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ORIGINAL ARTICLE

Is the threshold for postoperative prosthesis-patient mismatch the same for all prostheses?

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Abstract

Purpose The effective orifice area index (EOAI) is used to define the prosthesis-patient mismatch (PPM) after aortic valve replacement (AVR). However, few studies have so far evaluated whether the cutoff value for PPM varies across prostheses. This study assessed the hemodynamics in patients given a mechanical valve and then re-evaluated the validity of the commonly accepted threshold.

Methods The subjects included 329 patients that underwent AVR with a St. Jude Medical Regent valve. The transvalvular pressure gradient and EOAI were determined echocardiographically, and the commonly accepted threshold was analyzed in relation to survival.

Results The mechanical valves very often yielded a postoperative transvalvular pressure gradient >10 mmHg, and thus, clinically significant residual pressure, regardless of the EOAI. The slope of the curve describing the relationship between the transvalvular pressure gradient and EOAI was gentler than that reported for bioprosthetic valves, for which the pressure gradient rises sharply at EOAI <0.85 cm^2/m^2. The commonly defined PPM did not affect the long-term survival or regression of the left ventricular mass index.

Conclusions The relationship between the transvalvular pressure gradient and the EOAI in patients given a mechanical prosthesis differed from the reference standard. These data suggest the need to reconsider the appropriate cutoff value for PPM in relation to different prostheses.

Keywords Aortic valve replacement · Aortic root · Prosthesis

Introduction

Aortic valve replacement (AVR) in patients with a small aortic annulus can lead to an unfavorable outcome. Surgeons need a prospective strategy to avoid prosthesis-patient mismatch (PPM) [1, 2]. The consequence of PPM is the persistence of an abnormally high transvalvular pressure gradient, resulting in an increase in left ventricular work.

The PPM in the aortic position is generally defined as an effective orifice area index (EOAI) < 0.85 cm^2/m^2. The cutoff value for the PPM is estimated according to the relationship between the EOAI and the transvalvular pressure gradient after AVR. Pibarot et al. [1] found that the transvalvular pressure gradient increased steeply when the EOAI was <0.85 cm^2/m^2. Although their findings were based on echocardiographic measurements in patients given non-mechanical prostheses, the same EOAI is commonly used as the threshold for PPM, even in patients with a mechanical valve. Few studies have so far evaluated the relationship between the EOAI and transvalvular pressure gradient after AVR with a mechanical valve in a large patient series. Therefore, the objective of this study was to investigate the relationship between these two variables in patients given a mechanical prosthesis and to reconsider the definition of PPM.

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Patients and methods

Patients

The subjects of this study were 329 patients that underwent elective AVR with a St. Jude Medical Regent mechanical valve (St. Jude Medical, Inc., St. Paul, MN) at this institution between July 2005 and February 2011. The mean age was 65.2 ± 11.1 years. Seventy percent ($n = 231$) of the patients were females. The mean body surface area (BSA) was 1.55 ± 0.18 m^2 (range 1.16–2.07 m^2). The preoperative patient characteristics are summarized in Table 1. The study followed the guidelines of the Ethical Review Board of Jichi Medical University. All patients had previously granted permission for use of their medical records for research purposes.

Operative techniques

Aortic valve surgery was performed via standard median sternotomy. Cardiopulmonary bypass was initiated after cannulation of the ascending aorta, superior vena cava, and inferior vena cava. A left ventricular vent was inserted via the right upper pulmonary vein. Antegrade/retrograde cold blood cardioplegia was administered intermittently to maintain cardiac arrest. Moderate hypothermia was applied. The diseased aortic valve was completely excised, and the diameter of the aortic annulus was measured with valve sizers (St. Jude Medical) for selection of the appropriately sized prosthesis. A bioprosthesis was usually selected for patients older than 70 years of age at this institution. However, a mechanical valve was selected based on the patient's preference, anticoagulation requirements, or small aortic annulus in some patients older than 70 years of age. A St. Jude Medical Regent mechanical valve was implanted in the intra-annular position with the use of everted mattress sutures of 2-0 braided polyester in 310 patients and with the use of interrupted sutures of 2-0 braided polyester in 19 patients. The surgical data, including hospital mortality and its causes, are shown in Table 2. Associated procedures included coronary bypass grafting in 39 patients (12 %), mitral valve replacement in 67 patients (20 %), and mitral annuloplasty in 18 patients (5 %). Warfarin sodium was started on the day of surgery, with a target prothrombin time ratio (international normalized ratio) of 2.0–3.0.

