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The Ross operation: a Trojan horse?†

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Aims The Ross operation is the operation of choice for children who require aortic valve replacement (AVR) and may also provide a good option in selected adult patients. Although the autograft does not require anticoagulation and has a superior haemodynamic profile, concern regarding autograft and allograft longevity has risen. In this light, we report the 13-year results of our prospective autograft cohort study.
Methods and results Between 1988 and 2005, 146 consecutive patients underwent AVR with a pulmonary autograft at Erasmus Medical Center Rotterdam. Mean age was 22 years (SD 13; range 4 months–52 years), 66% were male. Hospital mortality was 2.7% ($N = 4$); during follow-up four more patients died. Thirteen-year survival was $94 \pm 2\%$. Over time, 22 patients required autograft reoperation for progressive neo-aortic root dilatation. In addition, eight patients required allograft reoperation. Freedom from autograft reoperation at 13 years was $69 \pm 7\%$. Freedom from allograft reoperation for structural failure at 13 years was $87 \pm 5\%$. Risk factors for autograft reoperation were previous AVR and adult patient age.
Conclusion Although survival of the Rotterdam autograft cohort is excellent, over time a worrisome increase in reoperation rate is observed. Given the progressive autograft dilatation, careful follow-up of these patients is warranted in the second decade after operation.

Introduction

The autograft procedure was introduced by Donald Ross in 1967.[1] Ross initially used the scalloped subcoronary implantation technique to insert the pulmonary valve into the left ventricular (LV) outflow tract with encouraging results.[2] It became a worldwide-accepted procedure for aortic valve replacement (AVR) despite the need for specific surgical expertise to perform this complicated operation on both the aortic and pulmonary valve.

Initially, the Ross operation was employed using the subcoronary implantation technique, but over years most of the centres shifted towards the root replacement technique—the most commonly used implantation technique nowadays. Conservation of the autograft root appeared to be more versatile and associated with a decreased incidence of early and late failure when compared with the other techniques.[3,4]

Several studies reported satisfactory mid-term and long-term results of the Ross operation.[5–8]

The pulmonary autograft has excellent haemodynamic adaptation, there is no need for anticoagulation, patients can live an active lifestyle, and patient survival seems to be superior when compared with survival of patients with other valve substitutes.[2,5,9] However, in recent years the number of reports on the reoperation rate after the Ross operation using root replacement is becoming more and more extensive,[8,10–12] thus questioning the durability of the autograft.

The Ross operation has previously been claimed to be the next best thing to nature, but at present serious drawbacks are shown, raising the question whether or not this operation may turn out to be a Trojan Horse. In this regard, we evaluated our prospective cohort study of the Ross operation with emphasis on patient survival, durability of the autograft and pulmonary allograft, and the incidence of potential risk factors for reoperation after the Ross operation in children and adult patients.

Methods

Patients

From 1988 until 2005, 146 consecutive patients underwent the Ross operation at our institution. Preoperative patient characteristics are shown in *Table 1*. Twelve patients underwent previous AVR: six subcoronary homografts, three biological prostheses, and three mechanical prostheses were used. Approval from the Institutional Review Board was obtained for this prospective follow-up study; the Institutional Review Board waived informed consent.

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Table 1 Preoperative patient characteristics

	All patients ($n = 146$)	Patients <16 years ($n = 52$)	Patients ≥16 years ($n = 94$)
Mean age [years (SD; range)]	22.4 (13.4; 0.3–52)	8.0 (5.4; 0.3–15)	30.4 (9.1; 16–52)
Male gender	66% ($n = 96$)	67% ($n = 35$)	65% ($n = 61$)
Prior cardiac surgery[a]	33% ($n = 48$)	44% ($n = 23$)	27% ($n = 25$)
Prior AVR	8% ($n = 12$)	–	13% ($n = 12$)
Prior valvulotomy	18% ($n = 26$)	31% ($n = 16$)	11% ($n = 10$)
Prior balloon dilatation	20% ($n = 29$)	46% ($n = 24$)	5% ($n = 5$)
Aetiology			
Endocarditis	5% ($n = 8$)	6% ($n = 3$)	5% ($n = 5$)
Congenital (including bicuspid)	74% ($n = 108$)	90% ($n = 47$)	65% ($n = 61$)
Other (mainly prosthetic valve)	13% ($n = 18$)	2% ($n = 1$)	19% ($n = 17$)
Degenerative/rheumatic	8% ($n = 11$)	2% ($n = 1$)	11% ($n = 10$)
Aneurysm/dissection	1% ($n = 1$)	–	1% ($n = 1$)
Diagnosis			
Aortic valve regurgitation (AR)	30% ($n = 44$)	17% ($n = 9$)	37% ($n = 35$)
Aortic valve stenosis (AS)	32% ($n = 47$)	33% ($n = 17$)	32% ($n = 30$)
AR + AS	38% ($n = 55$)	50% ($n = 26$)	31% ($n = 29$)
Systolic LVF ($n = 140$)[b]			
Good (EF >50%)	83% ($n = 116$)	83% ($n = 39$)	82% ($n = 77$)
Impaired (EF 40–50%)	11% ($n = 16$)	17% ($n = 8$)	9% ($n = 8$)
Moderate/bad (EF <40%)	6% ($n = 8$)	–	9% ($n = 8$)
Sinus rhythm	100%	100%	100%
Creatinin [μmol/L (SD; range), $n = 145$]	63 (24; 12–157)	40 (13; 12–71)	75 (18; 38–157)
NYHA class ($n = 143$)			
I	42% ($n = 61$)	56% ($n = 29$)	34% ($n = 32$)
II	36% ($n = 53$)	21% ($n = 11$)	45% ($n = 42$)
III	15% ($n = 22$)	8% ($n = 4$)	19% ($n = 18$)
IV/V	5% ($n = 7$)	11% ($n = 5$)	2% ($n = 2$)
Ventilation support	2% ($n = 3$)	4% ($n = 2$)	1% ($n = 1$)
Type of operation			
Emergency (<24 h)	1% ($n = 1$)	–	1% ($n = 1$)
Urgent	13% ($n = 20$)	23% ($n = 12$)	9% ($n = 8$)
Elective	86% ($n = 125$)	77% ($n = 40$)	90% ($n = 85$)

