Cardiac reoperations following the Ross procedure in children: spectrum of surgery and reoperation results

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Abstract

OBJECTIVES: The Ross procedure is the preferred aortic valve replacement (AVR) choice in small children. Nonetheless, it is a complicated surgery and there are concerns that subsequent cardiac reoperations are exceptionally complex and associated with high morbidity and mortality. We examine the surgical spectrum and report outcomes of cardiac reoperations in patients who had undergone the Ross procedure during childhood.

METHODS: Records of 227 consecutive children (<18 years old) who had undergone the Ross procedure at our institution from 1991 to 2004 were reviewed. Our patient cohort was 50 patients who underwent 58 cardiac reoperations following the Ross procedure during the follow-up. Time-related outcomes were analyzed.

RESULTS: From 1992 to 2009, 50 patients, 37 males (74%), underwent cardiac reoperation at a mean age of 15.6 ± 5.2 years and a mean interval of 3.9 ± 3.0 years following the Ross procedure. Risk factors for cardiac reoperation following the Ross procedure on multivariable analysis were rheumatic fever, aortic regurgitation, concomitant cardiac surgery, use of fresh homografts and earlier era of surgery. Overall, 32 (55%) reoperations were isolated procedures whereas 26 (45%) were more complex involving 2–4 simultaneous cardiac procedures. In total, 92 procedures were performed including AVR (n = 31), homograft replacement (n = 23), mitral valve replacement (n = 18), mitral valve repair (n = 11), tricuspid valve repair (n = 5) and other (n = 4). There was no operative mortality and one late death. Survival was 98% at 10 years. During the follow-up, 8 of 50 patients required further cardiac surgery following initial reoperation with freedom from additional cardiac surgery of 82% at 10 years. Subsequent cardiac surgery risk was higher in patients with pre-operative aortic regurgitation and those who had concomitant surgery at time of Ross on log-rank analysis. Among survivors, 96% are in New York Heart Association class I/II.

CONCLUSIONS: A wide range of cardiac reoperations may be required in children following the Ross procedure, especially those with underlying rheumatic aetiology, aortic regurgitation and multivalvular involvement. Despite complexity, reoperation following the Ross procedure can be performed with low mortality and good mid-term results. This information should be taken into consideration during the selection of aortic valve substitute in children.

Keywords: Ross procedure · Aortic valve replacement · Reoperation · Rheumatic fever · Congenital heart disease

INTRODUCTION

The aortic valve can be commonly involved in various congenital and acquired pathologies in children thus requiring surgical intervention [1–3]. Although valve repair is the treatment of choice, aortic valve replacement (AVR) may be required in children in whom the valve is extensively damaged or following repair failure [1–3].

AVR in children is associated with distinct clinical and technical problems. Those problems are especially common in the smallest children owing to the lack of suitable small size prostheses and subsequent early and late problems related to compression of adjacent cardiac structures by the relatively large prosthesis, rapid prosthesis degeneration, lack of growth and poor compliance with anticoagulation regimen [2–4].

There is no ideal valve substitute and all options are associated with major limitations; the Ross procedure is no exception. The procedure is frequently censured for being complex and for creating a double valve disease that could require multiple complicated reinterventions. Modern literature showed that reoperation following the Ross procedure is not uncommon and often not limited to right ventricle to pulmonary artery (RV-PA) conduit change but may involve other cardiac structures owing to autograft failure, aortic dilatation with aneurysm formation and coronary anomalies, in addition to mitral and tricuspid valve

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disease [5–10]. Recent studies suggested that reoperations following the Ross procedure are especially complex and associated with high morbidity and mortality which may have implications on valve choice at time of initial AVR [5, 9, 11].

We aim in the current series to detail the range of surgeries and long-term outcomes following cardiac reoperation in patients who had undergone the Ross procedure during childhood.

