Mark G. Hazekamp
Heynric B. Grotenhuis
Paul H. Schoof
Marry E. Rijlaarsdam
Jaap Ottenkamp
Robert A.E. Dion

Results of the Ross operation in a Paediatric Population.
Chapter 8

Abstract

Purpose: To analyse the results of the mid-term clinical and echocardiographic follow-up of the pediatric Ross operation.

Materials and Methods: Echo-Doppler follow-up of 53 consecutive pediatric Ross procedures was performed between 1994 and 2003. Median age was 9.7 years at time of operation (2 weeks - 17.7 years). Six patients were younger than 3 months. Median age at follow-up was 15.6 years. Aortic valve/left ventricular outflow tract (LVOT) anomalies were congenital in 49 (92%). Seventy percent had previous surgery or balloon valvuoplasty. Root replacement was used in all. Thirteen patients (25%) had LVOT enlargement. Mean cross-clamp time was 113 (69 - 189) minutes.

Results: Early mortality occurred in 3 patients after emergency surgery following balloon failure (n = 1) and extended Ross following interrupted arch / VSD repair (n = 2). Late mortality was due to LV fibroelastosis in 2 patients and complicated pulmonary artery stenting in another. RVOT reoperations were required because of late homograft obstruction in 2 patients and because of pulmonary artery stenosis in another. Five patients (9.4%) were reoperated for pulmonary autograft dilatation (n = 3) and for leaflet fibrosis or perforation (n = 2). Autografts were repaired in two patients, while a mechanical valve was inserted in 3 cases. At 9 years the actuarial survival and event free survival were 89% and 74%, respectively. At last follow-up 90% of autograft diameters indexed to body surface area was above the 90th percentile of normal aortic root diameters. LVOT and RVOT gradients were low and autograft insufficiency was trivial to mild in 84% and mild to moderate in 16%. Autograft stenosis was not noticed.

Conclusion: The pediatric Ross procedure remains an important tool but autograft dilatation also occurs in the pediatric population. The significance of this finding has yet to be determined.
Introduction

The use of the pulmonary autograft was first reported in 1967 by Ross for the treatment of aortic valve disease in adults (1). Since that time, the Ross procedure has been increasingly applied to the pediatric population, including neonates and infants (2-6). Several advantages of the pulmonary autograft are of benefit for both the adult and pediatric patient group: the high rates of freedom of reoperation and the lack of need for anticoagulation (2-6). Especially for the pediatric population there are additional beneficial effects, like the potential for growth of the autograft and the ready availability of an inherently proper sized pulmonary autograft (2,3,5-9). However, pulmonary autograft growth and dilatation cannot be easily distinguished from each other and several reports indicate that both dilatation and growth occur in the growing subject (10). Despite conflicting reports about autograft dilatation causing aortic insufficiency, excess dilatation necessitating reoperation is one of the main concerns following the Ross operation (3-8).

We have reviewed our consecutive Ross operations in all patients younger than 18 year with an emphasis on maximal pulmonary autograft diameters in relation to body surface. Part of our experience has been described previously (11).

Material and methods

Patient population

From February 1994 to March 2003, 53 consecutive Ross procedures have been performed in patients younger than 18 years in our institution. The preoperative indication for the Ross procedure was aortic stenosis (AS) in 12 patients (23%), aortic regurgitation (AR) in 14 patients (26%) and a combination in 27 patients (51%). The underlying left ventricular outflow tract (LVOT) pathology was congenital in 48 patients (90%) while 3 patients had a pulmonary autograft procedure as a consequence of rheumatic heart disease and 2 following endocarditis of the aortic valve (AV). Bicuspid aortic valve was present in 64% of all cases. Median age at operation was 9.7 years (range: 2 weeks - 17.7 years), with a mean age of 9.15 ± 5.07 years. Six patients were operated at an age of 3 months or less. Forty-six patients were male (87%).

Thirty-seven patients (70%) had undergone surgery or percutaneous intervention(s) prior to the Ross procedure (Table 1). Of this group 11 patients (20%) had undergone more than one procedure prior to the pulmonary autograft procedure.
Informed consent was obtained from all included patients, with approval of the institutional ethics committee.

