Postoperative Exercise Tolerance After Aortic Valve Replacement by Small-Size Prosthesis

Functional Consequence of Small-Size Aortic Prosthesis

Pierre Becassis, MD,* Maurice Hayot, MD, PhD,† Jean-Marc Frapier, MD,‡ Florence Leclercq, MD,* Lionel Beck, MD,* Jérôme Brunet, MD,* Eric Arnaud, MD,* Christian Prefaut, MD, PhD,† Paul-André Chaptal, MD,‡ J. M. Davy, MD,* Patrick Messner-Pellenc, MD, PhD,* R. Grolleau, MD* Montpellier, France

OBJECTIVES

The objective of this study was to determine whether a small-size valve prosthesis contributes to exercise intolerance, as assessed by Vo2 measurement during an exhaustive cycle ergometer exercise.

BACKGROUND

The determinants of exercise capacity after mechanical aortic replacement are not well known. The selection of small valve sizes has, however, been described as an independent predictor of exercise intolerance as assessed by exercise duration. Maximal oxygen uptake (Vo2 max) is a good index of exercise tolerance.

METHODS

Fourteen patients were eligible, with a mean age of 62 ± 6 years. Before surgery, the mean left ventricular ejection fraction (LVEF) was 73 ± 8%. Two valve types with small diameter (19 to 21 mm) were used: Medtronic Hall and St Jude Medical. A healthy sedentary control group (n = 14) paired for age, weight and size was constituted. After one year of follow-up, cardiorespiratory tests were performed. In addition, the gradients through the prostheses were determined by continuous pulse Doppler at rest and immediately after the cardiorespiratory test.

RESULTS

The exercise tolerance was not significantly different between the control group and patient group: Vo2 peak (21.7 vs. 20.4 ml/kg/min; p = 0.42), workloads (115 vs. 93 W; p = 0.13) and ventilatory parameters were similar. The mean and peak gradients at rest and during exercise were not correlated with Vo2max.

CONCLUSIONS

Valve replacement by small aortic prosthesis does not seem to be a factor of exercise intolerance as assessed by Vo2 max in patients without LVEF dysfunction before surgery. (J Am Coll Cardiol 2000;36:871–7) © 2000 by the American College of Cardiology

In the case of a small aortic annulus, the choice of prosthesis size is very important. If a medium-size prosthesis is selected, the consequences include prolonged surgical procedure and increased operative risk (1) due to surgical root enlargement. A small size, however, may increase the risk of residual outflow obstruction (2). Moreover, small prosthesis size has been reported to be an independent factor in sudden death, particularly when the body surface area and prosthesis size are mismatched (3). Nevertheless, in current surgical practice, a small prosthesis is most frequently used in this indication.

A negative influence of small prosthesis size on exercise capacity has been suggested. This is thought to be due mainly to high transaortic gradients during exercise that are not observed at rest and also to other factors such as a smaller left ventricular cavity (4). After aortic valve replacement, the patient’s functional level usually improves, but the effective prosthetic valve area is smaller than that of healthy native valves. Few studies have described the exercise tolerance after valve implantation. Indeed, the determinants of exercise capacity after mechanical aortic replacement are not well known. Tatineni et al. (5) showed that, as expressed by exercise duration, prosthesis size is an independent predictor of exercise tolerance.

Maximal oxygen uptake (Vo2 max) is a good index of exercise capacity and is used for prognosis in cardiac disease (6). To our knowledge, the evaluation of exercise capacity as assessed by Vo2max, compared with that of control subjects, has not been studied in patients with small aortic prosthesis (≤21 mm). Hirooka et al. (7) compared the percentage of predicted peak oxygen consumption in relationship to four valve sizes (19 to 25 mm) without statistically significant results. In their study, predicted peak oxygen consumption tended to be lower, however, in patients with a prosthesis size of 19 mm than in those with a size of 25 mm. This suggests that patients with small aortic prostheses present an exercise intolerance. The mechanisms may involve a residual outflow obstruction at rest that is increased during exercise (2); however, we do not know whether hemodynamic characteristics of these small prostheses were a determinant of exercise tolerance. Hemodynamic evaluation of prosthesis...
follow-up of 28 surgery, the patients were prospectively studied with a mean 6) and St. Jude Medical (no. 19, n 5
21 mm) were implanted. After surgery, the patients were prospectively studied with a mean 6 months. The mean age of patients was
62.4 ± 6 years, with nine women and five men.

