

Ross Procedures in Children With Previous Aortic Valve Surgery



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ABSTRACT

BACKGROUND The Ross procedure in children is performed either as a primary operation, or a secondary operation after initial aortic valve surgery.

OBJECTIVES The study aimed to determine whether the outcomes of primary and secondary Ross procedure are similar.

METHODS All patients who underwent Ross procedure between 1995 and 2018 were included in the study. Outcomes were compared between those who had primary Ross procedure and those who had secondary Ross procedure, after aortic valve surgery. Propensity score matching for baseline characteristics and risk factors for death and reoperation was performed.

RESULTS Of 140 Ross procedures, 51.4% (n = 72 of 140) were primary operations, while 48.6% (n = 68 of 140) were secondary operations. Patients undergoing primary Ross procedure tended to be older (median age 8.6 years vs. 7.0 years; p = 0.10) and have a higher weight (28.9 kg vs. 19.4 kg; p = 0.07). There were no significant differences in survival or freedom from reoperation in the unmatched cohort. Propensity score matching resulted in 50 well-matched pairs. In the matched cohort, survival at 10 years was 90.0% (95% confidence interval [CI]: 77.5% to 95.7%) in the primary Ross group, compared with 96.8% (95% CI: 79.2% to 99.5%) in the secondary Ross group (p = 0.04). Freedom from autograft reoperation at 10 years was 82% (95% CI: 64.1% to 91.5%) in the primary Ross group, compared with 97.0% (95% CI: 80.4% to 99.6%) in the secondary Ross group (p = 0.03).

CONCLUSIONS Secondary Ross procedure performed after initial aortic valve surgery achieves superior long-term survival and freedom from autograft reoperation compared with primary Ross procedure. A strategy of initial aortic valve repair followed by delayed Ross procedure may provide better long-term survival and freedom from autograft reoperation. (J Am Coll Cardiol 2020;76:1564-73) Crown Copyright © 2020 Published by Elsevier on behalf of the American College of Cardiology Foundation. All rights reserved.

Aortic valve disease requiring surgery in childhood is a challenging condition for surgeons to manage, with inevitable need for reintervention (1). Aortic valve repair, although often feasible, has a high rate of reoperation (2-6). The Ross procedure provides better long-term freedom from reoperation but results in neonates and infants are disappointing (7-14). Our preferred strategy is initial aortic valve repair, followed by Ross procedure when reoperation is necessary. Our aim is to delay



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Ross procedure until after 1 year of age, in order to avoid the high infant mortality, and achieve better autograft longevity. However, it is unclear if there is a difference in outcomes when the Ross procedure is performed as a primary operation, compared with when it is done as a reoperation. We performed a retrospective analysis of all Ross procedures at a single institution to investigate the difference in outcomes between primary and secondary Ross procedures.

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METHODS

PATIENTS. A total of 541 aortic valve operations were performed between 1995 and 2018, of which 63.6% (n = 344 of 541) were aortic valve repairs, 25.9% (n = 140 of 541) were Ross procedures, 7.9% (n = 43 of 541) were mechanical aortic valve replacements, 2.4% (n = 13 of 541) were homograft aortic valve replacements, and 0.2% (n = 1 of 541) were bioprosthetic aortic valve replacements. This cohort included 101 aortic valve replacements performed after previous aortic valve surgery, of which 67.3% (68 of 101) were Ross procedures, 27.7% (n = 28 of 101) were mechanical aortic valve replacements, 4.0% (n = 4 of 101) were homograft aortic valve replacements and 1.0% (n = 1 of 101) were bioprosthetic aortic valve replacements. Of the 140 children who had Ross procedure and were included in the study, 51.4% (n = 72 of 140) underwent Ross procedure as a first surgery (primary Ross procedure) and 48.6% (n = 68 of 140) underwent Ross procedure after prior aortic valve surgery (secondary Ross procedure). The Ross procedure is our preferred approach whenever aortic valve replacement is required. Prosthetic aortic valve replacement is reserved for patients with rheumatic valve disease, those with connective tissue diseases, and those with infective endocarditis who are not suitable for Ross procedure due to severe annular destruction or critical illness. Ethics approval was granted by the Royal Children’s Hospital Human Research Ethics Committee. Data were collected retrospectively from hospital records. Follow-up was obtained from correspondence with patients’ cardiologists and general practitioners.

DEFINITIONS. Early mortality was defined as death within 30 days of surgery, or during the same hospital admission. Primary Ross procedure was defined as a Ross procedure without prior aortic valve surgery. Secondary Ross procedure was defined as a Ross procedure performed after previous surgical aortic valve repair or replacement (including surgical

valvotomy and leaflet repair but excluding balloon valvuloplasty). Simple valvotomy refers to surgical commissurotomy without additional repair techniques. Extended aortic valve repair refers to surgical techniques including leaflet thinning, leaflet patching, plication and triangular resection and sub-commissural annuloplasty.

OPERATIVE TECHNIQUE. The operative technique has been previously described (12). Briefly, all procedures were performed through a median sternotomy with aortobicaval cannulation, on full cardiopulmonary bypass at moderate systemic hypothermia. The pulmonary autograft is harvested and most commonly implanted as an aortic root replacement, with coronary reimplantation. Recently, a poly-(p-dioxanone) filament band (PDS, Johnson & Johnson, New Brunswick, New Jersey) has been used to reinforce the sinotubular junction. Right ventricle-to-pulmonary artery (RV-PA) continuity is re-established with 1 of a homograft (aortic or pulmonary), Contegra conduit (Medtronic, Minneapolis, Minnesota), or Freestyle conduit (Medtronic).

