Ross Procedure in Infants and Toddlers Followed Into Childhood

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Background—The Ross procedure is commonly used to treat aortic valve disease in pediatric and adult patients. For infants, data are limited regarding survival, reintervention, autograft growth, and function.

Methods and Results—The Ross procedure was performed in 27 infants <18 months of age (median age 5.7 months). All patients had congenital aortic stenosis (AS); associated lesions included subAS (n=9), supravalvular AS (n=2), coarctation (n=5), and interrupted aortic arch (n=2). Median follow-up was 6.1 years (range 0.2 to 12.9). There were 3 early deaths and no late deaths. Freedom from reintervention for homograft dysfunction was 87% at 8 years; freedom from autograft reintervention was 100%. Follow-up echocardiograms were available in 17 patients. Estimated peak autograft gradient was 55 mm Hg in one patient and <10 mm Hg in 16. Mild autograft insufficiency was seen in 4 patients; 13 had none. Autograft diameter was measured early postoperatively and at latest follow-up. The mean z score increased from 0.63 to 3.2 (P<0.01) at the annulus and from 0.26 to 2.2 (P<0.01) at the sinus. In a subgroup, the mean autograft z score increased significantly from the postoperative period to 1 year for both the annulus (0.72 to 3.2, P<0.01) and the sinus (0.26 to 2.2, P<0.01), but remained unchanged thereafter.

Conclusions—The Ross procedure effectively relieves AS in infants. Homograft reintervention occurred in 13% within 8 years. No patient developed significant autograft insufficiency or required autograft reintervention during the follow-up period. Dilatation of the autograft occurred during the first year after surgery and stabilized thereafter. (Circulation. 2005;112[suppl I]:I-390–I-395.)

Key Words: surgery ■ heart defects, congenital ■ pediatrics ■ aorta ■ valves

In recent years, the Ross procedure, which is replacement of the aortic valve with a pulmonary autograft, has been used for the treatment of aortic valve disease.1 Whereas outcomes after the Ross procedure in adults and older children are well described,2 experience in the infant population is not well characterized. In contrast to older patients, infants are often more critically ill, and almost all undergo the Ross procedure after failing prior interventions for congenital aortic stenosis; aortic insufficiency (AI) is a less common indication. Furthermore, infants are more likely to present with more complex left ventricular disease and other associated congenital anomalies.

The Ross procedure has a number of advantages for infants. The pulmonary autograft can be sized appropriately, is not prone to calcification, and has growth potential.3 The patients do not require anticoagulation therapy, which may be difficult to adjust in small infants. Short-term outcomes have been reported for these patients, but information regarding intermediate or long-term follow-up in the infant population is limited.4,5 Questions remain regarding the function of the homograft and autograft and the need for reintervention. Dilatation of the autograft and the development of autograft insufficiency have been reported in older age groups.6 This observation also warrants further investigation in the infant population.

Study Design

All infants <18 months of age who underwent the Ross procedure at the Children’s Hospital of New York Presbyterian or the Cardiothoracic Centre of Monaco between May, 1991, and July, 2004, were included in this retrospective series. Institutional Review Board approval was obtained. Medical records were reviewed for preoperative patient characteristics including age, body surface area, sex, original diagnosis, and prior interventions. The indication for the Ross procedure was recorded. Operative variables included additional procedures performed, size and type of homograft, bypass time, and cross clamp time. Postoperative data included length of hospital stay, the need for reintervention, and the occurrence of conduction abnormalities or neurological complications. Follow-up data on all survivors, including the need for reintervention, were obtained from primary cardiologists.

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Echocardiographic Analysis
Echocardiograms conducted before surgery, early postoperatively (11±9 days), at 1 year ±3 months postoperatively, and at latest follow-up (5.5±3.4 years) were reviewed by a single cardiologist blinded to the time point of study. The diameters of the pulmonary annulus and the native aortic annulus were measured on all preoperative studies for quantitative comparison. Qualitative assessment of left ventricular function and results of continuous wave Doppler analysis of the right ventricular outflow tract (RVOT) and left ventricular outflow tract (LVOT) were recorded from postoperative studies. Autograft insufficiency was qualitatively graded by color Doppler using a scale of 0 (none) to 4 (severe). Postoperative serial autograft measurements were obtained at the levels of the annulus and sinus (Figure 1). The diameter of the autograft annulus was measured at the hinge points of the valve leaflets. The sinus was measured at the largest diameter distal to the valve. All measurements were made off-line in systole, and an average of 3 measurements was used. We calculated \( z \) scores for autograft values on the basis of expected normal aortic dimensions for body surface area.

