

Defining Patient-Prosthesis Mismatch and Its Effect on Survival in Patients With Impaired Ejection Fraction

David A. Cotoni, DO, Robert T. Palac, MD, Lawrence J. Dacey, MD, and Daniel J. O'Rourke, MD

Department of Internal Medicine, Section of Cardiology, and Section of Cardiothoracic Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; and Section of Cardiology, Veterans Affairs Medical Center, White River Junction, Vermont

Background. How best to define patient-prosthesis mismatch (PPM) continues to be debated. Over time, the indexed effective orifice area has become the most widely used method. However, the clinical relevance of PPM remains controversial.

Methods. The indexed geometric orifice area and indexed effective orifice area were calculated for 143 patients having undergone aortic valve replacement with a normal left ventricular function 0.45 or less. Using the indexed geometric orifice area method, PPM was defined as nonsignificant if $1.2 \text{ cm}^2/\text{m}^2$ or greater and as significant if less than $1.2 \text{ cm}^2/\text{m}^2$. Using the indexed effective orifice area method, PPM was considered as nonsignificant if greater than $0.85 \text{ cm}^2/\text{m}^2$, as moderate if greater than $0.65 \text{ cm}^2/\text{m}^2$ and less than or equal to $0.85 \text{ cm}^2/\text{m}^2$, and as severe PPM if $0.65 \text{ cm}^2/\text{m}^2$ or less.

Results. The number of patients classified as having PPM differed according to the method used to predict its presence (PPM: Effective orifice area method = 72.7%; geometric method = 19.6%). Regardless of the method used to classify PPM there was no significant effect on mortality (adjusted hazard ratio: 2.65 at 1 year, 0.99 at 5 years, 0.92 at 9 years; $p =$ not significant). The postoperative mean transvalvular gradient ($17.1 \pm 6.5 \text{ mm Hg}$) and left ventricular function (0.50 ± 0.145) improved significantly compared with the preoperative findings.

Conclusions. The method used to calculate PPM resulted in significant classification discordance. However, regardless of classification, the presence of PPM did not adversely affect long-term outcome.

(Ann Thorac Surg 2011;91:692–9)

© 2011 by The Society of Thoracic Surgeons

The concept of aortic valve patient-prosthesis mismatch (PPM) was originally described by Rahimtoola in 1978 [1]. He identified a cohort of patients who presented with persistent symptoms following AVR that were found to have an “effective prosthetic valve area that was significantly less than that of a normal human valve.”

Over the past three decades, several studies have sought to determine if PPM is associated with adverse outcome, with conflicting results regarding the effect of PPM on early and late mortality [2–19]. Blais and colleagues [6] showed that the adverse impact of PPM on outcome is particularly important in patients with reduced left ventricular (LV) systolic function (ejection fraction [LVEF]) less than 0.40. This finding seems logical as the failing left ventricle should be more adversely affected by increased afterload of a mismatched valve replacement. However, contradictory results were reported by Jamieson and colleagues [18] who found no effect of PPM on outcome in patients with an LVEF 0.50 or less. Thus, the effect of PPM on outcome in patients with

reduced left ventricular systolic function remains unclear.

The second controversy that exists in the literature is “what is the appropriate definition of PPM?” There are two commonly employed methods to define PPM, each having advantages and disadvantages. The first method utilizes the valve’s geometric orifice area (GOA) calculated from the internal diameter of the prosthesis measured in vitro [20]. The second method uses echocardiography to calculate the effective orifice area (EOA) using an in vivo functional assessment of the implanted valve. More recently, referent values obtained from published data for EOA have been proposed as a standard for this measurement to be used intraoperatively to determine whether the implanted valve might result in PPM, and whether patients might require an aortic root enlargement procedure to accommodate a larger prosthesis to avoid developing PPM [21, 22]. Although consensus has grown around the use of indexed EOA to predict the potential for postoperative PPM, it is concerning that the prevalence of PPM using this method is high and might result in unnecessary aortic root enlargement procedures.

The variable incidence of PPM depending on the definition used, its conflicting association with outcome, and its apparent adverse effect on subjects with reduced

Accepted for publication Nov 16, 2010.

Address correspondence to Dr O'Rourke, Veterans Affairs Medical Center, Medical Service—Cardiology, 215 N Main St, White River Junction, VT 05009; e-mail: daniel.orourke@va.gov.

Abbreviations and Acronyms

AVR	= aortic valve replacement
BSA	= body surface area
CABG	= coronary artery bypass surgery
CI	= confidence interval
iEOA	= indexed effective orifice area
iGOA	= indexed geometric orifice area
HR	= hazard ratio
LVEF	= left ventricular ejection fraction
PPM	= patient-prosthesis mismatch

LVEF suggested that further investigation is warranted. In this study we applied the two most commonly used methods to define PPM to determine how often they are concordant, as well as their relationship with short-term and long-term outcome in a high-risk group of patients with an LVEF 0.45 or less who underwent aortic valve replacement (AVR). We hypothesized that patients who were concordant for the presence of PPM using both methods would be at highest risk for having adverse clinical outcomes related to PPM.