STATISTICAL METHODS. Data were analyzed using STATA version 13 (StataCorp LP, College Station, Texas). Continuous data were presented as mean ± SD, and skewed continuous data were expressed as median (interquartile range [IQR]). Discrete data were presented as percentages and frequencies of patients. Continuous variables were compared using the

ABBREVIATIONS AND ACRONYMS

- CI = confidence interval
- IQR = interquartile range
- RV-PA = right ventricle to pulmonary artery

TABLE 1 Baseline Characteristics Comparing Those Who Underwent Primary Ross Procedure With Those Who Had Prior Aortic Valve Surgery

	Primary Ross Procedure (n = 72)	Secondary Ross Procedure (n = 68)	p Value
Age, yrs	8.6 (3.1-14.0)	7.0 (1.0-12.2)	0.10
Weight, kg	28.9 (13.7-55.6)	19.4 (9.6-41.1)	0.07
Aortic valve morphology			
Unicuspid	0 (0.0)	6 (8.8)	0.01
Bicuspid	41 (56.9)	25 (36.8)	0.02
Tricuspid	31 (43.1)	37 (54.4)	0.24
Primary pathology			
Stenosis	17 (23.6)	22 (32.4)	0.25
Regurgitation	17 (23.6)	14 (20.6)	0.67
Mixed	30 (41.7)	29 (42.6)	0.91
Coarctation	9 (12.5)	8 (11.8)	0.89
Infective endocarditis	8 (11.1)	3 (4.5)	0.14
VSD	5 (6.9)	5 (7.4)	0.93
Interrupted arch	4 (5.6)	0 (0.0)	0.05
Endocardial fibroelastosis	1 (1.4)	2 (2.9)	0.53
RHD	2 (2.8)	0 (0.0)	0.17
TGA	0 (0.0)	2 (2.9)	0.14

Values are median (interquartile range) or n (%).
 RHD = rheumatic heart disease; TGA = transposition of great arteries; VSD = ventricular septal defect.

TABLE 2 Operative Details Comparing Patients Who Had a Primary Ross Procedure With Those Having Secondary Ross Procedure

	Primary Ross Procedure (n = 72)	Secondary Ross Procedure (n = 68)	p Value
XCT, min	166.4 ± 42.5	161.2 ± 55.0	0.54
CPB, min	233.9 ± 91.6	219.7 ± 50.8	0.27
Ross technique			
Root replacement	41 (56.9)	41 (60.3)	0.70
Ross-Konno	21 (29.2)	17 (25.0)	0.58
Inclusion cylinder	9 (12.5)	8 (11.8)	1.0
Subcoronary	1 (1.4)	2 (2.9)	0.61
PDS reinforcement	11 (15.3)	15 (22.1)	0.30
RV-PA conduit type			0.02
Pulmonary homograft	43 (59.8)	32 (47.1)	
Contegra xenograft	13 (18.1)	28 (41.2)	
Aortic homograft	13 (18.1)	7 (10.3)	
Freestyle xenograft	3 (4.2)	1 (1.5)	
RV-PA conduit size, mm	20.6 ± 0.5	19.2 ± 0.5	0.06
Length of hospital stay, days	19.3 ± 5.2	16.4 ± 3.5	0.65
Post-operative complications			
Early death	4 (5.6)	3 (4.4)	1.0
ECMO	0 (0.0)	1 (1.5)	0.49
Pacemaker	3 (4.2)	3 (4.4)	1.0

Values are mean ± SD or n (%).
CPB = cardiopulmonary bypass; ECMO = extracorporeal membrane oxygenation; RV-PA: right ventricle to pulmonary artery; XCT = cross-clamp time.

Kruskal-Wallis test, while discrete variables were compared using the chi-square test, unless group size was <10, in which case Fisher exact test was used. For the purpose of assessing the effect of era, the cohort was divided into 2 groups: 1995 to 2006 (n = 69) and 2007 to 2018 (n = 71). Time-dependent endpoints (i.e., survival and freedom from reoperation) were analyzed using the Kaplan-Meier method. Statistical significance was set as a p value <0.05.

Propensity score matching was used to assess the impact of reoperative Ross procedure on clinical outcomes, as has been previously described in detail (15). Propensity scores were generated using variables associated with reoperation and mortality after Ross procedure (age, weight, valve morphology, valve pathology [i.e., regurgitation, stenosis, and mixed]). Matching on the generated propensity scores was performed using 1:1 matching with a fixed caliper width set at 0.20 standard deviations of the logistic regression of the propensity score. The degree of balance of baseline characteristics between groups was assessed using standardized differences, where a difference of <10% was considered to reflect high degree of balance. Kaplan-Meier analysis was performed to estimate time dependent endpoints. An adjusted log-rank test stratified by quintiles of propensity scores was used to assess differences

between matched groups for time-dependent endpoints (16).

