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Valve Disease

Hemodynamic and Physical Performance During Maximal Exercise in Patients With an Aortic Bioprosthetic Valve

Comparison of Stentless Versus Stented Bioprostheses

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OBJECTIVES The objective of this study was to compare stentless bioprostheses with stented bioprostheses with regard to their hemodynamic behavior during exercise.

BACKGROUND Stentless aortic bioprostheses have better hemodynamic performances at rest than stented bioprostheses, but very few comparisons were performed during exercise.

METHODS Thirty-eight patients with normally functioning stentless ($n = 19$) or stented ($n = 19$) bioprostheses were submitted to a maximal ramp upright bicycle exercise test. Valve effective orifice area and mean transvalvular pressure gradient at rest and during peak exercise were successfully measured using Doppler echocardiography in 30 of the 38 patients.

RESULTS At peak exercise, the mean gradient increased significantly less in stentless than in stented bioprostheses (+5 ± 3 vs. +12 ± 8 mm Hg; $p = 0.002$) despite similar increases in mean flow rates (+137 ± 58 vs. +125 ± 65 ml/s; $p = 0.58$); valve area also increased but with no significant difference between groups. Despite this hemodynamic difference, exercise capacity was not significantly different, but left ventricular (LV) mass and function were closer to normal in stentless bioprostheses. Overall, there was a strong inverse relation between the mean gradient during peak exercise and the indexed valve area at rest ($r = 0.90$).

CONCLUSIONS Hemodynamics during exercise are better in stentless than stented bioprostheses due to the larger resting indexed valve area of stentless bioprostheses. This is associated with beneficial effects with regard to LV mass and function. The relation found between the resting indexed valve area and the gradient during exercise can be used to project the hemodynamic behavior of these bioprostheses at the time of operation. It should thus be useful to select the optimal prosthesis given the patient's body surface area and level of physical activity. (J Am Coll Cardiol 1999;34:1609–17) © 1999 by the American College of Cardiology

Recent studies (1,2) showed that stentless aortic bioprostheses have better hemodynamic performance at rest than their stented counterparts, and this is believed to be related to the stentless design that provides a larger effective orifice area (EOA) for the same prosthesis outer diameter size. Also, our team recently showed that during maximal exercise in stented bioprostheses, the increase in gradient is mainly determined by the indexed EOA at rest (3). Therefore, we hypothesized that stentless bioprostheses would have less increase in gradient during exercise in comparison with stented bioprostheses due to their larger resting indexed EOAs. We also hypothesized that the stentless bioprostheses might have the added advantage of increasing their EOA during exercise to a relatively greater extent than stented bioprostheses due to a possible expansion of the prosthesis valvular annulus. To our knowledge, there have been few studies of the hemodynamic behavior of stentless valves during exercise (4,5).

The objective of this study was, therefore, to compare the hemodynamic behavior of stentless and stented aortic bioprostheses during maximal exercise in comparable groups of patients. Because the hemodynamic behavior of the prosthesis could also influence the remodeling of the left ventricle (LV) after valve replacement, a secondary objective

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Abbreviations and Acronyms

EOA = effective orifice area
LV = left ventricular or ventricle
LVOT = left ventricular outflow tract
VO_2 = oxygen consumption

of the study was to compare the parameters of LV morphology and function in these two groups of patients.

METHODS

Patients. Fifty patients, 11 female and 39 male, with either a stented or a stentless bioprosthetic valve in the aortic position were randomly selected for the study. Of the 27 patients included in the stented valve group, 22 received a Medtronic Intact valve (Medtronic, Minneapolis, Minnesota), 2 received a Medtronic Mosaic valve, 2 received a Carpentier-Edwards pericardial valve (Baxter, Irvine, California) and 1 received a St-Jude X-Cell valve (St-Jude Medical, St. Paul, Minnesota). All the patients (n = 23) in the stentless valve group received a Medtronic Freestyle valve. The valve was implanted using the subcoronary technique in 22 patients and the root replacement technique in one patient. A complete Doppler echocardiographic evaluation was first performed at rest with the patient in the supine position to verify that all patients had a normal LV systolic function (ejection fraction >50%) and no evidence of prosthetic valve dysfunction. The protocol was approved by the authors' institutional review board, and all subjects gave informed written consent. Some of the data from the patients with a stented valve have been reported in a previous study (3).

Echocardiographic assessment of LV morphology and function at rest. Doppler echocardiographic examinations were performed with a Hewlett Packard Sonos 2000 Ultrasound system (Hewlett Packard, Andover, Massachusetts). From a parasternal LV long-axis view, standard recordings of two-dimensionally directed LV M-mode echocardiograms were obtained at rest with the patient in the left lateral decubitus position. Left ventricular minor axis internal dimension, posterior wall and septal thickness were measured at end-diastole and end-systole. Left ventricular mass was calculated using the corrected formula of the American Society of Echocardiography and was indexed for body surface area (6). The shortening fraction of the internal radius, the mid-wall radius and the length of the LV, as well as the fraction and velocity of the posterior wall thickening, were determined using the model proposed by Dumesnil et al. (7). The ejection fraction was calculated using the mid-wall radius and the longitudinal shortening fractions as previously described (8).

