Patient-Prosthesis Mismatch Can Be Predicted at the Time of Operation

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Background. **Patient-prosthesis mismatch is a frequent cause of high postoperative gradients in normally functioning prostheses. The objective of this study was to determine whether mismatch can be predicted at the time of operation.**

Methods. **Indices used to predict mismatch were valve size, indexed internal geometric area, and projected indexed effective orifice area (EOA) calculated at the time of operation, and results were compared with indexed EOA and mean gradients measured by Doppler echocardiography after operation in 396 patients.**

Results. **The sensitivity and specificity of these indices to detect mismatch, defined as a postoperative indexed EOA of 0.85 cm^2/m^2 or less, were respectively: 35% and 84% for valve size, 46% and 85% for indexed internal geometric area, and 73% and 80% for projected indexed EOA. Projected indexed EOA also correlated best with resting ($r = 0.67$) and exercise ($r = 0.77$) postoperative gradients.**

Conclusions. **The projected indexed EOA calculated at the time of operation accurately predicts mismatch as well as resting and exercise postoperative gradients, whereas valve size and indexed internal geometric area cannot be used for this purpose.**

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An important objective of aortic valve replacement is to minimize postoperative gradients to optimize the normalization of left ventricular mass and function, and it has been well demonstrated that patient-prosthesis mismatch is, by far, the most frequent cause of high postoperative gradients in normally functioning prostheses [1–5]. Recent studies also suggest that mismatch could theoretically be predicted at the time of operation, but this remains to be determined [5]. The primary objectives of this study were therefore (1) to determine whether mismatch and its consequences on resting and exercise postoperative gradients can actually be predicted at the time of operation, and (2) to compare the incidence of mismatch with regard to the type of valve substitute used for replacement.

In this context, there persists some confusion in the literature as to what variable should best be used to define mismatch as well as to the eventual consequences of mismatch on prognosis. Hence, in a recent study, Rao and colleagues [6] have shown that the projected indexed effective orifice area (EOA) calculated at the time of operation is an independent predictor of postoperative mortality. In contrast, Medalion and colleagues [7] attempted to identify mismatch on the basis of an indexed internal geometric area (IGA) calculated from the internal diameter of the prosthesis and the patient's body surface area. On this basis, they reported that mismatch was a rare phenomenon at least with the Carpentier-Edwards pericardial bioprosthesis and found no relation between this variable and postoperative mortality. An additional objective of this study was therefore to determine which of these two variables best correlates with mismatch after operation.

Material and Methods

Patients

Three hundred ninety-six patients were evaluated by Doppler echocardiography 18 ± 10 months after aortic valve replacement with either a stented bioprosthesis (51 patients, 67 ± 9 years), a stentless bioprosthesis (194 patients, 66 ± 10 years), a pulmonary autograft (96 patients, 45 ± 11 years), or an aortic homograft (45 patients, 43 ± 10 years). Among the patients with a stented bioprosthesis, 31 received a Medtronic Intact bioprosthesis (Medtronic Inc, Minneapolis, MN), 12 a Medtronic Mosaic, and 8 a St. Jude X-Cell (St. Jude Medical Inc, St. Paul, MN). All patients in the stentless bioprosthesis group received a Medtronic Freestyle, and all patients in the homograft group received a cryopreserved aortic homograft (Cryolife; Cryolife Inc, Kennesaw, GA). Results were also compared with a control group of 12 normal subjects who were matched for age and sex with the autograft or homograft subjects.

Doppler Echocardiography

Valve EOA and mean transvalvular gradient were measured at rest in all patients to assess the performance of

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Table 1. Internal Diameters of Bioprostheses[a]

Bioprosthesis	Labeled valve size (mm)				
	19	21	23	25	27
Medtronic Intact	16.6	18.5	20.3	22.1	23.7
Medtronic Mosaic	. . .	18.5	20.5	22.5	24.0
Medtronic Freestyle	16.0	18.0	20.0	21.5	23.5

[a] Internal diameters (mm) were provided by the manufacturers.

the valve substitute [1]. These variables were also measured during maximum exercise in the 12 normal subjects and in a subgroup of 55 patients as previously described [8].

Estimation of Patient-Prosthesis Mismatch

A postoperative indexed EOA of 0.85 cm^2/m^2 or less was considered evidence of mismatch on the basis of previous studies [1–3, 5, 9].