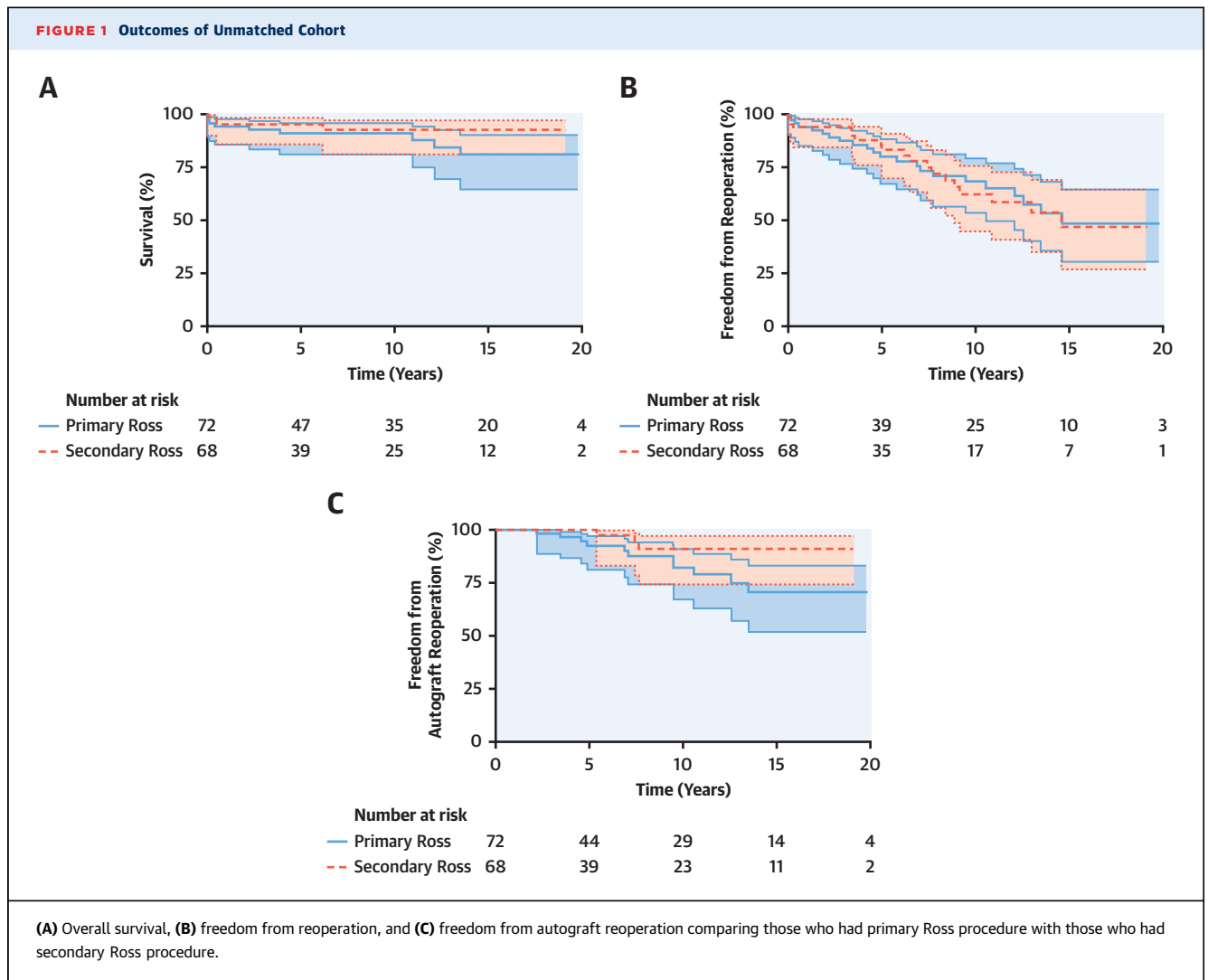
RESULTS

PATIENTS. There were a total of 140 Ross procedures performed in the study period, of which 51.4% (n = 72 of 140) were performed as a primary procedure, while 48.6% (n = 68 of 140) were performed as a reoperative procedure. Baseline demographics comparing patients who underwent primary Ross procedure with those who underwent secondary Ross procedure are presented in **Table 1**. It can be seen that patients undergoing a primary Ross procedure tended to be older (median age 8.6 years vs. 7.0 years; p = 0.10) and have a higher weight (28.9 kg vs. 19.4 kg; p = 0.07), although these differences did not reach statistical significance. Of the 68 patients, who had a secondary Ross procedure, 39.7% (n = 27 of 68) underwent isolated valvotomy, 47.1% (n = 32 of 68) underwent extended repair, 2.9% (2 of 68) underwent aortic valve replacement, 8.8% (n = 6 of 68) underwent initial valvotomy followed by valve repair, and 1.5% (n = 1 of 68) underwent valvotomy followed by aortic valve replacement. The median time from initial aortic valve surgery to Ross procedure was 4.2 years (IQR: 0.8 to 9.4 years).

Operative details comparing patients, who underwent primary and secondary Ross procedures are demonstrated in **Table 2**.

SURVIVAL. The early mortality was 5.6% (n = 4 of 72) in those undergoing primary Ross procedure, compared with 4.4% (n = 3 of 68) in those undergoing secondary Ross procedure. This difference was not statistically significant (p = 1.0). Detailed causes of death were provided in our previous publication (7). All early deaths occurred in neonates (n = 3 of 5, 60%) and infants (n = 4 of 24, 16.7%). Long-term survival is shown in **Figure 1A**. Survival at 10 and 15 years was 91% (95% confidence interval [CI]: 81.1% to 95.9%) and 80.9% (95% CI: 64.5% to 90.2%) in those undergoing primary Ross procedure, respectively, compared with 92.6% (95% CI: 81.1% to 97.3%) at both 10 and 15 years in those undergoing secondary Ross procedure. There was no significant difference in long-term survival between the 2 groups (p = 0.24).