The peak systolic wall stress was estimated by the method of Grossman et al. (9):

$$\text{Wall stress} = \frac{(\text{LVPs} \times \text{LVIDs})}{2 \times \left(\text{LVPWTs} \times \left(1 + \dfrac{\text{LVPWTs}}{2 \times \text{LVIDs}}\right)\right)}$$

where LVIDs and LVPWTs are the internal dimension and the posterior wall thickness of the LV at end-systole, respectively, and LVPs is the approximated LV systolic pressure, calculated by adding the systolic blood pressure and the peak transprosthetic gradient obtained from continuous wave Doppler recordings of the aortic jet velocity.

Exercise protocol. Patients were submitted to a maximal ramp upright bicycle exercise test beginning with an initial workload of 0 W, followed by continuous increments of 10 W/min. A 12-lead electrocardiogram was continuously recorded and blood pressure was measured every 2 min. The patients were encouraged to exercise until exhaustion or the appearance of symptoms. The test was stopped if there was an abnormal rise in blood pressure (diastolic pressure >110 mm Hg), ECG evidence of ischemia (>1 mm horizontal or downsloping S-T depression 0.08 s after the J point compared with the resting ECG) or significant arrhythmia. Respiratory gas analysis was carried out with a Q-Plex 1 system (Quinton Instrument Co., Bothel, Washington) to measure oxygen consumption (VO_2) and CO_2 production. Results were averaged over five breaths. Peak oxygen consumption was defined as the highest value of VO_2 obtained at the end of the test. The percentage of the predicted peak VO_2 for a given patient's age and gender was calculated from the mean values of peak VO_2 in the normal population (10). The anaerobic threshold was determined by two experienced observers using the V-slope method (11). Patients were considered to have reached their cardiorespiratory maximum if the respiratory exchange ratio was $\geq$1.10 or if it was $\geq$1.05 and the VO_2 had leveled off at the end of the test (12).

Doppler echocardiographic measurements during exercise. Doppler echocardiographic examinations were performed with the patient sitting on the bicycle: 1) at rest, and 2) at peak of maximal exercise just before stopping the test or within 2 min after test termination. Measurements performed at rest in the upright position included the transvalvular flow velocity using continuous wave Doppler, LV outflow tract (LVOT) flow velocity using pulsed-wave Doppler and LVOT diameter, as previously described (1,13,14). The same measurements were performed during exercise except for LVOT diameter which was assumed to have remained constant (15). The velocity recording was first performed in the transvalvular jet and then in the LVOT. From these measurements, we calculated the LV stroke volume from the product of the LVOT velocity-time integral and cross-sectional area, the cardiac output from the product of stroke volume and heart rate, the mean transvalvular flow rate from the quotient of stroke volume and systolic ejection time, the mean transvalvular pressure gradient using the modified Bernoulli equation with inclusion of subvalvular velocity and the EOA using the standard continuity equation. If the difference in heart rate between the time of transvalvular velocity recording and that of LVOT velocity recording was $>5\%$, the data was rejected to avoid potential errors in EOA and mean gradient due to changing hemodynamics in the early postexercise recovery period. The EOA was then indexed for body surface area.

Data and statistical analysis. For each patient, the change in valve EOA and mean gradient per change in transvalvular flow rate during exercise was calculated to assess and compare the flow dependence of these parameters in stentless bioprostheses versus in stented bioprostheses (16–18).

Data were expressed as mean ± SD and compared using a two-way analysis of variance for repeated measures followed by the Tukey test to evaluate the effects of exercise and bioprosthesis type (stentless vs. stented). If the normality test or the equality of variance test failed, the analysis of variance was performed on the logarithmic transform of the data. Statistical analysis of the association of variables was performed with the Pearson correlation coefficient or the determination coefficient adjusted for degrees of freedom when the relation was linear or nonlinear, respectively. Graphs were constructed with the corresponding regression equation using a curve-fitting software (Table Curve, Jandel Scientific, San Rafael, California). Values of $p < 0.05$ were considered significant.

A forward stepwise regression analysis was performed to identify factors that significantly influenced the change in valve EOA during exercise. The relevant variables tested for this analysis were: patient age and gender, prosthesis size, type of bioprosthesis, time interval since prosthesis implantation, mean flow rate, EOA and indexed EOA at rest and changes in mean flow rate and systolic blood pressure with exercise.

RESULTS

Measurement feasibility. Of the 50 patients recruited for the study, 38 patients achieved maximal exercise. The exercise test was stopped prematurely because of excessive blood pressure rise in seven patients and ST-segment depression in one patient. In addition, one patient stopped because he did not tolerate the mouth piece and three patients stopped because of claudication. Transvalvular flow velocity could be adequately measured in 37 of the 38 patients who completed the maximal exercise test, whereas it was possible to measure LVOT flow velocity (and therefore EOA and mean gradient) in 30 of the 38 patients.