Surgical Technique
The Ross procedure was performed using the root replacement technique. No rings, pledgets, or other reinforcements were used. The proximal suture line was extended below the native aortic annulus to take advantage of the natural support structure of the LVOT. When necessary, additional surgical procedures, such as a modified Konno procedure, were performed. The Konno technique in this infant population consisted of a vertical, full thickness incision in the interventricular septum oriented to the left of the papillary muscle of the conus. This was done after removal of the autograft. In addition, resection of fibrous muscular tissue from the LVOT was performed if indicated. All patients received antegrade cold blood cardioplegia delivered directly into the coronary arteries every 30 minutes as needed. The last dose is given in the aorta after completion of the aortic root reconstruction to check for bleeding and autograft competence.

Statistical Analysis
Values were characterized as mean ±1 standard deviation for continuous variables and as count and percent frequency for categorical variables. Using the follow-up data, Kaplan Meier estimates of freedom from reintervention were computed for the homograft and autograft. Autograft annulus and sinus dimensions were converted to \( z \) scores using normal aortic values. In a subgroup of patients with available echocardiograms, serial \( z \) scores early, 1-year postoperatively, and at latest follow-up were compared by paired Student’s \( t \) test. A probability value <0.05 was considered significant for all analyses.

Results
Patient Characteristics
All 27 infants <18 months of age who underwent the Ross procedure during the study period at 2 institutions were included; 20 from the Children’s Hospital of New York and 7 from the Cardiothoracic Centre of Monaco. Six patients were female and 21 were male. The median age at surgery was 5.7 months, with a range of 14 days to 17 months. Median weight was 5.5 kg and ranged from 3 kg to 10 kg. The primary diagnosis was isolated valvular aortic stenosis (AS) in 10 patients, all of whom had undergone an intervention before the Ross procedure. In addition to aortic valvular stenosis or annular hypoplasia, complex left-sided disease was present in 17 patients (Table 1).

Follow-up survival and reintervention data were available in the 24 surviving patients. Median follow-up was 6.1 years, with a range of 2.6 months to 12.9 years. Follow-up echocardiographic data were available for review in 17 of the 24 survivors. The median time of echocardiographic follow-up was 4.9 years, with a range of 0.8 to 12.9 years.

Prior Interventions
Before the Ross procedure, 26 of 27 patients underwent one or more interventions (Table 2). A primary Ross procedure was carried out in 1 patient with severe valvular and supravalvular AS. Aortic balloon valvuloplasty was performed in 15 patients; 1 patient subsequently underwent open surgical valvotomy. Eleven patients had undergone a surgical procedure before the Ross procedure: Surgical aortic valvotomy was performed in 10 patients, and 1 patient had an isolated coarctation repair. One patient underwent balloon dilatation of a recoarctation in the catheterization laboratory after surgical coarctation repair.
TABLE 2. Prior Interventions

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>11 (40%)</td>
</tr>
<tr>
<td>Valvotomy</td>
<td>10</td>
</tr>
<tr>
<td>Coarctation repair</td>
<td>5</td>
</tr>
<tr>
<td>Ventricular septal defect closure</td>
<td>3</td>
</tr>
<tr>
<td>Interrupted arch repair</td>
<td>2</td>
</tr>
<tr>
<td>Catheterization</td>
<td>16 (59%)</td>
</tr>
<tr>
<td>Balloon valvuloplasty</td>
<td>15</td>
</tr>
<tr>
<td>Balloon dilation recoarctation</td>
<td>1</td>
</tr>
</tbody>
</table>

n=26 of 27.

Indications for the Ross Procedure

Indications at the time of the Ross procedure are shown in Table 3. Mixed aortic valve disease was present in 11 patients after prior interventions. In addition to valvular AS, 8 patients had multiple levels of residual LVOT obstruction. Of the 4 patients with significant AI, 3 had balloon valvuloplasties and 1 had undergone a surgical valvotomy and resection of subaortic stenosis.

