Original Research

Medium-Term Results From Pulmonary Autografts After the Ross Procedure in Children and Adolescents

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Introduction: The Ross procedure is being used increasingly for the treatment of aortic valve problems in children, but the long-term prospects of the pulmonary autograft and its ability to grow continue to be controversial. This study summarises the experience of our centre from using the Ross procedure in children and adolescents.

Methods: During the period November 1996 to March 2004, 35 children aged 3 months to 18 years (mean 10.6 ± 5.4 years) and weighing 3.2-71 kg (mean 35.4 ± 19.8 kg) underwent the Ross procedure for the treatment of aortic valve disease (stenosis - 25, 71.4%; regurgitation - 5, 14.3%; mixed - 5). The majority of patients (n=26, 74.2%) had a history of aortic valve procedures. The technique employed was replacement of the aortic root with the pulmonary autograft. All patients were followed for 16-87 months (mean 37 months) with clinical and echocardiographic examinations, which were performed before discharge, 3-6 months later, and then every year.

Results: Perioperative mortality was zero. There was one late (sudden) death 3 years after the procedure. Actuarial 7-year survival was 97.1 ± 2.9% and freedom from reoperation for any reason was 100%. Two patients (5.7%) needed balloon dilatation because of pulmonary stenosis. All patients were in New York Heart Association functional class I. Haemodynamic parameters at the last follow-up examination were similar to those immediately post procedure: 12 patients (versus 11) had trivial and 3 mild aortic regurgitation. The pulmonary autograft followed the patient's body growth. The diameter of the aortic annulus increased from 19.1 ± 3.9 mm to 21.6 ± 2.8 mm and the diameter of the sinuses of Valsalva from 25.6 ± 5.8 mm to 28.7 ± 4.6 mm.

Conclusions: The Ross procedure seems to be the ideal solution for aortic valve problems in children, because of the small perioperative risk, the excellent haemodynamic results, and the potential of the autograft to grow, as shown by medium-term follow up.

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Aortic valve replacement using the patient's own pulmonary valve (pulmonary autograft) in children was first described in 1967 by Donald Ross.[1] For many years, the "Ross procedure" received only limited acceptance in the (paediatric) cardiac surgical community. During the last decade, however, interest in this procedure has been rekindled. The advantages of the use of the pulmonary autograft for aortic valve replacement, as opposed to the usual mechanical or biological prosthesis, are obvious: avoidance of anticoagulation therapy and the risk of thromboembolism or haemorrhage (mechanical valves);[2] no risk of degenera-

tion and destruction (biological prostheses, homografts).[3,4] What is more, since the pulmonary autograft appears to grow in parallel with the child's body growth, the Ross procedure frees the patient from the need for repeated replacements.[5,6] Thus, after the Ross procedure the child is able to enjoy an active way of life, without restrictions.

This study presents the medium-term results from the use of the Ross procedure in children and adolescents in our centre, focusing on an evaluation of the prospects of the pulmonary autograft.

Patients and methods

The study material comprised all the patients aged under 18 years who underwent the Ross procedure in our centre from November 1996 to March 2004. The patients' files were studied for the following: demographic data; initial diagnosis; history of aortic valve procedures (surgical or non-surgical); technical details of the Ross procedure; postoperative course; postoperative early and medium-term follow-up. Particular emphasis was given to data from the echocardiographic studies during patients' follow-up, which took place within 30 days after the procedure, 3-6 months later, and then every year.

Table 1. Patients' characteristics.

Number (male/female)	35 (26/9)
Age (range)	11.0 ± 4.5 years (3 days - 18 years)
Body weight (kg)	38.2 ± 18.2
Height (cm)	139.3 ± 24.3
Body surface area (m^2)	1.19 ± 0.38
Aortic valve pathology	
- Stenosis	25
- Regurgitation	5
- Mixed pathology	5
- Bicuspid valve	20
- Endocarditis	1
Preoperative NYHA class	
- I	17 (48.5%)
- II	13 (37.1%)
- III	4 (11.4%)
- IV	1 (2.8%)
Previous aortic valve procedures	28 (80%)
- Balloon valvuloplasty	14* (40%)
- Open valvulotomy	10 (28.6%)
- Both	2 (5.7%)
- Valvuloplasty	2 (5.7%)
Other procedures	
- Repair of aortic coarctation	1 (2.8%)
- Closure of ventricular septal defect	1 (2.8%)