Prediction of Mismatch

The feasibility of predicting mismatch at the time of operation was assessed by calculating the two variables proposed for this purpose, ie, the projected indexed EOA derived from the published normal value of EOA for the type and size of prosthesis being implanted divided by the patient's body surface area [5, 6] and the indexed IGA, as proposed by Medalion and colleagues [7] using the internal dimension values given in Table 1.

Statistical Analysis

Data were expressed as mean ± standard deviation and compared using analysis of variance to evaluate the effect of the type of valve substitute. Statistical analysis of the association of variables was performed with the Pearson correlation coefficient or the determination coefficient when the relation was linear or nonlinear, respectively. Values of p less than 0.05 were considered significant.

Results

Comparison of Hemodynamic Performance and Incidence of Mismatch

Patients with an autograft had similar resting and exercise valve hemodynamic performance when compared with the normal subjects (Table 2). The resting and exercise valve EOAs of the homografts were significantly lower than those of the autografts or the normal native valves, but their mean gradients were not statistically different. The hemodynamic performance of the homografts, autografts, and normal valves was superior to that of the bioprostheses as shown by the higher valve EOAs, and lower gradients at rest and during exercise. Patients with a stentless bioprosthesis had a significantly better valve performance than those with a stented bioprosthesis. Accordingly, the incidence of mismatch, ie, the percentage of patients with a postoperative indexed EOA of 0.85 cm^2/m^2 or less, was dramatically different ($p < 0.001$) depending on the type of valve substitute (Table 2), the highest incidence being observed in the stented bioprostheses.

Dependence of Transvalvular Gradients on Indexed EOA

We previously reported for the same group of patients a strong inverse relation between the mean gradients at rest ($r = 0.79$) or during exercise ($r = 0.90$) and the postoperative resting indexed EOA measured by Doppler echocardiography [5, 8]. Figure 1A shows the relation between the same mean resting gradients and the projected indexed EOA, a variable that could have been calculated at the time of valve sizing during operation. Not surprisingly, the correlation ($r = 0.67$) is slightly less than when using the indexed EOA actually measured in each patient after operation; this is possibly related to variance in hemodynamic conditions, differences in prosthesis manufacturing, or other unknown factors. Nonetheless, the relation indicates that the postoperative resting gradients can be predicted with some accuracy and

Table 2. Doppler Echocardiographic Data at Rest and During Maximum Exercise

Variable	Stented (n = 51)	Stentless (n = 194)	Homograft (n = 55)	Autograft (n = 96)	Control (n = 12)
Mean gradient (mm Hg)					
Rest (n = 408)	18 ± 9[a,b,c,d]	7 ± 5[a,b,c]	4 ± 3	2 ± 2	1 ± 1
Exercise (n = 67)	25 ± 11[a,b,c,d]	10 ± 7[a,b]	7 ± 4	3 ± 2	3 ± 2
Valve EOA (cm^2)					
Rest (n = 408)	1.32 ± 0.30[a,b,c,d]	1.84 ± 0.54[a,b,c]	2.47 ± 0.63[a,b]	3.09 ± 0.84[a]	3.46 ± 0.71
Exercise (n = 67)	1.60 ± 0.49[a,b,c,d]	2.40 ± 0.61[a,b]	2.74 ± 0.92[a,b]	3.59 ± 0.90	3.58 ± 0.80
Index EOA (cm^2/m^2)					
Rest (n = 408)	0.76 ± 0.16[a,b,c,d]	1.04 ± 0.29[a,b,c]	1.38 ± 0.30[a,b]	1.73 ± 0.42	1.80 ± 0.30
Exercise (n = 67)	0.90 ± 0.24[a,b,c,d]	1.32 ± 0.36[a,b]	1.40 ± 0.36[a,b]	1.95 ± 0.46	1.87 ± 0.34
Incidence of mismatch (Indexed EOA ≤ 0.85 cm^2/m^2)	36/51 (71%)[a,b,c,d]	57/194 (29%)[a,b,c]	2/55 (4%)	0/96 (0%)	0/12 (0%)

[a] $p < 0.05$ versus control. [b] $p < 0.05$ versus autograft. [c] $p < 0.05$ versus homograft. [d] $p < 0.05$ versus stentless bioprosthesis.

EOA = effective orifice area.