[a]Some patients had other prior cardiac surgery, i.e. VSD closure, subvalvular membrane resection.
[b]Systolic LV function based on echocardiographic or angiographic estimations.

Operation

Perioperative data are shown in *Table 2*. All surgical procedures were performed on cardiopulmonary bypass with moderate hypothermia. In three patients additional deep hypothermia with total circulatory arrest was needed for surgery on the aortic arch. Crystalloid cardioplegia and topical cooling were used for myocardial protection.

In most patients, the root replacement technique was employed, and the pulmonary autograft was inserted at the level of the annulus while care was taken to reduce the subannular muscular rim of the autograft by 3–4 mm. The proximal suture line of the autograft was constructed with interrupted sutures in 21% ($n = 30$) of the procedures, with running sutures in the remainder. In two patients, an autologous pericardial strip supported the proximal suture line.

In all patients the right ventricular outflow tract (RVOT) was reconstructed using an allograft, in 98% a pulmonary allograft was used and 99% of the allografts used were cryopreserved. Three patients required concomitant coronary artery bypass grafting (CABG) due to a procedural complication.

Follow-up

All patients were followed-up prospectively, contacted annually and interviewed over telephone. Patients over 16 years underwent standardized echocardiography biannually.[13]

In case of suspected complications the attending physician was contacted for verification. Valve-related events were defined according to the guidelines for reporting morbidity and mortality after cardiac valvular operations.[14] Hospital mortality and morbidity were registered and the causes of death were documented. Hospital mortality was defined as death of the patient within any time interval of operation if the patient was not discharged from the hospital. Failure of the autograft or pulmonary allograft was determined at the time of reoperation or death. Patient survival started at the time of Ross operation and ended at the time of death or at last follow-up. Survival of the autograft or pulmonary allograft started at the time of operation and ended when a reoperation or reintervention was done, when the patient died or at last follow-up. Two patients moved abroad and were lost to follow-up. Echocardiographic measurements were obtained for patients who did not die or did not require reoperation related to the Ross operation during follow-up.

The database was frozen on 1 October 2005. Total follow-up was 1269 patient years and was 99.3% complete.[15] Mean follow-up duration was 8.7 years (range 0–17.1 years).

Statistical methods

Descriptive statistical analysis of perioperative data was done. Continuous data are displayed as mean ± 1 SD and were compared using the unpaired *t*-test. Discrete data are presented as proportions and were compared using the χ^2 test or Fisher's exact test. Cumulative survival and freedom from reoperation or reintervention were analysed using the Kaplan–Meier method. Survival is displayed as proportion ± SE. Age-matched survival in the

Table 2 Perioperative details

	All patients ($n = 146$)	Patients <16 years ($n = 52$)	Patients ≥ 16 years ($n = 94$)
Aortic valve			
Bicuspid	61% ($n = 89$)	69% ($n = 36$)	56% ($n = 53$)
Tricuspid	32% ($n = 46$)	31% ($n = 16$)	32% ($n = 30$)
Prosthesis	7% ($n = 11$)	–	12% ($n = 11$)
Surgical technique			
Autograft root replacement	96% ($n = 140$)	100%	94% ($n = 88$)
Inlay autograft	4% ($n = 6$)	–	6% ($n = 6$)
Concomitant procedures			
CABG	2% ($n = 3$)	–	3% ($n = 3$)
LVOT enlargement	10% ($n = 14$)	21% ($n = 11$)	3% ($n = 3$)
Mitral valve surgery	1% ($n = 1$)	–	2% ($n = 1$)
Other[a]	11% ($n = 17$)	14% ($n = 8$)	10% ($n = 9$)
CPB time (min)	202 (114–685)	179 (118–465)	215 (114–685)
Cross-clamp time (min)	141 (90–240)	125 (90–240)	150 (90–238)
Circulatory arrest ($n = 3$, min)	30 (11–64)	15 ($n = 1$)	37 (11–64, $n = 2$))
Complications			
Bleeding/Tamponade	13% ($n = 19$)	2% ($n = 1$)	19% ($n = 18$)
Pacemaker	1% ($n = 1$)	2% ($n = 1$)	–
Perioperative MI	1% ($n = 1$)	–	1% ($n = 1$)
Early mortality	2.7% ($n = 4$)	2% ($n = 1$)	3% ($n = 3$)

CPB, cardio pulmonary bypass.
[a]Includes patients requiring tailoring of the ascending aorta or subvalvular membrane resection.

general population was calculated using the Dutch population life tables (http://statline.cbs.nl/). The log-rank test was used to compare Kaplan–Meier curves.