Table 1. Previous interventions.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon dilatation</td>
<td>11</td>
</tr>
<tr>
<td>Aortic valvotomy</td>
<td>15</td>
</tr>
<tr>
<td>Resection subaortic stenosis</td>
<td>13</td>
</tr>
<tr>
<td>Aortic valve repair</td>
<td>3</td>
</tr>
<tr>
<td>VSD closure</td>
<td>8</td>
</tr>
<tr>
<td>Coarctation or interrupted arch repair</td>
<td>9</td>
</tr>
<tr>
<td>Arterial switch operation</td>
<td>1</td>
</tr>
</tbody>
</table>

**Operative technique**

In all patients the pulmonary autograft was implanted using the root replacement technique. Reinforcement of proximal and distal suture lines with a strip of autologous pericardium was used in most patients. Continuous sutures were used in all. In all cases cardiopulmonary bypass with moderate hypothermia was used. Autograft harvesting was usually performed after aortic cross-clamping and antegrade administration of St Thomas cardioplegic solution. The mean cross-clamp time was 113 min (range: 69 - 189 min). Right ventricular outflow tract (RVOT) reconstruction was performed with cryopreserved pulmonary homografts (n = 47; mean diameter 22 mm), cryopreserved aortic homografts (n = 3; mean diameter 15 mm) or Contegra bovine jugular vein grafts (Medtronic Inc., USA) (n = 3; mean diameter 15 mm). The distal RVOT suture line was usually done during myocardial arrest while the proximal suture lines were performed on beating heart.

In 13 patients (25%) the aortic annular or LVOT diameter was considered as being too small and annular enlargement was performed in association with septal muscle myectomy and/or resection of subaortic fibrous tissue. In 3 of these 13 patients the LVOT was further enlarged by septal patch insertion (Ross-Konno procedure).

Associated procedures during the Ross operation were enucleation or resection of a discrete subaortic stenosis in 8 patients, ventricular septal defect (VSD) closure in 2 patients and mitral valve replacement in 1 patient. One patient with a VSD and aortic insufficiency repaired has previously been described elsewhere (12).
Follow-up
Follow-up was performed by analysis of operative reports, patient records and echo-Doppler studies at last follow-up. Body weight and height data at the time of last follow-up were collected and used to determine body surface area (BSA expressed in m²). The maximal diameter of the pulmonary autograft at sinus of Valsalva (SOV) level obtained by echocardiography was noted at the same last visit. Maximal autograft diameters were indexed for BSA and compared to normal values for aortic SOV diameters in relation to body surface area and age, as indexed by Roman (13). The degrees of pulmonary autograft and RVOT conduit insufficiency were indexed as being trivial, mild, moderate or severe. Gradients over the LVOT and RVOT were expressed in maximal Doppler gradients (mm Hg).

Of the 47 surviving patients 5 were lost to follow-up. Four of these patients came from non-European countries. With the exception of these 5 patients, recent follow-up data were available in all other patients.

Statistical analysis
Statistical analysis was performed with the use of SPSS-11. Descriptive statistics are expressed as median and range. Means are provided with standard deviations. Unpaired student t-test was used for comparison of unpaired data. P < 0.05 was considered to indicate statistically significant difference. The Kaplan-Meyer method was used to determine event-free survival curves.

Results

Postoperative complications
In the postoperative period 5 patients required a resternotomy for bleeding, while late pericardial effusions needed drainage in 3 patients. Complete heart block requiring pacemaker implantation occurred in 2 patients.

Early mortality
Early mortality occurred in 3 patients (5.6%) at the age of 1, 2 and 4 months. One neonate with critical valvular AS developed massive AR directly after balloon dilatation and underwent a Ross procedure on an emergency basis. This patient died in the intensive care unit as a result of multiple organ failure. Two other infants had been referred with LVOT obstruction following previous repair of interrupted aortic arch and VSD, 1 and 3 months before the Ross operation. One of them died as a result of preoperative poor left ventricular (LV) function. The other patient developed myocardial ischemia related to the coronary artery reimplantation and died early.
Chapter 8

Late mortality

Three patients died 13 months, 5 and 6 years after the Ross operation (5.6%). One patient with valvular AS received a Ross procedure at the age of 2.5 months following a failed attempt of balloon dilatation. Severe pulmonary hypertension persisted after surgery and this patient died 13 months later. A second patient received a Ross procedure at the age of 7 years but suddenly died at 5 years of follow-up. Pulmonary hypertension had been diagnosed in this patient several years postoperatively. In these 2 patients autopsy showed severe LV endocardial fibroelastosis. LV dimensions were within normal limits at the time of the Ross procedure. A third patient had a Ross operation at the age of 16 years. Pulmonary artery patch augmentation was performed after one year to relief distal RVOT homograft stenosis. Complications of stent placement for recurrent RVOT obstruction subsequently led to mortality 6 years after the Ross procedure.