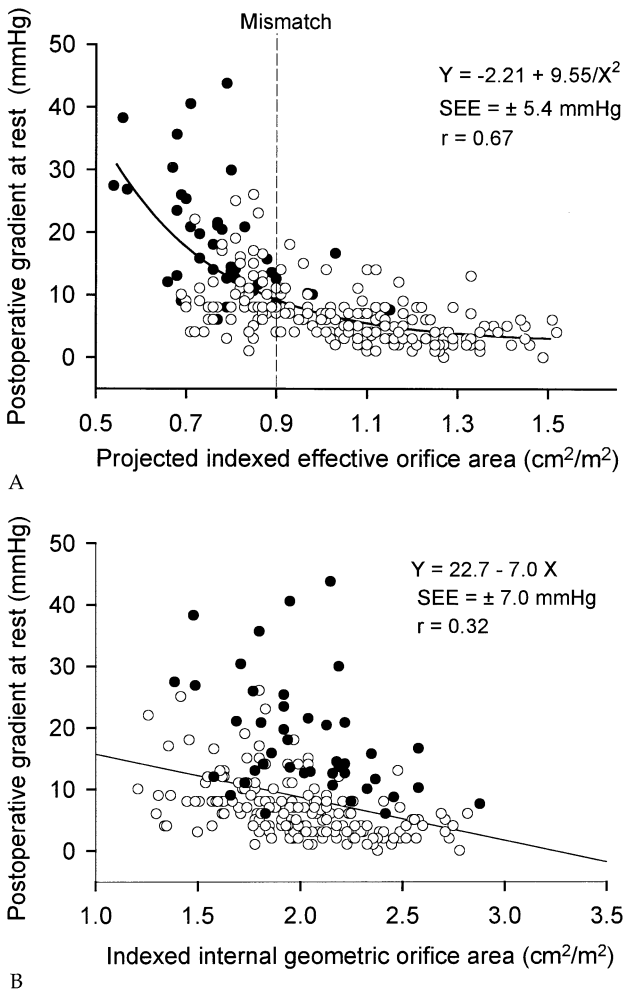

Fig 1. Correlation between the postoperative resting mean gradient and the indices calculated at the time of operation: projected indexed effective orifice area (A) and indexed internal geometric area (B). Open circles *indicate stentless bioprostheses;* closed circles *indicate stented bioprostheses. (*SEE = *standard error of the estimate.)*

that most patients with a high postoperative resting gradient could have been identified at the time of operation on the basis of a projected indexed EOA less than 0.80 to 0.90 cm^2/m^2. Figure 1B also shows that the correlation between the postoperative resting gradients and the indexed IGA is very poor and cannot be used to identify patients with a high gradient. Moreover, it is interesting to note that the threshold of 0.85 cm^2/m^2 arbitrarily proposed by Medalion and colleagues [7] to identify mismatch does not appear valid as none of the patients are below this value. Hence, this variable could not have been used at the time of operation to identify those patients who had a high gradient on the basis of mismatch. Likewise, there was no correlation between the resting gradient and valve size. Similar considerations can be observed when the projected indexed EOA and the indexed IGA are correlated to the postoperative exercise gradients (Fig 2). The projected indexed EOA is a good predictor ($r = 0.77$), whereas the indexed IGA ($r = 0.28$) is not.

Prediction of Patient-Prosthesis Mismatch

If mismatch is defined as a postoperative indexed EOA of 0.85 cm^2/m^2 or less, the variable that best predicts mismatch is a projected indexed EOA of 0.90 cm^2/m^2 or less (sensitivity 73%, specificity 80%) rather than 0.85 cm^2/m^2 (sensitivity 62%, specificity 87%). This slight discrepancy could be related to differences in patient selection compared with the reference studies or other unknown factors. As mentioned, no patient had an indexed IGA of 0.85 cm^2/m^2 or less. Obviously, the use of this criterion would have resulted in a sensitivity of 0% and a specificity of 100%. This is because of the fact that the IGA of the valve is much larger that its EOA, and it is therefore not relevant to use the same threshold. Nonetheless, even when using an optimal threshold (indexed IGA $\leq$ 1.80 cm^2/m^2), the sensitivity (46%) and specificity (85%) of the indexed IGA remain lower than that of the projected indexed EOA. Finally, the use of valve size of 21 mm or