The Cox proportional hazards regression analysis was used to evaluate the following variables as predictors for autograft reoperation over time: previous AVR, patient age, bicuspid valve disease, the surgical technique used (root replacement vs. inclusion cylinder technique), and haemodynamic diagnosis (regurgitation vs. stenosis vs. combined regurgitation and stenosis). First, all variables were entered into a univariable analysis. Next, all variables that were significant in the univariable analysis or showed a tendency towards significance ($P \leq 0.20$) were forced into the multivariable Cox regression analysis (enter method). The proportional hazards assumption was assessed for each variable through graphical inspection of the log minus log survival and the linearity assumption for continuous variables though the partial residuals. There was no indication of violation of the assumptions. A P-value ≤ 0.05 was considered statistically significant. All testing was performed two-sided. For all data analysis, SPSS 12.0.1 Windows (SPSS, Chicago, IL, USA) was used.

Results

Hospital mortality and late survival

Hospital mortality was 2.7% (four patients). Two patients, both female, died perioperatively. One 40-year-old patient died due to low output failure and the other patient, 4 months old, died of heart failure and severe arrhythmias.

One 26-year-old male patient died due to massive pulmonary emboli shortly after the operation. Finally, one 24-year-old female patient with Turner syndrome and extreme LV hypertrophy died due to mediastinitis and sepsis 13 days after surgery.

During follow-up four more patients died. There were one valve-related and three non-valve-related deaths. The valve-related death was a 12-year-old girl with severe juvenile rheumatic disease and severe aortic valve regurgitation and mitral valve incompetence resulting in progressive heart failure. She died 6 months after operation.[16]

Causes of the non-valve-related deaths included septic shock (*Candida albicans*) in one infant 51 days after autograft operation, heart failure resulting in cardiogenic shock in another infant 1.7 years after autograft operation, and an acute myocardial infarction in an adult patient 4.7 years after autograft operation. The latter patient died 2 months after autograft reoperation for structural valve deterioration with implantation of a mechanical prosthesis.

Overall, 13-year survival was $94.4 \pm 1.9\%$ (*Figure 1*). For patients younger than 16 years, the 13-year survival was $92.0 \pm 3.8\%$; for patients older than 16 years $95.7 \pm 2.1\%$ (log-rank test $P = 0.35$).

Reoperation

Twenty-four patients underwent a reoperation related to the Ross operation. Of these 24 patients, 16 patients required isolated pulmonary autograft replacement, six patients required simultaneous replacement of both the pulmonary autograft and allograft, and two patients required isolated pulmonary allograft replacement.

Progressive dilatation of the neo-aortic root was the main cause for autograft reoperation. *Table 3* shows details of each operation. Causes for allograft replacement were mainly structural failure, calcification, or senile degeneration of the valve. One patient had a recurrent episode of rheumatic fever involving the autograft, thus requiring a reoperation. Two patients underwent a reoperation without valve replacement. One patient underwent enlargement of the pulmonary outflow tract due to supravalvular pulmonary stenosis and the other patient required reoperation for constrictive pericarditis. One patient underwent balloon valvuloplasty of the RVOT to relieve supravalvular pulmonary stenosis.

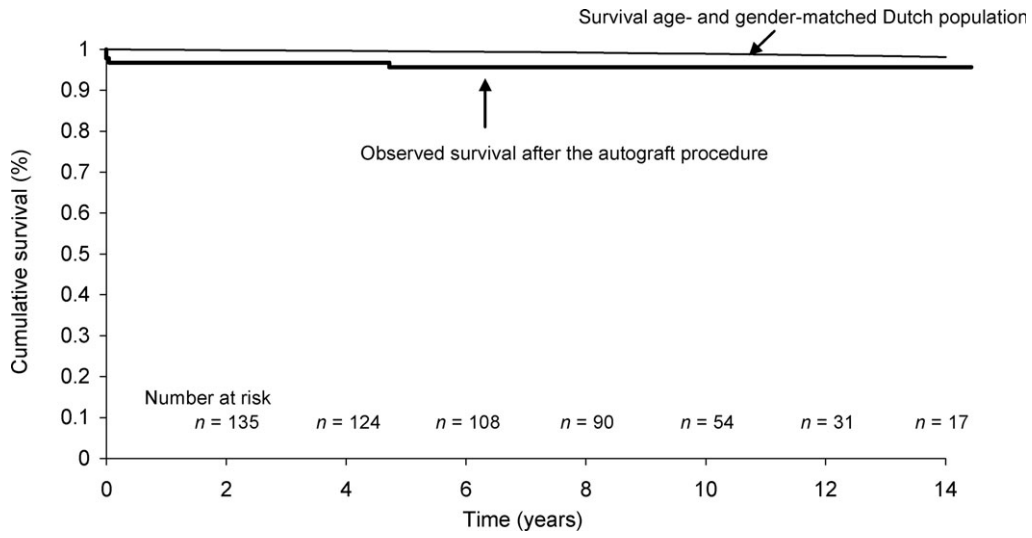

Figure 1 Observed cumulative survival after the Ross operation and survival of the age- and gender-matched general Dutch population.

