Midterm Echocardiographic Follow-Up After Ross Operation

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Background—The pulmonary autograft (Ross) operation is an attractive treatment for aortic valve disease, but hemodynamic follow-up is not well defined.

Methods and Results—One hundred thirty-two consecutive patients (62% male, mean age 40±11 years) were followed up to 5 years after the Ross operation. Echocardiography was performed early (within 30 days), 3 to 6 months, and yearly after surgery. The valve effective orifice area (EOA) and mean transvalvular gradient of both aortic and pulmonary valves were measured, and transvalvular regurgitation was assessed by using color Doppler echocardiography. EOA was indexed for body surface area. The hemodynamic performance was excellent for both the aortic and pulmonary valves early after surgery (gradient, 3±4 and 3±4 mm Hg, respectively). It remained stable thereafter for the aortic valve, whereas there was a significant deterioration of the EOA (−0.74±0.82 cm²) and gradient (+6±8 mm Hg) for the pulmonary valve, which occurred mostly during the first 6 months after surgery. This hemodynamic deterioration resulted in suboptimal (defined as an EOA index <0.85 cm²/m²) hemodynamics in 19.3% of the patients, to the extent that 3 (2%) of the 132 patients eventually had to be subjected to further surgery for severe pulmonary valve stenosis.

Conclusions—The pulmonary autograft provides continued excellent hemodynamics in the aortic position, whereas moderately high gradients can be found across the pulmonary homograft in some patients. Further studies are necessary to identify the factors responsible for the deterioration of the hemodynamic performance of the homograft in the pulmonary position and to determine its impact on right ventricular function and clinical status. (Circulation. 2000;102[suppl III]:III-10-III-14.)

Key Words: valves ■ grafting ■ hemodynamics ■ echocardiography

Successful aortic valve replacement with a pulmonary autograft was first described by Ross in 1967.¹ It has been shown to be an attractive and durable substitute for the aortic valve, but its hemodynamic behavior during follow-up is not well documented.²⁻⁷ Moreover, there is even less information regarding the hemodynamics of the homograft implanted in the pulmonary position.

The objective of the present study was therefore to evaluate patients who underwent the Ross operation with attention to the hemodynamics of the pulmonary autograft implanted in the aortic position and the pulmonary homograft implanted in the pulmonary position.

Methods

Patients

One hundred thirty-two consecutive adult patients (aged 20 to 59 years, mean 40±11 years) were followed up to 5 years after the Ross operation (mean follow-up 2.47±1.75 years). These patients were the survivors of a larger series of 134 patients, 2 of whom experienced perioperative death, the causes of which were aortic root rupture and myocardial infarction. The preoperative and operative data of the survivors are summarized in the Table. In the aortic position, the pulmonary autograft was implanted as a root replacement in 70.5% of the patients and as a valve replacement in 29.5%. Root replacement was favored because of our growing impression that there could be less regurgitation in the long term with the use of this technique; however, this point remains to be examined in longer term studies. Cryopreserved pulmonary homografts (Cryolife) were used in all patients as the substitute for the pulmonary valve.

Doppler Echocardiographic Measurements

Doppler echocardiographic examinations were performed early (7 to 30 days, 132 patients), 3 to 6 months (124 patients), and 1 year (106 patients) after surgery and annually thereafter (2 years, 84 patients; 3 years, 65 patients; 4 years, 66 patients; and 5 years, 42 patients). A Sonos 1500, 2500, or 5500 ultrasound system (Hewlett-Packard) was used.

Measurements performed from the echocardiograms included transvalvular flow velocity for the aortic valve with use of continuous-wave Doppler, left ventricular outflow tract (LVOT) flow velocity with use of pulsed-wave Doppler, and LVOT diameter, as previously described.⁸ The flow velocity across the pulmonary valve was measured by continuous-wave Doppler in the left parasternal short-axis view. From these measurements, the peak and mean transvalvular pressure gradients of the aortic and pulmonary valves were calculated by use of the modified Bernoulli equation, and the left ventricular stroke volume was calculated from the product of the
LVOT velocity-time integral and LVOT cross-sectional area. The valve effective orifice areas (EOAs) were determined by the standard continuity equation with use of the LVOT stroke volume for the calculation of both the aortic and pulmonary valve EOAs. Color flow Doppler was used to detect aortic and pulmonary valvular regurgitation, and severity was subjectively graded as trivial (0.5/4), mild (1/4), moderate (2/4), moderately severe (3/4), and severe (4/4). Pulmonary valve EOA was not calculated when there was pulmonary or aortic valve regurgitation.

Data and Statistical Analysis

Data are presented as mean±SD and were compared by ANOVA for repeated measures to evaluate the effect of time since the operation. 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 by using a curve-fitting software (Table Curve 4.0, SPSS Inc). Values of P<0.05 were considered significant.

