Original Article

Prosthesis-Patient Mismatch after Aortic Valve Replacement: A Single-Center Experience

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Abstract

Background: The impact of prosthesis-patient mismatch (PPM) on early and late outcomes after aortic valve replacement (AVR) remains controversial. In this study, we aimed to investigate the patient and surgery-related factors leading to various severities of PPM following AVR. **Methods:** Ninety-six patients who had undergone AVR with a prosthetic valve between 2001 and 2013 and later found to have PPM were enrolled. PPM was defined as the indexed effective orifice area (iEOA) of the aortic prosthesis to be ≤0.8 cm^2/m^2. PPM was considered to be of moderate or severe degrees if the iEOA was between 0.66 and 0.85 cm^2/m^2 or ≤0.65 cm^2/m^2, respectively. **Results:** The mean age of patients was 26 ± 15 years, and 51% of patients were female. Sixteen patients (15.2%) had mild PPM, 40 patients (38.1%) had moderate PPM, and 40 patients (38.1%) had severe PPM. The majority of our patients had surgery due to congenital causes. Prosthetic valve size and preoperative left ventricular outflow tract diameter were factors statistically related to PPM in the three groups ($P < 0.05$). There was only one death that was in severe PPM group due to severe heart failure. **Conclusion:** PPM is a substantial yet underrated clinical entity in patients undergoing prosthetic valve replacement surgery. Patients with smaller body surface areas, surgery at earlier age, and underlying congenital heart disease are more commonly prone to the development of PPM. As our center is referral for the patients affected with congenital aortic valve disease, mindful scheduling and performance of the aortic valve replacement surgery in this patient population is highly recommended.

Keywords: Aortic valve replacement, cardiac surgery, prosthesis-patient mismatch

Introduction

Prosthesis-patient mismatch (PPM) after aortic valve replacement (AVR) occurs when the prosthetic valve is functioning normally, but the effective orifice area (EOA) of the prosthesis is discrepantly small in relation to patient's body surface area (BSA). In this setting, the left ventricle has to produce a greater pressure to overcome the mechanical resistance encountered with resultant higher transvalvular pressure gradients.[1,2] PPM is detected not so infrequently after AVR and is diagnosed based on increased prosthetic gradients and decreased EOA in the presence of normal leaflet motion and structure. Theoretically, PPM has been suggested to occur by mechanisms. First: Baseline reductions in size of aortic annulus due to congenital pathologies, extensive annular calcification, and fibrosis and left ventricular hypertrophy. Second: Anatomical status of the inserted prosthesis that could create a relative flow obstruction.[3] The generally accepted value for diagnosis of PPM is an indexed EOA (iEOA) of ≤0.85 cm^2/m^2 which is the cutoff point when there is an increased measured gradient. In severe PPM, the iEOA is ≤0.65 cm^2/m^2.

As PPM has been suggested to increase morbidity and mortality based on severity, it is of paramount importance to recognize the risk factors leading to PPM and implement preventive measures to avert or reduce PPM after AVR. Recent advances in the field of percutaneous AVR particularly in high-risk patients with severely stenotic and calcified valves are also bring PPM to further clinical light.[4-6] In the present article, we aimed to assess existing data in our center and review recent growing body of evidence concerning PPM.

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Methods

Clinical and echocardiographic data of patients who had undergone surgical AVR between 2001 and 2013 were reviewed and 96 patients who fulfilled the criteria for PPM were selected. Data regarding age at time of first surgery, underlying disease resulting in valve replacement, clinical history, and related medical conditions were recorded. Echocardiographic variables including left ventricular outflow tract (LVOT) diameters before valve replacement, valvular gradients before and after surgery, presence of left ventricular hypertrophy, and left ventricular ejection fraction were reviewed. Surgery-related data including prosthesis size, EOA, concomitant surgeries, and the mortality rate were also recorded.