Table 3 Details on Ross operation-related reoperations

Patient	Sex	Age at Ross operation	Years to reoperation	Indication	Prosthesis implanted	Result
Isolated pulmonary autograft reoperation						
1	M	16	1.8	RF, AR	MP	Alive
2	M	28	4.5	RD, AR	MP	Died[a]
3	M	20	5.7	RD, AR	MP	Alive
4	F	27	6.7	RD, AR	MP	Alive
5	M	28	6.7	RD, AR	ALL	Alive
6	F	8	7.0	RD, AR	ALL	Alive
7	M	34	7.3	RD, AR	MP	Alive
8	M	16	7.6	RD, AR	MP	Alive
9	M	33	7.6	RD, AR	MP	Alive
10	M	39	8.6	RD, AR	MP	Alive
11	M	25	9.1	RD, AR	MP	Alive
12	M	26	10.1	RD, AR	MP	Alive
13	F	21	11.2	RD, AR	MP	Alive
14	F	26	11.7	RD, AR	MP	Alive
15	F	22	11.9	RD, AR	MP	Alive
16	M	22	12.9	RD, AR	MP	Alive
Pulmonary autograft + pulmonary allograft reoperation						
17	M	26	3.1	Reiter, RD, AR	MP, pALL	Alive
18	M	15	7.7	RD, AR, PR, PS	ALL, pALL	Alive
19	F	29	8.3	RD, AR, PR	MP, pALL	Alive
20	F	41	9.3	RD, AR, PR	MP, pALL	Alive
21	M	16	9.5	RD, AR, PS	MP, pALL	Alive
22	M	18	13.1	RD, AR, PR	ALL, pALL	Alive

M, male; F, female; RF, rheumatic fever; AR, aortic regurgitation; RD, root dilatation; Reiter, Reiter's disease; PR, pulmonary regurgitation; PS, pulmonary stenosis; MP, mechanical prosthesis implanted as a conduit; ALL, allograft; pALL, pulmonary allograft.
[a]This patient died 2.5 months after the reoperation.

Freedom from reoperation for autograft failure at 5 years was $97.7 \pm 1.3\%$ and at 13 years was $69.2 \pm 6.6\%$ (*Figure 2*). Freedom from autograft reoperation was significantly better for patients younger than 16 years when compared with patients aged 16 years and older at the time of operation [at 13 years 92.1 ± 5.4 vs. $56.7 \pm 9.6\%$ (log-rank test $P = 0.02$)].

Freedom from allograft reoperation for structural failure at 5 years was $99.2 \pm 0.8\%$ and at 13 years was $87.1 \pm 5.5\%$ (*Figure 3*). Freedom from allograft reoperation for structural failure did not differ for patients younger than 16 years when compared with patients aged 16 years and older at the time of operation [80.0 ± 1.1 vs. $92.5 \pm 3.8\%$ at 13 years (log-rank test $P = 0.73$)].

Univariable predictors of autograft reoperation were previous AVR (HR 2.8; 1.1–7.1; $P = 0.03$) and adult patient age (HR 5.0; 1.2–21.1; $P = 0.03$). After multivariable analysis adult patient age remained the only significant predictor of autograft reoperation (HR 4.6; 1.01–21.1; $P = 0.05$) (*Table 4*).

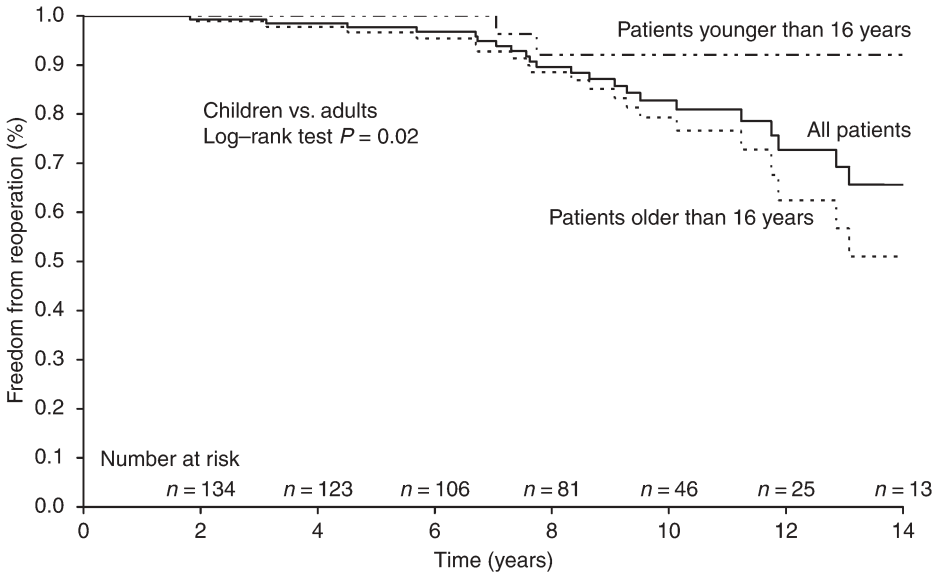

Figure 2 Overall freedom from autograft reoperation and freedom from autograft reoperation for adult patients (16 years and older) vs. children.