* One patient underwent two procedures and another three.
NYHA – New York Heart Association

Patients

A total of 35 patients (26 male, 74.2%), mean age 10.6 ± 4.5 years (range, 3 days to 18 years), underwent the Ross procedure. Demographic characteristics, main aortic valve pathology, and haemodynamic consequences are shown in Table 1. Twenty-eight patients (80%) had a history of aortic valve procedures involving either invasive catheterisation or surgery. One patient had undergone balloon aortic valvuloplasty twice, and another one three times, prior to the Ross procedure. The latter patient also underwent surgical aortic valvuloplasty because of rupture of the non-coronary aortic valve cusp during the last balloon procedure. One patient had a history of aortic coarctation repair; another had a ventricular septal defect closure.

Surgical technique

All the Ross procedures were performed by the same surgeon (MP). The usual cardiopulmonary bypass was used (direct cannulation of the *venae cavae*) under moderate hypothermia (28°C). Myocardial protection was achieved with antegrade administration of cold blood cardioplegia (4°C), initially via the aortic root and then via the coronary ostia, every 20 minutes. The left ventricle was always vented with a catheter via the right superior pulmonary vein. Access to the aortic valve was achieved through transection of the ascending aorta along a curved line, starting from the anterior aortic wall, and extending with a slight downwards inclination to the posterior aortic wall in the middle of the non-coronary sinus of Valsalva, thus enabling excellent exposure of the valve. In all cases the aortic root replacement technique was used, with re-implantation of the coronary arteries to the pulmonary autograft. Running suture was used for the coronary sinuses of Valsalva and interrupted sutures for the non-coronary one.

In all but two cases, small discrepancies between the diameters of the aortic annulus and the pulmonary autograft were managed either by appropriate arrangement of the stitches during suturing or with the aid of a muscular flap from the right ventricular outflow tract, which was used to extend the pulmonary

autograft. Plication of the aortic annulus was necessary in two patients, where the diameter of the annulus was at least 3 mm larger than that of the autograft.

For reconstruction of the right ventricular outflow tract (RVOT) a cryopreserved pulmonary homograft was used in the first 19 patients (53.4%) and a bovine valved allograft (Contegra™) in the next 16 (45.7%), since homografts of appropriate size were not available. RVOT reconstruction was always performed on a beating heart. The size of the allograft used for the reconstruction was the largest permitted. The intraoperative data are given in Table 2.

Medium-term follow up

Surgical mortality was defined as the percentage of patients who died within 30 days of the procedure, and in-hospital mortality as the percentage who died during the same hospitalisation. All patients underwent a clinical examination, clinical evaluation according to the New York Heart Association (NYHA) classification, chest X-ray, electrocardiogram, and echocardiogram before their discharge from the hospital, 3-6 months later, and once yearly thereafter. The echocardiographic study included colour Doppler for evaluation of any insufficiency of the pulmonary autograft, scored according to the method of Perry et al.[8] The mean and peak flow velocities were measured with continuous wave Doppler and the mean and peak pressure gradients were calculated. The transverse dimensions of the pulmonary autograft were measured at the level of the aortic annulus, at the maximum diameter of the Valsalva sinuses, and at the sinotubular junction. A haemodynamic echocardiographic study was also performed along the length of the pulmonary autograft and the Contegra™.

Table 2. Intraoperative and postoperative data.

Cardiopulmonary bypass time: range (mean ± standard deviation)	135-410 (200.4 ± 48.6) min
Aortic cross clamp time: range (mean ± standard deviation)	101-185 (130.9 ± 18.4) min
Conduit for RVOT reconstruction:	
- Homograft	19 (54%)
- Bovine valved allograft (Contegra™)	16 (46%)
Conduit diameter, range (median)	12-27 (20) mm
Length of mechanical ventilation	11.5 ± 6.9 hours
Length of ICU stay, range (median)	1-13 (2) days
Length of hospital stay, range (median)	6-42 (8) days

ICU – intensive care unit; RVOT – right ventricular outflow tract.