REOPERATIONS. Long-term freedom from reoperation is shown in **Figure 1B**. Freedom from reoperation at 10 and 15 years was 68.3% (95% CI: 53.4% to 79.3%) and 48.5% (95% CI: 30.3% to 75.6%) in those undergoing primary Ross procedure, respectively, compared with 62.2% (95% CI: 44.7% to 75.6%) and



47.0% (95% CI: 26.9% to 64.8%) in those who underwent secondary Ross procedure, respectively. There was no significant difference between the groups ($p = 0.89$). There were no peri-operative deaths at the time of reoperation after Ross procedure.

Long-term freedom from autograft reoperation is shown in **Figure 1C**. Freedom from autograft reoperation at 10 and 15 years was 82.2% (95% CI: 67.1% to 90.8%) and 70.7% (95% CI: 51.8% to 83.3%) for patients undergoing primary Ross procedure, respectively, compared with 90.9% (95% CI: 74.2% to 97.0%) at both 10 and 15 years for patients undergoing secondary Ross procedure. The difference between the 2 groups did not reach statistical significance ($p = 0.07$). Details of autograft reoperations are summarized in **Table 3**.

Freedom from reoperation on the RV-PA conduit at 10 and 15 years was 77.3% (95% CI: 62.9% to 86.7%)

and 54.7% (95% CI: 35.8% to 70.2%) for the primary Ross procedure group, respectively, compared with 69.6% (95% CI: 51.2% to 82.2%) and 54.0% (95% CI: 32.3% to 71.4%) for the secondary Ross procedure group, respectively. This difference was not statistically significant ($p = 0.92$).

In addition to the reoperations, there were 8 transcatheter procedures performed on the RV-PA conduit: 5 balloon valvuloplasties, 2 RV-PA conduit stents, and 1 Melody valve (Medtronic) implantation. Freedom from any RV-PA conduit reintervention at 10 and 15 years was 77.4% (95% CI: 63.0% to 86.8%) and 52.3% (95% CI: 33.8% to 67.9%) in the primary Ross procedure group, respectively, compared with 60.5% (95% CI: 43.2% to 74.1%) and 52.2% (95% CI: 33.9% to 67.7%) in the secondary Ross procedure group, respectively. This difference was not statistically significant ($p = 0.60$).

TABLE 3 Details of Autograft Reoperation

Pathology	Age at Ross Procedure (Years)	Primary or Secondary Procedure	Cause of Reoperation	Time to Reoperation (Years)	Type of Reoperation
Bicuspid aortic valve, AS, Shone complex	11.6	Primary	Autograft stenosis	10.5	Valve repair and ascending aorta replacement
Bicuspid aortic valve, mixed AS/AR	3.6	Primary	AR due to autograft dilatation	13.5	Root replacement with porcine root
Dilated aortic root, AR	8.9	Primary	AR due to autograft dilatation	12.6	Valve-sparing aortic root replacement
Aortic valve endocarditis, AR	0.8	Primary	AR due to autograft dilatation	9.5	Mechanical Bentall procedure
Bicuspid aortic valve, AR post-BAV	8.3	Primary	AR due to autograft dilatation	4.9	Annuloplasty, STJ reduction, leaflet plication
Bicuspid aortic valve, mixed AS/AR post-BAV	18	Primary	AR due to autograft dilatation	6.9	Mechanical Bentall procedure
Bicuspid aortic valve with AS, interrupted aortic arch	0.5	Primary	AR due to autograft dilatation	3.4	Annuloplasty, STJ reduction, leaflet plication
Congenital AS, mixed AR/AS post-failed BAV	0.1	Primary	AR due to autograft dilatation	9.5	Annuloplasty, cusp resuspension
Rheumatic heart disease, AS	17.5	Primary	AR due to autograft leaflet prolapse	2.2	Mechanical aortic valve replacement
Dysplastic trileaflet valve, small annulus, AS	3.8	Primary	AR due to autograft dilatation	7.1	Mechanical aortic valve replacement
Trileaflet valve with prolapsing left coronary cusp, AR	0.2	Primary	AR due to autograft dilatation	4.6	Leaflet plication, annuloplasty
Congenital AS and aortic coarctation	1.1	Secondary	AR due to autograft dilatation	7.4	Annuloplasty, STJ reduction
Prolapsing right coronary cusp with failed leaflet extension, AR	15.7	Secondary	AR due to autograft dilatation	5.4	Mechanical Bentall procedure
Bicuspid aortic valve, AS	0.9	Secondary	AR due to autograft dilatation	7.6	Leaflet plication, annuloplasty

AS = aortic stenosis; AR = aortic regurgitation; BAV = balloon aortic valvuloplasty, STJ = sinotubular junction.

Freedom from reoperation on the RV-PA conduit at 5 years was 100% for the Freestyle xenograft, 91.9% (95% CI: 81.6% to 96.6%) for the pulmonary homograft, 89.2% (95% CI: 63.2% to 97.2%) for the aortic homograft, and 73.1% (95% CI: 46.6% to 87.9%) for the Contegra xenograft. These differences did not reach statistical significance ($p = 0.10$).

Furthermore, there was no impact of era on mortality ($p = 0.94$), autograft reoperation rate ($p = 0.68$), or overall reoperation rate ($p = 0.58$).

PROPENSITY SCORE-MATCHED GROUPS. Propensity score matching was performed to account for baseline difference between the group of patients who had primary Ross procedure and those who underwent secondary Ross procedure. This resulted in 50 well-matched pairs, as shown in [Table 4](#). Notably, there was no difference between the groups in terms of age ($p = 0.54$), weight ($p = 0.60$), or aortic valve morphology ($p = 0.65$). The use of PDS reinforcement of the sinotubular junction did not differ significantly between the groups (14% vs. 20%; $p = 0.60$).