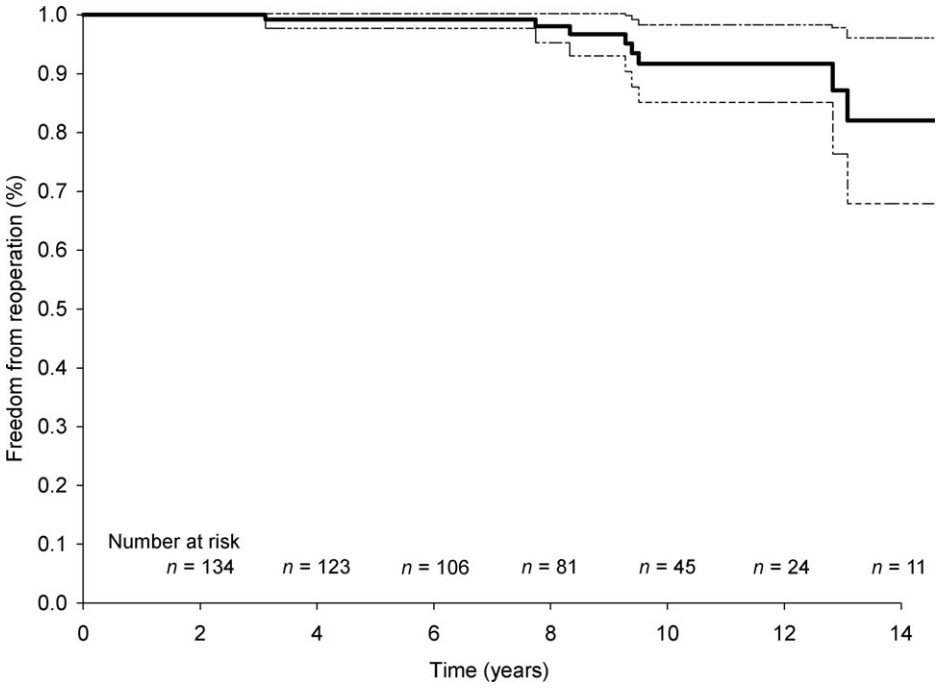

Figure 3 Freedom from pulmonary allograft reoperation for all 146 patients. The dotted lines indicate upper limit and lower limit of the 95% CI.

Other valve-related events

During follow-up two patients developed endocarditis (0.16%/patient year), complicated by a stroke in one patient. In one patient allograft endocarditis occurred and was treated with antibiotics. One patient developed pulmonary emboli (0.08%/patient year). Bleeding events, valve thrombosis, or non-structural failure were not observed.

Functional status at follow-up

During the last follow-up, 95% of the patients were in New York Heart Association (NYHA) class I or II. Eleven per cent of the patients had moderate to severe aortic regurgitation, 3% with moderate to severe pulmonary regurgitation, and 8% of the patients had moderate to severe pulmonary stenosis.

Discussion

Our study shows that the autograft procedure initially fulfils the prospect with regard to excellent long-term survival and avoidance of anticoagulation therapy. Especially children, patients who want to live an active lifestyle and women who want to become pregnant benefit the most from this

Table 4 Risk factors for autograft reoperation

Risk factors	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Previous AVR	2.8 (1.1–7.1)	0.03	1.2 (0.4–4.2)	0.74
Adult patient age	5.0 (1.2–21.1)	0.03	4.6 (1.01–21.1)	0.05
Bicuspid valve	0.52 (0.23–1.2)	0.13	0.6 (0.2–1.7)	0.36
Sex	0.80 (0.32–1.96)	0.62	0.7 (0.3–1.8)	0.45
Surgical technique	0.20 (0.0–24.8)	0.53	0.0 (0.0–0.0)	0.98
Haemodynamic diagnosis				
AS	1.0		–	
AR	1.5 (0.5–4.2)	0.5	1.03 (0.3–3.2)	0.96
AR + AS	0.9 (0.3–2.7)	0.9	0.7 (0.2–2.4)	0.56

operation. However, with time we also observed an increase in reoperations related to the Ross operation, confirming the scepticism about the superior durability of this procedure.

In our prospective cohort study, the survival of patients who undergo a Ross operation is excellent when compared with survival of patients receiving other valve substitutes, and is even comparable with the general age- and gender-matched population. The question remains if this can be ascribed solely to the autograft procedure. Patient selection bias is not unlikely since our Ross patients are mainly those who undergo elective surgery, present with no or mild symptoms of dyspnoea, usually have isolated aortic valve disease, and a normal preoperative cardiac rhythm.[17] However, in the prospective randomized trial by Yacoub and co-workers,[18] the pulmonary autograft was compared with the allograft, and a survival advantage on the long-term was observed in favour of the pulmonary autograft.

Nevertheless, we observed a worrisome increase in autograft reoperations in the second decade after the Ross operation. The main cause for reoperation after the Ross operation is dilatation of the neo-aortic root. Due to this dilatation, coaptation of the cusps is lost and aortic regurgitation occurs. Reporting a small but persistent increase in root dimensions and neo-aortic root regurgitation over time, a previous study by our institution anticipated that more reoperations would be necessary in the upcoming years.[19] These findings are also confirmed by other studies.[8,10]

Although the exact causes of autograft root dilatation still have to be determined, several factors may play a role. One of those factors is the root replacement technique.

Performing the autograft root replacement technique requires surgical expertise and the application of this technique varies among surgeons.[9] The autograft can be inserted at annular or subannular level and with or without scalloping the muscle rim to a minimum below the valve cusps. Also, continuous or interrupted sutures can be used for the proximal suture line. Finally, the length of the autograft root can vary. Some surgeons keep it as short as possible, whereas others leave the complete length of the pulmonary artery distal to the sino-tubular junction of the pulmonary artery (http://www.ctsnet.org/doc/2380).

In our institution, all reoperations were in patients who underwent the root replacement technique.

When the autograft is inserted as an inclusion cylinder, the native aorta is supporting the pulmonary autograft and may thus prevent it from dilatation. However, the number of autografts implanted as an inclusion cylinder in our institution is small and follow-up duration limited, so any speculations should be interpreted with caution.