Before surgery, 13 patients had aortic stenosis; one had a predominant insufficiency. All were free of significant coronary artery disease: mean left ventricular ejection fraction (LVEF) was 73 ± 8% (using digital subtraction angiography), and the mean stenotic aortic gradient was 71 ± 25 mm Hg. All patients were in sinus rhythm before and after surgery and without exercise contraindication.

Control group. The healthy control group, matched for gender, height and weight, was constituted at the same period. It was composed of 14 normal sedentary subjects without history of cardiovascular or pulmonary disease based on the results of clinical, echocardiographic, electrocardiographic (ECG), and spirographic examination. All subjects gave signed consent to participate in the study after the design and risks of protocol were explained to them. The study was also approved by the hospital ethics committee.

Spirographic measurements. Conventional spirographic measurements were performed on a digital spirometer (Pulmonet III, SensorMedics, Yorba Linda, California). The lung function study included force expiratory volume in 1 s (FEV1) and vital capacity (VC). The FEV1/VC ratio was then calculated. The predicted values were those of Quanjer (10).

Doppler echocardiography. A complete echocardiographic and Doppler examination was performed at rest in the sitting position with SONOS 1500 Hewlett Packard using a 2.5 duplex mechanical transducer. The usual data were collected using M-mode, two-dimensional and continuous-wave Doppler.

Maximal velocities across the prosthesis were measured by continuous-wave Doppler from the apical view. Indeed, the high-velocity jets were best recorded from the cardiac apex, correlated with cardiac catheterization findings (11). From the highest velocities obtained, the transprosthetic pressure drop was calculated according to the Bernoulli equation (12). Mean gradients were obtained by integrating the Doppler velocity signals (13). The effective orifice area was calculated with the continuity equation, using the pulsed Doppler (13,14). Doppler measurements were performed at rest and early after peak exercise, during the first minute of recovery, using the same location of the Doppler sampler, in the sitting position.

Cardiorespiratory exercise testing. Exercise tests were performed on an electrically braked cycle ergometer with heart rate, blood pressure and ECG monitoring under the supervision of a physician. The subjects breathed through a low-resistance valve (2700 Hans Rudolf, Kansas City, Kansas) with the nose clamped. Expired flow and oxygen and carbon dioxide partial pressures were continuously monitored on a breath-by-breath basis using a cardiopulmonary exercise test (CPX Medical Graphics System, Medical Graphics, St. Paul, Minnesota). Ventilation (VE, liter/ min BTPS), O2 uptake (VO2 ml/min and ml/kg/min STPD), and CO2 production (VCO2, liter/min STPD) were calculated by averaging the breath-by-breath data over 30 s. We also determined the respiratory gas exchange ratio (R = VCO2/VO2) and the ventilatory equivalents for O2 (VE/VO2) and CO2 (VE/VCO2). The ventilatory threshold (VT) was determined as the level of VO2 at which an increase in VE/VO2 was observed without a simultaneous change in VE/VCO2 (15). The maximal minute ventilation at peak exercise (VEmax) values were predicted by VEmax = measured FEV1 × 35 (16). The ventilatory reserve (VR) at maximal exercise was calculated as follows: [100 – (100 × measured VEmax/predicted VEmax)] (17).