Patients clinical characteristics. Table 1 shows the preoperative and operative data for the 38 patients who completed the maximal exercise study. These data show no significant difference between the two groups and as well, the patients operated on for dominant aortic stenosis had no difference in preoperative mean gradient (50 ± 21 vs. 47 ± 18 mm Hg) or indexed EOA (0.36 ± 0.07 vs. 0.37 ± 0.07 cm^2/m^2), and the patients operated on for dominant aortic regurgitation or mixed dysfunction had no difference in the severity of regurgitation.

Left ventricular morphology and function. Table 2 shows that, at the time of the exercise study, several parameters of LV morphology and function were significantly better in the patients with a stentless bioprosthesis as compared with the patients with a stented prosthesis. Moreover, on the basis of the criteria (LV mass index >110 g/m^2 for women and >134 g/m^2 for men) proposed by Devereux et al. (19), 1 of 19 (5%) patients with a stentless bioprosthesis had LV hypertrophy compared with 6 of 19 (32%) of patients with a stented bioprosthesis.

Maximal exercise capacity. Maximal exercise capacity as estimated by maximal workload, peak VO_2 or anaerobic threshold did not significantly differ between patients with a stentless bioprosthesis and those with a stented bioprosthesis (Table 3).

Validation of echocardiographic measurements. There was a strong correlation and agreement between the resting EOA measured in the supine position and that measured in the upright sitting position: EOA upright = 0.10 + (0.95 × EOA supine), r = 0.97, standard error of estimate (SEE) = ±0.14 cm^2, $p < 0.001$). There also was a very good correlation (r = 0.83, SEE = ±1.19 L/min, $p < 0.001$) between VO_2 and the cardiac output measured by Doppler echocardiography at peak exercise.

Baseline Doppler echocardiographic data (Table 4). In the upright rest position, patients with a stentless bioprosthesis had similar cardiac index and mean transvalvular flow rate but higher valve EOA and lower mean gradient when compared with patients with a stented bioprosthesis. Despite a similar indexed prosthesis size in both groups (Table 1), the indexed EOA was significantly higher in stentless bioprostheses, thus reflecting their superior hemodynamic performance at rest.

Changes in Doppler echocardiographic data with maximal exercise (all patients). On average, cardiac index increased by 123 ± 41% (+3.11 ± 0.89 L/min/m^2, $p < 0.001$) and mean flow rate increased by 53 ± 24% (+132 ± 60 ml/s, $p < 0.001$), whereas EOA increased by 10 ± 13% (+0.21 ± 0.27 cm^2, $p < 0.001$) and mean gradient increased by 96 ± 53% (+8 ± 7 mm Hg, $p < 0.001$) with maximal exercise.

Comparison of stentless versus stented bioprostheses. Despite similar increase in cardiac index and mean flow rate with exercise, the patients with a stentless bioprosthesis had significantly ($p = 0.002$) less increase in mean gradient (Table 4). The changes in gradient per change in flow rate were also significantly lower in stentless bioprostheses (+4 ± 4 vs. +13 ± 10 mm Hg/100 mls^{-1}; $p = 0.002$).

The EOA increased significantly with maximal exercise in both groups and there was no significant difference

Table 1. Patient Characteristics

	Stented (n = 19)	Stentless (n = 19)	p Value
Gender			NS
Female	5 (26.3%)	3 (15.8%)	
Male	14 (73.7%)	16 (84.2%)	
Age (yr)	65 ± 11	64 ± 7	NS
Body surface area (m^2)	1.78 ± 0.20	1.85 ± 0.14	NS
Dominant valvular dysfunction			NS
Stenosis	16 (84.2%)	14 (73.7%)	
Regurgitation	1 (5.3%)	2 (10.5%)	
Mixed dysfunction	2 (10.5%)	3 (15.8%)	
Preoperative LV mass index (g/m^2)	148 ± 63	152 ± 28	NS
Preoperative LV ejection fraction (%)	64 ± 11	62 ± 9	NS
Prosthesis size (mm)			NS
19	1 (5.3%)	0 (0%)	
21	2 (10.5%)	2 (10.5%)	
23	2 (10.5%)	1 (5.3%)	
25	8 (42.1%)	6 (31.6%)	
27	5 (26.3%)	10 (52.6%)	
29	1 (5.3%)	0 (0%)	
Average	24.8 ± 2.5	25.5 ± 2.0	NS
Prosthesis size indexed for BSA (mm/m^2)	14.0 ± 1.5	13.9 ± 1.5	NS
Time interval since implantation (yr)	4.1 ± 2.2	3.0 ± 1.2	NS
Blood pressure (mm Hg)			
Systolic	140 ± 22	138 ± 18	NS
Diastolic	78 ± 15	75 ± 10	NS
Hypertension on therapy	5 (26.3%)	4 (21.1%)	
Diabetes	1 (5.3%)	2 (10.5%)	

Data presented are mean value ± SD or number of patients. BSA = body surface area; LV = left ventricular; NS = nonsignificant.

between the groups for the change in EOA with maximal exercise both in absolute (Table 4) and relative terms (stented: 9 ± 13% versus stentless: 11 ± 14%, p = 0.56). There also was no significant difference between stentless and stented bioprostheses in regard to the change in EOA per change in flow rate (+0.15 ± 0.15 vs. +0.08 ± 0.18 $cm^2/100\ mls^{-1}$; p = 0.30). In multivariate analysis, the change in mean flow rate with exercise was the only independent determinant of the change in EOA during exercise.