Patients and Methods

This study was approved by the Institutional Review Board at Dartmouth College (Project no. 15351).

Patient Population

Our institutional echocardiographic database and the Dartmouth-Hitchcock Medical Center component of the Northern New England Cardiovascular Disease Study Group valve database were merged [23]. The merged database was searched to identify patients having undergone an AVR. We identified 697 consecutive patients who underwent AVR between January 1, 1992 and December 31, 1999. Of these patients, 143 (20.5%) had a preoperative LVEF 0.45 or less and comprised the study group. At our institution, a follow-up transthoracic echocardiogram is routinely obtained at six weeks in all patients who have undergone valve surgery. For patients followed long-term at our institution, a yearly transthoracic echocardiogram is often obtained.

The presence of PPM was ascribed to each study subject retrospectively by applying definitions published for the geometric and functional methods [2, 4, 21, 22]. The geometric method, as defined by Blackstone and colleagues [5], is based on the indexed GOA calculated from the prosthesis geometric internal orifice diameter divided by the body surface area. Using this method, a patient-prosthesis size less than $1.2 \text{ cm}^2/\text{m}^2$ has been considered to represent PPM. The functional method, as defined by Pibarot and colleagues [8] and the American Society of Thoracic Surgeons, is an in vivo method in which an EOA is measured by echocardiography after implantation. We calculated an indexed EOA for each patient by dividing the referent EOA for each valve type by the patient's body surface area. Patient-prosthesis

mismatch was defined as being present when the referent indexed EOA is $0.85 \text{ cm}^2/\text{m}^2$ or less. This may be further subcategorized into moderate PPM ($> 0.65 \text{ cm}^2/\text{m}^2$ and $\leq 0.85 \text{ cm}^2/\text{m}^2$) and severe PPM ($\leq 0.65 \text{ cm}^2/\text{m}^2$) [5, 22, 24].

An example calculation for the indexed EOA and GOA are as follows. A 21-mm Carpentier-Edwards Perimount bioprosthesis: Body surface area = 2.13 m^2 ; referent EOA value = 1.3 cm^2 [Ref 21]; indexed EOA = $1.3 \text{ cm}^2/2.13 \text{ m}^2$; and indexed EOA = 0.61 cm^2 . Referent internal diameter for 21 mm = 2.0 cm [Ref 5]: Body surface area = 2.13 m^2 ; indexed GOA = $\pi r^2/\text{body surface area}$; indexed = $3.14 (1 \text{ cm}^2)/2.13 \text{ m}^2$; and indexed GOA = 1.47 cm^2 .

The merged database contained the clinical and surgical characteristics and echocardiographic findings for all study patients. Baseline data were collected on patient demographics, comorbidities, prior cardiac history, cardiac anatomy and function, surgical indication and priority, procedural information, and outcomes, including in-hospital mortality [25, 26].

The National Death Index was used to obtain data on 30-day and long-term survival. Mortality through October 31, 2008 was determined by a probabilistic match of the registry to the National Death Index (US Department of Health and Human Services) [27, 28] using a combination of name, Social Security number, date of birth, gender, date last known alive, and state of last known residence. The accuracy of the National Death Index is between 92% and 99%, depending on which patient identifiers are available [29, 30].

Statistical Methods

Continuous variables were compared using the Student *t* test expressed as mean \pm standard deviation. Categorical variables were compared by χ^2 analysis. Baseline and follow-up measurements were compared by the Student *t* test for paired samples. Long-term survival was calculated using Kaplan-Meier analysis. Logistic regression and Cox proportional hazards modeling was used to compare adjusted survival for patients with versus without PPM, adjusting for age, sex, diabetes, concomitant coronary artery bypass grafting, preoperative New York Heart Association class, preoperative LVEF, and the type of valve. Adjusted hazard ratios were reported with 95% confidence intervals and *p* values. Microsoft EXCEL 2007 (Microsoft Corporation, Redmond, WA), STATA (Release 9.0; Stata Corporation, College Station, TX) software, and R 2.5.0 statistical software (R Foundation for Statistical Computing, Wein, Austria) were used to perform statistical analyses. Statistical significance was defined as a 2-tailed *p* value less than 0.05.