Operative Course

At the time of the Ross procedure, 20 patients required a concurrent surgical procedure (Table 4). In addition to the 3 patients with primary mitral valve anomalies, 1 patient developed subendocardial ischemia with severe mitral regurgitation due to persistent severe LVOT obstruction before surgery. A Konno modification to relieve subaortic obstruction was necessary in 20 (74%) of the 27 patients. Replacement of the native pulmonary valve was accomplished with a pulmonary homograft in 15 patients, an aortic homograft in 10 patients, and a porcine heterograft in 2 patients. Homograft size ranged from 9 mm to 20 mm. Mean cardiopulmonary bypass time was 178±34 minutes, and mean cross-clamp time was 122±24 minutes. Median length of hospital stay was 10 days, with a range of 7 to 111 days.

Mortality

There were 3 deaths within 1 day of the Ross procedure. A 1-month-old child had right ventricular infarction and died on postoperative day 1. Transfer of the right coronary artery was technically difficult in this patient because of the large discrepancy in size between the small native aorta and the much larger pulmonary autograft. A patient with complex LVOT obstruction and severe pulmonary hypertension died after homograft rupture. The third patient experienced cardiopulmonary arrest secondary to bilateral tension pneumothoraces immediately after surgery and was unable to be resuscitated. There were no deaths during the follow-up period.

TABLE 3. Indications for the Ross Procedure

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
</tr>
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<tbody>
<tr>
<td>AS/Al</td>
<td>11</td>
</tr>
<tr>
<td>Complex LVOTO</td>
<td>8</td>
</tr>
<tr>
<td>AI</td>
<td>4</td>
</tr>
<tr>
<td>AS</td>
<td>4</td>
</tr>
</tbody>
</table>

TABLE 4. Concurrent Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Konno</td>
<td>20</td>
</tr>
<tr>
<td>Mitral Valve repair</td>
<td>4</td>
</tr>
<tr>
<td>Ventricular septal defect closure</td>
<td>2</td>
</tr>
<tr>
<td>Atrial septal defect closure</td>
<td>2</td>
</tr>
<tr>
<td>Patent ductus arteriosus ligation</td>
<td>2</td>
</tr>
<tr>
<td>Aortic arch repair</td>
<td>1</td>
</tr>
</tbody>
</table>

n=20.

Morbidity

No patient required reoperation in the immediate postoperative period. One patient had clinical seizure activity noted within 24 hours postoperatively and was treated with phenobarbital. At 4 months of age, the patient had a normal neurological examination and the medication was discontinued. Complete heart block occurred in 3 patients in the immediate postoperative period. One patient required a permanent pacemaker, 1 patient died secondary to bilateral pneumothoraces, and 1 patient regained normal sinus rhythm. Transient second-degree atrioventricular block was seen in 1 patient.

Preoperative Dimensions

Preoperative echocardiographic data were analyzed in 14 patients. There was a significant difference between the size of the native aortic annulus and the native pulmonary annulus at the time of the Ross procedure. The mean pulmonary annulus diameter (1.0±0.2 cm, range 0.66 to 1.19) was greater than the mean aortic annulus diameter (0.7±0.2 cm, range 0.37 to 1.21, P<0.01), with a mean pulmonary annulus z score of 1 and a mean aortic annulus z score of −2. The median difference in annulus diameter was 43%, with a maximum difference of 55%.

Follow-Up

Homograft

Homograft reintervention was performed in a total of 4 patients, 3 for obstruction and 1 for insufficiency. One patient had surgical replacement of an 11-mm pulmonary homograft with a valved conduit 9 years postoperatively because of severe pulmonary insufficiency. Two patients with significant homograft obstruction underwent surgical replacement of porcine heterografts with pulmonary homografts at 13 months and 4.5 years after the Ross procedure. Of note, porcine heterografts are no longer used for RVOT reconstruction. One patient who had a 15-mm pulmonary homograft placed at 7 months of age underwent stent placement for relief of homograft obstruction 10 years postoperatively. Overall freedom from homograft reintervention was 87% at 8 years (Figure 2).

