



Long-term outcomes of Ross and Ross–Konno operations in patients under 15 years of age

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Abstract

Objective The Ross operation is an excellent surgical option for young children, regardless of aortic pathology type. However, failure rates are concerning during the second postoperative decade. We sought to determine the predictors of long-term outcomes after Ross and Ross–Konno operation performed in childhood.

Methods We performed 34 Ross and 9 Ross–Konno operations in pediatric patients (age < 15 years) from 1996 to 2016, and retrospectively evaluated the long-term results.

Results The postoperative follow-up period was 13.5 ± 3.9 years. In the Ross group, there were one inpatient death and one death after discharge. There were no inpatient deaths in the Ross–Konno group. There were 6 reoperations in the Ross group and 1 in the Ross–Konno group for left ventricular outflow tract (LVOT). Cumulative survival rates were 96.8% and 100% in the Ross and Ross–Konno groups, respectively. The reoperation free rate for LVOT /RVOT (right ventricular outflow tract) were 98.6/85.5% and 91.9/63.4% in the 5th and 10th years of follow-up, respectively. Patients who underwent the operations at age > 8.6 years had higher risks of reoperation for LVOT. Aortic annulus measurements > 24 mm or aorta/pulmonary artery diameter (Ao/PA) ratios > 1.2 conferred higher risks of reoperation for LVOT.

Conclusions Long-term outcomes after Ross and Ross–Konno operations in children were satisfactory. However, new-onset aortic regurgitation was progressive and reoperation was needed in some children. Age, aortic annulus diameter, and Ao/PA ratio may be able to predict of long-term outcomes after Ross and Ross–Konno operations.

Keywords Ross operation · Ross–Konno operation · Left ventricular outflow tract · Aortic annulus diameter · Aortic-pulmonary artery diameter ratio

Introduction

Ross and Ross–Konno procedures were first described in 1967 [1, 2] and were first performed at our institution in 1996. These operative procedures relieve severe left ventricular outflow tract obstruction (LVOTO) caused by a narrow aortic root by simultaneously enlarging the proximal aorta and the LVOT. These procedures have some advantages that include maintenance of normal hemodynamics, fewer thromboembolic complications, and no requirement for anti-coagulation therapy. Ross and Ross Konno procedures are

suitable for young children, regardless of aortic valve pathology type. However, high failure rates are concerning during the second postoperative decade.

We performed 76 Ross and Ross–Konno operations. Among these, we reviewed the results of 43 patients who underwent these surgeries in childhood (age < 15 years) to determine the predictors that may have an impact on the outcomes. The current study aimed to evaluate the long-term survival and the reoperation rate who underwent Ross and Ross–Konno operations, and clarify the cause of reoperation.

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Patients and methods

Patients

This research is a retrospective study in a single facility. In this study, we evaluated the survival of patients after Ross and Ross–Konno operation, the postoperative cardiac function by angiography and echocardiogram, and the reoperation rate for LVOT and Right Ventricular Outflow Tract (RVOT) reconstruction. Follow-up is done on an outpatient basis, but in cases, where they cannot come in such as moving, we contacted them by telephone. We evaluated the records of 43 patients who underwent 34 Ross and 9 Ross-Konno operations in childhood (age < 15 years) at our institute from 1996 to 2016. We included those with follow-up over 5 years resulting in only two being excluded. The preoperative diagnoses included: congenital aortic valve stenosis (AS): 12 patients; aortic valve stenosis with regurgitation (AsR): 20 patients; aortic valve regurgitation (AR): 9 patients; infectious endocarditis (IE): 2 patients.

Concomitantly performed surgeries included: 5 ventricular septal defect (VSD) closures, 1 coarctation of the aorta repair, and 1 coronary arteriovenous fistula (AV) repair. Four patients underwent aortic valvotomy and 3 patients underwent VSD closure prior to the Ross and Ross Konno operation. The research ethics committee at our institution approved this study (approval number #3596), and 43 patients provided informed consent prior to participation in the study.