Table 2. Comparison of Left Ventricular Morphology and Function at Rest Between Patients With a Stented Bioprosthesis and Patients With a Stenless Bioprosthesis

	Stented (n = 19)	Stentless (n = 19)	p Value
End-diastolic dimension (mm)	48 ± 5	45 ± 2	0.02
End-systolic dimension (mm)	28 ± 4	26 ± 3	NS
End-diastolic septum thickness (mm)	13 ± 4	12 ± 2	NS
End-diastolic posterior wall thickness (mm)	11 ± 2	11 ± 3	NS
LV mass (g)	219 ± 81	180 ± 38	NS
LV mass index (g/m^2)	122 ± 42	99 ± 19	0.04
Posterior wall thickening fraction	0.58 ± 0.13	0.70 ± 0.20	0.03
Posterior wall thickening velocity (s^{-1})	1.63 ± 0.44	2.16 ± 0.69	0.008
Internal radius shortening fraction	0.42 ± 0.05	0.42 ± 0.06	NS
Mid-wall radius shortening fraction	0.23 ± 0.03	0.21 ± 0.05	NS
Longitudinal shortening fraction	0.17 ± 0.10	0.25 ± 0.10	0.02
Ejection fraction	0.72 ± 0.07	0.75 ± 0.07	NS
Peak systolic wall stress ($kdynes/cm^2$)	114 ± 35	78 ± 23	< 0.001

Data presented are mean value ± SD. LV = left ventricular; NS = nonsignificant.

Table 3. Comparison of Maximal Workload and Oxygen Consumption During Maximal Exercise Between Patients With a Stented Bioprosthesis and Patients With a Stentless Bioprosthesis

	Stented (n = 19)	Stentless (n = 19)	p Value
Maximal workload (Watts)	118 ± 53	129 ± 41	NS
Rest VO$_2$ (ml/kg/min)	4.4 ± 0.8	4.0 ± 0.7	NS
Anaerobic threshold (ml/kg/min)	12.7 ± 3.6	14.7 ± 3.9	NS
Peak VO$_2$ (ml/kg/min)	25.8 ± 8.2	27.2 ± 6.8	NS
% of predicted peak VO$_2$	110 ± 29	112 ± 32	NS

Data presented are mean value ± SD. VO$_2$ = oxygen consumption; NS = nonsignificant.

Dependence of exercise transvalvular gradients on resting indexed EOA. A strong inverse exponential relation was found in all patients between the mean gradient either at rest or during peak exercise and the resting indexed EOA (Fig. 1, Panels A and B). As previously found in our study of patients with a stented valve (3), there also was a strong inverse correlation between the increase in gradient with maximal exercise and the resting indexed EOA (Fig. 2). However, in the previous study the relation was linear whereas in this study, that included a group of patients with a wider range of indexed EOA (0.56–1.75 cm^2/m^2 vs. 0.56–0.98 cm^2/m^2), this relation was exponential. The analysis of Figures 1 and 2 shows that patients with a stented or a stentless bioprosthesis were distributed on different sections of the same exponential curves. Most patients with a stented bioprosthesis had an indexed EOA ≤0.85–0.90 cm^2/m^2 and were therefore on the steep portion of the exponential curves. Consequently, in these patients the gradient was relatively high at rest (Fig. 1, Panel A) and increased markedly with maximal exercise (Fig. 2). In contrast, most patients with a stentless bioprosthesis had a larger indexed EOA at rest and were, therefore, on the flat portion of the curves where the resting gradient was low and little increase in gradient occurred during exercise.

DISCUSSION

Comparison with previous studies. Several studies in patients with an aortic bioprosthesis have reported a significant increase in mean gradient during exercise, but important variations were observed among patients, depending on valve model and size (4,5,20–23). To our knowledge, this is the first study that compared the hemodynamic performance in patients with stented versus stentless bioprostheses during maximal exercise. Previous studies in similar bioprostheses were performed during submaximal exercise, and, in most cases, the EOA was not measured.