The exercise test consisted of a 3-min rest period, followed by the maximal exercise test, which started with a 3-min warmup at 20 W with a minimum constant pedalling

### Abbreviations and Acronyms

- FEV1: Forced expiratory volume in 1 s
- HR: Heart rate
- LVEF: Left ventricular ejection fraction
- MH: Medtronic Hall
- R: Respiratory gas exchange ratio (VCO2/VO2)
- SJM: St Jude Medical
- VC: Vital capacity
- VE: Minute ventilation at peak exercise
- VE,max: Maximal oxygen uptake
- VE2: Peak oxygen consumption
- VR: Ventilatory reserve
- Vt: Ventilatory threshold
- Wmax: Maximal workload

### Methods

**Patients.** From March 1993 to September 1994, a total of 14 small aortic valve prostheses (≤21 mm) were implanted. Two types of valve were used: Medtronic Hall (no. 21, n = 6) and St. Jude Medical (no. 19, n = 7; no. 21, n = 1). After surgery, the patients were prospectively studied with a mean follow-up of 28 ± 6 months. The mean age of patients was 62.4 ± 6 years, with nine women and five men.

Before surgery, 13 patients had aortic stenosis; one had a predominant insufficiency. All were free of significant coronary artery disease: mean left ventricular ejection fraction (LVEF) was 73 ± 8% (using digital subtraction angiography), and the mean stenotic aortic gradient was 71 ± 25 mm Hg. All patients were in sinus rhythm before and after surgery and without exercise contraindication.

**Control group.** The healthy control group, matched for gender, height and weight, was constituted at the same period. It was composed of 14 normal sedentary subjects without history of cardiovascular or pulmonary disease based on the results of clinical, echocardiographic, electrocardiographic (ECG), and spirographic examination. All
rate of 60 rpm. For the patients, the workload was then increased by 10 W every minute. For the healthy control subjects, the workload increment (20 or 30 W) was chosen to obtain an exercise duration between 8 and 12 min, which is the optimal range for obtaining the highest values of peak VO₂ (18). Subjects were asked to continue exercise until exhaustion (VO₂ peak). The criteria for prematurely stopping the test were defined as follows: serious cardiac arrhythmia, fall in blood pressure, ECG changes compared to resting value, and chest pain.

For every subject, the observation of at least three of the four following criteria was necessary to consider that VO₂ peak was obtained: stability of heart rate (HR) at a value close to the predicted maximal HR; stability of oxygen uptake despite the increase in workload; respiratory ratio >1.10; and the inability of the subject to maintain a pedalling rate of 50 rpm (17).

Protocol. The study protocol included spirometric values at rest and maximal cardiopulmonary exercise testing for both groups. The echocardiography Doppler measurements at rest and early after peak exercise, during the first minute of recovery, were performed for the aortic prosthesis group using the same location of Doppler sample, in the sitting position and by the same physician.

Statistical analysis. All data are expressed as mean ± standard deviation (SD). The Student t test for unpaired observations was used for between-group comparison when the normality distribution (Kolmogorov-Smirnov test) and the equality of variance (Levene median test) were verified. When these conditions of normality were not obtained, a statistical analysis was performed for the aortic prosthesis group using the same location of Doppler sample, in the sitting position and by the same physician.

RESULTS

Anthropometric and spirometric characteristics. As shown in Table 1, the anthropometric parameters did not differ significantly between the two groups. The spirometric data (Table 2) showed that FEV1 and VC were significantly lower in patients than in controls; the FEV1/VC ratio was not significantly different.

Exercise testing. The results of maximal exercise testing are summarized in Table 3. Exercise capacity, expressed as VO₂ peak or %predicted VO₂ max, was not significantly different between the two groups (Fig. 1). Similarly, no difference was observed in the ventilatory parameters (VE, VR and the ventilatory equivalents for VO₂ and VCO₂). Patients with the SJM prosthesis had an exercise tolerance comparable to those with MH. However, the maximal heart rate expressed as a percentage of predicted value (% predicted HRmax) was lower in the patient group than in controls (82 ± 11 vs. 91 ± 9 beats/min; p = 0.03). The maximal R (Rmax) was higher (p = 0.03) in the controls, but a mean value above 1.1 was observed in both groups. No event occurred in either group to lead to an interruption of exercise testing.