Table 1 Preoperative patient characteristics (329 total patients)

Characteristics	
Age (years; mean ± SD)	65.2 ± 11.1
Female sex	231 (70 %)
NYHA class III or IV	136 (41 %)
Body surface area (m^2; mean ± SD)	1.55 ± 0.18 (range 1.16–2.07)
Aortic valve lesion	
AS	155 (47 %)
ASR	72 (22 %)
AR	102 (31 %)
Hypertension	136 (41 %)
Diabetes	46 (14 %)
Ischemic heart disease	51 (16 %)
Atrial fibrillation	72 (22 %)
Hemodialysis	29 (9 %)
LVEF <0.40	38 (12 %)

The number and percentage of patients are shown unless otherwise indicated

AR aortic regurgitation, *AS* aortic stenosis, *ASR* aortic stenosis and regurgitation, *LVEF* left ventricular ejection fraction, *NYHA* New York Heart Association

Table 2 Surgical data (329 total patients)

Characteristics	
Cross-clamp time (min; mean ± SD)	
Isolated procedure	113 ± 22
Concomitant procedures	168 ± 41
Method of implantation	
Everted mattress sutures	310 (94 %)
Interrupted sutures	19 (6 %)
Implanted valve size (mm)	
17	116 (35 %)
19	118 (35 %)
21	67 (20 %)
23	27 (8 %)
25	1 (0 %)
Concomitant procedures	
Coronary artery bypass grafting	39 (12 %)
Mitral valve replacement	67 (20 %)
Mitral annuloplasty	18 (5 %)
Maze procedure	18 (5 %)
Mitral valve repair	7 (2 %)
Perioperative death	7 (2 %)
Complication	
Cerebral infarction	6 (2 %)
Need for intra-aortic balloon pump insertion or percutaneous cardiopulmonary support	4 (1 %)

The number and percentage of patients are shown unless otherwise indicated

Echocardiography

Standard M-mode cardiac dimensions were determined according to the American Society of Echocardiography criteria. M-mode echocardiograms were obtained for the measurement of the end-diastolic septal thickness, left ventricular end-diastolic dimension, left ventricular end-systolic dimension, and left ventricular end-diastolic posterior wall thickness. All Doppler measurements were averaged from more than three cycles in patients with sinus rhythm and from more than five cycles in those with atrial fibrillation. Maximum pressure gradients were calculated using the Bernoulli equation. The effective orifice area (EOA) was calculated according to the continuity equation: $EOA = (LVOT^2_{diameter} \times 0.785 \times TVI_{LVOT})/TVI_{aortic\ valve}$, where LVOT is the diameter of the left ventricular outflow tract, and TVI is the time velocity integral of the LVOT or aortic valve.

Follow-up

The mean follow-up time was 31.1 ± 18.5 months (range 0–68 months) and was 99.1 % complete. The clinical status of each patient was evaluated by means of direct hospital visits and telephone interviews. Follow-up transthoracic echocardiographic data were obtained for 106 (32 %) of the 329 patients at 13.1 ± 11.5 months after surgery. The most recently obtained echocardiographic measurements were used for patients who underwent echocardiographic study more than once during the follow-up period.

Definition of PPM

The projected EOAI was calculated as the EOA reported by the valve manufacture divided by the patient's BSA. The PPM was graded according to the EOAI as no mismatch (EOAI > 0.85 cm^2/m^2), moderate mismatch (EOAI 0.65–0.85 cm^2/m^2), or severe mismatch (EOAI < 0.65 cm^2/m^2).

Statistical methods

Data are reported as the mean ± SD. The actuarial survival was calculated by the Kaplan–Meier method. Differences in the actuarial survival between patients with and without PPM were analyzed by the log-rank test. A Cox proportional hazards model was used to identify predictors of survival. Variables for which a p value <0.15 was obtained in the univariate analysis were included in the multivariate analysis. All analyses were performed with the SPSS software package (version 10.1; SPSS Inc. Chicago, IL). A p value of 0.05 was considered to be significant.

Results

Surgical outcomes

Hospital mortality was 2.1 % (7 patients). The causes of hospital death were pneumonia ($n = 4$), stroke ($n = 1$), intestinal necrosis ($n = 1$), and prosthetic valve endocarditis ($n = 1$). Six patients (1.8 %) experienced postoperative cerebral infarction. Four patients (1.2 %) required perioperative intra-aortic balloon pumping or percutaneous cardiopulmonary support for hemodynamic instability.