Surgical management

Indications for surgery

Infants and children with congenital AS and narrow aortic annuli are the best candidates for Ross and Ross–Konno procedures. If the aortic and pulmonary valve annuli are approximately the same size, or if the aortic valve annulus is slightly narrowed, a standard Ross operation is performed. A small aortic annulus is frequently found in patients with AS. When the LVOT is stenotic in addition to AS, a Konno incision is made at the aortic root wall to dilate the annulus, and then the Ross operation is performed. Thus, this procedure was termed the Ross–Konno operation [3, 4]. We performed the Ross–Konno operation on nine patients in this study. In the segment of the aortic root enlarged by the Konno incision, we usually trimmed the remaining part of the RVOT area into a U-shape so that it could be used as an autograft or filler material. However, if it could not be used because there were not enough remaining segments, we used the patient's own pericardium.

Ross and Ross–Konno procedure techniques

After the initiation of cardiopulmonary bypass (CPB) and induction of mild hypothermia and cardiac arrest using cold crystalloid for cardioplegia, the aortic valve was inspected. When a repair of the aortic valve did not seem durable, a Ross operation was performed. First, a pulmonary autograft was harvested from the RVOT, and then the base of the aorta was incised. Thereafter, the entire aortic wall was removed, leaving behind an annulus and a button-shaped coronary artery.

A pulmonary autograft was precisely transposed onto the aortic annulus and the RVOT was reconstructed using an allograft or an expanded polytetrafluorethylene (e-PTFE) 3-valved pericardial conduit.

At the autograft anastomosis, we ran a continuous suture along 2/3 of the posterior side, and then, because we expected the grafts to grow, the anterior 1/3 was knotted-sutured. During a Ross operation, the surgeon must be careful not to damage the valves of the pulmonary artery (PA). It is also important to preserve the septal branches as well as the branches of the septal branches of the left anterior descending artery when collecting the pulmonary autograft, in the wearing of the aortic annulus. Close attention should be paid to the new aortic valve as it is divided into three sections at 120° angles. This prevents the right coronary artery from bending or overstretching, particularly at the coronary artery button implantation site. Furthermore, in the outflow tract reconstruction, it is important to ensure that the right ventricle-PA morphology creates a smooth arch. In cases of distant autograft dilatation, it is recommended that reinforcement of the annulus be achieved using a Dacron® felt (INVISTA, Wichita, KS, USA) and autologous pericardium.

We used handmade conduits for RVOT reconstructions and the specified valve types. The conduit compositions (total $n = 36$) included: autologous pericardial conduits (14 patients), xeno-pericardial conduits (8 patients), a tissue-engineered graft (1 patient), valved aortic autografts (4 patients), and direct anastomoses of the posterior wall (9 patients).

The valve types used in the procedures (total $n = 36$) included: no valve (2 patients), autologous pericardium (25 patients), and e-PTFE (9 patients). Recently, we used an allograft for the RVOT in 7 patients (Table 1). All allografts were provided by the Tokyo University Tissue Bank.

Statistical analyses

Continuous data are presented as means \pm standard deviations (SD). Categorical variables were analyzed using the Chi-squared test or Fisher's exact test. Continuous variables were examined using the Student's *t* test or the Mann–Whitney *U* test. Kaplan–Meier curves were generated to compare

Table 1 Methods of RVOTR

Hand-made conduit	36
Conduit	
Autologous pericardial roll	14
Xeno-roll	8
Tissue-Engineered graft	1
Valved aortic autograft	4
Direct anastomosis of posterior wall	9
Valve	
None	2
Autologous pericardium	25
e-PTFE	9
Homograft	7

Table 2 Patient profile

Variable	Mean ± SD
Age (years)	9.5 ± 7.9
Male/female	31/12
Body weight (kg)	20.6 ± 9.8
CPB duration	223.3 ± 42.5
ACC time (min)	167.7 ± 90.2
Follow-up (years)	13.5 ± 3.9