Results

The characteristics of the entire study population are presented in Table 1. The mean age of the population was 70.4 ± 12.5 years and was predominately male (72.0%). While relatively few patients had a history of tobacco use (24.2%), diabetes (20.3%), prior stroke (13.3%), or previ-

Table 1. Patient Characteristics of the Entire Study Cohort

Patient Characteristics	Values
Age (mean, years)	70.4 ± 12.5
Sex (% male)	72
Body surface area (m ²)	1.9 ± 0.2
Tobacco use (%)	24.2
Hypertension (%)	47.6
Diabetes (%)	20.3
Preoperative diagnosis (%)	
Aortic stenosis	78.6
Aortic regurgitation	10.3
Both	11.1
Previous CABG (%)	10.5
History of heart failure (%)	78.3
Prior stroke (%)	13.3
Preoperative creatinine (mean, mg/dL)	1.3 ± 1.5
Preoperative NYHA (mean)	3.2 ± 0.64
Preoperative LVEDP (mean, mm Hg)	25.4 ± 9.4
Preoperative LVEF (mean)	0.35 ± 0.08
Prosthesis type	
Bioprosthesis	61.3
Mechanical	38.7

CABG = coronary artery bypass graft; LVEDP = left ventricular end diastolic pressure; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

ous coronary artery bypass surgery (10.5%), a history of heart failure (78.3%) and hypertension (47.6%) were frequent. The majority of patients undergoing valve replacement had a history of severe aortic stenosis (78.6%), while 11.1% had mixed aortic valve disease and 10.3% had severe aortic regurgitation. The pathologic processes for valve replacement included degenerative valve disease (80.4%), congenital (13.3%), rheumatic (4.9%), and other (1.4%). Average body surface area was 1.9 m² ± 0.2 m². The mean preoperative creatinine was 1.3 mg/dL ± 1.5 mg/dL. The average LVEF was 0.35 ± 0.08. No patients were taken to the operating room emergently. At the time of valve surgery, almost half of the patients (48.3%) had concomitant CABG. The majority of patients received a bioprosthesis (61.3%); Hancock II (39.9%; Medtronic, Minneapolis, MN) or Carpentier-Edwards Perimount (22.4%; Edwards Lifesciences, Irvine, CA). A mechanical prosthesis was implanted in the remaining patients (38.7%); Medtronic-Hall (24.4%; Medtronic) or St Jude HP model (13.3%; St. Jude Medical, Inc, St. Paul, MN) prosthesis.

We found that the number of patients classified as having PPM differed according to the method used to predict its presence (Table 2). Of the 143 patients, 104 were classified as having PPM when using indexed EOA in comparison with 28 when using indexed GOA. Using the indexed EOA method, patients with PPM were older, more often received a bioprosthetic valve, and had less tobacco use. In contrast, using the indexed GOA method patients were younger, more hypertensive, had a larger

body surface area, and more often received a mechanical valve. Regardless of the method used to define PPM, groups did not differ with respect to the following: diabetes, history of congestive heart failure, prior stroke, functional class, left ventricular end-diastolic pressure, LVEF, and aortic valve gradient.

The concordance between the two methods used to define PPM is shown in Figure 1. Sixty-five patients (45.5%) were concordantly classified as having PPM (19.6%) or not having PPM (25.9%) using the two methods (left lower quadrant and right upper quadrant, respectively). In contrast, 78 patients (54.5%) were found to be discordant, which are plotted in the left upper and right lower quadrants. Seventy-six of the discordant patients met PPM criteria using the indexed EOA method; however, they did not meet criteria using indexed GOA. The remaining two discordant patients met PPM criteria using indexed GOA and not indexed EOA. Linear regression was used to assess the relationship between EOA and GOA. Not surprisingly, the relationship between the methods was poor ($x = \text{GOA}$, $y = \text{EOA}$; $y = 0.2x + 0.91$, $r = 0.20$, $R^2 = 0.04$, standard estimate of the error = 0.32, $p = 0.02$).

Adjusted hazard ratios for death for patients having PPM defined by both methods compared with patients without PPM are shown in Figure 2. Regardless of the method used to classify PPM there was no significant effect on short-term or long-term mortality. However, mortality approached statistical significance in patients within the first postoperative year classified as having severe PPM, using the indexed EOA method. The adjusted hazard ratios corrected for age, sex, diabetes, preoperative LVEF, and prosthesis type were greater than one for indexed EOA and indexed GOA at each time frame postprocedure.

The risk-adjusted survival for patients with PPM and no PPM are displayed in Figure 2. Overall, survival was similar throughout the nine-year follow-up period. There was a nonstatistically significant decline in survival in the first postoperative year in patients classified as having PPM using the indexed EOA.