Follow-up data

Twenty-four patients (7.3 %) died during the follow-up period. The actuarial 1-, 3-, and 5-year survival rates were 94.7, 91.2, and 86.2 %, respectively. A univariate analysis identified age, preoperative New York Heart Association (NYHA) class III or IV, diabetes, ischemic heart disease, hemodialysis, ejection fraction <0.4, aortic stenosis, and concomitant coronary artery bypass grafting as predictors of post-discharge mortality, defined as death from any cause at any time after discharge. PPM was not associated with late mortality in the univariate analysis. The multivariate analysis showed diabetes and preoperative NYHA class III or IV to be independent predictors of late mortality (Table 3). There was no significant difference in survival between the aortic valve lesions, although patients with aortic regurgitation did tend to have a better survival (p value = 0.292).

Echocardiographic data

Transthoracic echocardiographic data obtained at discharge are summarized in Table 4.

Both the EOAI and the corresponding mean left ventricular aortic pressure gradient (LVAo-PG) were obtained in 266 (81 %) of the 329 patients at discharge. The relationship between the EOAI and the mean LVAo-PG at discharge is shown in Fig. 1. In comparison to the curve previously reported by Pibarot and Dumesnil [1], the approximate curve was gentler, and the patients with a mechanical valve achieved a higher LVAo-PG, even though the corresponding EOAI was comparable. The echocardiographic measurements obtained at follow-up showed a trend similar to that at discharge (Fig. 2).

Table 3 Results of the Cox proportional hazards analysis for post-discharge mortality

	HR	95 % CI	*P* value
Late mortality			
Diabetes	2.7	1.1–6.9	0.034
Preoperative NYHA class III or IV	2.9	1.1–7.6	0.028

Post-discharge mortality defined as death from any cause at any time after discharge

CI confidence interval, *HR* hazard ratio, *NYHA* New York Heart Association

Table 4 Hemodynamic values at discharge per labeled valve size (329 total patients)

Variable	Labeled valve size (mm)				
	17 ($n = 116$)	19 ($n = 118$)	21 ($n = 67$)	23 ($n = 27$)	25 ($n = 1$)
Maximum LVAo-PG (mmHg)	31.9 ± 11.3	30.3 ± 11.9	27.5 ± 9.9	27.5 ± 12.2	37.0
Mean LVAo-PG (mmHg)	17.8 ± 6.3	16.2 ± 6.5	15.7 ± 5.6	16.7 ± 7.9	18.0
EOA (cm^2)	1.41 ± 0.37	1.63 ± 0.39	1.84 ± 0.49	2.38 ± 0.52	2.19
EOAI (cm^2/m^2)	0.98 ± 0.26	1.03 ± 0.27	1.08 ± 0.33	1.30 ± 0.29	1.27

Values are the mean ± SD, except when shown for only 1 patient

EOA effective orifice area, *EOAI* effective orifice area index, *LVAo-PG* left ventricular aortic pressure gradient

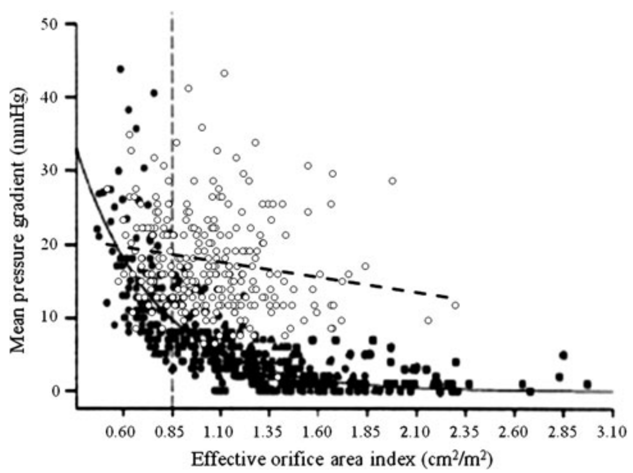

Fig. 1 Scatter plot showing the relation between postoperative mean transvalvular pressure gradient and effective orifice area index at discharge in patients given a mechanical (St. Jude Medical Regent) valve (*open circles*). *Dashed line* is the exponential curve ($n = 266$, $Y = 20.99 \exp[-0.299X]$) drawn from our data. *Solid line* (*filled circles*) is the exponential curve reported by Pibarot and Dumesnil [1]