Doppler hemodynamic evaluations in the prosthetic group: Rest and exercise data analysis. At rest, the mean and peak transaortic gradients were, respectively, 21 ± 8 and 35 ± 13 mm Hg. With exercise, these gradients increased in all patients: the mean gradient increased to 33 ± 14 and the peak to 57 ± 24 mm Hg; the acceleration time of flow velocity increased to 3.01 ± 0.54 to 3.59 ± 0.78 (p = 0.03). We did not observe a significant difference for mean (p = 0.70) or peak exercise (p = 0.75) gradients (Fig. 2) in the subgroups of patients with the 19-mm prosthesis versus the 21-mm prosthesis. These exercise gradients also did not differ (Fig. 3) for SJM versus MH: (p = 0.82 for mean exercise gradients; p = 0.74 for peak exercise gradients). A significant correlation between the

<table>
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<tr>
<th>Table 1. Anthropometric Values of Control Group and Patients</th>
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<td><strong>Control Group</strong></td>
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<td>Age (yrs)</td>
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<td>Weight (kg)</td>
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<td>BMI</td>
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BMI = body mass index.

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<th>Table 2. Spirometric Values of Control Group and Patients</th>
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<td><strong>Control Group</strong></td>
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<tr>
<td>FEV1 (liter)</td>
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<td>%pred FEV1</td>
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<td>VC (liter)</td>
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<td>%pred VC</td>
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<td>FEV1/VC</td>
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FEV1 = forced expiratory volume in 1 s (liter/sec); %pred FEV1 = percentage of predicted FEV1; %pred VC = percentage of predicted VC; VC = vital capacity (liter).

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<th>Table 3. Cardiorespiratory Exercise Measurement in Control Group and Patients</th>
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<tr>
<td><strong>Control Group</strong></td>
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<td>VO₂ peak/mi/min</td>
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<td>%pred VO₂ max</td>
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<td>Wmax (watts)</td>
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<td>VEmax liter/min</td>
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<td>%pred VEmax</td>
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<td>%VR</td>
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<td>VE/VO₂</td>
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<td>VE/VCO₂</td>
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<td>Basal HR (beats/min)</td>
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<td>R</td>
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<td>Vt (ml/min)</td>
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HR = heart rate; %pred VO₂ max = percentage of predicted VO₂ max; %pred VE = percentage of predicted VEmax; %pred HRmax = percentage of predicted HRmax; R = respiratory gas exchange ratio (V̇CO₂/V̇O₂); V̇Emax = minute ventilation at peak exercise; Vt = ventilatory threshold; VO₂ peak = peak oxygen consumption; VR = ventilatory reserve; Wmax = maximal workload.
resting peak gradient and early after peak exercise gradient was found (Fig. 4). No significant correlation was observed between exercise capacity (VO₂ max or maximal workload [Wmax]) and the following data: prosthesis area, rest and early after peak exercise gradients (Fig. 5), body surface, or the body surface/prosthesis area ratio.

However, a significant correlation existed between the prosthesis area at rest and the values of mean and early after peak exercise gradients (respectively, $y = 71.5 - 34.0X$, $r = -0.80$, $p < 0.01$; and $y = 117.9 - 54.4X$, $r = -0.74$, $p < 0.01$). Finally, when we compared subgroups of patients with two different prosthesis sizes (19 or 21 mm), we did not observe a difference in VO₂ peak.

**DISCUSSION**

To our knowledge, this study was the first to compare the exercise tolerance between a healthy control group and a small aortic prosthesis group. The main result was a similar exercise tolerance, expressed by VO₂ peak or Wmax, with no significant differences between the patient and control groups. The use of a small aortic prosthesis, therefore, did not appear to induce exercise intolerance. Moreover, the mean and peak gradients at rest and early after peak exercise were not correlated with VO₂ peak. Although the values of these gradients were higher than those usually observed in medium-size aortic prostheses, this did not seem to be a cause of exercise limitation.