The EOA was calculated as the LVOT cross-sectional area multiplied by LVOT velocity time integral divided by the aortic jet velocity time integral. iEOA was calculated by dividing EOA to patient's body surface area (BSA). Significant PPM was defined as the iEOA of the aortic prosthesis to be ≤0.8 cm^2/m^2. PPM was considered to be of moderate or severe degrees if the iEOA was between 0.66 and 0.85 cm^2/m^2 or ≤0.65 cm^2/m^2, respectively. Mild PPM was defined when iEOA was about 0.8 cm^2/m^2. The first accessible postsurgical echocardiogram-containing data regarding iEOA were used to evaluate for PPM. Follow-up data were obtained from the patient records and outpatient clinic forms.

Statistical analysis

Mean value, standard deviation, and frequency were used as descriptive analysis. For evaluation, the distribution of data one-sample Kolmogorov–Smirnov test was used. Qualitative data were compared with Chi-square test. Mean values were compared using independent-samples *t*-test or Mann–Whitney U-test. Logistic regression was used to identify multivariate independent predictors of PPM. Odds ratios were reported with 95% confidence intervals. Multivariate analysis was done using STATA version 11 (StataCorp. LLC, Texas, USA).

Results

Most of our patients were relatively young with the mean age of patients being 26 ± 15 years at time of first surgery [Table 1]. Thirty-nine patients had undergone at least two times of surgery. All the participants had mechanical prosthesis.

Mild PPM was present in 16 patients (15.2%), moderate PPM in 40 patients (38.1%), and severe PPM in the remaining 40 patients (38.1%). The comparisons between three groups in terms of demographic and clinical symptoms are shown in Table 2.

There was a significant relationship between age at first operation and presence of PPM (P = 0.034). However, no significant relationship was found between age at first operation and each subgroup of PPM perhaps due to relatively smaller number in each subgroup.

Table 1: The demographic, clinical, and surgery-related data in all patients

	Mean±SD, *n* (%)
Sex (female/male)	49/47
Age	26.75±15.09
BSA	1.61±0.18
F/C	
I	22 (25.6)
II	45 (52.3)
III	16 (18.6)
IV	3 (3.5)
Valve size	20.67±2.11
LVOT diameter	19.727±4.35
PPG in first postoperative echocardiography	43.72±21.42
MPG in first postoperative echocardiography	27.08±12.97
PPG maximum in follow-up	66.05±23.58
MPG maximum in follow-up	38.67±14.79
LVEF	52.42±5.87

BSA: Body surface area, F/C: Functional class, PPG: Peak pressure gradient, MPG: Mean pressure gradient, SD: Standard deviation, LVEF: Left ventricular ejection fraction, LVOT: Left ventricular outflow tract

Table 2: The comparison of demographic and clinical symptoms in three groups of patients

	Mild PPM (%)	Moderate PPM (%)	Severe PPM (%)	*P*
Sex				
Male	10 (62.5)	16 (40)	22 (55)	0.84
Female	6 (37.5)	24 (60)	18 (45)	
CAD	1 (6.3)	3 (7.7)	1 (2.5)	0.38
Dyspnea	14 (87.5)	32 (82.1)	32 (80)	0.54
Asymptomatic	1 (6.3)	6 (15)	7 (17.5)	0.34
F/C				
I	5 (38.5)	9 (27.3)	7 (21.2)	0.32
II	7 (53.8)	18 (54.5)	16 (48.5)	
III	1 (7.7)	6 (18.2)	8 (24.2)	
IV	0	0	2 (6.1)	

CAD: Coronary artery disease, F/C: Functional class, PPM: Prosthesis-patient mismatch

Forty-nine of patients (51%) were female. No statistically significant relationship between gender and presence of mismatch was found. Regarding the functional capacity, most reported to be in New York Heart Association Functional Classification II, but the differences between groups regarding to clinical symptoms were not statistically significant ($P > 0.05$).

Interestingly, eighty-two of our patients with mismatch (85%) had a history of AVR due to a form of congenital heart disease (mainly congenital aortic stenosis, bicuspid aortic valve, and subvalvular aortic stenosis). Other underlying causes of AVR were rheumatic heart disease (9.5%) or aortic regurgitation (5.5%) due to endocarditis or miscellaneous causes.

