves in patients with PPM. Larger cohort studies with echocardiograph data as well as EOA and pressure gradients are needed to further facilitate valve choice when PPM is suspected.

Some studies that have enrolled small cohorts have warned about the negative impact of PPM on QOL, especially on the physical component.<sup>9,20</sup> Because PPM is associated with higher transprosthetic gradients, with physical exercise, a rise in the gradient may come close to the values shown in mild and moderate native valve aortic stenosis.21 The median values of the QOL measurements in the present study were close to the SF-12's normal values. The values of the QOL mental component did not show a statistically significant difference in either group's patients with or without PPM. The physical component of the questionnaire revealed statistically significantly lower scores in patients with a biological prosthesis and PPM than in patients with a biological prosthesis without PPM. After adjusting for age and sex, however, there was no statistical difference. This difference was not observed in the mechanical prosthesis group, either. The freedom from angina during follow-up also did not differ between the groups. These results are similar to those published by Hoffman et al,12 who found only a difference in the physical component of the QOL survey, and by Urso et al<sup>22</sup> (163 patients enrolled), who found lower physical scores in older patients. Sportelli et al<sup>4</sup> (152 patients enrolled) and Reskovic Luksic et al<sup>23</sup> (46 patients included) failed to demonstrate a difference in QOL for patients who have PPM. Once again, neither of these studies performed subanalyses for biological or mechanical prostheses.

Perioperative results are affected mainly by the type of valve implanted, but the hemodynamic properties of each valve type can also influence the outcome. In every biological prosthesis, structural valve degeneration will happen to some extent over time. Structural valve degeneration in prostheses with PPM and with higher transprosthetic gradients could lead to further augmentation of gradients, especially during physical exercise. The transprosthetic gradients, however, remain the same over time in a mechanical prosthesis.<sup>24</sup> Although the surgeon must strive to implant the largest valve possible if PPM is suspected in a biological prosthesis, if this is not possible, then a mechanical valve, a sutureless valve implantation, or a root enlargement procedure should be considered. The root enlargement procedure is a debated contemporary issue. It can be safely performed but requires that both the surgeon and the center where the procedure is performed have advanced experience. According to available publications, however, the volume of procedures does not contribute to operative risk.25 Aortic root enlargement is a valuable tool to help prevent PPM in both mechanical and biological valves. If a risk of PPM is suspected, the surgeon should consider another prosthetic model with a better hemodynamic profile. In the present study, the frequency of PPM with Trifecta and Epic valves raised an additional concern regarding valve choice, but further clarification is needed by way of larger, randomized studies and echocardiographic follow-up. As the clinical indications for transcatheter AVR use expand rapidly, the size of the implanted biological prosthesis should be carefully planned.

#### **Study Limitations**

The present study has several substantial limitations. First, the study was observational and lacked randomization. More extensive prospective randomized trials are needed to explore these results and their clinical application. Second, the study was performed in a single center. Third, the response rate for the QOL survey was 87.6%, and data were not available for all patients enrolled in the study. The present study results should only be interpreted as observational and hypothesis-generating because of the nature of their exploratory data analysis.

## **Conclusions**

Patient-prosthesis mismatch is common after biological valve implantation and substantially affects long-term survival and QOL. If the risk of PPM after the implantation of a biological prosthesis is suspected, prospective strategies to avoid PPM at the time of the operation are warranted. Aortic root enlargement or the choice of another prosthetic model with better hemodynamic performance could be considered according to local practice and expertise.

## **Article Information**

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Author Contributions: Milos Matkovic was involved in the conceptualization of the study, investigation of the medical case, methodology design, and the writing of the manuscript. Nemanja Aleksic was involved in the methodology design and the writing of the manuscript. Ilija Bilbija was involved in conceptualization of the study, the methodology design, and the writing of the manuscript. Ana Antic was involved in the data curation and validation of the findings as well as the writing of the manuscript. Marko Cubrilo was involved in the methodology design and the writing of the manuscript. Jelena Milin Lazovic was involved in the data curation, statistical analysis, and software management of this study. Aleksandar Milojevic was involved in the data curation and validation of the findings as well as the writing of the manuscript. Igor Zivkovic was involved in the methodology design and the writing of the manuscript. Svetozar Putnik was involved in the investigation of the medical case, the methodology design, and the supervision and writing of the overall manuscript.