Survival comparing the matched groups is shown in [Figure 2A](#). Survival at 10 and 15 years was 90.0% (95% CI: 77.5% to 95.7%) and 82.6% (95% CI: 65.7% to 91.7%) in the primary Ross procedure group,

respectively, compared with 96.8% (95% CI: 79.2% to 99.5%) at both 10 and 15 years in the secondary Ross procedure group. This represented a statistically significant difference ($p = 0.04$).

Overall freedom from reoperation, comparing the matched groups, is shown in [Figure 2B](#). Freedom from reoperation at 10 and 15 years was 66.5% (95% CI: 48.9% to 79.2%) and 49.8% (95% CI: 30.7% to 66.4%) in the primary Ross procedure group, respectively, compared with 74.9% (95% CI: 53.9% to 87.3%) and 56.5% (95% CI: 31.7% to 75.4%) in the secondary Ross procedure group, respectively. This difference was not statistically significant ($p = 0.22$).

Freedom from reoperation on the autograft, comparing matched groups, is shown in [Figure 2C](#). Freedom from autograft reoperation at 10 and 15 years was 82% (95% CI: 64.1% to 91.5%) and 74.1% (95% CI: 54.2% to 86.3%) in the primary Ross procedure group, respectively, compared with 97.0% (95% CI: 80.4% to 99.6%) at both 10 and 15 years in the secondary Ross procedure group. This difference was statistically significant ($p = 0.03$).

Freedom from reoperation on the RV-PA conduit at 10 and 15 years was 73.5% (95% CI: 55.7% to 85.0%) and 56.2% (95% CI: 36.7% to 71.8%) in the primary

Ross procedure group, respectively, compared with 78.3% (95% CI: 57.5% to 89.8%) and 61.1% (95% CI: 36.1% to 78.8%) in the secondary Ross procedure group. This difference did not reach statistical significance ($p = 0.36$).

DISCUSSION

Pediatric aortic valve disease presents a challenge to surgeons due to the competing aims of minimizing transvalvular gradient and degree of regurgitation, permitting ongoing somatic growth and minimizing reoperation rates. In young children, options include a strategy of initial valve-sparing approaches (valvuloplasty, valvotomy, and valve repair) or the Ross procedure (1). The Ross procedure has shown excellent results in young adults, superior to what can be achieved with a prosthetic valve replacement (15,17-21). Application of the Ross procedure in children has also provided good long-term outcomes. However, there are higher rates of autograft reintervention. Furthermore, in infants the early mortality rate is high, in the range of 16% to 22% (7,8,11).

In order to address the shortcomings of early Ross procedure, our unit has pursued a strategy of aortic valve repair followed by secondary Ross procedure if required (3). Our strategy has always been to do aortic valve repair as the first procedure, then perform Ross procedure at a later stage beyond infancy and, ideally, in adolescence when the child is fully grown. This strategy did not change over the study period (7,12). We always try to repair the valve, and the Ross procedure is performed when the aortic valve is deemed not suitable for repair by the operating surgeon (7,12). We have previously demonstrated superior freedom from reoperation following surgical aortic valve repair compared with balloon aortic valvuloplasty in infants and children (2). As such, surgical aortic valve repair has become our preferred intervention for initial aortic valve surgery, and balloon valvuloplasty is rarely used (7). We accept the potential need for reoperation following primary aortic valve repair, in the hope of avoiding the high mortality of Ross procedure in infancy, and achieving a more durable outcome from the autograft (2). However, it has been unclear if the outcomes of secondary Ross procedure would be similar to those of the primary Ross procedure. Additional potential risks that may be encountered during redo sternotomy and dissection of adhesions could compromise the outcomes of the Ross. Hence, we reviewed our results, comparing primary and secondary Ross procedures (Central Illustration).