A forward stepwise regression analysis was performed to identify factors that significantly influenced the valve EOA of the pulmonary homograft. The relevant variables tested for this analysis were as follows: patient age, sex, and body surface area; homograft size; age and sex of the homograft donor; year of surgery; risk factors at the time of operation (systemic hypertension, pulmonary hypertension, smoking, hyperlipidemia, obesity, and chronic renal insufficiency); and concomitant coronary artery disease.

Results

Pulmonary Autograft Function

Regarding the pulmonary autograft implanted in the aortic position, 39.2% to 53.6% of the patients had mild (1/4) aortic regurgitation depending on the follow-up interval (Figure 1A). Three percent of the patients had moderate (2/4) regurgitation early after surgery, and this proportion increased with time (14.3% at 5 years). Indeed, the severity of regurgitation progressed from 0.5/4 or 1/4 to 2/4 during follow-up in 8 patients. One patient with an autograft implanted as a valve replacement had moderately severe (3/4) regurgitation early after surgery, which regressed to 1/4 thereafter. One patient with an autograft implanted as a root replacement had 2/4 regurgitation at discharge, which progressed to 3/4 regurgitation 1 year after surgery. This patient became symptomatic and was subjected to further surgery. Overall, there was no significant difference in the incidence and severity of regurgitation between autografts implanted with use of the root replacement technique and those implanted with use of the valve replacement technique.

Early after surgery, the average EOA of the aortic valve substitute was close to 3.00 cm², which is very similar to that of normal native aortic valves (Figure 2A). Thereafter, the valve EOAs of the aortic valve remained stable, resulting in low mean gradients at all follow-up intervals (Figure 2B). There was no significant difference between the average valve EOAs of the autografts implanted with use of the root replacement technique (1 year, 3.19±0.85 cm²; 5 years, 2.87±0.91 cm²) and the average valve EOAs of the autografts implanted with use of the valve replacement technique (1 year, 3.12±1.04 cm²; 5 years, 2.94±1.02 cm²).
Figure 3A shows the relationship between the mean gradients measured 1 year after surgery and the aortic valve EOAs indexed for body surface area for data from the patients who underwent the Ross operation compared with previously published data from 51 patients with a stented bioprosthesis, 85 patients with a stentless bioprosthesis, and 10 normal healthy control subjects also studied in our laboratory.8 As can be seen, the patient data fall on different sections of the same exponential curve depending on the type of aortic valve substitute they received. Hence, the majority (70.6%) of the subjects with a stented bioprosthesis have values suggestive of patient-prosthesis mismatch (indexed EOA $\leq 0.85$ cm$^2$/m$^2$)8–11; therefore, their values appear on the steeper portion of the curve with relatively high gradients. In contrast, most patients (71.8%) with a stentless bioprosthesis, all Ross patients except 1, and all control subjects had an indexed EOA $>0.85$ cm$^2$/m$^2$, and their values are on the flatter portion of the curve with relatively low gradients.

Pulmonary Homograft Function
The homografts implanted in the pulmonary position showed a low incidence (<10.5%) of moderate (2/4) regurgitation, and none had moderately severe (3/4) or severe (4/4) regurgitation (Figure 1B).

The pulmonary valve EOAs were, on average, similar to normal early after surgery but progressively decreased there-
eration at the level of the proximal anastomosis, whereas in the 2 others, it corresponded to sclerotic thickening and/or calcifications at the valvular level. In all cases, the impression was that this could be due to a rejection phenomenon.

A forward stepwise regression analysis was performed to identify the preoperative and operative factors that are associated with postoperative pulmonary valve EOA. In univariate analysis, the patient’s body surface area ($P=0.03$), homograft size ($P=0.009$), and preoperative history of systemic hypertension ($P=0.02$) correlated with the pulmonary valve EOA measured 1 year after surgery. In multivariate analysis, homograft size ($P=0.01$) and history of systemic hypertension ($P=0.03$) were the only independent factors associated with pulmonary valve EOA at 1 year. The pulmonary valve EOA increased with increasing homograft size and with history of systemic hypertension. No preoperative or operative factor was found to be associated with pulmonary valve EOA measured early after surgery.

**Discussion**

**Comparison With Previous Studies**

Previous Doppler echocardiographic studies of patients undergoing the Ross procedure were performed in smaller series (24 to 87 patients), and in most cases, only the gradients and not the EOAs were reported, and the data for the pulmonary homograft were not available. Current recommendations clearly suggest that aortic (and, by extension, pulmonary) valve hemodynamics should be evaluated by reporting both transvalvular gradients and EOAs, because EOAs are much less flow dependent and more accurately reflect the intrinsic degree of stenosis, if any. Moreover, previous studies in patients with aortic bioprostheses have shown that the indexed EOA can be used to determine whether there is any degree of patient-prosthesis mismatch, and it is also the parameter that most accurately predicts postoperative gradients both at rest and during maximal exercise.