The comparisons between three groups in terms of echocardiographic and surgery-related data are demonstrated in Table 3. As shown in Table 3, chosen prosthetic valve size and patient's LVOT diameter had a statistically significant relationship with the presence of mismatch in the three groups ($P < 0.05$).

The mean LVOT diameter in affected patients was 19.7 mm and LVOT diameter before surgery had a significant relationship with the presence and severity of mismatch ($P = 0.034$). There were no significant differences between groups in regard to other surgery-related variables.

The mean left ventricular ejection fraction in affected patients was 52.4%. The lowest reported ejection fraction was 30%. No statistically significant relation was found between mismatch and presence of other medical conditions including chronic renal disease and thyroid or liver abnormalities.

In our study, 84.8% of patients were followed clinically and only 15.2% had undergone redo surgery. Two patients refused the redo operation. Mortality was reported in one patient in the severe PPM group due to advanced heart failure.

The results of multivariate analysis are shown in Table 4. This model was adjusted for factors that were significant in univariate analysis and also age at first operation as an important predictor of PPM. Age at first operation and LVOT diameter were two predictors of PPM at multivariate analysis [Table 4].

Table 3: The comparison of echocardiographic and surgery-related data in three groups of patients

	Mild PPM (%)	Moderate PPM (%)	Severe PPM (%)	*P*
Valve size	21.20±1.42	21.38±1.44	20.05±2.28	0.01
LVOT diameter	21±1.41	20.47±4.76	18.52±4.68	0.03
PPG maximum	56.81±21.13	66.35±27.73	70.26±21.16	0.10
MPG maximum	32.21±11.96	38.22±16.66	41.28±13.99	0.19
LVEF	50.62±5.73	52.70±4.94	53.67±5.94	0.14
LVH after	3 (18.8)	6 (16.2)	8 (21.6)	0.83
Death	0	0	1 (2.5)	0.41
Discharge information				
CFU	13 (81.3)	34 (85)	34 (87.2)	0.76
Reoperation	1 (6.3)	1 (6.3)	2 (5.1)	
Refuses redo surgery	0	0	2 (2.6)	

PPG: Peak pressure gradient, MPG: Mean pressure gradient, LVEF: Left ventricular ejection fraction, LVH: Left ventricular hypertrophy, CFU: Clinical follow-up, LVOT: Left ventricular outflow tract, PPM: Prosthesis-patient mismatch

Table 4: Multivariable analyses of patient-prosthesis mismatch

	OR	*P*	95% CI
Age at first operation	0.94	0.03	0.88-0.99
LVOT diameter	0.55	0.02	0.33-0.90
Valve size	0.95	0.65	0.78-1.1

OR: Odds ratio, CI: Confidence interval, LVOT: Left ventricular outflow tract

Discussion

PPM is a relevant subject in both mechanical and bioprosthetic valves. Measured prosthetic valve gradient is directly related to the amount of flow passing through the valve. Transvalvular flow is determined by cardiac output which in turn is greatly affected by body surface area. When the BSA is large and the EOA is small, increased transprosthetic gradients and thus PPM could ensue.[5] From practical point of view, it has been shown that when iEOA becomes <0.85 cm^2/m^2, transprosthetic gradients (as measured by Doppler echocardiography) are elevated. However, the European Association of Cardiovascular Imaging recommends a cutoff value of <0.7 cm^2/m^2 in obese patients (body mass index ≥35 kg/m^2) as not to overdiagnose this group.[4] Although PPM is a very common cause of increased gradients post-AVR, other causes including pannus ingrowth, thrombosis, high cardiac output states, and degenerative changes in bioprosthetic valves should be taken in to account during patient workup. It must also be kept in mind that there are situations when both PPM and other factors of valvular dysfunction exist concurrently. Hence, if the severity of increased transvalvular gradients could not be explained by PPM alone, other pathologies should be actively sought. If the leaflet motion or morphology is not intact, valvular dysfunction is more likely. Transesophageal echocardiography might be more helpful in this regard.[5-8]