The mean time until the last follow up was 4.1 ± 2.4 years (range 2.3-7.4 years), including all the patients who were discharged from hospital (n=35).

Statistical analysis

Results are presented as mean ± standard deviation. The calculation of the patient's medium-term survival was performed using the Kaplan-Meier method. Student's t-test was used for the analysis of quantitative parameters, with a statistical significance of $p<0.05$. The software used was Microsoft Excel and the Statistical Package for the Social Sciences, version 10.0 for Windows 2000 (SPSS, Chicago, Ill., USA). The transverse diameters of the aortic annulus and Valsalva sinuses were compared with the normal body surface area values.[9]

Results

Mortality

There were no perioperative deaths. One child aged 5 years died suddenly three years after the procedure. He was admitted to the emergency room in a shock status, and initial resuscitation was unsuccessful. An emergency sternotomy was performed, but did not reveal any cause for the patient's clinical condition, nor could the patient be saved. The post mortem found no problem related to the coronary vessels or valves. The cause of death was considered to be ventricular arrhythmia.

The 7-year survival for all patients of the study was calculated as 96 ± 3%.

Morbidity

The postoperative complications are shown in Table 3. Arrhythmias and conduction system abnormalities were the most common. Three patients needed inotropic support for 12-48 hours postoperatively. One patient underwent reexploration of the sternotomy because of bleeding on the first postoperative day. Three patients had pneumothorax after removal of the chest drain tubes, but in no case did a chest tube need to be reinserted. Two patients had pericardial effusion. In one case the fluid was drained with a needle under echocardiographic guidance, while in the other, the effusion responded to conservative treatment with diuretics.

Duration of mechanical respiratory support and

Table 3. Postoperative complications of the Ross procedure.

Complication	Patients (%)
Arrhythmia	5 (14.3)
- ventricular extrasystoles	2 (5.7)
- nodal rhythm	2 (5.7)
- transient atrial fibrillation	1 (2.8)
Low cardiac output syndrome	3 (8.6)
Pneumothorax	3 (8.6)
Pericardial effusion	2 (5.7)
Pleural effusion	2 (5.7)
Reexploration for bleeding	1 (2.8)

stay in the intensive care unit are shown in Table 2. No reoperations were needed during early or medium-term follow-up because of problems with the neo-aortic valve (pulmonary autograft). Two patients needed balloon dilatation of the homograft used for reconstruction of the RVOT because of stenosis.

Patients' functional condition

Preoperatively, 18 patients (56.3%) were in NYHA class I, 11 (34.5%) were in class II, and 3 (9.4%) in class III. At last follow up all surviving patients (n=34) were in NYHA class I.

Echocardiographic assessment of pulmonary autograft

The medium-term echocardiographic examination showed that the pulmonary autografts had excellent haemodynamic behaviour. The peak pressure gradient across the aortic valve was 7.4 ± 4.0 mmHg on discharge and 6.9 ± 3.9 mmHg at follow-up, remaining essentially the same (p=0.3) (Table 4). Eleven patients (31.4%) had mild and 3 (8.6%) mild-to-moderate aortic regurgitation on discharge from hospital. The same grade of regurgitation remained at last follow up (Table 4).

Our patients had normal somatic growth, as shown by the increase of body surface area from 1.19 ± 3.8 m^2 at the time of operation to 1.37 ± 0.3 m^2 (p=0.04) at last follow up. The diameter of the neo-aortic annulus (pulmonary autograft) increased from 19.6 ± 3.7 mm at discharge to 22 ± 2.8 mm (p<0.004) at last follow up. The diameter of the sinuses of Valsalva also increased, from 26.1 ± 5.7 mm at discharge to 29.1 ± 4.4 mm (p<0.004) at last follow up. The growth of the annulus and the sinuses of Valsalva was in proportion to the increase in body surface area (Figures 1 and 2). Moreover, the diameter of the neo-aortic annulus was within normal limits for the body surface area, both at discharge and at last follow up. However, the sinuses of Valsalva showed early dilatation after surgery, with 75% of patients having a diameter at the level of the sinuses of Valsalva above the normal 95th percentile. Subsequently, the increase in diameter paralleled the increase in body surface area.