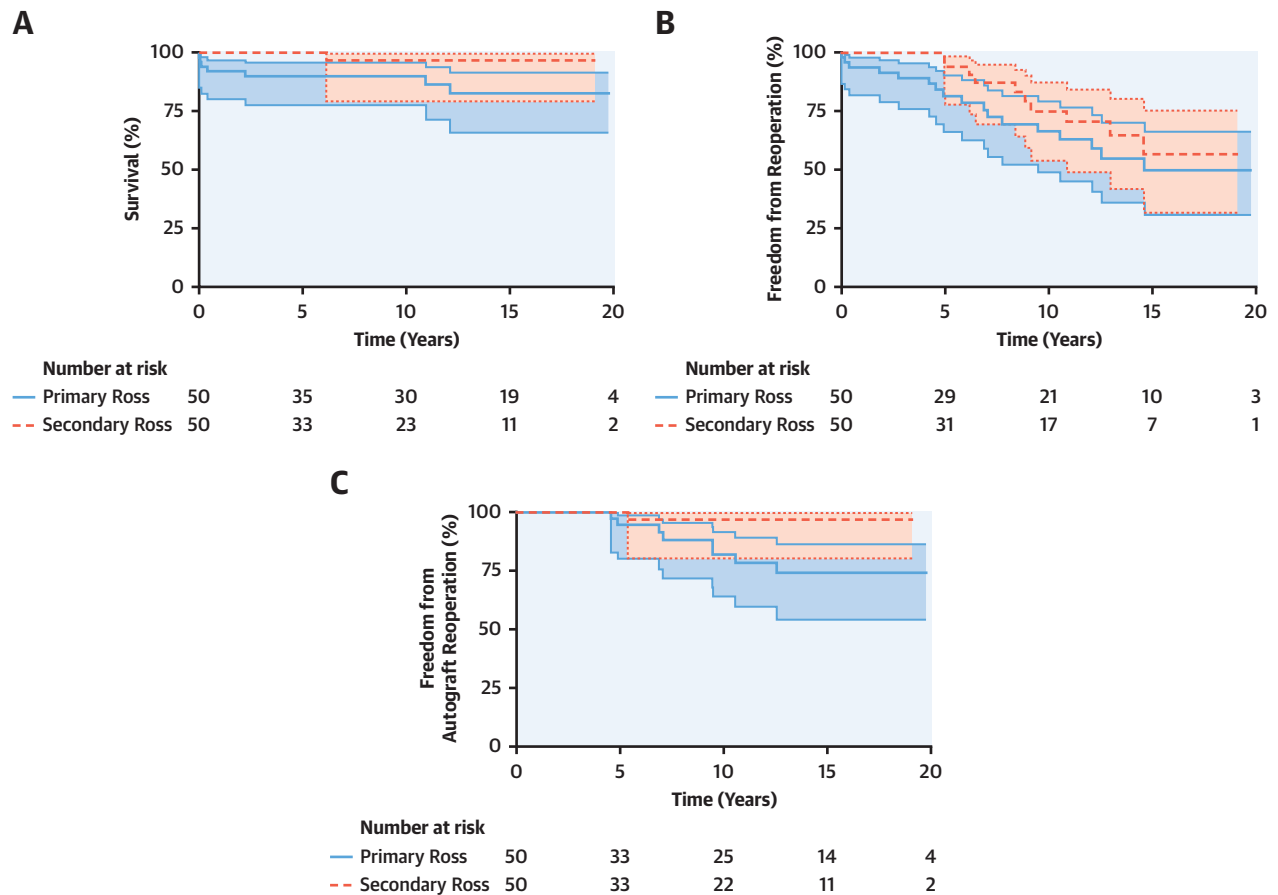
TABLE 4 Baseline Characteristics Comparing Those Who Underwent Primary Ross With Those Who Had Prior Aortic Valve Surgery After Propensity Score Matching

	Primary Ross Procedure (n = 50)	Secondary Ross Procedure (n = 50)	p Value	Standardized Difference
Age, yrs	7.3 (1.9-13.2)	7.7 (3.2-13.3)	0.54	0.12
Weight, kg	25.1 (14.1-45.0)	23.5 (13-44.2)	0.60	0.10
Aortic valve morphology				0.08
Unicuspid	0 (0)	1 (2)	0.50	
Bicuspid	23 (46)	23 (46)	0.58	
Tricuspid	27 (54)	26 (52)	0.50	
Primary pathology				0.05
Stenosis	14 (28)	12 (24)	0.65	
Regurgitation	10 (20)	12 (24)	0.63	
Mixed	26 (52)	26 (52)	0.55	
Aortic coarctation	6 (12)	5 (10)	1.00	0.06
Infective endocarditis	6 (12)	3 (6)	0.49	0.21
VSD	6 (12)	4 (8)	0.74	0.13
Interrupted aortic arch	0 (0)	0 (0)	—	0
Endocardial fibroelastosis	0 (0)	1 (2)	1.00	0.20
RHD	1 (2)	0 (0)	1.00	0.20
TGA	0 (0)	0 (0)	—	0
PDS reinforcement	7 (14)	10 (20)	0.60	0.11
RV PA conduit type				0.03
Pulmonary homograft	29 (58)	27 (54)		
Contegra xenograft	7 (14)	18 (36)		
Aortic homograft	11 (22)	4 (8)		
Freestyle xenograft	3 (6)	1 (2)		

Values are median (interquartile range) or n (%), unless otherwise indicated.
 Abbreviations as in Table 1.

In the unmatched groups, survival and reoperation rates were similar between primary and secondary Ross procedures. Conversely, there was a trend toward higher autograft reoperation in the primary Ross group, although this did not reach statistical significance. It must be noted that patients who underwent primary Ross are somewhat older and had higher weight, although these differences were not statistically significant. The median time from initial aortic valve surgery to Ross procedure was over 4 years, demonstrating that the strategy of initial valve repair allowed for a significant delay of the Ross procedure. Ivanov et al. (9) reported similar findings, with a median time from initial valve repair to Ross procedure of 5.2 years. This is especially important given the poor results with Ross procedure in neonates and infants as compared with the excellent results reported in older children and young adults.

In order to account for this difference in baseline characteristics between the 2 groups, we performed propensity score matching to balance baseline characteristics as well as the risk factors for mortality and reoperation. The produced 50 well-matched pairs. We

FIGURE 2 Outcomes of Matched Cohort

(A) Survival, (B) freedom from reoperation, and (C) freedom from autograft reoperation comparing, in a propensity score-matched cohort, those who had primary Ross procedure with those who had secondary Ross procedure.