PATIENTS AND METHODS

Inclusion criteria

From 1991 to 2004, 227 children underwent AVR with the Ross procedure at the King Faisal Specialist Hospital and Research Center in Riyadh, Saudi Arabia. The median age at time of the Ross procedure was 12.1 years (range 1 week–18 years); 15 patients (7%) were under 1 year of age at time of surgery. Follow-up of those children revealed that 50 patients, our current patient cohort, required cardiac reoperation following the Ross procedure from 1992 to 2009. Those patients were identified using our surgical database. Clinical, operative and outcome data were abstracted from the medical records. Approval of this study was obtained from the Research Ethics Board at our institution and individual consent was waived.

Patient cohort

Fifty patients who had undergone the Ross procedure during childhood and required subsequent cardiac reoperation were identified. They were 37 males (74%) and 13 females (26%). The mean age at time of the Ross procedure was 11.7 ± 4.3 years (range 2.4 months–18 years), and the mean age at time of first cardiac reoperation was 15.6 ± 5.2 years (range 1.2–27.5 years) with a mean interval between the Ross procedure and first reoperation of 3.9 ± 3.0 years (range 1 month–11.8 years).

Underlying aortic valve pathology was rheumatic fever in 37 patients (74%) and congenital heart disease in 13 patients (26%). Haemodynamic manifestation of aortic valve disease prior to the Ross procedure was regurgitation in 37 patients (74%), stenosis in 7 patients (14%) and mixed in 6 patients (12%). Prior to the Ross procedure, three patients had undergone prior cardiac surgery including aortic coarctation repair, aortic arch reconstruction with ventricular septal defect (VSD) closure and sub-aortic membrane resection (n = 1 each). At time of the Ross procedure, 23 patients (46%) had undergone concomitant cardiac procedures such as mitral valve repair (n = 21), VSD closure (n = 1) and ascending aortic aneurysm repair (n = 1). Eight patients (16%) had required aortic annular enlargement (modified Ross-Konno) at time of the Ross procedure.

The Ross procedure technique

Our Ross procedure technique has been described previously [2, 12, 13]. In summary, the pulmonary autograft was implanted as a full root with coronary transfer in all cases. The proximal suture line was performed using running polypropylene sutures. In patients with narrow left ventricular outflow tract (LVOT), a modified Ross-Konno technique was used by dividing the fibrous annulus of the aortic valve down to the septum to open up the LVOT without utilizing a VSD patch. RV-PA continuity was established with a homograft in all patients. The immediate post-operative results were assessed in all patients in the operating room by means of transoesophageal echocardiography.

Follow-up

Late outcomes were determined from recent office visits at King Faisal Specialist Hospital and Research Center or from direct correspondence with patients’ families. The mean follow-up duration following the Ross procedure was 11.7 ± 5.2 years and the mean follow-up duration following cardiac reoperation was 7.8 ± 5.2 years.

Statistical analysis

All the data were analyzed with the SAS software program (version 9; SAS Institute, Inc., Cary, NC, USA). Data are presented as frequency, median with range or mean ± SD as appropriate, with the number of non-missing values indicated. Estimates for long-term survival or freedom from reoperation were made by the Kaplan–Meier method. Differences between survival curves were evaluated with the log-rank statistic. Cox regression was used to determine the independent predictors of late outcomes.

RESULTS

Risk factors for cardiac reoperation following the Ross procedure

Among the 227 children who had undergone the Ross procedure, there were 58 cardiac reoperations in 50 patients in addition to 7 patients who underwent percutaneous pulmonary valve replacement. Overall freedom from cardiac reoperation following the Ross procedure was 95% at 1 year and 59% at 15 years (Fig. 1a and b). Overall freedom from all-cause cardiac reoperation was higher for patients with underlying congenital aortic valve disease compared with those with underlying rheumatic fever (69 vs. 44%, P = 0.002; Fig. 2). At 15 years following the Ross procedure, freedom from autograft replacement was 82%, freedom from homograft replacement (including percutaneous pulmonary valve) was 74%, freedom from autograft or homograft replacement was 61% (Fig. 3) and freedom from cardiac reoperation other than autograft or homograft replacement was 85% (Fig. 4).