Of the 143 patients in our cohort, 103 had preoperative and 6-week postoperative LVEF and transvalvular gradient assessments. These data are presented in Table 3. Overall, the LVEF and transvalvular gradients were similar in both the indexed GOA and indexed EOA groups. The mean transvalvular gradient and LVEF were also similar in the 24 patients who were concordant for PPM. The mean preoperative LVEF ranged from 33.5% to 37.4%, respectively, and the mean transvalvular gradients ranged from 37.9 mm Hg to 46.5 mm Hg, respectively, across all subgroups of classification. The 6-week postoperative LVEF increased and the mean transvalvular gradient decreased in all subgroups regardless of how they were classified. There was a strong correlation between indexed EOA and postoperative mean gradient ($r^2 = 0.81$) and a moderate correlation between indexed GOA and postoperative

Table 2. Patient Characteristics Stratified by the Presence of Patient-Prosthesis Mismatch Determined by Each Method

Characteristics	Indexed EOA Method		p Value	Indexed GOA Method		p Value
	PPM (n = 104)	No PPM (n = 39)		PPM (n = 28)	No PPM (n = 115)	
Age (mean, years)	73.4	62.2	<0.01	65.8	71.6	0.03
Sex (% male)	70.2	79.5	0.27	60.0	76.1	0.08
Body surface area (m ²)	1.91	1.90	0.84	1.97	1.89	0.04
Tobacco use (%)	21.2	38.5	0.04	30.0	24.8	0.56
Hypertension (%)	52.9	35.9	0.07	66.7	43.4	0.02
Diabetes (%)	19.2	23.1	0.61	20.0	20.4	0.97
Concomitant CABG (%)	52.9	43.6	0.32	46.7	51.3	0.65
Preoperative diagnosis (%)						
Aortic stenosis	79.8	53.9		80.0	70.8	
Aortic regurgitation	7.7	15.4		3.3	11.5	
Both	12.5	30.8	0.01	16.7	17.7	0.39
History of heart failure (%)	77.9	79.5	0.84	80.0	77.9	0.80
Prior stroke (%)	12.5	15.4	0.65	16.7	12.4	0.54
Preoperative creatinine (mean, mg/dL)	1.4	1.1	0.36	1.9	1.1	0.02
Preoperative NYHA (mean)	3.2	3.0	0.13	3.2	3.2	0.71
Preoperative LVEDP (mean, mm Hg)	24.7	23.9	0.70	27.0	23.8	0.16
Preoperative LVEF	0.353	0.333	0.16	0.352	0.346	0.72
Prosthesis						
Bioprosthesis	78.8	15.4		26.7	70.8	
Mechanical	21.2	84.6	<0.01	73.3	29.2	<0.01

CABG = coronary artery bypass graft; EOA = effective orifice area; GOA = geometric orifice area; LVEDP = left ventricular end diastolic pressure; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PPM = patient-prosthesis mismatch.

mean gradient ($r^2 = 0.64$) as seen in Figure 3. Despite the correlation of both methods with postoperative mean gradient, there is considerable variability in predicting postoperative mean transvalvular gradient on a case by case basis.

In our patient population, the majority of patients (86%) had a mean transvalvular gradient less than 20 mm Hg at 6 weeks postoperation, which is considered to be within normal limits for prosthetic valves. A minority of patients had a mean gradient 30 mm Hg or greater (4%, $n = 6$) and even fewer patients had a mean gradient 40

mm Hg or greater (1%, $n = 2$). We evaluated the sensitivity and specificity for both methods to predict a postoperative mean transvalvular gradient greater than 20 mm Hg. Using the indexed GOA method, the sensitivity and specificity are 40% and 81%, respectively. Using the indexed EOA method, the sensitivity and specificity are 100% and 32%, respectively. Additionally, we calculated the positive predictive value of these methods in our patient population. The positive predictive value for each method was poor and not statistically different; indexed GOA 18% versus indexed EOA 19%, $p =$ not significant.

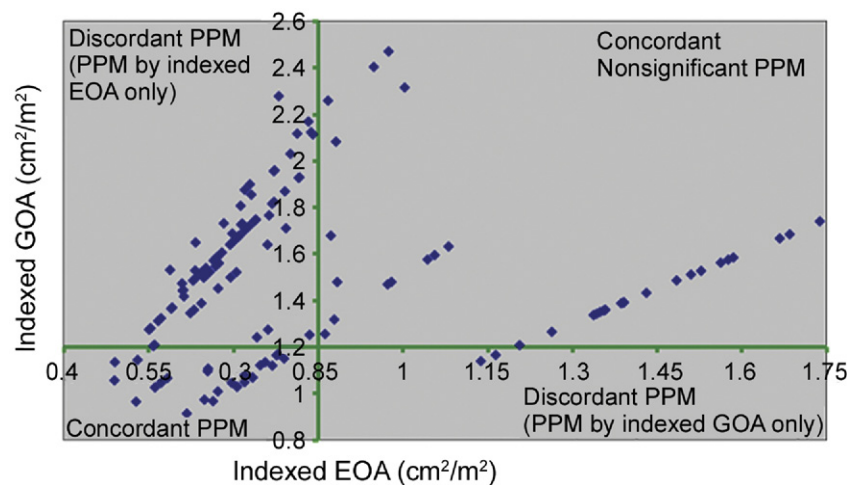
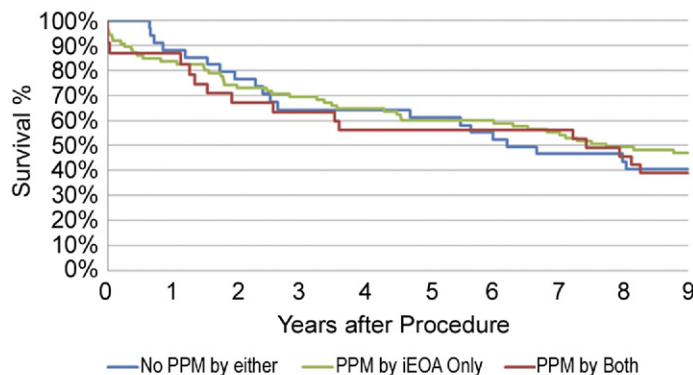