Medium-term echocardiographic evaluation of the pulmonary homograft

In contrast to the pulmonary autograft, the pulmonary homograft used for RVOT reconstruction showed no increase in size. As a result, the pressure gradient across the homograft increased significantly, from 9.2 ± 3.9 mmHg immediately after the procedure to 15.8 ± 9.5 mmHg at follow up, with a range of 7.8-49 mmHg (p=0.03). Two patients (5.7%) needed balloon dilatation because of homograft stenosis. Another two patients had peak pressure gradient (on cardiac catheterisation) of 40 mmHg along the conduit. Five patients had mild and one patient moderate regurgitation of the pulmonary homograft valve. All

Table 4. Echocardiographic findings.

Variable	Discharge	Medium-term follow up	p
Body surface area (m^2)	1.19 ± 3.7	1.37 ± 0.3	0.04
Diameter of aortic annulus (mm)	19.6 ± 3.7	22 ± 2.8	<0.005
Diameter of sinuses of Valsalva (mm)	26.1 ± 5.7	29.1 ± 4.4	<0.005
Peak pressure gradient (mmHg)	7.4 ± 4.0	6.9 ± 3.9	0.3
Aortic regurgitation (pulmonary autograft)	n = 35	n = 34*	
- none	21 (60.0%)	20 (58.8%)	
- mild (0-1+/4+)	11 (31.4%)	11 (32.3%)	
- mild-moderate (1-2+/4+)	3 (8.6%)	3 (8.8%)	

*Not including one patient who died during follow up.

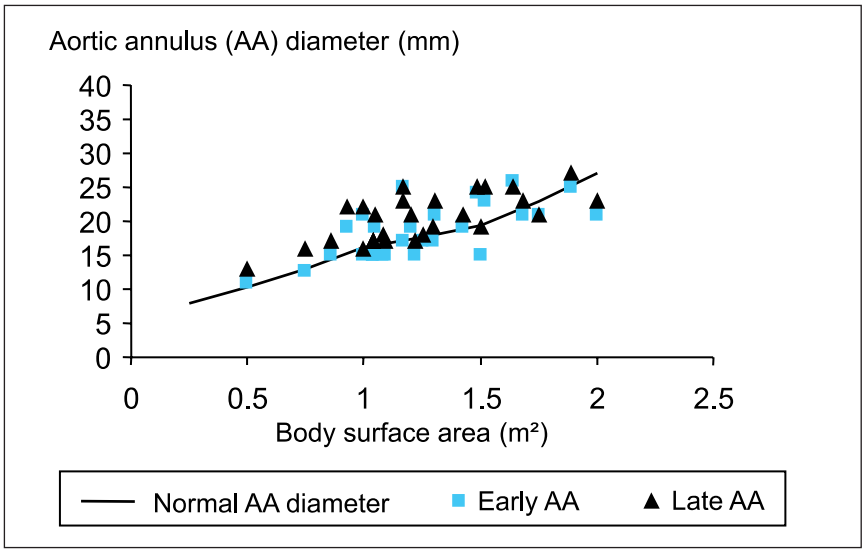

Figure 1. Relation between diameter of the (pulmonary autograft) aortic annulus (AA) and body surface area after the Ross procedure. In the majority of patients the AA diameter was within the 95% confidence interval for the normal population and the AA was seen to grow during the follow-up following the curve for normal growth.