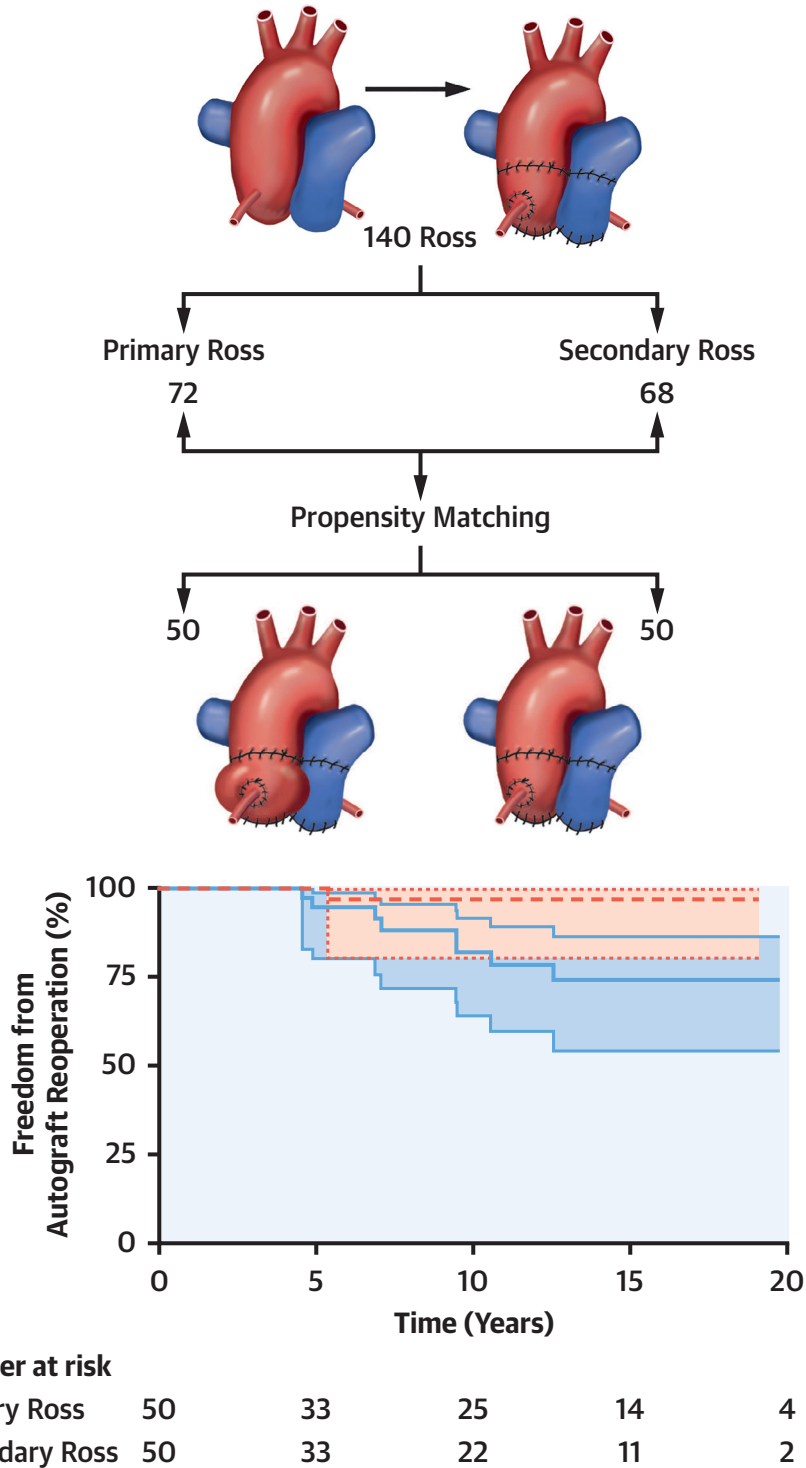
found a significantly better survival as well as freedom from autograft reoperation in the secondary Ross procedure group.

It is not immediately obvious why mortality and freedom from autograft reoperation should be lower in the secondary Ross group. Intuitively, one would think reoperation would pose additional risks, such as sternal re-entry and dissection of adhesions. However, other groups have also observed improved results with reoperative Ross procedure compared with primary Ross in both children and adults (22,23). It has been previously postulated that the post-surgical adhesions present after prior sternotomy may provide an additional extrinsic support for the autograft, thus preventing dilatation and subsequent failure due to regurgitation (23). Although higher rates of homograft failure have previously been observed in

secondary Ross procedure (24), we found similar freedom from reoperation on the RV-PA conduit regardless of whether Ross was performed as a primary or secondary procedure.

In recent years, there has been a growing consensus that stabilization of the autograft may be an important factor in preventing late dilatation in some patients. Superb results have been reported with stabilized Ross procedure in young adults (15,25). It is difficult to achieve such stabilization of the autograft in this challenging group of growing children. Thus, fibrous thickening of aortic and pulmonary artery tissue may provide similar support and contribute to improved longevity of the autograft in the redo setting in children. It is interesting to draw comparisons to the better autograft performance in the setting of reoperation, with the effect of PDS band

CENTRAL ILLUSTRATION Propensity-Matched Comparison of Primary and Secondary Ross Procedure in Children



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Design of the propensity score-matched study and the key finding of improved freedom from autograft reoperation in the secondary Ross procedure group.

support of the sinotubular junction. We have previously demonstrated that PDS band was associated with less late aortic regurgitation (12). We believe that although this band is completely absorbed within 6 months, it creates an increased amount of fibrous tissue at the sinotubular junction, thus reducing the rate of autograft dilatation. This may be a similar phenomenon to that occurring in the setting of reoperation, in which an increased amount of fibrosis around the aorta and autograft is already present.

Overall, these findings suggest that the approach of performing a delayed Ross procedure after initial repair can provide better results than those achieved with primary Ross procedure.

STUDY LIMITATIONS. This study is limited by its retrospective and nonrandomized nature. Although propensity score matching resulted in 2 well-matched groups, it cannot account for unidentified sources of bias in this model due to the limited cohort size.