Fig 1. Comparison between the indexed geometric orifice area (GOA) and effective orifice area (EOA). (PPM = patient-prosthesis mismatch.)

Fig 2. Risk-adjusted survival stratified by patient-prosthesis mismatch (PPM) definition. Adjusted for age, sex, diabetes, preoperative left ventricular ejection fraction, and prosthesis type. (CI = confidence interval; EOA = effective orifice area; GOA = geometric orifice area; HR = hazard ratio.)



Number of Patients Alive	30 days	5 years	7 years	9 years
No PPM by either (n=37)	37	24	19	17
PPM by iEOA only (n=104)	94	59	54	43
PPM by Both (n=28)	25	17	17	12

	Indexed GOA method PPM <1.2 cm ² /m ²		Indexed EOA method PPM <0.85 cm ² /m ²		Indexed EOA method PPM <0.65 cm ² /m ²	
	HR*	p-value 95% CI	HR	p-value 95% CI	HR	p-value 95% CI
1 year	2.56	0.25 (0.52 - 12.57)	2.29	0.31 (0.47 - 11.25)	2.65	0.08 (0.90 - 7.80)
5 years	1.54	0.30 (0.69 - 3.45)	1.54	0.33 (0.64 - 3.72)	0.99	0.98 (0.48 - 2.03)
9 years	1.45	0.27 (0.75 - 2.78)	1.19	0.65 (0.56 - 2.54)	0.92	0.79 (0.50 - 1.70)

Comment

In this study, we retrospectively applied two accepted methods for defining PPM in a patient population with compromised LVEF undergoing aortic valve replacement. We found that the method used to calculate PPM would have resulted in significant preoperative classification discordance. Both methods used to define PPM were related to postoperative mean transvalvular gradient. Also, the early hazard was greatest in the subgroups that were classified as having PPM using both methods,

or those having severe PPM using indexed EOA method. Importantly, the presence of PPM did not significantly impact long-term survival beyond the early postoperative period.

A significant portion of the study population was discordant for PPM when using indexed EOA. The majority (97.4%) of the discordant patients received bioprosthetic valves. The meaning of this finding is unclear; however, it has been reported previously [13, 15]. Florath and colleagues [13] reported lower rates of severe PPM

Table 3. Comparison of Transvalvular Gradients and Left Ventricular Ejection Fraction Versus Patient-Prosthesis Mismatch Defined by the Indexed GOA and EOA Methods

Variable	Indexed GOA Method		Indexed EOA Method			Concordant PPM
	Nonsignificant PPM (n = 77)	PPM (n = 26)	Nonsignificant PPM (n = 24)	Moderate PPM (n = 53)	Severe PPM (n = 26)	Using Both Methods (n = 24)
Mean orifice area (cm ²)	1.62 ± 0.27	1.09 ± 0.06	1.3 ± 0.34	0.73 ± 0.05	0.59 ± 0.05	1.08 ± 0.06 (GOA) 0.66 ± 0.1 (EOA)
Mean transvalvular pressure gradient (mm Hg)						
Preoperative	40.3 ± 16.9	45.1 ± 20.7	44.2 ± 18.3	37.9 ± 15.9	46.5 ± 19.9	43.1 ± 20.2
Postoperative (6-weeks)	15.7 ± 6.7	17.2 ± 6.3	13.6 ± 6.3	16.2 ± 6.7	17.9 ± 6.3	17.1 ± 6.5
Change in mean gradient (Preop minus postop)	-24.7 ± 16.2	-27.9 ± 19.3	-30.4 ± 18.0	-21.7 ± 15.0	-28.5 ± 18.6	-26.0 ± 18.9
LVEF:						
Preoperative	0.343 ± 0.077	0.356 ± 0.068	0.335 ± 0.078	0.338 ± 0.076	0.374 ± 0.065	0.350 ± 0.067
Postoperative (6-weeks)	0.509 ± 0.134	0.502 ± 0.141	0.505 ± 0.127	0.492 ± 0.136	0.54 ± 0.133	0.50 ± 0.145
Change in ejection fraction (Postop minus preop)	+0.165 ± 0.14	+0.148 ± 0.116	+0.169 ± 0.105	+0.153 ± 0.119	+0.166 ± 0.119	+0.15 ± 0.117

EOA = effective orifice area; GOA = geometric orifice area; LVEF = left ventricular ejection fraction; PPM = patient-prosthesis mismatch.