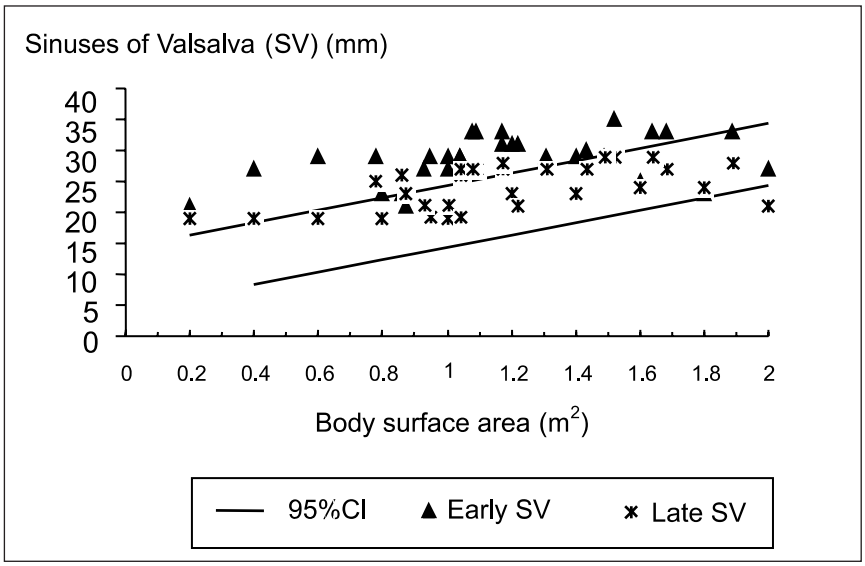

Figure 2. Relation between the diameter of the sinuses of Valsalva (SV) of the pulmonary autograft and body surface area after the Ross procedure. There was an early postsurgical dilatation in >75% of patients, with SV diameter exceeding the 95% confidence interval (CI) for normal values. During medium-term follow up the SV grew in parallel with the curve of normal population growth.

remained asymptomatic throughout the study period, with normal function and slight dilatation of the right ventricle. None of the patients needed reoperation because of dysfunction of the pulmonary homograft.

Medium-term echocardiographic evaluation of the Contegra™ allograft

The Contegra™ allograft has been used in our centre since November 2000 for RVOT reconstruction in all patients who undergo the Ross procedure. The use of the Contegra™ was necessitated initially by the lack of homografts of suitable size. Early echocardiographic studies showed that the Contegra™ is a very good substitute for a pulmonary homograft. In three patients (8.8%) mild insufficiency of the Contegra™ valve was diagnosed and remained stable until the last echocardiographic follow up. The peak systolic pressure gradient was 11 ± 3.9 mmHg after the procedure, and 12.4 ± 6.7 mmHg at last follow up (p=0.35).

Discussion

The results of this study show that the Ross procedure is an excellent option for aortic valve replacement in paediatric patients. The surgical mortality in our series was zero and compares extremely favourably with other series of Ross procedures,[6,8-10] being less than that for replacement of the aortic valve with a mechanical prosthesis[11] or an aortic homograft.[12,13]

The most common complication in our patients was arrhythmia. This can be explained by the fact that children who undergo the Ross procedure usually have a myocardium that has been exposed for a long time to pressure and/or volume overload. On top of this there is the effect of ischaemia during the procedure, which increases the possibility of postoperative ventricular dysfunction and the appearance of arrhythmias (ventricular or supraventricular tachycardia). The only late death in our series was attributed to arrhythmia, as in other series.[4,14] The incidence of all complications in the immediate postoperative period is comparable with data reported in the latest international literature.[4,8,10,14]

Without "bringing owls to Athens", we would like to stress that the growth of the pulmonary autograft by 13% during the medium-term follow-up was an important finding of our study. This increase closely paralleled the 15% increase in body surface area during the same follow-up period. However, there was a clear difference in growth between the neo-aortic annulus (pulmonary autograft) and the sinuses of Valsalva. The diameter of the neo-aortic annulus was within normal limits in the majority of patients immediately after the Ross procedure and increased throughout the medium-term follow-up, following the expected growth curve for a normal population. In contrast, the sinuses of Valsalva showed a significant initial increase in diameter, which should be attributed to the early postoperative dilatation of the pulmonary autograft as a result of its exposure to the high pressures of the systemic circulation. However, from then on the increase in size of the sinuses of Valsalva paralleled the normal growth curve, with no indication of aneurysmal dilatation, a finding that testifies to the normal growth of the pulmonary autograft. Simon et al[6] and Solymar et al[15] have reported similar results.