In the group of 17 patients with follow-up echocardiograms, 15 did not require homograft reintervention. Continuous wave Doppler estimated peak gradients across the RVOT were <20 mm Hg in 3 patients, 20 to 40 mm Hg in 6 patients, and >40 to 55 mm Hg in 6 patients. Of the 6 patients with RVOT gradients of >40 to 55 mm Hg, 3 had received aortic homografts and 3 had received pulmonary homografts.
In the 2 patients who underwent homograft replacement for obstruction, the estimated peak gradient across the RVOT was 100 mm Hg and 50 mm Hg before reoperation.

**Autograft**

No patient required reintervention for the autograft during the follow-up period. Echocardiographic evaluation of the autograft was carried out in 17 patients. All 17 patients had qualitatively normal left ventricular function at latest follow-up. Autograft insufficiency was mild in 4 patients; 13 patients had no autograft insufficiency. Continuous wave Doppler analysis of the LVOT revealed a peak estimated Doppler gradient of 10 mm Hg in 16 patients. One patient who underwent a Ross procedure with Konno modification for AS/subAS developed an LVOT gradient of 56 mm Hg related to a fibromuscular ridge in the subaortic area that has remained stable from 1 to 3.2 years postoperatively.

**Autograft Diameter**

The autograft was no more than mildly dilated (z score <3) in 16 of 17 patients at the annulus and in 15 of 17 patients at the sinus within the first month after the Ross procedure. The z score of both the autograft annulus and sinus diameter significantly increased from the early to the latest follow-up (Figure 3). The autograft annulus mean z score rose from 0.63 to 3.2 (P<0.01) and the autograft sinus mean z score rose from 0.26 to 2.5 (P<0.01). In a subset of patients, echocardiograms were available 1 year ±3 months postoperatively. Figure 4 and Figure 5 demonstrate the change in individual z score values for the autograft annulus and sinus early, at 1 year, and at latest follow-up. For both the autograft annulus and autograft sinus, the z score significantly increased within the first year postoperatively, but no significant change in the autograft annulus or sinus z score was noted from 1 year after surgery to latest follow-up. In this subgroup of 8 patients, the aortic valve anatomy was bicuspid in 5, tricuspid in 2, and unknown in 1. The original lesion was AS in 7 and AS/subAS in 1, whereas the indication for the Ross procedure was AS in 2, AI in 2, and AS/AI in 4. All 8 patients underwent a Ross procedure with Konno modification.

**Discussion**

The Ross procedure has been carried out in older children and adults with low mortality. In a study of 86 children (mean age 11 years) after Ross procedure, Elkins et al\(^3\) reported an early mortality rate of 3.5%. Marino et al\(^8\) reported an early mortality rate of 1.5% in a cohort of 66 patients (mean age 10.8 years) after the Ross procedure. Infants most often have a different substrate of disease than older patients. In the series of infants undergoing the Ross procedure reported here, there was a high incidence of complex lesions involving multiple levels of left ventricular obstruction and associated lesions. The Ross procedure was performed after one or more prior interventions to relieve obstruction in the majority of patients; primary AI was not the indication for the operation. There were 3 deaths among the 27 infants in this series, and there was no late mortality. Solymar et al\(^4\) reported 1 late death in a cohort of 8 infants undergoing the Ross procedure, and Ohye et al\(^5\) reported no deaths in a cohort of 10 infants. Despite increased complexity, size issues, and the necessity for more extensive surgery, it appears that in experienced
hands, infant mortality for the Ross operation is similar to reported results for older patients.

Morbidity in this series included complete heart block that was permanent in 1 infant. Marino et al\(^8\) reported transient complete heart block in 4 older patients, none of whom required a permanent pacemaker. Complete heart block requiring a permanent pacemaker was reported by Pessotto et al\(^9\) in 1 patient (0.9%) in a cohort of 111 patients (median age 15.7 years) after the Ross procedure. Both Ohye et al and Marino et al each reported the use of extracorporeal membrane oxygenation in 1 infant.\(^5\)\(^8\) No patient in our analysis required extracorporeal membrane oxygenation. Ohye et al\(^5\) reported seizures in 2 infants after the Ross procedure (20%). One infant (4%) in our study had a postoperative seizure. Marino et al\(^8\) reported additional morbidities including perioperative ventricular tachycardia in 18 patients (27.2%) requiring discharge on antiarrhythmic medication, and reoperation for bleeding in 3 patients. Neither of these complications was noted in the present study.