CPB cardiopulmonary bypass time, ACC aorta cross clamp

the survival rates between the Ross and Ross–Konno groups. Wilcoxon and Kruskal–Wallis trials with log-rank tests were used in the survival analysis. A Cox proportional hazards regression analysis was performed to evaluate the following variables as predictors for reoperation secondary to LVOT pathology: age, sex, previous cardiac operation, and pre-operative aortic valve variables (AR, aortic annulus diameter, and aorta/pulmonary artery diameter [Ao/PA]). The proportional hazard assumption was met for all variables. Multivariate Cox proportional hazard models were developed using the significant ($p \leq 0.10$) univariate predictors. We showed with cut-off values whether the risk of reoperation for LVOT pathology increased according to the receiver operating characteristic (ROC) curve. The data were analyzed using JMP Version 12 (SAS Institute Inc., Cary, NC, USA), and were considered significant if $P < 0.05$.

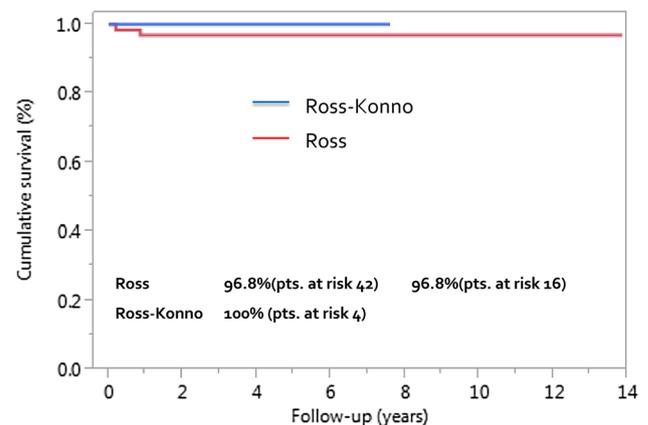
Results

The baseline characteristics of the 43 patients under 15 years of age are summarized in Table 2. At the time of surgery, the mean age was 9.5 years (range 5 months to 15 years) and the mean body weight was 20.6 kg (range 5–50 kg).

Table 3 Mortality and morbidity

	Ross ($n=34$)	Ross-Konno ($n=9$)
Hospital death	1(CHF)	0
Late death	1(CHF)	0
Reoperation for LVOT		
Procedure	AVR:5 Konno:1	Bentall:1
Causes	AR:3 AsR:2 IE:1	AR:1
Age at Ross (years)	8.0–15	12
Interval (years)	0.2–10.7	5
Reoperation for RVOT		
Procedure	RVOTR:3 PVR:1 PTA:9	RVOTR:1 PTA:1
Age at Ross (years)	0.9–10	0.5–5.6
Interval (years)	0.2–12.9	5.8–8.0

CHF congestive heart failure, IE infective endocarditis, AVR Aortic Valve Replacement, PTA percutaneous transluminal angiography, RVOTR right ventricular outflow tract reconstruction

**Fig. 1** Kaplan–Meier curve of survival rate for Ross/Ross–Konno operations

The mean CPB time was 223.3 ± 42.5 min, and the mean cardiac arrest time was 167.7 ± 90.23 min. The mean post-operative follow-up period was 13.5 ± 3.9 years (range 5–19 years; Table 2). In the Ross group, there was one inpatient death and one late death after discharge. A 13-year-old boy died of perioperative congestive heart failure on post-operative day 54. The underlying cause of the late death was chronic heart failure in the 10th postoperative month. There were no deaths in the Ross–Konno group (Table 3). The cumulative survival rate was 96.8% in the 5th and 10th follow-up years in the Ross group, and 100% in the Ross–Konno group (Fig. 1).

There were 22 significant complications in 21 patients. Seven patients required reoperation for LVOT pathology as follows: five patients underwent aortic valve replacement surgeries, one underwent a Konno operation, and one underwent a Bentall operation. The reasons for the reoperations included AR in four patients, ASR in 2, and IE in 1. Of the patients who underwent reoperation, the age range at initial surgery was 8–15 years in the Ross group and 12 years in the Ross–Konno group. The interval from the initial surgery to reoperation was 0.2–10.7 years in the Ross group and 5 years in the Ross–Konno group. The incidence of new-onset AR and AsR was 13.8% (AR: 4; AsR:2), and autograft dilatation was the leading cause of new-onset AR. The average length of time between the initial surgery and the progression to AR grade III was 8.3 years.