Among the cohort of 50 patients who underwent reoperation following the Ross procedure, 42 patients had one reoperation and 8 patients had two reoperations. Some patients required multiple simultaneous cardiac procedures at time of each cardiac reoperation. Thirty-two (55%) of cardiac reoperations were isolated cardiac procedures, 20 (35%) were two simultaneous procedures, 4 (7%) were three simultaneous procedures and 2 (3%) were four simultaneous procedures. In total, 92 procedures were performed during those 58 reoperations including AVR (n = 31), RV-PA conduit change (n = 23), mitral valve replacement (n = 18), mitral valve repair (n = 11), tricuspid valve repair...
Factors associated with a higher risk of cardiac reoperation after the Ross procedure were sought. Significant factors for cardiac reoperation on multivariable analysis were underlying rheumatic fever [parameter estimate (PE): 0.89 ± 0.29, \( P = 0.002 \)], concomitant cardiac surgery at time of the Ross procedure (PE: 0.98 ± 0.27, \( P = 0.001 \)), pre-operative aortic regurgitation (PE: 0.89 ± 0.28, \( P = 0.002 \)), earlier era of surgery (PE: 0.20 ± 0.06, \( P < 0.001 \)) and the use of fresh homografts (PE: 0.61 ± 0.28, \( P = 0.03 \)).

**Time-related results following first cardiac reoperation**

Following cardiac reoperation, there were no operative mortalities and one late death 1.2 years following surgery. Overall survival was 98% at 10 years following reoperation.

Eight patients required subsequent cardiac reoperation. Freedom from additional surgery following first cardiac reoperation was 96% at 1 year and 82% at 10 years (Fig. 5).

There was a trend for higher need for subsequent cardiac reoperation in patients with pre-Ross aortic regurgitation when compared with stenosis by log-rank analysis (10-year freedom
from second reoperation 57 vs. 85% for stenosis, \( P = 0.024 \); Fig. 6) and in patients who had undergone concomitant cardiac surgery at time of the Ross procedure (10-year freedom from second reoperation 69 vs. 92% for those who had not undergone concomitant cardiac surgery, \( P = 0.12 \); Fig. 7). On multivariable analysis, none of the examined variables were found significant for subsequent second cardiac surgery following initial reoperation, likely due to the small sample size and small number of events.

Among survivors, 96% are in New York Heart Association functional class I/II.

**DISCUSSION**

The Ross procedure is considered by many as the aortic valve substitute of choice in small children as it is associated with excellent haemodynamic and cardiac recovery; it offers growth potential and does not require long-term anticoagulation [1–3, 6, 12, 13]. The early expectation was that autograft longevity will be better than that of any available prosthesis and that reoperation when required will be simple and limited mainly to RV-PA conduit change.

Nonetheless, increased follow-up exposed the fact that reoperation was not as infrequent as anticipated and often involved multiple valves in addition to the coronaries and ascending aorta [2, 5, 7–12].

Complex future reoperations following the Ross procedure may impose high morbidity and mortality risk that is more than that of simpler reoperations following AVR with stented prostheses. This reoperation complexity is a fact that should be taken into consideration at time of any cardiac surgery and could influence the type of the primary procedure offered to the patient.

A recent review from the Mayo clinic reported that 144 procedures were performed in 56 patients who required cardiac reoperations following the Ross procedure. Despite low hospital mortality (one patient), surgical morbidity was high and results were beset by four additional deaths at a median follow-up of 8 months [11]. Our study was consequently designed to examine the spectrum and complexity of procedures required at time of cardiac reoperation following the Ross procedure in children at our institution.