Hemodynamic performance of stentless versus stented bioprostheses. This study definitely shows that stentless bioprostheses have less increase in gradient during maximal

Table 4. Change in Doppler Echocardiographic Data With Exercise in Patients With a Stented Bioprosthesis and Patients With a Stentless Bioprosthesis

	Baseline (Rest Upright)	Maximal Exercise	Change With Maximal Exercise	p Value Effect of Exercise	p Value Effect of Prosthesis	p Value Factors Interaction
Cardiac index (L/min/m^2)				< 0.001	NS	NS
Stented (n = 14)	2.68 ± 0.62	5.91 ± 1.09†	+3.18 ± 0.71†			
Stentless (n = 16)	2.53 ± 0.42	5.58 ± 1.10†	+3.04 ± 1.05†			
Mean flow rate (ml/s)				< 0.001	NS	NS
Stented (n = 14)	256 ± 50	383 ± 105†	+125 ± 65†			
Stentless (n = 16)	241 ± 37	377 ± 69†	+137 ± 58†			
Effective orifice area (cm^2)				< 0.001	< 0.001	NS
Stented (n = 14)	1.46 ± 0.32	1.60 ± 0.49*	+0.15 ± 0.22*			
Stentless (n = 16)	2.15 ± 0.45¶	2.40 ± 0.61¶†	+0.26 ± 0.30†			
Indexed effective orifice area (cm^2/m^2)				< 0.001	< 0.001	NS
Stented (n = 14)	0.82 ± 0.13	0.90 ± 0.24*	+0.08 ± 0.12*			
Stentless (n = 16)	1.18 ± 0.25¶	1.32 ± 0.36¶†	+0.14 ± 0.18†			
Mean transvalvular gradient (mm Hg)				< 0.001	< 0.001	NS
Stented (n = 14)	13 ± 5	25 ± 11†	+12 ± 8†			
Stentless (n = 16)	5 ± 4¶	10 ± 7¶†	+5 ± 3§†			

*$p < 0.05$. †$p < 0.001$, exercise versus baseline. §$p < 0.01$. ¶$p < 0.001$, stentless versus stented bioprostheses.
NS = nonsignificant. Data presented are mean value ± SD.

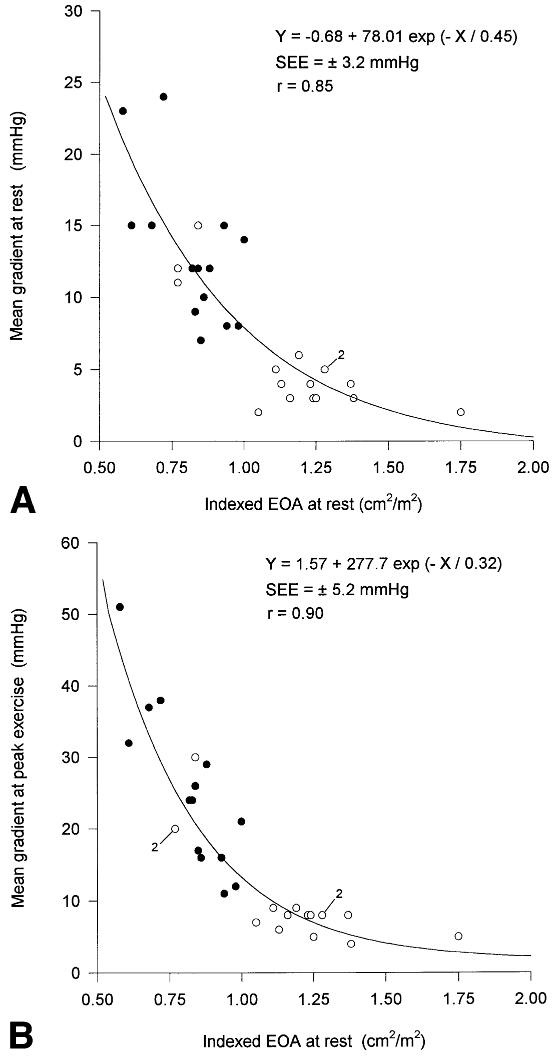

Figure 1. Correlation between mean transvalvular gradient and indexed EOA at rest in patients with a stentless **(open circle)** or a stented **(solid circle)** bioprosthesis. **Panel A** and **panel B** show this relation for mean gradient measured at rest and during peak exercise, respectively. EOA = effective orifice area.

exercise than stented bioprostheses, despite similar increases in mean flow rate. In both cases, the EOA also increased during exercise thus minimizing the increase in gradient that could have occurred had the EOA remained constant. In Figure 3, the solid lines are the relations between the indexed EOA and the gradients observed at rest and during exercise and the dashed line represents the gradients that would have been observed during exercise given similar increases in mean flow rates and constant EOAs. The reduction in gradient due to the increase in EOA is in the order of 24%. To explain the apparent discrepancy in the order of magnitude between the increase in EOA (+10 ± 13%) and the reduction in gradient (−24 ± 10%), one must remember that gradient is a squared function of flow and EOA.

However, this study did not confirm our hypothesis stating that stentless bioprostheses might have a greater intrinsic capacity for EOA enlargement due to the flexibility of their annulus. The Freestyle bioprosthesis is surrounded by a polyester covering which might limit its potential to expand with exercise.