CONCLUSIONS

Secondary Ross procedure performed after initial aortic valve surgery achieves superior long-term survival and freedom from autograft reoperation

compared with primary Ross procedure. A strategy of initial aortic valve surgery followed by delayed Ross procedure may provide better long-term survival and freedom from autograft reoperation in aortic valve disease in children.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND

PROCEDURAL SKILLS: In children undergoing cardiac reoperation after previous aortic valve surgery, a secondary Ross procedure can be associated with better survival and freedom from autograft failure than can a primary Ross procedure.

TRANSLATIONAL OUTLOOK: Prospective studies are required to confirm the safety and durability of secondary Ross procedures in pediatric patients undergoing reoperation for aortic valve disease.

REFERENCES

- Bouhout I, Ba PS, El-Hamamsy I, et al. Aortic valve interventions in pediatric patients. *Semin Thorac Cardiovasc Surg* 2019;31:277-87.
- Siddiqui J, Brizard CP, Galati JC, et al. Surgical valvotomy and repair for neonatal and infant congenital aortic stenosis achieves better results than interventional catheterization. *J Am Coll Cardiol* 2013;62:2134-40.
- d'Udekem Y, Siddiqui J, Seaman CS, et al. Long-term results of a strategy of aortic valve repair in the pediatric population. *J Thorac Cardiovasc Surg* 2013;145:461-7.
- Benson L. Neonatal aortic stenosis is a surgical disease: an interventional cardiologist view. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu* 2016;19:6-9.
- Hraška V, Sinzobahamvya N, Haun C, et al. The long-term outcome of open valvotomy for critical aortic stenosis in neonates. *Ann Thorac Surg* 2012;94:1519-26.
- Vergnat M, Asfour B, Arenz C, et al. Contemporary results of aortic valve repair for congenital disease: lessons for management and staged strategy. *Eur J Cardiothorac Surg* 2017;52:581-7.
- Donald JS, Wallace FRO, Naimo PS, et al. Ross operation in children: 23-Year experience from a single institution. *Ann Thorac Surg* 2020;109:1251-9.
- Mookhoek A, Charitos E, Hazekamp MG, et al. Ross procedure in neonates and infants: a European multicenter experience. *Ann Thorac Surg* 2015;100:2278-84.
- Ivanov Y, Drury NE, Stickley J, et al. Strategies to minimise need for prosthetic aortic valve replacement in congenital aortic stenosis—value of the Ross procedure. *Semin Thorac Cardiovasc Surg* 2020;32:509-19.
- Martin E, Laurin C, Jacques F, et al. More Than 25 Years of Experience With the Ross Procedure in Children: A Single-Center Experience. *Ann Thorac Surg* 2020;110:638-44.
- Luciani GB, Lucchese G, Carotti A, et al. Two decades of experience with the Ross operation in neonates, infants and children from the Italian Paediatric Ross Registry. *Heart* 2014;100:1954-9.
- Tan Tanny SP, Yong MS, d'Udekem Y, et al. Ross procedure in children: 17-year experience at a single institution. *J Am Heart Assoc* 2013;2:e000153.
- Konstantinov IE. Is Ross operation in neonates and infants justified? Aortic valve repair may postpone Ross operation. *Eur J Cardiothorac Surg* 2015;47:e170-1.
- Konstantinov IE, d'Udekem Y, Brizard CP. Ross operation or aortic valve Repair in neonates and infants? *J Thorac Cardiovasc Surg* 2014;148:362-3.
- Buratto E, Shi WY, Wynne R, et al. Improved survival after the Ross procedure compared with mechanical aortic valve replacement. *J Am Coll Cardiol* 2018;71:1337-44.
- Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. *J Thorac Cardiovasc Surg* 2007;134:1128-35.
- David TE, Ouzounian M, David CM, et al. Late results of the Ross procedure. *J Thorac Cardiovasc Surg* 2019;157:201-8.
- Mokhles MM, Körtke H, Stierle U, et al. Survival comparison of the Ross procedure and mechanical valve replacement with optimal self-management anticoagulation therapy. *Circulation* 2011;123:31-8.
- Mazine A, David TE, Rao V, et al. Long-term outcomes of the Ross procedure versus mechanical aortic valve replacement propensity-matched cohort study. *Circulation* 2016;134:576-85.
- Sharabiani MT, Dorobantu DM, Mahani AS, et al. Aortic valve replacement and the Ross

operation in children and young adults. *J Am Coll Cardiol* 2016;67:2858-70.

21. El-Hamamsy I, Eryigit Z, Stevens LM, et al. Long-term outcomes after autograft versus homograft aortic root replacement in adults with aortic valve disease: a randomised controlled trial. *Lancet* 2010;376:524-31.

22. Alsoufi B, Al-Halees Z, Manlihot C, et al. Superior results following the Ross procedure in

patients with congenital heart disease. *J Heart Valve Dis* 2010;19:269-77.

23. Knott-Craig CJ, Goldberg SP, Pastuszko P, et al. The Ross operation for aortic valve disease: previous sternotomy results in improved long-term outcome. *J Heart Valve Dis* 2007;16:394-7.

24. Sakaguchi H, Elkins RC, Lane MM, et al. Effect of prior aortic valve intervention on results of the Ross operation. *J Heart Valve Dis* 2003;12:423-9.

25. Skillington PD, Mokhtes MM, Takkenberg JJ, et al. Twenty-year analysis of autologous support of the pulmonary autograft in the Ross procedure. *Ann Thorac Surg* 2013;9:823-9.

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