Among the patients in our study, five younger adults had undergone either annuloplasty or plication of the fibrous tissue beneath the commissures of the non-coronary aortic sinus. We performed reoperations for AR exacerbations that were grade III or higher, and for left ventricular volume overload.

There were four patients in whom the annulus was reinforced with Dacron felt or autologous pericardium. These annuli did not show decreases in performance. However, there were two patients in whom retraction of the commissure of the original aortic valve led to worsening AR and resulted in reoperation.

Five patients underwent reoperation for RVOT obstruction (RVOTO). Four of those patients had RVOT repairs and one had pulmonary valve replacement (PVR) because of pulmonary stenosis induced by conduit degeneration. Catheter interventions to manage RVOT were required ten times in nine patients because of stenotic pulmonary autografts. Among the patients requiring reoperation, the age range at initial surgery was 0.5–10 years for both groups, and the interval from initial surgery to reoperation ranged from 0.2 to 12.9 years for both groups (Table 3).

In the Ross group, the reoperation-free rate for the LVOT was 98.2% in the early postoperative period, and 90.3% in the 5th and 10th follow-up years. In the Ross–Konno group, the reoperation-free rate for the LVOT was and remains 87.5% from the early postoperative period, through to 10 year follow-up (Fig. 2). We reviewed the preoperative aortic and pulmonary annular diameters of the patients younger than 15 years of age. There were significant differences in age, aortic annulus diameter, and the Ao/PA ratio between the patients who underwent reoperation to manage the LVOT and those who did not require reoperation. The univariate predictors identified for age [hazard ratio (HR) 1.33; 95% confidence interval (CI) 0.92–1.98; $P=0.05$], aortic annulus diameter (HR 1.48; 95% CI 1.05–1.61; $P=0.04$), and Ao/PA diameter ratio (HR 1.65; 95% CI 1.15–2.56; $P=0.03$) were significant contributors to the reoperation

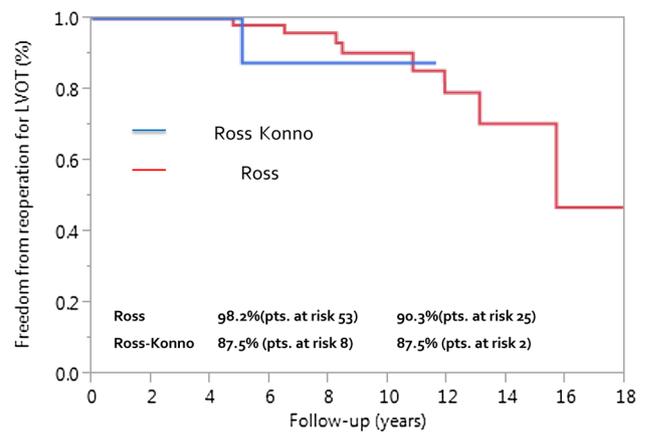


Fig. 2 Kaplan–Meier curve of freedom reoperation for LVOT

Table 4 Cox proportional hazards regression analysis was performed to evaluate the following variables as predictors for reoperation for LVOT

Factor	HR	95% CI	P value
Age	1.33	0.92–1.98	0.06
Sex	1.12	0.85–1.47	0.46
Previous cardiac operation	0.83	0.64–1.69	0.19
Aortic regurgitation	1.16	0.90–1.55	0.12
Aortic annulus diameter	1.48	1.05–1.61	0.04
Ao/PA diameter ratio	1.65	1.15–2.56	0.03

rates. In the multivariate analysis, no combination of univariate predictors reached significance because of the small number of events. (Table 4).

According to the ROC curve showing reoperations for LVOT pathology, the cut-off value for age was 8.6 years [area under the curve (AUC) 0.76] (Fig. 3a). Cut-off values for aortic diameter > 24 mm (AUC: 0.78) and Ao/PA ratios > 1.2 (AUC 0.78) were also determined. Better outcomes were observed when the aortic annulus diameters were < 24 mm or the Ao/PA ratios were < 1.2 (Fig. 3b, c).