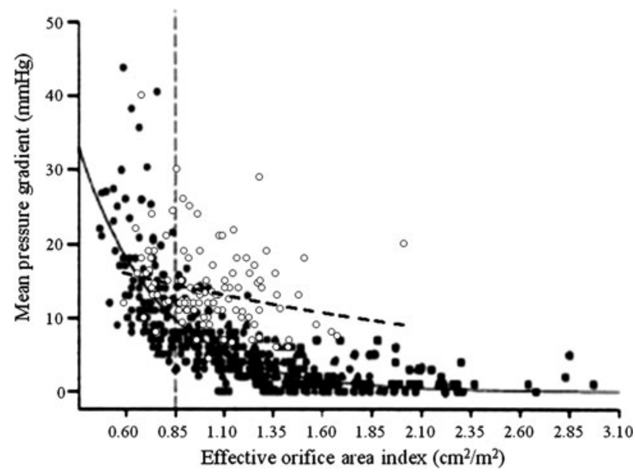

Fig. 2 Scatter plot showing the relation between postoperative mean transvalvular pressure gradient and effective orifice area index at follow-up in patients given a mechanical (St. Jude Medical Regent) valve (open circles). The *dashed line* represents the exponential curve ($n = 106$, $Y = 20.12 \exp[-0.41X]$) drawn from our data. The *solid line* (*filled circles*) represents the exponential curve reported by Pibarot and Dumesnil [1]

Relationship between PPM and outcomes

The projected EOAI showed that a moderate PPM was found in 27 patients (8 %) at discharge. None of these patients with a moderate PPM died or experienced from major adverse valve-related cardiac events during the follow-up period. No patient had a severe PPM. There was no difference in the survival between patients with a moderate PPM and those without PPM (Fig. 3). PPM did not affect regression of the left ventricular mass index (LVMI) at follow-up (Table 5).

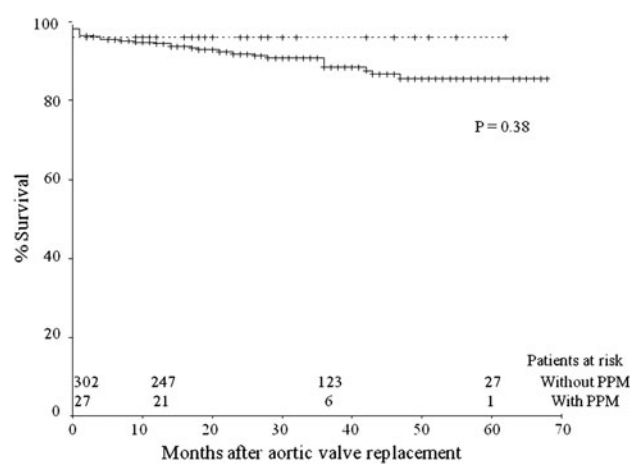

Fig. 3 Kaplan-Meier survival curves for patients with moderate prosthesis-patient mismatch (PPM [*dotted line*]) and those without PPM (*solid line*). There was no statistical difference in survival between the two groups

Discussion

Rahimtoola noted the problem of the PPM after AVR [3]. The basic principle of the PPM is a low postoperative EOAI leading to the persistence of an abnormally high

Table 5 Left ventricular mass index over time in patients with and without ppm

	PPM ($n = 27$)	No PPM ($n = 302$)
LVMI (g/m^2)		
Before surgery	160 ± 38	194 ± 69
At discharge	119 ± 62	157 ± 68
At follow-up[a]	107 ± 21	133 ± 40
Reduction in LVMI (%)		
Before surgery → at follow-up	24.7 ± 19.8	25.2 ± 23.4[b]

Prosthesis-patient mismatch, defined as an effective orifice area index <0.85 cm^2/m^2 at discharge

LVMI left ventricular mass index, *PPM* prosthesis-patient mismatch

[a] The most recent echocardiographic measurements were used in patients that underwent more than one echocardiographic study during the follow-up period

[b] $P = 0.960$ versus PPM

transvalvular gradient, which may pose a risk in terms of clinical status and survival. Although the clinical effect of a PPM on the prognosis remains unclear, some studies have indicated that patients with a PPM after AVR are at risk for decreased postoperative physical capacity and decreased short-term survival [1, 2, 4, 5]. The degree to which a PPM affects the survival depends on specific patient characteristics such as the age, body size, and left ventricular function [6–8]. Therefore, surgeons need to pay careful attention to both the selection of the prosthesis and the surgical method to prevent PPM in patients with a small aortic annulus.