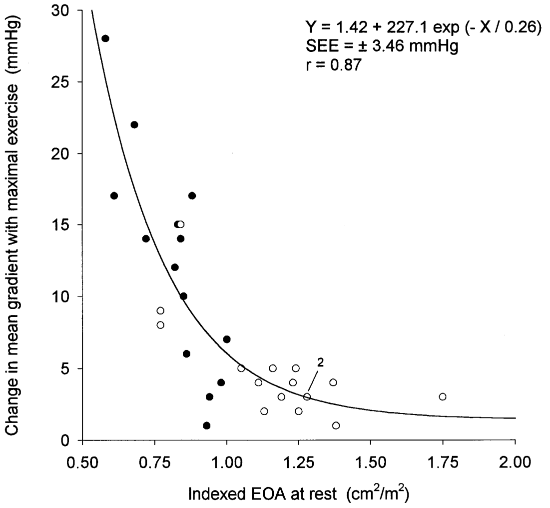

Figure 2. Correlation between the change in mean transvalvular gradient with maximal exercise and indexed EOA at rest in patients with a stentless **(open circle)** or a stented **(solid circle)** bioprosthesis. EOA = effective orifice area.

Given these observations, the superior hemodynamic performance of the stentless bioprostheses appears mainly to

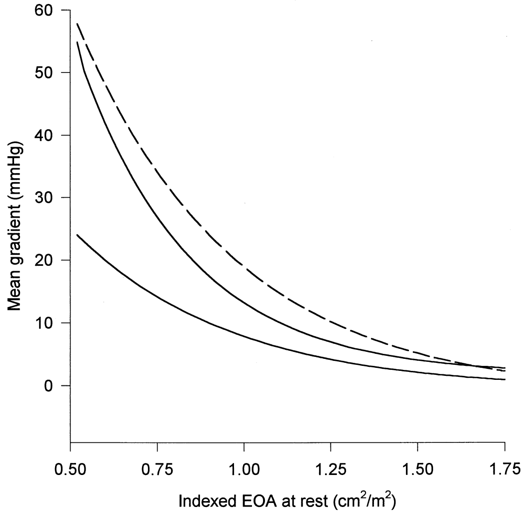

Figure 3. Mean gradient observed at rest **(lower solid line)** and during peak exercise **(upper solid line)** and expected mean gradient at peak exercise **(dashed line)** as a function of indexed EOA at rest. The exponential curves representing the observed gradient at rest and during peak exercise were constructed using the regression equations given in Figure 1. The curve representing the expected behavior of gradient during maximal exercise **(dashed line)** was derived from the resting curve **(lower solid line)** assuming incremental increase in mean flow rate and a constant EOA during exercise. EOA = effective orifice area.

be related to a question of sizing, i.e., to their larger EOA in relation to the patient's body surface area resulting in a larger EOA and a lower gradient at any given flow level. This conclusion is strongly supported by the relations given in Figures 1 and 2. A larger indexed EOA can be due either to a larger EOA in relation to the prosthesis outer diameter size or to the fact that, for the stentless bioprostheses, a larger prosthesis can be inserted into a smaller patient, as previously reported for the Freestyle and Toronto SPV valves (St. Jude Medical, St. Paul, Minnesota) (1,24,25). In this study, however, the indexed EOAs were much larger in the stentless bioprostheses despite a similar average valve size indexed for body surface area, suggesting that the main factor in these patients was a larger EOA in relation to the prosthesis outer diameter size.

Influence on exercise capacity and LV morphology. Although stentless bioprostheses had better hemodynamics than stented bioprostheses at rest and during exercise, there was no difference in maximal exercise capacity between the two groups. For all practical purposes, even in the patients with the smallest indexed EOAs, the resting and exercise gradients were similar to those observed in mild to moderate aortic stenosis (18) and probably not high enough to affect maximal exercise capacity.

Furthermore, our results suggest that the lesser gradients observed at rest and during exercise in stentless bioprostheses might have a beneficial effect on LV mass and function. Indeed, despite similar baseline characteristics, the patients with a stentless bioprosthesis had a significantly smaller LV mass than the patients with a stented bioprosthesis. This result is consistent with the previous study of Jin et al. (2) showing that stentless bioprostheses are associated with greater decrease in LV wall stress and better regression of LV hypertrophy than stented prostheses. The very significant differences in posterior wall thickening and ventricular longitudinal shortening also suggest a better recuperation of subendocardial myocardial function in the patients with a stentless bioprosthesis (7), which is also consistent with the lower residual systolic wall stress found in these patients. Further longitudinal studies are necessary to confirm these findings as well as to determine their potential impact on long-term morbidity and mortality.

Study limitations. Since Doppler echocardiographic measurements were performed with the patient in the upright position and during exercise, one cannot exclude completely that the true maximal transvalvular velocities were not always recorded. However, the very good correlation ($r = 0.90$; $p < 0.0001$) obtained between the gradient during maximal exercise and the indexed EOA at rest tends to confirm a certain coherence in the results. The recordings of the LVOT velocities and the measurement of the LVOT diameter, which determine stroke volume, cardiac output and EOA, can be affected by experimental conditions. However, the strong correlation that we obtained between the cardiac output measured at peak exercise by Doppler echocardiography and peak VO_2 supports the validity of these measurements. Although Doppler echocardiographic recordings during exercise, particularly those of LVOT velocities, are technically demanding, this study shows that they are feasible and reliable.