Risk factors

The proposed risk factors are smaller aortic annulus (<20–21 mm), larger body surface area, left ventricular hypertrophy, and implantation of bioprosthetic valves (as compared to mechanical valves), older age, hypertension, renal failure, and diabetes. Some studies have shown an association between female gender and PPM because of smaller body surface area and a smaller aortic annulus in females.[1,4,5,8,9] However, we did not find any relation between PPM severity and prevalence in regard to gender. We also did not find an association between BSA and severity of mismatch, similar to the study by Astudillo *et al*. of 311 prosthesis mismatch patients.[1] Postoperative valvular mean gradients have been indicated to be one of important factors in PPM after valve replacement. Our patients had increased mean gradients in the first postoperative echocardiography (27.08 ± 12.97), but relation with subgroups of PPM was not significant perhaps due to relatively small sample size. The patients were all relatively young and mechanical valves were used. Coronary risk factors and other medical conditions were not prevalent and did not show significant relation to PPM severity in our study group.

Morbidity and mortality

A meta-analysis of 34 observational studies involving 27,186 patients reported considerable reductions in global and cardiac-related survival during long-term follow-up of patients with PPM after AVR that increases by PPM severity and is persistent over time. However, this meta-analysis included both mechanical and bioprosthetic valves. Mechanical valves are more prevalently used in younger patients who frequently have an active lifestyle, and therefore, greater flow across the valve, on the other hand, PPM might result in more rapid valvular degeneration in older patients with bioprosthetic valves, so this study is considered to have heterogeneities in results.[4-8]

Association of PPM and increased mortality could be explained by a number of elements. There is a potentially higher risk of congestive heart failure, lack of regression of left ventricular hypertrophy and abnormal coronary flow reserve, persistence of possibility of exercise-induced arrhythmias, and continued bleeding tendencies associated with aortic stenosis. The gradients also increase substantially by exercise. This point makes PPM more hazardous in young patients with a longer expected life expectancy and a more active lifestyle.[9-16]

Those with baseline LV dysfunction and reduced myocardial reserve have a worse prognosis, and hence, low-flow low gradient state should be kept in mind while evaluating patients with AVR in the context of LV dysfunction.[5,10,17]

As our affected patients were rather in younger age group with the majority having preserved left ventricular function, early and late mortality was not clearly prevalent as the impact of PPM on mortality has been reported to relate to older age, LV dysfunction, and concurrent coronary bypass grafting. In our study, we had only one death in severe PPM. As our center is a tertiary center, patients with severe PPM would be referred for redo valve surgery as soon as clinical worsening seems to begin that might have led to decreased mortality rates.

Preventive strategies

PPM is a potentially preventable phenomenon. Multiplying patient's BSA by 0.85 is a mean of estimating the smallest iEOA needed to avert PPM and select the best matching prosthesis size and type accordingly. If the desired EOA is not easily achieved by available prosthesis, surgical aortic root enlargement could be considered. The use of newer generation valves might have help improve the achieved hemodynamics.[5,12]

Although more relevant in older and high-risk group, recent studies have shown lower incidence of PPM with transcatheter AVR (TAVR). However, there is a greater rate of paravalvular regurgitation. The Placement of Aortic Transcatheter Valves trial which was a multicenter, randomized controlled trial that aimed to compare surgical AVR with TAVR concluded that in high-risk patients with severe aortic stenosis, PPM is less frequent in the transcatheter group.[6,7]

The number of affected patients in our center was matching to other studies. Our patients, however, were much younger, and congenital causes of AVR were far more common. These might be due to the point that our hospital is a referral center for congenital heart disease patients, and this important subgroup might have actually been underrated in studies performed by other centers.

In summary, based on our study, we recommend meticulous measurement of LVOT diameter in patients referred for AVR. Discussion with surgical team should be contemplated in cases of LVOT/aortic annulus diameters below 21 mm.

Conclusion

PPM is believed to lead to adverse effects on patient survival and quality of life after AVR. Every effort should be taken to minimize this risk. Greater emphasis should be put in preoperative evaluation of young patients undergoing AVR particularly those with congenital aortic abnormalities. As for older patients, with the increased performance of TAVR, further studies are needed to focus on the prevalence of PPM, and it outcomes in this subset of rather high-risk patients.

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Conflicts of interest

There are no conflicts of interest.

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