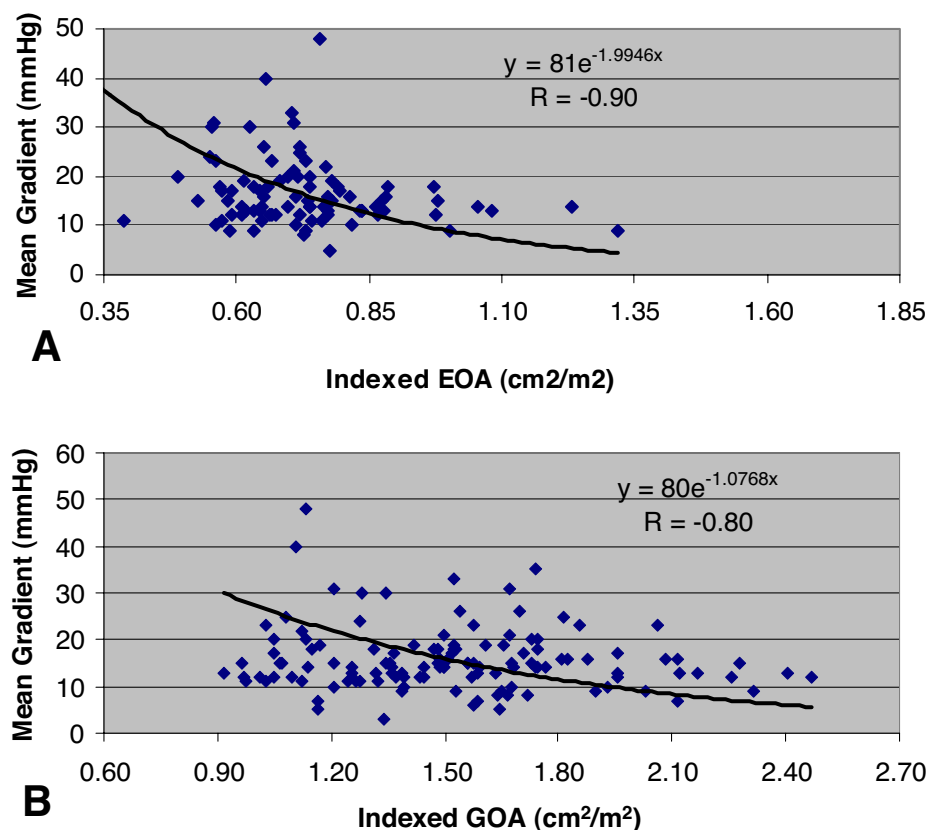


Fig 3. Relationship between patient-prosthesis mismatch method and postoperative mean gradient. (A) Functional method; (B) geometric method. (EOA = effective orifice area; GOA = geometric orifice area.)

in a subset of patients receiving stentless bioprosthetic valves. This finding is also supported by Kunadian and colleagues [15] who reported significantly ($p < 0.01$) improved indexed EOA in a meta-analysis involving ten randomized controlled trials involving patients receiving stentless valves. The discordance of the two methods has been reported by Tasca and colleagues [16] in patients receiving bioprosthetic valves. The discordance between the two methods has been attributed to the different criteria used to calculate the indexed GOA based on manufacturer valve type. As a result, the indexed GOA method is believed to overestimate EOA, especially in patients receiving a bioprosthesis compared to a mechanical prosthesis [16]. The correlation of indexed EOA with postoperative valve gradients has been previously shown and reported to be highly predictive of adverse outcomes [3, 6, 2, 21], while indexed GOA was felt not to be predictive of postoperative valve gradients. In contrast to these results, our study showed a relationship between postoperative mean gradient and indexed EOA, as well as indexed GOA (Fig 3). Despite this correlation, each method is limited by either a low specificity (indexed EOA method) or a low sensitivity (indexed GOA method). Importantly, the ability to predict having an elevated postoperative gradient greater than 20 mm Hg using either method to define PPM at the time of surgery was poor (ie, low positive predictive value). In our study the majority of the patients (86%) had a postoperative mean gradient in the normal range. Lastly, regardless of

which method was used to define the presence of PPM, long-term survival was unaffected.