Reoperation

A total of 8 patients required reoperation. Five patients (9.4%) were reoperated for insufficiency and/or dilatation of the pulmonary autograft. Two patients were reoperated for valvular failure of the pulmonary autograft. One patient presented with a valvular insufficiency 3 years after the Ross procedure: at reoperation a delineated perforation near the hinge of the right coronary autograft cusp was observed and subsequently repaired with an autologous pericardial patch. A second patient returned with fibrosis and shortening of one of the autograft leaflets 2 years after the Ross procedure. In this patient who had undergone an arterial switch operation in the past, an insufficient aortic valve had been replaced by the pulmonary autograft that in fact was the aortic valve before the arterial switch operation (14). At reoperation the autograft was replaced by a mechanical prosthesis.

Autograft dilatation with mild to severe AR led to reoperation in 3 patients. Maximal autograft diameter (at sinus Valsalva level) was 63 mm in one patient. This patient underwent a Bentall procedure with insertion of a mechanical valve prosthesis. Mechanical valve replacement was performed in a second patient and valve sparing root remodelling was done in the third patient. The age at the time of the Ross procedure had been 5.5, 3 and 6 years, respectively.

Three patients were reoperated for right-sided homograft obstruction. Two homografts were replaced 5 and 8 years after the Ross operation (Ross performed at the age of 1 month and 4.8 years, respectively). In a third patient distal homograft obstruction required patch enlargement 1 year after the Ross procedure.

Midterm survival

Kaplan-Meyer analysis showed a survival and event free survival rate of 89 and 74% at 9 years of follow-up, respectively (Figure 1).
Results of the Ross operation in a paediatric population

Figure 1. Survival and event free survival.

Functional status
The mean follow-up was 5.5 years (range: 0.9 - 8.2 years). At last follow-up all survivors were in New York Heart Association class I, without using medication.

Autograft function
Maximal autograft diameters (at sinus level) were indexed to body surface area (m²) and compared to normal values for aortic root diameters in infants, children and young adults (Figure 2). At last follow-up 90% of autograft diameters indexed to body surface area was above the 90th percentile of normal aortic root diameters. Median diameter was 37 mm (range: 22 - 45 mm). Bicuspid aortic valve vs tricuspid valve showed no significant difference for risk of developing aortic root dilatation (P = 0.218).

Figure 2. Autograft diameter vs body surface area.
In all patients mean LVOT gradients were less than 5 mm Hg, including all patients with an extended Ross or Ross-Konno procedure. Moderate pulmonary autograft insufficiency at last follow-up was observed in 6 patients (11%), while 17 patients had mild autograft regurgitation.

**Homograft function**

RVOT obstruction was rare in our patients; in only 3 cases a moderate degree of stenosis was noticed, with a maximum Doppler RVOT gradient ranging between 37 and 45 mm Hg. Mean maximal RVOT gradient of the entire population was 23 mm Hg, ranging between 7 and 45 mm Hg. Moderate homograft insufficiency was observed in only 4 patients, while 13 patients had only trivial to mild homograft regurgitation.

**Discussion**

In the pediatric group aortic valvular disease can frequently be treated without the need for valve replacement. Balloon dilatation, open commissurotomy, cusp shaving as well as repair procedures for insufficient valves are the first choice. Subaortic obstruction is also frequently amenable to resection of fibrous or muscular tissue. Valve replacement may be postponed for years in this way. Seventy percent of our patients had undergone one or more procedures prior to their Ross operation (Table 1) leading in this series to a mean age of 9.15 years at the time of the autograft procedure.

When aortic valve replacement in children can no longer be postponed, replacement with the pulmonary autograft has important advantages. The use of anticoagulants can be avoided as well as the occurrence of early failure as observed with homografts in children. Above all the autograft increases in size commensurate with body growth (10). Therefore, the pulmonary autograft is superior to any other available aortic valve substitute for the growing child.

Alternative surgical options to the Ross procedure should however, always be considered. Mechanical valves can be used in older children if a size of 21 mm or larger can be inserted. Severe LVOT obstruction can be repaired sometimes without the need for aortic valve replacement. However, in our series aortic valve pathology or hypoplastic annulus was present in all Ross-Konno patients.

During our 10-year experience we came across some additional technical benefits of the Ross procedure. Enlargement of annulus or septum which is often required in congenital aortic valve disease, is easily accomplished when the root is removed and may be accomplished without the insertion of patch material, using the extended muscular rim of the autograft. Moreover, any associated subaortic VSD can be addressed in a similar fashion by using the muscular rim of the autograft to make an extended inflow anastomosis including the VSD (12). In tunnel-form LVOT obstruction incision of the muscular septum
and subsequent enlargement with patch material (Ross-Konno procedure) will provide a satisfactory solution in almost all cases.