Most of the stented bioprostheses were Medtronic Intact valves, whereas all the stentless bioprostheses were Medtronic Freestyle bioprostheses. Other bioprosthetic or mechanical valves may demonstrate different changes in EOA with exercise and therefore different increases in gradient given the same indexed EOA at rest. The power to detect differences in EOA behavior during exercise is also limited by the low number of patients in each group, but the results nonetheless suggest that the change in gradient with exercise is much more related to the resting EOA rather than to its relative change during exercise.

Also, this study was carried out in a relatively homogenous group of patients, i.e., sedentary patients between 55 and 75 years old with a normal LV systolic function. In a more heterogeneous group of patients with regard to patient age, LV function and physical training conditions, the correlation between mean gradient and the resting indexed EOA might have been lower than that observed in this study. For instance, given the same indexed EOA at rest, young athletes might have had a higher gradient than predicted at peak exercise due to a supranormal cardiac output, whereas inversely, older patients with depressed LV function might have had lower gradients.

Clinical implications. These findings further confirm the importance of valve sizing with regard to the hemodynamic behavior of a prosthesis. Indeed, our results show that, regardless of the type of bioprosthesis, the resting indexed EOA is the best predictor of postoperative gradients whether at rest or during exercise. Furthermore, the relations found in this study can be used to project postoperative gradients at the time of operation and should thus be useful to select the optimal prosthesis given a patient's body surface area and level of physical activity. Figure 4 illustrates the relations between the resting and exercise gradients observed in this study and the indexed EOAs calculated from the patient's body surface area and the published normal values for the prosthesis being implanted (1), a calculation that can be made in the operating room. The correlations are slightly less significant than those shown in Figure 1, probably due to differences in prosthesis manufacturing and other unknown factors. Nonetheless, they show that these postoperative gradients could have been predicted from information available at the time of operation. They also further confirm that the projected indexed EOA should ideally be no less than 0.90 cm^2/m^2 in order to minimize postoperative gradients. It should be emphasized that the normal values for the EOA of stented bioprostheses were taken from in vitro data whereas for the stentless bioprostheses, these values were taken from in vivo data because it has been shown that, contrary to stented bioprostheses, in

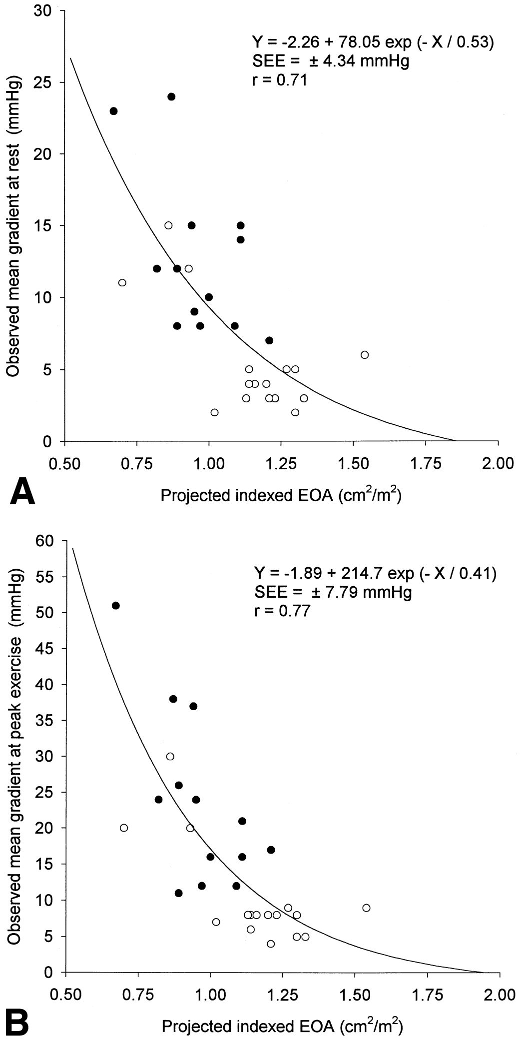

Figure 4. Correlation between mean transvalvular gradients observed in patients and the projected indexed EOA calculated by indexing the normal values of valve EOA for patients' body surface area. Normal values of EOA were determined for each model and size of prosthesis using a previous study from our laboratory (1). The normal value of EOA for the St-Jude X-Cell stented valve was not available in the published literature. **Panel A** and **panel B** show this relation for mean gradient measured at rest and during peak exercise. **(open circle)** = Stentless bioprostheses; **(solid circle)** = stented bioprostheses. EOA = effective orifice area.

vitro data for stentless bioprostheses grossly overestimate in vivo EOAs (1).

Conclusions. Stentless bioprostheses have a better hemodynamic performance than stented bioprostheses during exercise mostly because of their larger resting EOA rather than a greater intrinsic capacity for EOA enlargement. This is associated with beneficial effects with regard to LV mass and function. The strong exponential relations found between the resting indexed valve EOA and the gradients at rest and during exercise further confirm that the postoperative hemodynamic behavior of a bioprosthesis can largely be predicted from this parameter at the time of operation. These relations should therefore be useful to select the optimal valve given a patient's body surface area and level of physical activity.