**Autograft reoperation**

Despite excellent survival and superior haemodynamics following the Ross procedure, recommendation for this procedure has been declining, especially in older children in whom there are other alternatives. This is mainly due to concerns about the development of aortic root dilatation, with or without subsequent autograft regurgitation [7–10]. Several risk factors have been identified to be associated with late autograft failure and subsequent reoperation including bicuspid aortic valve, rheumatic fever, especially when associated with dilated aortic annulus, geometric mismatch between the aortic and pulmonary valves and aortic regurgitation [7–10, 12, 14–18]. In a review from our
institution of children who underwent the Ross procedure for congenital and acquired aortic valve disease, we found that 15-year freedom from autograft reoperation was 82% and that freedom from reoperation was significantly influenced by underlying pathology, haemodynamic manifestation of aortic valve disease and concomitant valve surgery [12]. We also found that better patient selection can be associated with a significant reduction in autograft replacement requirement. For example, the expected 15-year freedom from autograft reoperation in children with congenital aortic stenosis and no concomitant cardiac pathology is >95% compared with 50% in children with rheumatic fever, aortic regurgitation and concomitant mitral involvement [12]. Moreover, we found that changes in patient selection that we had adopted by avoiding the Ross procedure in those with active rheumatic fever, associated mitral involvement, pure aortic regurgitation and dilated aortic annulus, along with technical modification such as careful trimming of the muscle cuff below autograft cusps and proximal suture line enforcement of marginally dilated annuli, have all been associated with significant increase in autograft longevity [12, 17]. Therefore, we suspect that the requisite for autograft replacement will further decrease in the current era and subsequently cardiac reoperations following the Ross procedure may become simpler.

Of note, among 31 AVR procedures at time of cardiac reoperation in our current series, none of the patients required root replacement and all had stented prostheses inserted within the autograft annulus. Accordingly, none of the patients had coronary injury or required extensive aortic reconstruction.

In other words, AVR following the Ross procedure was not more complex than redo replacement of stented prosthesis. This may be different from the experience reported in other centres such as the Mayo clinic where 38% of patients had aortic root replacement and 21% had ascending aorta and arch reconstruction at time of reoperation [11]. Their higher requirement for aortic root and ascending aorta surgery may be explained by different patient population with likelihood that patients at the Mayo clinic were older and had more preoperative bicuspid aortic valve with related regurgitation, dilated annulus and aortic wall pathology [11]. Although it has been shown that the annulus, root and ascending aorta endure progressive dilatation following the Ross procedure, none of the patients in our paediatric population so far required root surgery [7–10]. We appreciate that redo root surgery is a complex and morbid operation when needed but it has not been necessary in our patient population thus far [11, 13, 19]. Of course, those patients continue to need monitoring for possible development of root dilatation or aneurysm formation that may require aortic wall reintervention in the future.

Of note, several authors described surgical modifications to prevent autograft dilatation such as a reduction in aortic annulus diameter and wrapping the pulmonary autograft with an absorbable mesh, glutaraldehyde-fixed bovine pericardium or encasing it in a Dacron tube to prevent dilatation. Those techniques are suitable only for patients who will not need future autograft growth because the outer shell prohibits this [20]. Further follow-up is required to confirm the hypothetical advantages of those modifications. Another notable advance is the progress in valve preserving root-replacement techniques. Those techniques have been successfully used following the Ross procedure in patients with root dilatation and autograft regurgitation and may increase autograft longevity despite aortic wall reintervention [21].

**Homograft reoperation**

Reoperation for RV-PA conduit change is a continuous problem following the Ross procedure [5–7, 11–13, 18, 22, 23]. In a review from our institution of children who underwent the Ross procedure for congenital and acquired aortic valve disease, we found that 15-year freedom from homograft reoperation was 74% and that freedom from conduit replacement was significantly influenced by homograft type and size [12]. Twenty-three patients in our series required RV-PA conduit change as an isolated procedure or simultaneous to other procedures. In experienced hands, RV-PA conduit change is a relatively simple procedure and has been associated with low morbidity and operative mortality [5–7, 11–13, 18, 22, 23]. RV-PA conduit replacement will likely continue to be the most common type of reoperation following the Ross procedure. However, it is important also to note recent advances in percutaneous pulmonary valve replacement that have allowed cardiologists to address this problem without surgical intervention [24]. Seven patients at our institution who had undergone the Ross procedure during childhood had percutaneous pulmonary valves implanted with good immediate and short-term results; however, longer follow-up is needed to confirm those encouraging preliminary outcomes.