The absence of reoperation for RVOTO was 85.5%, 63.4% in the 5th and 10th years of follow-up (Fig. 4). The autologous pericardial conduit and valve was the most frequently used conduit in reoperations for RVOT.

Discussion

Children younger than 15 years who underwent the Ross or Ross–Konno operations in our facility had a sustained low risk of death over time, but the reoperation rates were relatively high. This fact emphasizes the need for further study to determine the risk factors for reoperation so as to

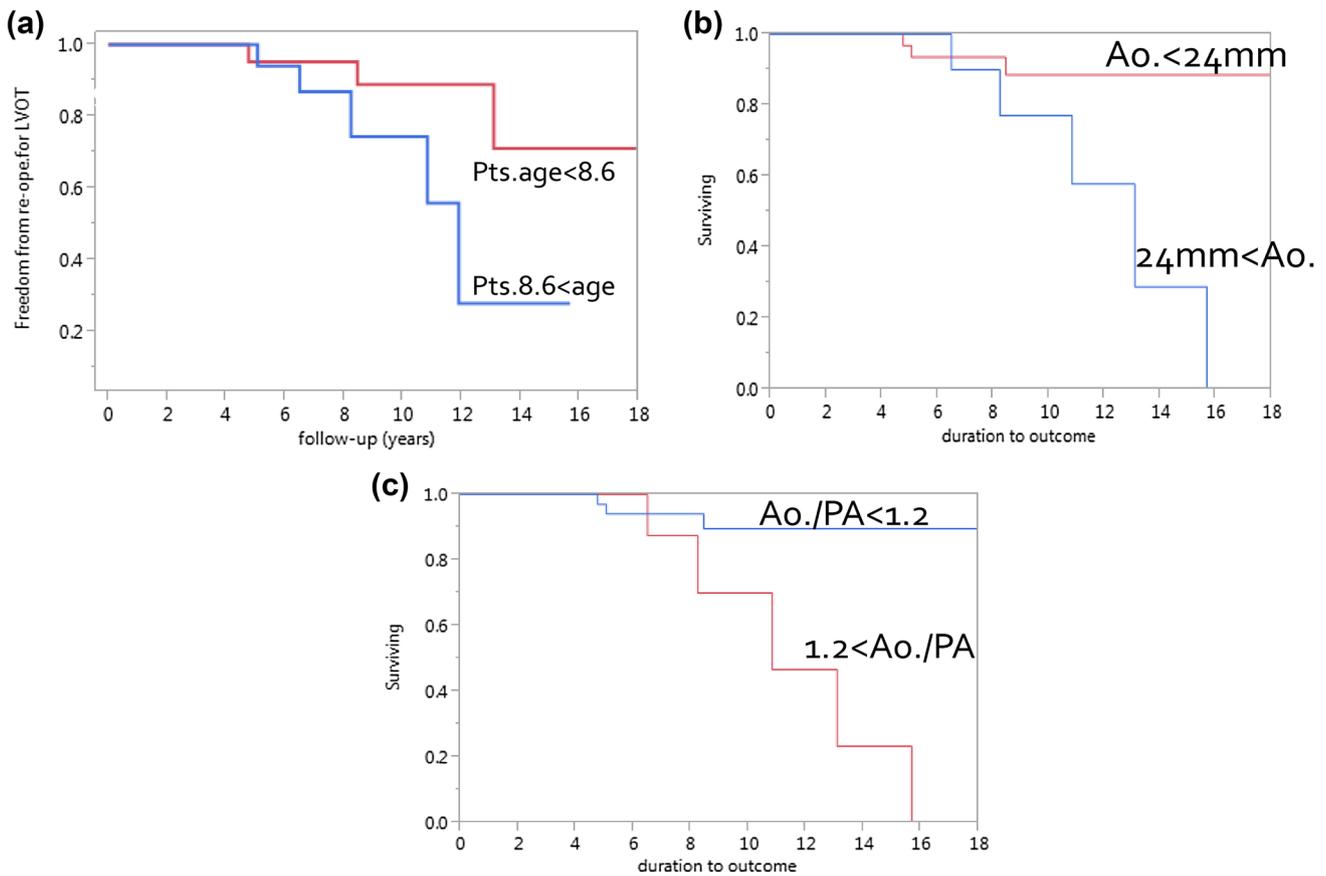


Fig. 3 Risk factors for reoperation for LVOT after Ross and Ross-Konno operation in patients younger than 15 years. **a** Freedom from reoperation for LVOT. According to the ROC curve of the reoperation for LVOT, the cut off value of age was calculated as 8.6 years.

Better outcome was observed in the group aortic annulus diameter less than 24 mm **(b)** or Ao/PA ratio less than 1.2 **(c)** compared to diameter more than aortic annulus diameter more than 24 mm or Ao/PA ratio more than 1.2

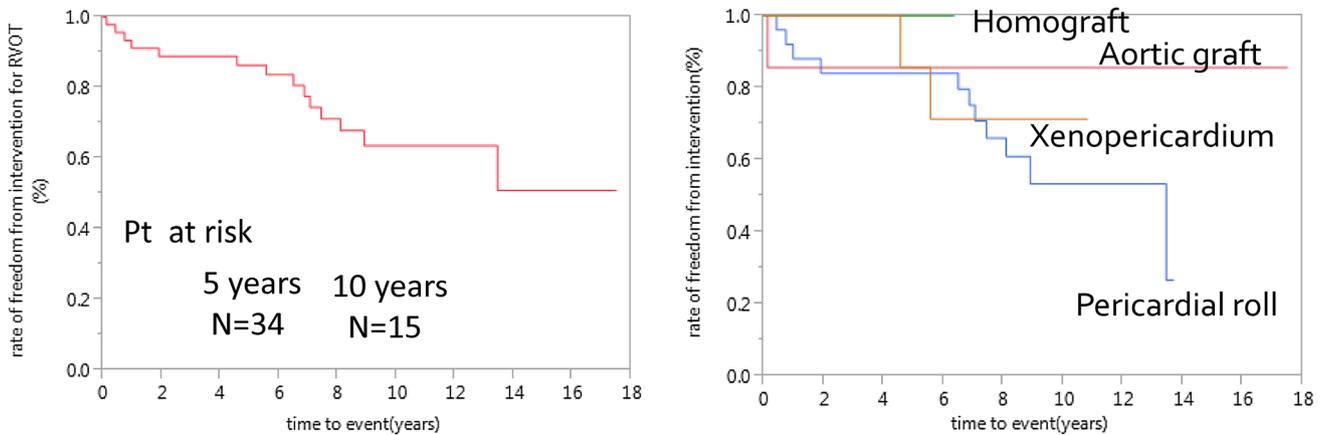


Fig. 4 Kaplan–Meier curve of freedom reoperation for RVOT

minimize or prevent recurrences in these young children. In our assessment of reoperations performed to manage the LVOT, age, preoperative aortic valve annulus diameter, and the Ao/PA diameter ratio were identified as predictive

risk factors. As these three factors could be extracted from the univariate analysis, we calculated their cut-off values, although they were not powerful. Our data show that the patients who underwent Ross or Ross–Konno operations at

an age > 8.6 years had a higher risk of reoperation for LVOT pathology. There are other reports that have confirmed variable age-related outcomes after the Ross operation in children [5]. Infants more commonly have left-sided heart disease and experience higher mortality, but they have excellent long-term autograft durability. Children and young adults tend to have a sustained, albeit low, risk of death over time. In addition to assessing survival, the long-term durability of the autograft across the age groups was an outcome of primary interest. Previous series have reported 74–100% freedom from LVOT reoperation at 10 years in pediatric patients who underwent Ross operation. However, nearly all comprised mixed age group cohorts [6–8].