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#### References

- Rahimtoola SH. The problem of valve prosthesis-patient mismatch. *Circulation*. 1978;58(1):20-24. doi:10.1161/01. cir.58.1.20
- Ternacle J, Pibarot P, Herrmann HC, et al. Prosthesis-patient mismatch after aortic valve replacement in the PARTNER 2 trial and registry. *JACC Cardiovasc Interv.* 2021;14(13):1466-1477. doi:10.1016/j.jcin.2021.03.069
- Lancellotti P, Pibarot P, Chambers J, et al. Recommendations for the imaging assessment of prosthetic heart valves: a report from the European Association of Cardiovascular Imaging endorsed by the Chinese Society of Echocardiography, the Inter-American Society of Echocardiography, and the Brazilian Department of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2016;17(6):589-590. doi:10.1093/ehjci/ jew025
- Sportelli E, Regesta T, Salsano A, et al. Does patientprosthesis mismatch after aortic valve replacement affect survival and quality of life in elderly patients? *J Cardiovasc Med (Hagerstown)*. 2016;17(2):137-143. doi:10.2459/ JCM.000000000000000292
- Jamieson WRE, Ye J, Higgins J, et al. Effect of prosthesispatient mismatch on long-term survival with aortic valve replacement: assessment to 15 years. *Ann Thorac* Surg. 2010;89(1):51-58; discussion 9. doi:10.1016/j. athoracsur.2009.08.070
- Hernandez-Vaquero D, Garcia JM, Diaz R, et al. Moderate patient-prosthesis mismatch predicts cardiac events and advanced functional class in young and middle-aged patients undergoing surgery due to severe aortic stenosis. *J Card Surg*. 2014;29(2):127-133. doi:10.1111/jocs.12265
- Hong S, Yi G, Youn YN, Lee S, Yoo KJ, Chang BC. Effect of the prosthesis-patient mismatch on long-term clinical outcomes after isolated aortic valve replacement for aortic stenosis: a prospective observational study. *J Thorac Cardiovasc Surg.* 2013;146(5):1098-1104. doi:10.1016/j. jtcvs.2012.07.101
- Chen J, Lin Y, Kang B, Wang Z. Indexed effective orifice area is a significant predictor of higher mid- and long-term mortality rates following aortic valve replacement in patients with prosthesis-patient mismatch. *Eur J Cardiothorae Surg*. 2014;45(2):234-240. doi:10.1093/ejcts/ezt245
- Concistrè G, Dell'aquila A, Pansini S, et al. Aortic valve replacement with smaller prostheses in elderly patients: does patient prosthetic mismatch affect outcomes? *J Card Surg.* 2013;28(4):341-347. doi:10.1111/jocs.12136
- Dumesnil JG, Pibarot P. Prosthesis-patient mismatch: an update. *Curr Cardiol Rep.* 2011;13(3):250-257. doi:10.1007/ s11886-011-0172-7
- Weber A, Noureddine H, Englberger L, et al. Ten-year comparison of pericardial tissue valves versus mechanical prostheses for aortic valve replacement in patients younger than 60 years of age. *J Thorac Cardiovasc Surg.* 2012;144(5):1075-1083. doi:10.1016/j.jtcvs.2012.01.024
- 12. Hoffmann G, Abraham-Westphal S, Attmann T, et al. Impact of patient-prosthesis mismatch following aortic valve replacement on long-term survival and quality of life. *Thorac Cardiovasc Surg.* 2020;68(2):124-130. doi:10.1055/s-0038-1666973