Sievers *et al.*[20] report the results of a single centre, single surgeon's experience with another implantation technique, the subcoronary implantation technique. They show good functional results with only 2.6% of the patients requiring a reoperation thus far. However, their follow-up period does not extend beyond 10 years, and longer-term follow-up may prove differently. Also the subcoronary implantation technique is technically much more challenging.

Interestingly, in the reports on the Ross operation that showed a high incidence of reoperation, more than one surgeon performed the initial operation.[8,10,12] In studies where only one surgeon performed the Ross operation, incidence of reoperation was lower.[9,20] This suggests that larger experience is correlated with improved durability.

Another factor that is supposed to play a role in autograft dilatation is bicuspid valve disease.[21] It is known that a bicuspid aortic valve is associated with aortic wall abnormalities.[22] Since the pulmonary valve has the same embryonic origin as the aortic valve, these abnormalities could also be present in the pulmonary artery. Microscopic evaluation of pulmonary autografts reveals media abnormalities, intimal proliferation, and adventitial fibrosis suggestive of chronic exposure to high pressure.[6,23,24] However, in a recent autograft explant study no association was observed between bicuspid valve disease and histological changes in explanted pulmonary autografts.[25]

In the present study, adult patient age tended to be associated with higher autograft reoperation rates (8% at 13 years for patients under the age of 16 years when compared with 44% for adults). Other reports confirm the observation that fewer reoperations are seen in children.[26–28] However, Luciani *et al.*[10] found an opposite effect of patient age on autograft dilatation, but not on reoperation. A possible explanation is that the pulmonary autograft has the capacity to increase in diameter in the paediatric patient.[27] Whether it grows or simply dilates in line with somatic growth in children, is still a matter of debate.

Finally, patients who had previously undergone AVR (six subcoronary homografts, three biological prostheses, three mechanical prostheses) may also be at greater risk for pulmonary autograft reoperation in the future. In this regard, it might be relevant that after complete removal of the valve substitute, the remaining fibrotic annular area is

removed in part as well, without leaving a fixed plane for insertion of the pulmonary autograft.

Despite the high autograft reoperation rate in our study population, the pulmonary allograft is well preserved; only eight patients required reoperation, which is comparable with other studies.[5,8] The main reason for allograft reoperation in the present study was degeneration with calcification of the allograft. Vogt *et al.*[28] determined in their study the viability of cryopreserved allografts and found both total destruction of cellular elements in endothelial cells of allografts and immunological rejection in allografts used in the RVOT. Since the allograft is a non-viable valve substitute it is predisposed to calcify, and eventually at risk for reintervention and therefore affects the durability of the Ross operation on the longer term. Still, the ideal conduit for the RVOT in adults as well as in children has to be found. In the near future there might be an interesting role for tissue engineering for this valve substitute. Considering the limitations of the existing valve substitutes this new concept of creating a viable valve out of human cells shows encouraging results.[29]

Another recent development, percutaneous valve implantation, may be applied to the degenerated pulmonary allograft. Since stenosis is the main indication for undergoing percutaneous valve replacement and since the homograft in the RVOT is subject to calcification, this could be an alternative to surgery.[30]

During follow-up, endocarditis and thrombo-embolic complications were uncommon in our study patients; bleeding events and valve thrombosis did not occur. This underlines that, in this regard, the Ross operation indeed allows patients to live their life to the fullest.

Clinical implications

In our centre, the Ross operation is now an operation performed only in infants and children. In adults it has been abandoned because of the high reoperation rate and because of the great complexity and difficulties that may be encountered at the eventual reoperation.

Other alternatives for the Ross operation are the mechanical prosthesis, bioprosthesis, and homograft with their advantages and disadvantages. Mechanical prostheses are designed to last a lifetime but require lifelong anticoagulation therapy due to their increased thrombogenicity. Even though anticoagulation therapy is relatively safe, it does increase the risk of bleeding complications. For smaller children no artificial valves of adequate size are available and the Ross operation remains the solution of choice. Furthermore, in children or patients who want to life an active lifestyle it is preferable to avoid the use of anticoagulation therapy. And also for women in child-bearing age the mechanical prosthesis has several disadvantages, including not only a higher mortality risk during pregnancy mainly due to valve thrombosis, but also a higher risk of embryopathy with oral anticoagulants.[31]

After the Ross operation, patients require no anticoagulation therapy similar to the bioprosthesis and homograft. However, tissue valves have a limited durability and therefore the patient almost certainly requires a reoperation later in life. Because of the large number of patients who return to our centre for reoperation in the second decade after the initial procedure, we need to ensure close follow-up of the patients and be prepared for more reoperations in the near future.

Conclusions

Although the Ross operation is associated with excellent patient survival in our institution, there is a considerable increase of autograft failure requiring reoperation. Careful follow-up is necessary in the second decade after the operation and greater insight into the mechanism of the pulmonary autograft dilatation is needed.

Finally, uniform well-defined and detailed technical guidelines for autograft root replacement need to be established if the Ross operation is to be maintained as a surgical option for AVR with optimal benefits and enhanced durability for the patients.

Conflict of interest: none declared.