In 1 patient with neo-aortic valve insufficiency following the arterial switch operation a ‘switch-back’ procedure was performed. The valve was replaced with the neopulmonary valve, which originally was the anatomic aortic valve. Bringing back the native aortic valve to the LV certainly has a lot of intuitive appeal (14).

Early mortality in our series occurred only in neonatal patients or young infants. Six patients underwent the Ross procedure at an age of 3 months or less. Mortality in this age group was relatively high with 4 of 6 patients dying (3 in-hospital deaths and 1 late death). One patient died as a result of multiple organ failure following an emergency Ross procedure. Balloon dilatation had resulted in severe aortic valve insufficiency and cardiac arrest. Two patients had valvular and subvalvular LVOT obstruction following repair of interrupted aortic arch type B and VSD 1 and 3 months earlier. One of them had severely depressed LV function and died of low output failure following the Ross procedure. Ischemia probably caused by unrecognized left coronary artery kinking led to mortality in the other patient with previous IAA/VSD repair. Finally, one patient died 13 months after a Ross procedure (performed at the age of 2 months) due to severe pulmonary hypertension and LV failure. Autopsy confirmed the presence of severe LV fibroelastosis. Prior to the Ross operation diastolic LV dysfunction with a minor suspicion of fibroelastosis was present. LV-dimensions were within normal ranges.

LVOT obstruction following IAA/VSD repair is common and the use of the Ross-Konno procedure is very attractive. Care should be taken with coronary artery transfer as the diameter of the pulmonary autograft will usually be considerably larger than that of the aortic root. Starnes et al. reported their experience with the pulmonary autograft procedure for residual LVOT obstruction following IAA/VSD repair with good results. They even suggest that for IAA/VSD and small LVOT a primary Ross-Konno procedure with arch repair may be the procedure of choice (2,15-17).

Endocardial fibroelastosis has been reported as being a risk factor for an adverse outcome in neonatal critical aortic stenosis (18). Biventricular repair may not always be the ideal solution for this subgroup and the Norwood procedure and subsequent univentricular repair can be a better option.

Dilatation and autograft valve failure as has been described in several series of adult patients (3-8) also occurred in our pediatric population. The majority of patients showed annular diameters in excess of 90th percentile of normal aortic root diameters and 3 patients were even reoperated for valve failure in association with excessive root dilatation. The meaning of this observation is not clear, as progression of autograft dilatation was not common in this series. Serial assessment by echocardiography and careful clinical follow-up will provide more insight in the coming years. Although exact criteria for reoperation
because of dilatation are not available, the rate at which dilatation occurs and maximal
diameter related to body surface area should be taken in consideration.

In some patients the superior capacity of juvenile tissues to remodel appears to be
inadequate to prevent aneurysmal dilatation and valve failure of the pulmonary autograft.
Although one might believe that a Ross procedure performed in the neonatal period would
suffer less from autograft dilatation than a Ross performed at a later age, some evidence
exists that autograft dilatation can also occur following a neonatal Ross operation (Ziemer,
personal communication 2003). Initial bicuspid aortic valve appeared to be no risk factor
for developing dilatation either; despite suggestions in literature our study showed no
difference in dilatation between the two groups (19).

Reinforcing proximal and distal autograft suture lines with autologous pericardial
strips was used in most of our patients, but apparently did not provide protection from
dilatation. The use of large coronary buttons to replace the native pulmonary sinuses and
reinforcement of the ‘non-coronary’ sinus wall of the pulmonary autograft by leaving the
noncoronary aortic sinus in situ, have been reported to be of benefit (20).

Root dilatation is not the only mechanism of autograft failure. In one of our patients
leaflet fibrosis occurred leading to replacement by a mechanical prosthesis. Leaflet
dysfunction without associated root dilatation has been described by others before (21).
The mechanism of autograft leaflet shortening by fibrosis is not known. It may be the
result of improper tissue handling at the time of operation but autograft leaflet failure may
also be the result of a (connective) tissue disorder.

In summary, we believe that the Ross procedure is of great use in the pediatric population
as it provides a unique growing aortic valve substitute together with the above-described
additional technical advantages such as an adequate solution for otherwise difficult to
treat obstructive LVOT’s. Nevertheless, in our opinion the Ross procedure should only be
considered when valve-sparing techniques can no longer provide a solution for pediatric
aortic valve disease.
Results of the Ross operation in a paediatric population

References