**Other valves reoperation**

A significant number of our patients (n = 29) required mitral reoperation following the Ross procedure. Simultaneous mitral valve repair at time of the Ross operation was a risk factor not only for mitral reoperation but also for autograft failure, especially in patients with rheumatic fever [12, 17]. Mitral valve replacement with a mechanical prosthesis following the Ross operation abolishes the major advantage of the Ross procedure of avoiding anticoagulation. It is therefore our current policy that we do not perform the Ross procedure in patients with rheumatic fever and multivalvular involvement except in selected patients. Obviously, mitral reoperation is a product of underlying pathology rather than a direct complication of the Ross procedure. Nonetheless, mitral pathology should be taken into consideration at time of initial AVR for the above-mentioned reasons.

On the contrary, although tricuspid valve regurgitation can be associated with underlying cardiac pathology, secondary tricuspid valve regurgitation can be a result of RV-PA conduit failure and subsequent right ventricular dilatation and therefore a direct complication of the Ross procedure. With proper surveillance for conduit failure and timely management, this problem seems to be uncommon. Only five patients in our series required tricuspid valve repair at time of reoperation, which was associated with low morbidity and durable results.

**Study limitations**

This case series is subject to the limitations inherent in all retrospective observational studies such as selection bias and lack of randomization. Additionally, the small cohort size, and multiple variables in this series that reflect the heterogeneous nature of patients, change in patient selection criteria and development of different surgical modifications related to the management of the autograft and homograft all preclude sophisticated statistical
analyses and limit the power of the study to identify clinically significant risk factors.

SUMMARY

Cardiac reoperations are not infrequent following the Ross procedure in children and may involve the autograft, homograft, aorta and other valves. Multiple simultaneous cardiac procedures may be necessary at time of cardiac reoperation, some related to original cardiac pathology and the others directly related to the Ross procedure. Nonetheless, complex cardiac reoperations can be performed at experienced centres with minimal early morbidity and good mid-term outcomes. Better patient selection and technical modifications have mitigated the need for autograft replacement and could potentially further simplify cardiac reoperation following the Ross procedure. Those favourable results support the continuous consideration of the Ross procedure as a valid option in a surgeon’s armamentarium in the treatment of aortic valve disease in selected children.

Conflict of interest: none declared.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr V. Hraska (Sankt Augustin, Germany): You have achieved excellent results with this challenging group of failing Ross patients requiring reoperation and have demonstrated that reoperation is not only safe but effective as well with a really promising outcome. On the other hand, the incidence of reoperation in your cohort is not trivial. Freedom from reoperation following a Ross procedure was less than 60% in 10 years of follow-up. Reoperation on the right ventricular outflow tract due to conduit failure is unavoidable, so I do not want to discuss this issue. However, the incidence of autograft failure is worrisome. Thirty-one patients out of 227 operated on underwent mechanical aortic valve replacement which represents 14% incidence of autograft failure with 82% freedom from autograft reoperation at 15 years of follow-up. What was the mechanism of autograft failure?

Dr Alsoufi: The majority of those failures, as I mentioned, were in the rheumatic valve disease patients. The mechanism of failure we found is different, in fact, from that reported in series which include Western populations. I was anticipating such a question and have a slide.

Dr Hraska: You can just describe the mechanism.

Dr Alsoufi: As you can see, half of the patients had recurrent inflammatory disease: in some this was clearly recurrent rheumatic fever, and in others was this vague, unspecified inflammatory disorder. The other half had the unusual aortic cusp dilatation, failure of coaptation or aneurysm formation. Most of these failures were in children who had the Ross procedure prior to 1999. In 1999, we adopted technical modifications and changed selection criteria. Subsequently, we have seen much less autograft reoperation. But the model failure is a little bit different, especially in rheumatic patients, than is seen in the Western populations, where the majority are bicuspid aortic valve and AI.

Dr Hraska: The underlying morphology and the mechanism of failure precluded you from using any type of valve-sparing operation; is that correct?