References

1. Ross DN. Replacement of aortic and mitral valves with a pulmonary autograft. *Lancet* 1967;**2**:956–958.
2. Chambers JC, Somerville J, Stone S, Ross DN. Pulmonary autograft procedure for aortic valve disease: long-term results of the pioneer series. *Circulation* 1997;**96**:2206–2214.
3. Elkins RC, Lane MM, McCue C. Pulmonary autograft reoperation: incidence and management. *Ann Thorac Surg* 1996;**62**:450–455.
4. Kouchoukos NT, Davila-Roman VG, Spray TL, Murphy SF, Perrillo JB. Replacement of the aortic root with a pulmonary autograft in children and young adults with aortic-valve disease. *N Engl J Med* 1994;**330**:1–6.
5. Elkins RC. The Ross operation: a 12-year experience. *Ann Thorac Surg* 1999;**68**:S14–S18.
6. Carr-White GS, Afoke A, Birks EJ, Hughes S, O'Halloran A, Glennen S, Edwards S, Eastwood M, Yacoub MH. Aortic root characteristics of human pulmonary autografts. *Circulation* 2000;**102**:III15–21.
7. Takkenberg JJ, Dossche KM, Hazekamp MG, Nijveld A, Jansen EW, Waterbolk TW, Bogers AJ. Report of the Dutch experience with the Ross procedure in 343 patients. *Eur J Cardiothorac Surg* 2002;**22**:70–77.
8. Kouchoukos NT, Masetti P, Nickerson NJ, Castner CF, Shannon WD, Davila-Roman VG. The Ross procedure: long-term clinical and echocardiographic follow-up. *Ann Thorac Surg* 2004;**78**:773–781 (discussion).
9. Yacoub MH, Klieverik LM, Melina G, Edwards SE, Sarathchandra P, Bogers AJ, Squarcia U, Sani G, van Herwerden LA, Takkenberg JJ. An evaluation of the Ross operation in adults. *J Heart Valve Dis* 2006;**15**:531–539.
10. Luciani GB, Casali G, Favaro A, Prioli MA, Barozzi L, Santini F, Mazzucco A. Fate of the aortic root late after Ross operation. *Circulation* 2003;**108**(Suppl. 1):II61–II67.
11. Luciani GB, Favaro A, Casali G, Santini F, Mazzucco A. Reoperations for aortic aneurysm after the Ross procedure. *J Heart Valve Dis* 2005;**14**:766–772, discussion 772–763.
12. Brown JW, Ruzmetov M, Fukui T, Rodefeld MD, Mahomed Y, Turrentine MW. Fate of the autograft and homograft following Ross aortic valve replacement: reoperative frequency, outcome, and management. *J Heart Valve Dis* 2006;**15**:253–259, discussion 259–260.
13. Willems TP, Takkenberg JJ, Steyerberg EW, Kleyburg-Linkers VE, Roelandt JR, Bos E, van Herwerden LA. Human tissue valves in aortic position: determinants of reoperation and valve regurgitation. *Circulation* 2001;**103**:1515–1521.
14. Edmunds LH Jr, Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. *Ad Hoc* Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity of The American Association for Thoracic Surgery and The Society of Thoracic Surgeons. *J Thorac Cardiovasc Surg* 1996;**112**:708–711.
15. Clark TG, Altman DG, De Stavola BL. Quantification of the completeness of follow-up. *Lancet* 2002;**359**:1309–1310.
16. Schoof P, van Suylen RJ, Bos E. Homograft root replacement for juvenile rheumatoid aortic valve incompetence. *Ann Thorac Surg* 1992;**54**:602–603.

17. Klieverik LM, Noorlander M, Takkenberg JJ, Kappetein AP, Bekkers JA, van Herwerden LA, Bogers AJ. Outcome after aortic valve replacement in young adults: is patient profile more important than prosthesis type? *J Heart Valve Dis* 2006;**15**:479–487 (discussion).
18. Aklog L, Carr-White GS, Birks EJ, Yacoub MH. Pulmonary autograft versus aortic homograft for aortic valve replacement: interim results from a prospective randomized trial. *J Heart Valve Dis* 2000;**9**:176–188, discussion 188–179.
19. Takkenberg JJ, van Herwerden LA, Galema TW, Bekkers JA, Kleyburg-Linkers VE, Eijkemans MJ, Bogers AJ. Serial echocardiographic assessment of neo-aortic regurgitation and root dimensions after the modified Ross procedure. *J Heart Valve Dis* 2006;**15**:100–106, discussion 106–107.
20. Sievers HH, Hanke T, Stierle U, Bechtel MF, Graf B, Robinson DR, Ross DN. A critical reappraisal of the Ross operation: renaissance of the subcoronary implantation technique? *Circulation* 2006;**114**:I504–I511.
21. David TE, Omran A, Ivanov J, Armstrong S, de Sa MP, Sonnenberg B, Webb G. Dilation of the pulmonary autograft after the Ross procedure. *J Thorac Cardiovasc Surg* 2000;**119**:210–220.
22. Roberts CS, Roberts WC. Dissection of the aorta associated with congenital malformation of the aortic valve. *J Am Coll Cardiol* 1991;**17**:712–716.
23. Takkenberg JJ, Zondervan PE, van Herwerden LA. Progressive pulmonary autograft root dilatation and failure after Ross procedure. *Ann Thorac Surg* 1999;**67**:551–553, discussion 553–554.
24. Niwaya K, Knott-Craig CJ, Lane MM, Chandrasekaren K, Overholt ED, Elkins RC. Cryopreserved homograft valves in the pulmonary position: risk analysis for intermediate-term failure. *J Thorac Cardiovasc Surg* 1999;**117**:141–146, discussion 146–147.
25. Schoof PH, Takkenberg JJM, Van Suylen RJ, Zondervan PE, Hazekamp MG, Dion RAE, Bogers AJJC. Degeneration of the pulmonary autograft: an explant study. *Thorac Cardiovasc Surg* 2006;**132**:1426–1432.
26. Elkins RC, Lane MM, McCue C. Ross operation in children: late results. *J Heart Valve Dis* 2001;**10**:736–741.
27. Simon P, Aschauer C, Moidl R, Marx M, Keznickl FP, Eigenbauer E, Wolner E, Wollenek G. Growth of the pulmonary autograft after the Ross operation in childhood. *Eur J Cardiothorac Surg* 2001;**19**:118–121.
28. Vogt PR, Stallmach T, Niederhauser U, Schneider J, Zund G, Lachat M, Kunzli A, Turina MI. Explanted cryopreserved allografts: a morphological and immunohistochemical comparison between arterial allografts and allograft heart valves from infants and adults. *Eur J Cardiothorac Surg* 1999;**15**:639–644, discussion 644–645.
29. Hoerstrup SP, Kadner A, Melnitchouk S, Trojan A, Eid K, Tracy J, Sodian R, Visjager JF, Kolb SA, Grunenfelder J, Zund G, Turina MI. Tissue engineering of functional trileaflet heart valves from human marrow stromal cells. *Circulation* 2002;**106**:I143–I150.
30. Khambadkone S, Coats L, Taylor A, Boudjemline Y, Derrick G, Tsang V, Cooper J, Muthurangu V, Hegde SR, Razavi RS, Pellerin D, Deanfield J, Bonhoeffer P. Percutaneous pulmonary valve implantation in humans: results in 59 consecutive patients. *Circulation* 2005;**112**:1189–1197.
31. Yap SC, Takkenberg JJ, Witsenburg M, Meijboom FJ, Roos-Hesselink JW. Aortic stenosis at young adult age. *Expert Rev Cardiovasc Ther* 2005;**3**:1087–1098.