Our findings raise the question of how best to determine PPM. The concept of PPM originally defined by Rahimtoola [1] was described in patients presenting with the clinical syndrome resulting from PPM. Over the past several decades there has been much interest to better define PPM using echocardiography criteria, and more recently to determine if PPM can be predicted prior to surgery. In our study we found significant discordance in classification depending on the method used to define PPM.

Patient-prosthesis mismatch using indexed EOA was reported to be an independent risk factor for short-term mortality in a study conducted by Blais and colleagues [6] involving 1,266 patients. In this study the increase in relative risk mortality at 30 days was noted to be 2.1-fold for moderate PPM and 11.4-fold for severe PPM. It was also noted that in every category of PPM the presence of a reduced preoperative LVEF (<0.40) was associated with increased mortality. In our study, we found a similar trend in the early hazard associated with PPM, irrespective of the method used to define it; however, it was nonsignificant.

The influence of PPM on long-term survival is controversial. A recent study by Mohty and colleagues [17] involving 2,576 patients, using indexed EOA, noted moderate PPM to be an independent predictor of late mor-

tality in patients with an LVEF of less than 0.50 only. Severe PPM was noted to be an independent predictor of late mortality in patients less than 70 years old and with a body mass index less than 30 kg/m². In contrast, Jamieson and colleagues [18] also recently investigated influence of indexed EOA on mortality in 3,343 patients. After 15 years of follow-up, PPM was not found to adversely affect survival. Similar findings were noted by Howell colleagues [19] using indexed EOA to assess PPM in 801 patients. The in-hospital and 5-year survival rates for moderate and severe PPM were similar. Thus, PPM was not found to be an independent risk factor of mortality. In our study, we selected patients with a LVEF 0.45 or less with the assumption that PPM would have a more significant impact on survival in this population. However, we did not find this to be true. In addition the severity of PPM did not adversely affect short-term or long-term survival, irrespective of the method used to define its presence.

The suggestion of aortic root enlargement has been endorsed in the literature for patients having PPM by indexed EOA [16, 17]. The theory is that enlarging the aortic root would allow for a larger valve to be placed and therefore prevent the potential for developing PPM. However, in our study PPM did not have a negative impact on long-term mortality, nor did it have a significant impact on postoperative valve gradients. Also, our data suggest that the indexed EOA may over-classify patients with stented valves as having PPM. This is important because over-classification may lead to unnecessary aortic root enlargement in an attempt to correct presumed PPM, which results in a procedure with higher mortality. Based on our data more than half (53%) of the 143 patients studied were discordant for PPM using the indexed EOA and would have undergone unnecessary aortic root enlargement.

Our study has limitations. First, the number of subjects in our cohort is smaller compared with the most recently published studies. However, our study is unique in that it assessed both methodologies used to define PPM and encompasses a comprehensive data set. This includes a relatively long 9-year follow-up period with preoperative and 6-week postoperative echocardiographic data. Second, we studied a select group of patients having reduced LVEF and PPM and did not include all patients having PPM during this time period. We intentionally selected this group with the assumption that they would have a higher incidence of adverse events secondary to the presence of PPM. Third, because of our small sample size we were unable to analyze hazard ratios for patients meeting PPM by indexed GOA.

The presence of PPM calculated using two different accepted methods in patients who have undergone AVR with reduced left ventricular systolic function did not influence long-term mortality. Our study raises questions that could be answered by a national PPM registry directed at identifying echocardiogram parameters to help predict the clinical syndrome of PPM.