Dr Alsoufi: Yes, absolutely. Subsequent to this, I think in some adult patients, we have experience with aortic valve reimplantation. We have done a root-sparing autograft reoperation, preserving the valve but changing the root, but this was in patients who had the Ross procedure in adulthood. The patient cohort presented consists of patients who had the
Ross procedure during childhood. The leaflets in the majority of them were not good because of the recurrent inflammatory disorder. You cannot preserve.

Dr Hraska: Okay. Is mechanical aortic valve replacement only, without root replacement, justifiable when the long-term future of the neoaortic root is unclear? Can you comment on that?

Dr Alsoufi: This definitely a good question, and I am already trying to get echocardiograms in those patients who had the aortic valve replaced, and I want to see if the aortic root continues to be pathological.

I believe that the procedure is justifiable as it is a much simpler and safer procedure than the more complex redo root replacement which is associated with high risk of bleeding or coronary problems.

What happens to the root is interesting. We have quite a long follow-up so far, and it seems that despite progressive root dilatation in our patient population, none of them has yet reached a point that requires aortic root replacement. They need continued follow-up, but our experience so far is a course that has a simplified approach. We have not needed to redo the root yet in any of these patients.

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**EDITORIAL COMMENT**

Reoperations after paediatric Ross operation

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The population in their study is different from most reports on paediatric Ross operations from western countries, as it contains a much higher percentage of children who were operated on for rheumatic heart disease. This explains the relatively early reoperations: in the majority, replacement of the pulmonary autograft valve was done by a stented prosthesis and (re-) repair or replacement of the mitral valve.

The mortality of these reoperations was very low despite the fact that almost half of the reoperations were complex, with two to four simultaneous cardiac procedures. It has to be noted that reoperation for autograft dilatation was not necessary in any of their patients. All failing autograft valves could be replaced by stented prostheses that were placed inside the pulmonary autograft root, without the need to perform a root replacement. This also differs from other series and is probably explained by earlier reoperation of the autograft valve when root dilatation has not yet become significant. On the other hand, no repairs of the autograft valve are reported by the authors. This seems logical when considering the nature of rheumatic valve disease and the high chance of another reoperation when repairing the valve.

What can we learn from the experience of Alsoufi et al.? First of all, patient selection for the Ross operation is of paramount importance. Children with rheumatic heart disease are poor candidates for the Ross procedure. Especially when the aortic valve presents with annular dilatation and regurgitation and when the mitral valve is also damaged by rheumatic fever, one should refrain from doing a Ross operation. It was reported and histologically documented by Kumar et al. in 1999 and later in 2006 that the pulmonary autograft will frequently suffer from rheumatic degeneration once it is transposed to the aortic position. The reason for this is not entirely clear. Why does a pulmonary valve, that is often the only valve untouched by rheumatic fever, suffer from the rheumatic process once it is placed in the aortic position? [2, 3]. Concomitant rheumatic mitral valve disease should also be considered as a reason to avoid a Ross operation. Multiple valve involvement carries a higher risk of early reoperation and replacement of a mitral valve with subsequent anticoagulation abolishes one of the main purposes of the Ross technique.

A second lesson from this study is that it is again confirmed that aortic valve insufficiency increases the risk of pulmonary autograft failure and reoperation [1]. Recently, this was stressed by David et al. who found that aortic annular dilatation and valvular insufficiency do increase the risk of autograft failure even when annular reduction techniques were used during the Ross operation [4].

Finally, as was also reported by Stulak et al. [5] in 2010, reoperations after the Ross operation are often complex, with multiple concomitant procedures. The pulmonary autograft valve is usually lost at reoperation. Valve sparing root replacement and autograft valve repair have been reported, but the outcomes of these techniques in the longer term need to be awaited [6]. In experienced hands, reoperation after a Ross procedure can have a low mortality but there may be considerable morbidity. For all these reasons, careful patient selection is what a Ross operation should begin with.

**Conflict of interest:** none declared.

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