**Pulmonary Autograft Function**

As in previous studies, the present study confirms the excellent hemodynamic performance of the pulmonary autografts after the Ross operation; the gradients and EOAs for this valve are, in fact, very similar to normal. The prevalence and severity of aortic regurgitation found in the present study are also low and similar to those reported by Elkins et al and Daenen et al but somewhat higher than those reported by Kouchoukos et al. This could be due to the fact that Kouchoukos et al used different numerical grades to assess the regurgitation severity (0/3 [no regurgitation] to 3/3 [severe regurgitation]). Furthermore, it must be emphasized that amounts of regurgitation ≤2/4 are generally subclinical.

**Pulmonary Homograft Function**

Relatively high gradients at the level of the pulmonary homografts in some patients have previously been reported; in these studies, the incidences for peak gradients >20 to 25 mm Hg were 16% to 26%, whereas they were 4% to 5% for peak gradients >40 to 50 mm Hg.

The present study confirms these findings, but more important, it demonstrates that the suboptimal hemodynamics observed in some patients at the level of the pulmonary homograft are not present immediately after operation but appear progressively during the first year after surgery. Given that this deterioration occurs relatively late after surgery, this finding would suggest that it is probably not due to any immediate technical problem during surgery or to any degree of patient-prosthesis mismatch at the time of surgery.

That the deterioration would affect only selected patients is somewhat puzzling. Previous studies have postulated that this phenomenon might be due to an immunologic reaction resulting in fibrocalcification and a stenotic process generally located in the vicinity of the proximal or distal anastomosis. Indeed, the findings in our explanted valves tend to support this hypothesis.

Previous studies have identified the following as independent predictors of homograft failure in the pulmonary position: young age (<4 years) at surgery, smaller homograft size, use of aortic instead of pulmonary homograft, earlier operative year, and longer aortic cross-clamp time. In the present study, a smaller homograft size was also found to be associated with greater mortality in children undergoing right ventricular outflow tract reconstruction with a pulmonary homograft. In the present study, a smaller homograft size was found to be associated with smaller pulmonary valve EOA 1 year after surgery. These findings could suggest that smaller homografts are more prone to deterioration or that a similar degree of deterioration in a larger homograft does not result in any significant stenosis, given that there remains a relatively large EOA and that the relationship between gradients and indexed EOAs is exponential with significant gradients occurring only below a certain threshold (Figure 3). Our multivariate analysis also showed that systemic hypertension was associated with greater pulmonary valve EOA, a finding that is both surprising and intriguing. Further studies are necessary to confirm this result as well as to elucidate the underlying pathophysiological mechanism, if any.

**Use of Indexed EOA to Predict Gradients**

The results in Figure 3 further confirm that the indexed EOA is by far the best predictor of postoperative transvalvular gradients in the aortic position regardless of the type of valve substitute being used. Also, the results demonstrate that the pulmonary valve is governed by the same hemodynamic principles as the aortic valve, with a similar relationship between gradients and indexed EOAs being found and the value of 0.85 cm$^2$/m$^2$ appearing to be a threshold for the appearance of higher gradients.

**Clinical Implications**

When present, the stenotic deterioration of the pulmonary homograft appears to stabilize 1 year after surgery in most patients. However, it may progress, as evidenced by our 3 patients who were subsequently subjected to further surgery for severe stenosis. Therefore, patients with early evidence of homograft stenosis should be monitored closely for this valve.
tolerated when the peak gradient is $<50$ mm Hg.\(^\text{16}\) Hence, further surgery should probably be considered only if the patient becomes symptomatic or if the gradient continues to progress and/or there is evidence of right ventricular dysfunction.

The results of the present study also suggest that there are probably advantages to implanting the largest possible homograft in relation to body surface area to avoid pulmonary homograft stenosis. However, this will not necessarily prevent the appearance of stenosis in all cases, and future research in this area is certainly necessary. Some investigators have proposed the use of anti-inflammatory or immunosuppressive therapy,\(^\text{22}\) but as of yet, the benefits of this treatment have not been proven. Recently, Couetil et al\(^\text{21}\) have proposed a new approach consisting of direct anastomosis between the remaining pulmonary artery trunk and the infundibulum and the creation of a monocusp tailored from the anterior pulmonary artery wall as means of reconstructing the pulmonary valve, but the advantages of this approach remain to be demonstrated.

**Conclusion**

This midterm Doppler echocardiographic study shows that the Ross operation provides continued excellent hemodynamics in the aortic position, and from a hemodynamic standpoint, it is possibly the ideal operation for this valve. However, the results also show a progressive deterioration of the pulmonary valve during the first 6 months after surgery in up to 19% of the patients. This deterioration usually stabilizes after 1 year, but it progressed to the extent that 3 of our 132 patients had to be subjected to further surgery for progressively severe pulmonary stenosis. Future improvement of the Ross procedure should be oriented toward the search for new methods to prevent the deterioration of the pulmonary homografts. Given the rate of subsequent surgery and the progressive appearance of moderate valvular regurgitations, longer term studies are also needed to determine the relative benefits of this procedure compared with a standard aortic valve replacement.

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**References**

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