In addition, in our series we had 11 patients with mild and 3 with mild-to-moderate insufficiency of the neo-aortic valve, which remained stable throughout the medium-term follow up, despite the observed dilation of the Valsalva sinuses. The observation that the insufficiency did not worsen with time shows that the pulmonary valve in the aortic position preserves valvular function. This could be due to the growth of the pulmonary autograft and the reconfiguration of the valve leaflets. The phenomenon of passive dilatation of the pulmonary autograft was reported by Schoof et al[16] in an animal study. However, in clinical practice significant insufficiency of the pulmonary valve in the aortic valve position as a result of dilatation of the autograft has only been seen in a small number of patients.[17,18] Of course, since in our series we had no reoperations for neo-aortic valve dysfunction, we could not carry out pathologoanatomical examinations of valve tissue to prove that there was real growth of the pulmonary autograft. However, the growth was proved indirectly, since the neo-aortic valve remained without insufficiency for a considerable time span. Otherwise, the initial passive dilatation would have led to more and more severe insufficiency since the valve cusps could not coapt.

Another important finding of this study is the relatively stable function of the autograft valve in patients with a bicuspid aortic valve, of whom there were 20 (57%) in our series. The incidence of insufficiency in those patients (8/20, 40%) was similar to that in patients with a tricuspid aortic valve (5/12, $p=0.96$). Therefore, always bearing in mind the relatively short follow-up period (2.3-7.4 years), we can claim tentatively that the Ross procedure in patients with a bicuspid aortic valve does not entail early insufficiency of the pulmonary autograft. Of course, a longer follow-up period would be necessary for such a conclusion to be powerful.

The world literature reports pulmonary autograft insufficiency rates of 1-7% following the Ross procedure in paediatric patients,[5,9,10] which are much lower than those reported for aortic valve replacement with a mechanical (36%) or biological (72%) prosthesis in children.[11] In our series, we had no patient who needed reoperation because of the pulmonary autograft, while only two patients needed balloon dilatation because of pulmonary stenosis. These good results, however, may be due to our relatively short follow-up period compared to other series.

As regards the behaviour of the pulmonary homograft in the RVOT reconstruction, in our series there were 4 patients (of the 19 who received a pulmonary homograft, 21%) who had pulmonary stenosis (two needed balloon dilatation). This relatively high percentage, in comparison with other series,[19,20] confirms that the RVOT is the "Achilles' heel" of the Ross procedure.[19] The degeneration of the pulmonary homograft is due to the body's immune response.[19] We consider that, in contrast to the pulmonary autograft, the homograft is unable to adapt itself to the increasing size of the heart and the increasing stroke volume and begins to degenerate at an early stage.

Another finding of our study that is worthy of

comment is the behaviour of the Contegra™ allograft used for the RVOT reconstruction. The Contegra™ allograft is a biological conduit taken from a bovine jugular vein, fixed in glutaraldehyde, which bears a tricuspid venous valve. Since November 2000, the Contegra™ allograft has been used in 16 patients at our centre. The main reason was the unavailability of pulmonary homografts of suitable size. Our experience from the use of the Contegra™ in the Ross procedure has already been published.[21] In terms of haemodynamic behaviour, we consider it to be an attractive alternative solution to the pulmonary homograft in the Ross procedure. Only 3 of our patients developed mild-to-moderate postoperative insufficiency, which remained stable throughout the follow-up period, while the pressure gradient across the valve did not increase substantially. Advantages of the Contegra™ conduit are its "off-the-shelf" availability; its ease of use, in terms of conforming with the required shape and suturing; the variety of sizes (internal diameter 12-22 mm); as well as the lack of need for extension cephalad or caudad from the centrally placed valve. These advantages, along with its very good haemodynamic behaviour, have led us to consider this graft as our first choice for the RVOT reconstruction in the Ross procedure.

The limitations of this study include the relatively small number of patients and the short follow-up period, in comparison with other series.

To summarise, our seven-year experience with the Ross procedure, using a pulmonary autograft to replace the aortic root, confirms the suitability and safety of this procedure in paediatric patients with aortic valve disease. The Ross procedure produces excellent haemodynamic results, while avoiding the need for anticoagulation therapy. It thus offers the patient an active lifestyle. The chance of a technical error is small in experienced hands. Finally, the pulmonary autograft in the aortic valve position shows normal growth despite an early phase of passive dilatation.

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