References

1. Rahimtoola SH. The problem of valve prosthesis-patient mismatch. *Circulation* 1978;58:20-4.
2. Gillinov AM, Blackstone EH, Rodriguez LL. Prosthesis-patient size: measurement and clinical implications. *J Thorac Cardiovasc Surg* 2003;126:313-6.
3. Rao V, Jamieson WRE, Ovanov J, Armstrong S, David TE. Prosthesis-patient mismatch affects survival after aortic valve replacement. *Circulation* 2000;102[19 Suppl 3]:III-5-9.
4. Hanayama N, Chrsitakis GT, Mallidi HR, et al. Patient prosthesis mismatch is rare after aortic valve replacement: valve size may be irrelevant. *Ann Thorac Surg* 2002;73:1822-9.
5. Blackstone EH, Cosgrove DM, Jamieson WRE, et al. Prosthesis size and long-term survival after aortic valve replacement. *J Thorac Cardiovasc Surg* 2003;126:783-96.
6. Blais CB, Dumesnil JG, Baillet R, Simard S, Doyle D, Pibarot P. Impact of valve prosthesis-patient mismatch on short-term mortality after aortic valve replacement. *Circulation* 2003;108:983-8.
7. Fuster RG, Montero Argudo JA, Albarova OG, et al. Patient-prosthesis mismatch in aortic valve replacement: really tolerable? *Eur J Cardiothorac Surg* 2005;27:441-9.
8. Pibarot P, Honos GN, Durand LG, Dumesnil JG. The effect of prosthesis-patient mismatch aortic bioprosthetic valve hemodynamic performance and patients clinical status. *Can J Cardiol* 1996;12:379-87.
9. Pibarot P, Dumesnil JG, Lemieux M, Cartier P, Metras J, Durand LG. Impact of prosthesis-patient mismatch on hemodynamic and asymptomatic status, morbidity and mortality after aortic valve replacement with a bioprosthetic heart valve. *J Heart Valve Dis* 1998;7:207-16.
10. Frapier JM, Rouvière P, Razcka F, Aymard T, Albat B, Chaptal PA. Influence of patient-prosthesis mismatch on long-term results after aortic valve replacement with a stented bioprosthesis. *J Heart Valve Dis*. 2002;11:543-51.
11. Medalion B, Blackstone EH, Lytle BW, White J, Arnold JH, Cosgrove DM. Aortic valve replacement: is size important? *J Thorac Cardiovasc Surg* 2000;119:963-74.
12. Pibarot P, Dumesnil JG, Cartier PC, Métras J, Lemieux MD. Patient-prosthesis mismatch can be predicted at the time of operation. *Ann Thorac Surg* 2001;71(5 Suppl):S265-8.
13. Florath I, Albert A, Rosendahl U, Ennker IC, Ennker J. Impact of valve prosthesis-patient mismatch estimated by echocardiographic-determined effective orifice area on long-term outcome after aortic valve replacement. *Am Heart J* 2008;155:1135-42.
14. Mascherbauer J, Rosenhek R, Fuchs C, et al. Moderate patient-prosthesis mismatch after valve replacement for severe aortic stenosis has no impact on short and long-term mortality. *Heart* 2008;94:1639-45.
15. Kunadian B, Vijayalakshmi K, Thornley A, et al. Meta-analysis of valve hemodynamics and left ventricular mass regression for stentless versus stented aortic valves. *Ann Thorac Surg* 2007;84:73-9.
16. Tasca G, Mhagna Z, Perotti S, et al. Impact of prosthesis-patient mismatch on cardiac events and midterm mortality after aortic valve replacement in patients with pure aortic stenosis. *Circulation* 2006;113:570-6.
17. Mohty D, Dumesnil JG, Echahidi N, et al. Impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement. *J Am Coll Cardiol* 2009;53:39-47.
18. Jamieson WRE, Ye J, Higgins J, et al. Effect of prosthesis-patient mismatch on long-term survival with aortic valve replacement: assessment to 15 years. *Ann Thorac Surg* 2010;89:51-9.
19. Howell NJ, Keogh BE, Ray D, et al. Patient-prosthesis mismatch in patients with aortic stenosis undergoing isolated aortic valve replacement does not affect survival. *Ann Thorac Surg* 2010;89:60-4.

20. Muneretto C, Bisleri G, Negri A, Manfredi J. The concept of patient-prosthesis mismatch. *J Heart Valve Dis* 2004;13(Suppl 1):S59-62.
21. 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;36:1131-41.
22. Koch CG, Khandwala F, Estafanous FG, Loop FD, Blackstone EH. Impact of prosthesis-patient size on functional recovery after aortic valve replacement. *Circulation* 2005;111:3221-9.
23. Birkmeyer NJO, Marrin CAS, Leavitt BJ, et al. Trends toward declining mortality with aortic and mitral valve replacement surgery. *Circulation* 1998;98:60.
24. Edmunds LH Jr, Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. *Ann Thorac Surg* 1996;62:932-5.
25. Malenka DJ, O'Connor GT, Quinton H, et al. Differences in outcomes between women and men associated with percutaneous transluminal coronary angioplasty. *Circulation* 1996;94(9 Suppl):II99-104.
26. O'Connor GT, Plume SK, Olmstead EM, et al. Multivariate prediction of in-hospital mortality associated with coronary artery bypass graft surgery. Northern New England Cardiovascular Disease Study Group. *Circulation* 1992;85:2110-8.
27. Wentworth DN, Neaton JD, Rasmussen WL. An evaluation of the Social Security Administration master beneficiary record and the national death index in the ascertainment of vital status. *Am J Public Health* 1983;73:1270-4.
28. National Death Index Plus: Coded Causes of Death. National Death Index User's Manual. Hyattsville, MD: US Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Center for Health Statistics; 1997.
29. Williams BC, Demitrack LB, Fries BE. The accuracy of the National Death Index when personal identifiers other than Social Security number are used. *Am J Public Health* 1992;82:1145-7.
30. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax nationwide death search. *Am J Epidemiol* 1994;140:1016-9.