**Methods.** All patients in our study had a body surface area of less than 1.7 m², for which the usual recommendation is...
implantation of a small aortic prosthesis (3). The evaluation of exercise tolerance by VO2max measurement in patients with a small aortic prosthesis was easily obtained without adverse complication. In addition, a noninvasive hemodynamic study by Doppler echocardiography was also possible at rest and early after peak exercise in all patients. However, we did not compare the Doppler echocardiographic data with reference standard catheterization data. Indeed, in the smaller 19- and 21-mm sizes, the difference between Doppler and catheter gradients may be more than 20 mm Hg, particularly at high flow rates (19). In previous studies where close agreement between catheter and Doppler data was shown, the subgroup of small valve sizes was not well represented (19,20). Nevertheless, from an ethical point of view, performance of this invasive evaluation did not appear to be sufficiently justified in our study.

Exercise tolerance. In terms of VO2 peak, we found a preserved exercise tolerance; no statistically significant difference existed in the level of maximal exercise between the two groups when this parameter was expressed as %predicted VO2max or maximal workload. Only maximal HR was slightly higher in the control group, probably linked to a nonsignificantly higher maximal workload (115 ± 39 vs. 93 ± 36; p = 0.13; NS). Despite a mild restrictive

![Figure 4. Correlation between rest and early after peak exercise prosthesis gradients. (The correlation does not persist if we suppress the leverage point in the upper right corner of the graph.)](image)

![Figure 5. No correlations between peak gradients (rest and early after exercise) and VO2 max were observed. Open square = early after exercise peak gradient; closed circle = rest peak gradient.](image)
respiratory syndrome, the patients had a normal breathing pattern, with no differences between the two groups for VE\textsubscript{max} or ventilatory equivalents. The ventilatory threshold occurred slightly sooner in the patients but was not significantly different, which suggested there was no muscular impairment. The use of a small aortic prosthesis did not seem to induce an exercise intolerance.

The hemodynamic performance and exercise capacity did not differ between the patients with SJM and those with MH. In the subgroups, with two different diameters (19 and 21 mm) and two types of prostheses, the exercise tolerance did not significantly differ.

It would of course be helpful to compare these exercise tolerance measurements with preoperative data, but in this study the main etiology for which aortic valve replacement was indicated was a predominant aortic stenosis (13/14 patients). Therefore, we did not conduct cardiorespiratory testing before surgery because it is classically contraindicated in this pathology.

All patients presented a preserved left ventricular systolic function before surgery. Respiratory functional exploration performed two years after surgery found impaired respiratory function with a mild restrictive syndrome, probably associated with the thoracic surgery. The spirometric abnormalities we observed have already been described at the two-month follow-up after cardiac surgery (21).

Doppler hemodynamic data and VO\textsubscript{2max}. The VO\textsubscript{2max} was not correlated with the hemodynamic parameters (i.e., the transprosthetic gradients at rest and early after peak exercise) and the functional surface of the valve. Many previous studies have used cardiac catheterization for hemodynamic valuation, but this procedure introduced additional risks to patients, especially during exercise. The use of noninvasive Doppler echocardiography during exercise was an excellent means of studying the hemodynamic modifications.

Similar to the data reported by Wiseth et al. (4), the gradients during exercise were correlated with the resting gradients. In addition, rest and exercise prosthetic gradients did not differ between the two valve types or between the two sizes. This was true despite the mechanical differences, with a bi-leaflet tilting-disk design in SJM prostheses and a single tilting-disk design, with a less homogeneous velocity distribution across the valve orifice, in MH prostheses (19).

The transaortic Doppler exercise measurement was performed early after peak exercise, in the first minute of active recovery. This was not really the “peak exercise,” but hemodynamic conditions are very similar between peak and early active recovery of a maximal exercise test (22). Indeed, although HR and cardiac output rapidly decrease, the stroke volume is maintained or increased due to an increment of venous return (23).