Previous studies have characterized PPM by various parameters, including valve size, internal geometric area of the prosthesis, pressure gradient across the aortic valve, exercise-induced pressure gradient, and the EOAI [9–13]. PPM is widely defined on the basis of the EOAI, which has been found to consistently correlate with postoperative pressure gradient. Pibarot and colleagues described the PPM cutoff value according to the relation between the postoperative pressure gradient and EOAI. They found that mean LVAo-PG increased exponentially when the EOAI was <0.8–0.9 cm^2/m^2 and, therefore concluded that the threshold for PPM in the aortic position lies at an EOAI of 0.85 cm^2/m^2 [1]. Similarly, Dumesnil and Yoganathan [14] considered the ideal EOAI to be not less than 0.9–1.0 cm^2/m^2 because a small decrease in EOAI produces a rapid rise in the mean pressure gradient during exercise. Therefore, an EOAI of 0.85 cm^2/m^2 is commonly considered the threshold for PPM, regardless of which prosthesis is implanted. However, it should be noted that the data were derived from patients that underwent AVR with a non-mechanical prosthesis. Few studies have so far evaluated the relationship between the EOAI and mean LVAo-PG in patients given a mechanical valve or addressed the question of whether a mechanical valve and bioprosthesis differ in this regard.

The current study evaluated the relationship between the EOAI and the mean LVAo-PG in patients given a mechanical valve, and compared the findings with those previously reported. The current patients given a mechanical valve achieved a higher LVAo-PG than that of previously reported patients given a bioprosthesis, even though the corresponding EOAIs were comparable. The mean LVAo-PG in most of the patients exceeded 10 mmHg, which, according to Pibarot's original exponential curve, is a clinically significant postoperative residual pressure gradient. The steep increase in LVAo-PG was not found among the patients when the EOAI was <0.85 cm^2/m^2 in the current series. The appropriate EOAI for PPM should be higher in patients with a mechanical valve than in patients with a tissue valve, assuming that the principle of PPM is the negative impact of the residual pressure gradient.

The relationship between the EOAI and the mean LVAo-PG reported by some investigators differs from that reported by Pibarot and colleagues [1]. Sakamoto and colleagues [15] showed a correlation between the EOAI and mean LVAo-PG in patients given a Carpentier-Edwards Perimount valve. The exponential curve they obtained was gentler than that reported by Pibarot and Dumesnil [1] and they concluded that an EOAI of at least 2.0 cm^2/m^2 might be needed to avoid a PPM in patients undergoing AVR with a tissue valve. Dalmau and associates evaluated hemodynamic performance of the Carpentier-Edwards Perimount Magna and Medtronic Mosaic bioprostheses [16]. The correlation they reported between the EOAI and mean LVAo-PG was close to that reported by Sakamoto and colleagues [15]. Dalmau et al. [16] also showed a difference in the relationship between these variables for pericardial versus porcine bioprostheses. The current findings suggest that the PPM cutoff value might differ between types of prosthetic valves. An EOAI more than 2.0 cm^2/m^2 is required to avoid a residual pressure gradient (i.e., postoperative mean LVAo-PG exceeding 10 mmHg) according to Fig. 2. The current application of the same EOAI value to all types of valves could account for the conflicting results between series concerning the effect of PPM on clinical outcomes.

There were some limitations associated with the current study. First, the patient group was not exceptionally large, making it difficult to draw strong conclusions. Second, the follow-up period was short. The effect of PPM can be manifested long after surgery. Third, the echocardiographic data were obtained at rest; it is unclear whether we would obtain the same results during exercise.

In summary, the results of AVR with a Regent mechanical valve were satisfactory despite the fact that most patients had a postoperative mean pressure gradient >10 mmHg. The relationship between the postoperative pressure gradient and EOAI in patients given a St. Jude Medical Regent mechanical valve differed from that reported in patients given a non-mechanical valve. This finding implies the need to determine the appropriate EOAI cutoff value for the PPM in relation to the type of prosthesis used. The current results need to be confirmed in a larger patient series.

Conflict of interest The authors have no conflicts of interest to declare.

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