Elkins et al\(^3\) reported that 1 patient of 86 required a reoperation for homograft stenosis during a mean follow-up period of 30 months after the Ross procedure. Pessotto et al\(^9\) reported that 2.7% of patients required reintervention for the homograft at a median of 29 months after the Ross procedure. Similar to the incidence in older patients, freedom from reintervention for homograft dysfunction in this infant study was 87% at 8 years; Ohye et al\(^5\) demonstrated a freedom from reintervention of 75\(\pm\)15% at 4 years, and Solymar et al\(^4\) did not report reinterventions for the homograft in their study group of 8 infants during the median follow-up period of 4.9 years. Reoperation for the homograft in the infant population might be expected to occur more frequently than in older populations because of size limitations at the time of surgery; however, the impact of smaller conduits on reoperation in infants may not be important until later in childhood or adolescence.

In this series, there was no more than mild dilatation of the autograft observed within 1 month postoperatively in the majority of patients (94% at the annulus, 88% at the sinus), whereas studies in older children and adults after the Ross procedure have shown dilatation of the annulus and/or sinus immediately after surgery.\(^10,11\) It is possible that early autograft dilatation does not occur in the infant population because of the exposure of the pulmonary valve to high pulmonary vascular resistance. Carr-White\(^12\) et al demonstrated that the pulmonary autografts of patients with higher preoperative pulmonary arterial pressures had more ordered elastic fibers (less elastin fragmentation) and hypothesized that this may be protective against dilatation after the Ross procedure. The pulmonary autograft in infants may therefore be more suited than older autografts to handle the immediate increase in pressure from the systemic vascular bed.

In our study population, autograft dilatation occurred within the first year postoperatively, with a mean \(z\) score at 1 year of 3.2 for the annulus and 2.2 for the sinus, and further dilatation was not seen with longer follow-up. This pattern of early dilatation of the autograft followed by stabilization after the Ross procedure also was reported in 2 smaller series of infants.\(^5,5\)

Several reports on adults have shown significant dilatation of the autograft over time with subsequent development of autograft insufficiency,\(^6\) whereas others have demonstrated either no dilatation or mild dilatation without the development of autograft insufficiency.\(^12,13\) Reports in pediatric populations have also shown autograft dilatation without the development of significant autograft insufficiency.\(^11,14\) In the present infant series, no significant autograft insufficiency occurred despite evidence of autograft annulus and sinus dilatation. Solymar et al\(^4\) also showed no significant autograft insufficiency despite autograft sinus dilatation within the first year after the Ross procedure in an infant cohort (\(z\) score from 0.2 to 2.2). Others, however, have reported a few patients with significant autograft insufficiency occurring in children and infants after the Ross procedure. Elkins et al\(^3\) reported moderate autograft insufficiency in 2 of 23 children, with an increase in autograft annulus \(z\) score from \(-0.48\) to 1.3 late postoperatively. Ohye et al\(^5\) reported the development of significant autograft insufficiency in 2 of 10 infants who demonstrated dilatation of the sinotubular junction (mean change in \(z\) score 2.1), although neither patient required reintervention for the autograft during the follow-up period of 48 months. The explanation for the relative lack of severe autograft insufficiency after the Ross operation in infants may relate to differences in indications for the procedure. The infant population is unique from the older pediatric and adult populations because primary AI is a rare indication in this age group. As a result, in contrast to older patients, the aortic annulus is often not dilated at the time of the Ross procedure and no reduction in annulus size is needed.

Limitations of this study include the retrospective nature of data collection and the relatively small number of patients with echocardiograms available for study. In addition, the intermediate-term results reported here could change significantly as the patients reach late childhood and beyond.

This study demonstrates that the Ross procedure is an effective surgical technique for the relief of complex LVOT obstruction in the infant population. Reintervention for homograft dysfunction occurred in 4 of 27 patients. Autograft dilatation occurred within the first year after surgery and did
not progress during the median echocardiographic follow-up time of 4.9 years. No significant autograft insufficiency has developed. Continued monitoring of autograft diameter and neoaortic valve function is warranted to assess the future course of autograft dilatation.

Acknowledgments
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References
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