Comparison with previous studies. Very few studies have specifically investigated the parameters influencing exercise capacity and exercise hemodynamics in patients after aortic valve replacement, especially with a small-size prosthesis. Tatineni et al. (5) showed in patients with an aortic prosthesis that the ejection fraction and other parameters of left ventricular function were not predictive of exercise capacity. Only age and valvular size were independent predictors of exercise tolerance, which might be explained by the higher gradients in small prostheses (2). But in their study, the exercise tolerance was evaluated by exercise duration, and the correlation with prosthesis size was weak ($r = 0.41$; $p < 0.05$). Moreover, these data were not compared with those of a control group, and during these invasive studies the ability to complete exercise may have been limited in the patients, which would explain the moderate increase in gradient. Nitter-Hauge et al. (24) showed, in 10 patients with MH of usual size (21 to 27 mm), a mean gradient of 2.9 mm Hg at rest and increasing to 6.8 mm Hg during exercise.

Using Doppler echocardiography for a subgroup of 14 patients with MH 21 mm, Wiseth et al. (4) reported mean and peak gradients, at rest in supine position, of, respectively, 15 ± 4 and 30 ± 8, increased to 24 ± 6 and 47 ± 11 mm Hg during exercise. Aris et al. (25) reported, for 12 patients with SJM 19 mm, a mean resting gradient of 22 ± 7 mm Hg, increased during supine exercise to 32 ± 10 mm Hg, and for 16 patients with MH 20 mm, a mean resting gradient of 17 ± 5 mm Hg, increased to 24 ± 8 mm Hg.

In another study by Tatineni et al. (5), 12 patients had prosthesis sizes ≤21 mm (data extracted from figure), and their peak exercise gradients ranged from 22 to 52 mm Hg. For Wiseth et al. (4), the range was from 25 to 67 mm Hg, and in our study it was from 25 to 103 mm Hg. Thus, our data show mean gradients at rest and during exercise that are comparable to those of Aris et al. (25) (21 ± 8 vs. 22 ± 7 and 33 ± 14 vs. 32 ± 10 mm Hg, respectively), but the peak exercise gradients were higher in our study probably because one patient had values near 100 mm Hg at exercise.

More recently, Kadir et al. (26) studied the hemodynamic performance in patients with small-size SJM, using dobutamine echocardiography. They observed an increase in mean transvalvular gradient from 22 ± 4.9 mm Hg at rest to 41.9 ± 9 mm Hg at maximum stress (respectively, 21 ± 8 mm Hg and 33 ± 14 in our study).

Concerning the comparison between the exercise capacity in patients with SJM and MH, our finding was similar to that observed in the prospective randomized trial of Fiore et al. (27): their study could not detect a difference in clinical performance or dobutamine stress transesophageal Doppler echocardiography between SJM and MH.

If we summarized these data, we may conclude that our method of measuring the transvalvular gradient in sitting position, at rest, and immediately after exercise was reliable and comparable to other methods (dobutamine stress).

Conclusions. In patients without preliminary ventricular dysfunction who presented a small body surface (<1.7 m²), the implantation of small aortic prostheses did not provoke an alteration in exercise tolerance compared with controls.
This demonstrates that the high values of gradient observed in small-sized prostheses at rest and during exercise, in comparison with those of medium sizes, are not correlated with exercise tolerance. Thus, the residual outflow obstruction seems to have no functional consequence.

Finally, in cases of small aortic root, the use of SJM or MH valve prostheses with diameters <21 mm did not appear to be a factor of exercise intolerance. This was so despite higher rest and exercise gradients than those observed in “medium”-sized prostheses.

Reprint requests and correspondence: Dr. Pierre Becassie, Service de Cardiologie B, Hopital A. de Villeneuve, 371 Avenue Doyen Gaston Giraud, 34000 Montpellier, France.

REFERENCES