Clinical vignette

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Pacemaker Twiddler syndrome

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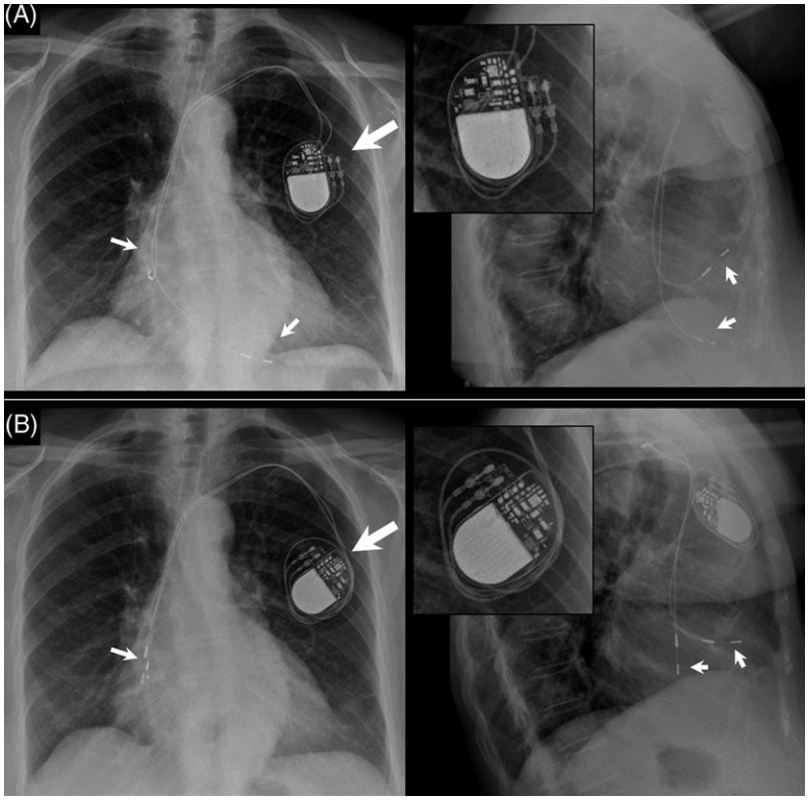

A 76-year-old woman diagnosed of sick sinus syndrome received in March 2006 a dual-chamber pacemaker with leads placed in the right atrium and right ventricle (arrows, Panel A). The leads were inserted without complications through axillary vein and secured with sutures to the pectoral muscle. A routine pacemaker follow-up performed 3 months later revealed no capture nor sensing of the ventricular lead, even at maximum output, and a considerable increase in the thresholds in the atrial lead. A chest X-ray (Panel B) showed displacement of both leads, especially the ventricle one, retracted and floating in the right atrium (arrows) with windings of the leads around the pulse generator (detail). Electrodes were replaced and the generator fixed to the underlying pectoral muscle. The patient admitted having twisted the pacemaker 'playing' with it. Twiddler syndrome, known as the rolling-up of the generator within the pacemaker pocket by the patient intentionally or not, frequently results in leads dislocation, diaphragmatic stimulation, and loss of capture. It is a rare but dangerous cause of lead dislodgement. Patients at risk for this condition include elderly and obese, because their relaxed subcutaneous tissue facilitates the rotation, and mentally handicapped patients. Clinical presentation includes those symptoms related with the failure of the cardiac pacemaker and other symptoms such as abdominal pulsation and stimulation of the pectoral muscle. Limiting the pocket size, suturing the device to the muscle, and the use of a Parsonnet pouch after the first episode may avoid the occurrence of this surprising but potentially fatal complication.