The risk of LVOT reoperation in this study varied significantly across the age groups [9], with the reoperation after a Ross operation being rare in children younger than 1 year. These findings are consistent with those of previous smaller studies [10, 11]. Similarly, a series that evaluated slightly different age groups reported that fewer LVOT reoperations were performed at the 10-year postoperative mark among patients who were younger (age 1–12 years) vs. older (age 13–17 years) at the time of the initial surgery (73.3% vs. 46.1%, respectively) [12]. Jonas mentioned that the results for teenagers undergoing complete aortic root replacement have been less satisfactory [13]. Some children experienced complications including early outgrowth and calcification, as well as regurgitation due to excessive dilation of the neo-aortic root and neo-aortic valve. The pulmonary valve is histologically identical to the aortic valve at birth and undergoes postnatal differentiation. Thus, it is possible that Ross procedures performed in younger patients will allow the autograft to differentiate into a histology similar to that which would have occurred in the native aorta and aortic valve, which could potentially lead to a more durable autograft [14]. Mauro et al. compared the Ross and Ross–Konno aortic root procedures when they were performed in children before and after the age of 18 months. They concluded that the Ross and Ross–Konno operations confer sound survival benefits in younger patients as opposed to older ones [15]. From our risk assessment, we recommend that the Ross procedure be performed in children under the age of 8.6 years.

Age and autograft dilatation were the leading causes of reoperation in our series. The predictors for reoperation due to autograft dilatation, according to the univariate analysis, were dilated aortic annulus, and dilated autograft. AR was previously reported to be a risk factor for autograft dilatation in many series [16, 17]. Several groups have proposed technical modifications to the procedure to avoid autograft dilatation. In our series, five younger adults had either annuloplasty or plication of the fibrous tissue beneath the commissures of the non-coronary aortic sinus. None of these patients required reoperation on the autograft. We retrospectively calculated the preoperative aortic annulus diameter

and the Ao/PA ratio for patients younger than 15 years of age, and also calculated the extent to which new-onset AR was detected. Previously there were no studies that determined these cut-off values. Hence, the data of this study may provide important prognostic information to help guide clinical decision-making.

There have been some cases in which RVOT reconstruction or a related intervention was performed in the long-term period. We used handmade conduits for our RVOT reconstructions. Pulmonary allografts are used in other countries for reconstruction of the RVOT; however, in Japan, these allografts are not easily available, so other methods are used. Pulmonary and aortic xenografts are not suitable for right-sided heart systems, especially in young patients. For that reason, alternate conduits including autologous pericardial conduits and autologous tissue alone are used in RVOT reconstructions. Two significant advantages of these conduits are that concomitant anticoagulation therapy is unnecessary and they are resistant to infection;

Although we expected autologous pericardium to be superior to a xenograft, both were found to yield poor long-term outcomes. In an early series, we used a three-leaved valve and conduit created with autologous pericardial tissue, but these valves calcified easily and ultimately progressed to dysfunction. This may be the cause of early RVOT events. Subsequently, we changed to 1- or 2-valved conduits created with autologous pericardium or e-PTFE. One reason for the late incidences of RVOT pathology in those young children may be due to early metabolism-induced hyper-calcification.

In recent years, allografts have become less available, but its usage displays a 100% reoperation-free rate for RVOT operations. As reported previously [18, 19], allografts can be expected to be used in RVOT reconstructions.

This study had several limitations. First, this was a retrospective study. Patient selection and operative care have improved over the years, with likely improved outcomes. Although we included a relatively large patient cohort, the survival analyses showed that the number of patients remaining at-risk after 10 years of follow-up was too small to allow for reliable outcome estimates. During the past 20 years, the follow-up rate decreased to 89%. We showed with cut-off values whether the risk of reoperation for LVOT pathology increased according to the receiver operating characteristic (ROC) curve. The value of AUC is not so strong which is a maximum of 0.78, but we thought that setting the cut-off value should help with selection of a procedure.

In summary, long-term outcomes after Ross and Ross–Konno procedures in young children were satisfactory and could prevent reoperations requiring autografts. However, new-onset AR was progressive and reoperation was needed in some children older than 8 years of age when there was an Ao/PA diameter mismatch. These patients must be followed very carefully.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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