- Pocock SJ, Clayton TC, Altman DG. Survival plots of timeto-event outcomes in clinical trials: good practice and pitfalls. *Lancet*. 2002;359(9318):1686-1689. doi:10.1016/S0140-6736(02)08594-X
- 14. Durko AP, Pibarot P, Atluri P, et al. Essential information on surgical heart valve characteristics for optimal valve prosthesis selection: expert consensus document from the European Association for Cardio-Thoracic Surgery (EACTS)-The Society of Thoracic Surgeons (STS)-American Association for Thoracic Surgery (AATS) Valve Labelling Task Force. Eur J Cardiothorac Surg. 2021;59(1):54-64. doi:10.1093/ejcts/ezaa263
- Blais C, Dumesnil JG, Baillot R, Simard S, Doyle D, Pibarot P. Impact of valve prosthesis-patient mismatch on short-term mortality after aortic valve replacement. *Circulation*. 2003;108(8):983-988. doi:10.1161/01. CIR.0000085167.67105.32
- Pibarot P, Dumesnil JG, Lemieux M, Cartier P, Métras J, Durand LG. Impact of prosthesis-patient mismatch on hemodynamic and symptomatic status, morbidity and mortality after aortic valve replacement with a bioprosthetic heart valve. J Heart Valve Dis. 1998;7(2):211-218.
- Rao V, Jamieson WR, Ivanov J, Armstrong S, David TE. Prosthesis-patient mismatch affects survival after aortic valve replacement. *Circulation*. 2000;102(19 Suppl 3):III5-III9. doi:10.1161/01.cir.102.suppl\_3.iii-5
- Fukuhara S, Shiomi S, Yang B, et al. Early structural valve degeneration of Trifecta bioprosthesis. *Ann Thorac Surg.* 2020;109(3):720-727. doi:10.1016/j.athoracsur.2019.06.032
- Kattach H, Shah BN, Harden S, et al. Premature structural failure of Trifecta bioprosthesis in midterm follow-up: a single-center study. *Ann Thorac Surg.* 2021;112(5):1424-1431. doi:10.1016/j.athoracsur.2020.11.026
- Koch CG, Khandwala F, Estafanous FG, Loop FD, Blackstone EH. Impact of prosthesis-patient size on functional recovery after aortic valve replacement. *Circulation*. 2005;111(24):3221-3229. doi:10.1161/ CIRCULATIONAHA.104.505248
- Pibarot P, Dumesnil JG. Hemodynamic and clinical impact of prosthesis-patient mismatch in the aortic valve position and its prevention. *J Am Coll Cardiol*. 2000;36(4):1131-1141. doi:10.1016/s0735-1097(00)00859-7
- Urso S, Sadaba R, Vives M, et al. Patient-prosthesis mismatch in elderly patients undergoing aortic valve replacement: impact on quality of life and survival. *J Heart Valve Dis*. 2009;18(3):248-255.
- Reskovic Luksic V, Dosen D, Pasalic M, Separovic Hanzevacki J. Impact of mild patient prosthesis mismatch on quality of life in patients with preserved ejection fraction after isolated aortic valve replacement for aortic stenosis. *Int J Cardiol.* 2017;227:225-228. doi:10.1016/j.ijcard.2016.11.138
- Kim DJ, Lee S, Joo HC, Youn YN, Yoo KJ, Lee SH. A retrospective comparison of hemodynamic and clinical outcomes between two differently designed aortic bioprostheses for small aortic annuli. *J Clin Med.* 2021;10(5):1063. doi:10.3390/jcm10051063
- Yu W, Tam DY, Rocha RV, Makhdoum A, Ouzounian M, Fremes SE. Aortic root enlargement is safe and reduces the incidence of patient-prosthesis mismatch: a meta-analysis of early and late outcomes. *Can J Cardiol*. 2019;35(6):782-790. doi:10.1016/j.cjca.2019.02.004