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REFERENCES

1. Dumesnil JG, LeBlanc MH, Cartier P, et al. Hemodynamic features of the Freestyle aortic bioprosthesis as compared to stented bioprosthesis. Ann Thorac Surg 1999;66 Suppl S:S130–3.
2. Jin XY, Zhang ZM, Gibson DG, et al. Effects of valve substitute on changes in left ventricular function and hypertrophy after aortic valve replacement. Ann Thorac Surg 1996;62:683–90.
3. Pibarot P, Dumesnil JG, Jobin J, et al. Usefulness of the indexed effective orifice area at rest in predicting an increase in gradient during maximal exercise in patients with a bioprosthesis in the aortic valve position [In press]. Am J Cardiol 1999;83.
4. Donatelli F, Triggiani M, Mariani MA, et al. Rest and exercise hemodynamics of stentless porcine bioprostheses in aortic position. Cardiologia 1994;39:41–7.
5. Eriksson MJ, Brodin LA, Dellgren GN, Radegran K. Rest and exercise hemodynamics of an extended stentless aortic bioprosthesis. J Heart Valve Dis 1997;6:653–60.
6. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450–8.
7. Dumesnil JG, Shoucri RM, Laurenceau JL, Turcot J. A mathematical model of the dynamic geometry of the intact left ventricle and its application to clinical data. Circulation 1979;59:1024–34.
8. Dumesnil JG, Shoucri RM. Effect of the geometry of the left ventricle on the calculation of ejection fraction. Circulation 1982;65:91–8.
9. Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest 1975;56:56–64.
10. Jones NL, Makrides L, Hitchock C, McCartney N. Normal standard for an incremental progressive cycle ergometer test. Am Rev Respir Dis 1985;131:700–8.
11. Nishijima H, Sato I, Matsumura N, et al. Ventilatory anaerobic threshold before and after cardiac valve surgery. Jpn Circ J 1993;57:208–14.
12. Mahler DA. American College of Sport Medicine Guidelines for Exercise Testing and Prescription. Baltimore, MD: Lippincott, Williams & Wilkins, 1995.
13. Dumesnil JG, Honos GN, Lemieux M, Beauchemin J. Validation and applications of indexed aortic prosthetic valve areas calculated by Doppler echocardiography. J Am Coll Cardiol 1990;16:637–43.
14. Pibarot P, Honos GN, Durand LG, Dumesnil JG. Substitution of left ventricular outflow tract diameter with prosthesis size is inadequate for calculation of the aortic prosthetic valve area by the continuity equation. J Am Soc Echocardiogr 1995;8:511–7.
15. Rassi A, Crawford MH, Richards KL, Miller JF. Differing mechanisms of exercise flow augmentation at the mitral and aortic valves. Circulation 1988;77:543–51.
16. Shively BK, Charlton GA, Crawford MH, Chaney RK. Flow depen-

dence of valve area in aortic stenosis: relation to valve morphology. J Am Coll Cardiol 1998;31:654–60.

17. Takeda S, Rimington HM, Chambers JB. The use of the pressure drop-flow slope as a measure of severity in patients with aortic stenosis (abstr). J Am Coll Cardiol 1998;31 Suppl A:A246.
18. Burwash IG, Pearlman AS, Kraft CD, et al. Flow dependence of measures of aortic stenosis severity during exercise. J Am Coll Cardiol 1994;24:1342–50.
19. Devereux RB. Detection of left ventricular hypertrophy by M-mode echocardiography. Anatomic validation, standardization, and comparison to other methods. Hypertension 1987;9 Suppl II:II19–26.
20. Jaffe WM, Coverdale HA, Roche AHG, et al. Rest and exercise hemodynamics of 20 to 23 mm allograft, Medtronic Intact (porcine), and St. Jude medical valves in the aortic position. J Thorac Cardiovasc Surg 1990;100:167–74.
21. Van den Brink RBA, Verheul HA, Visser CA, et al. Value of exercise Doppler echocardiography in patients with prosthetic or bioprosthetic cardiac valves. Am J Cardiol 1992;69:367–72.
22. Wiseth R, Levang OW, Tangen G, et al. Exercise hemodynamics in small (≤21 mm) aortic valve prostheses assessed by Doppler echocardiography. Am Heart J 1993;125:138–46.
23. Munt BI, Legget ME, Healy NL, et al. Effects of aortic valve replacement on exercise duration and functional status in adults with valvular aortic stenosis. Can J Cardiol 1997;13:346–50.
24. Del Rizzo DF, Goldman BS, Joyner CP, et al. Initial clinical experience with the Toronto stentless porcine valve. J Cardiac Surg 1994;9:379–85.
25. Westaby S, Amarasena N, Long V, et al. Time-related hemodynamic changes after aortic replacement with the Freestyle stentless xenograft. Ann Thorac Surg 1995;60:1633–9.