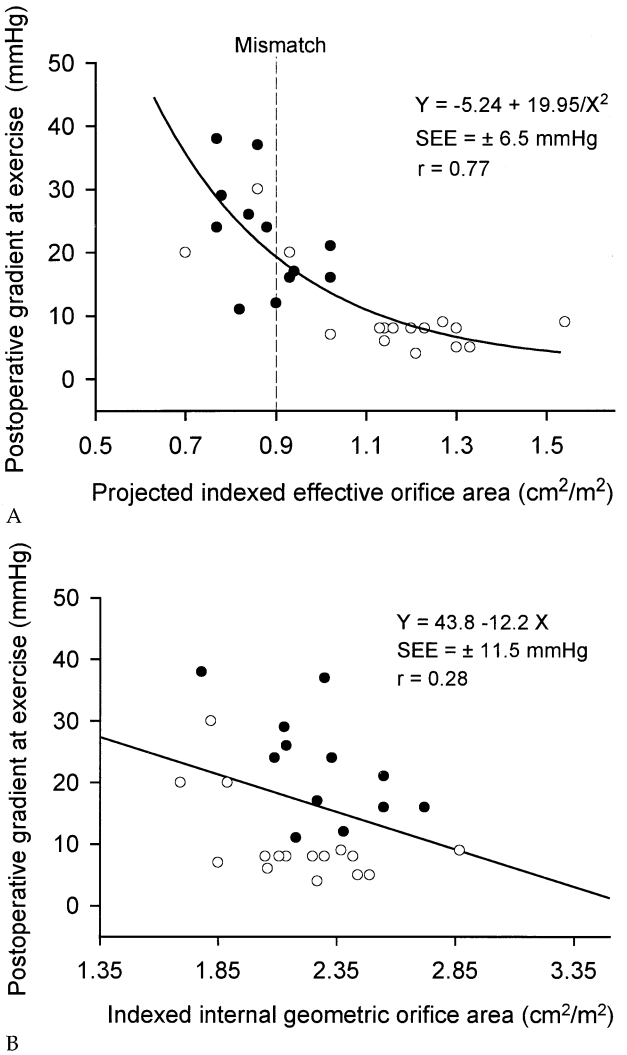

Fig 2. Correlation between the postoperative exercise mean gradient and the indices calculated at the time of operation: projected indexed effective orifice area (A) and indexed internal geometric area (B). Symbols and abbreviations are as in Figure 1.

less for the prediction of mismatch would have yielded a sensitivity of only 35% with a specificity of 84%.

Comment

The pathophysiology of patient-prosthesis mismatch and its consequences on the regression of left ventricular hypertrophy as well as on mortality and morbidity have recently been reviewed in detail [5]. Briefly, mismatch occurs when the size of the orifice of the prosthesis is too small in relation to patient's body size, and it results in inappropriately high gradients. The consequences are lesser regression of left ventricular hypertrophy, lesser improvement in functional class, and decrease in long-term survival [5].

A major finding of this study is that mismatch can in fact be predicted at the time of the operation from the reference value of EOA for the prosthesis being implanted and the patient's body surface area. In contrast, the indexed IGA correlates poorly with postoperative gradients, and it therefore should not be used to predict mismatch. In this context, it should be emphasized that there are important differences between the IGA and the EOA of a valve. First, the IGA is calculated from the internal orifice diameter of the valve assuming a circular orifice; this assumption is not entirely valid because the valve leaflets always occupy a part of this orifice. Second, contrary to the valve EOA, which is a physiologic variable that represents the cross-sectional area occupied by transvalvular flow, the IGA represents the geometric or anatomic area of the valve. And previous studies have shown the ratio between the IGA and the EOA may vary quite extensively depending on the type and size of prosthesis [10, 11]. Hence, IGA grossly overestimates EOA and in varying proportions, and therefore it cannot be used to predict gradients that, based on hydrodynamics, are directly related to EOA and not IGA. Likewise and partly for the same reasons, valve size is also not adequate to predict mismatch, and in addition, it does not take into account the patient's cardiac output requirements.

Accordingly, the conclusions of studies using either the indexed IGA [7] or valve size as a marker of mismatch may not be valid and should therefore be interpreted with great caution. In particular, it becomes obvious that an indexed IGA of 0.85 cm^2/m^2 or less cannot be used to identify mismatch or to estimate its prevalence.

In conclusion, this study shows that the projected indexed EOA calculated at the time of operation accurately predicts resting and exercise postoperative gradients and, consequently, the potential occurrence of an eventual mismatch. It should therefore be a useful variable to calculate when contemplating strategies designed to avoid mismatch. In contrast, our results also show that valve size and indexed IGA cannot be used for this purpose.

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