The Pulmonary Autograft After the Ross Operation: Results of 25-Year Follow-Up in a Pediatric Cohort

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Background. **Progressive autograft dilation and need for later reoperation remain major concerns of the Ross procedure. The study investigates the clinical outcome after the Ross operation, including a longitudinal analysis of autograft dimensions over 25 years.**

Methods. **From November 1991 to April 2019, 137 patients underwent a Ross procedure at the University Hospitals of UCL (Université catholique de Louvain)-Brussels and Ghent. Inclusion criteria were less than or equal to 18 years of age and pulmonary autograft implantation by root replacement. Outcome focused on survival, reoperation rate, and autograft size evolution through linear mixed-model analysis.**

Results. **A Ross or Ross-Konno operation was performed in 110 (80%) and 27 (20%) patients at a median age of 10.4 (interquartile range [IQR], 4.7-14.3) years and 0.5 (IQR, 0.04-5.2) years, respectively. Overall 10-year and 20-year survival was 87% ± 3% and 85% ± 3%, respectively, but was 93% ± 3% for isolated Ross patients. Right ventricular outflow tract–conduit exchange was required in 20.3%, whereas autograft-related reoperation was performed in 14 (10.7%) patients at a median interval of 14 (IQR, 9-16) years, for aortic regurgitation (n = 2) and autograft dilation (n = 12). Autograft z-values increased significantly at the sinus and sinotubular junction (STJ) compared with the annulus (annulus = 0.05 ± 0.38/y, sinus = 0.14 ± 0.25/y, STJ = 0.17 ± 0.34/y; $P = .015$). The z-value slope for autograft dimensions was significantly steeper for Ross-Konno vs Ross patients (annulus: $P = .029$; sinus: $P < .001$; STJ: $P = .012$), and for children having aortic arch repair (annulus: $P = .113$, sinus: $P = .038$; STJ: $P = .029$).**

Conclusions. **The Ross operation offers children requiring aortic valve replacement an excellent survival perspective, with an acceptable risk of autograft reoperation within the first 25 years. Contrary to the autograft annulus, dilation of the sinus and STJ size is of concern. Closer surveillance of autograft dimensions might be required in patients who underwent a Ross-Konno procedure or aortic arch reconstruction.**

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The treatment of aortic valve disease in pediatric patients yields various options, from catheter-based balloon valvuloplasty or surgical valve repair to valve replacement. Despite improving results of valve-preserving techniques, the majority of these sick valves ultimately need to be replaced.[1-3] The Ross operation is the preferred alternative, based on obvious advantages as the lack of the prosthesis-related complications, the avoidance of lifelong anticoagulation and the growth potential in younger children. Disadvantages as the creation of a dual valve disease by the obligatory need for a pulmonary valve substitute with limited durability, and a hazardous risk of autograft reoperation for dilation with or without valve dysfunction remain of concern.[4,5]

Most studies focusing on the fate of the pulmonary autograft have follow-up times limited to 10 years to 15 years, or are confounded by mixing pediatric and adult patients. The Leiden group recently reported on a 22-year experience with the Ross procedure in a cohort comprising 74% pediatric and 26% adult patients. They found a cumulative incidence of autograft reoperation of

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20% to 31% at 15 to 20 years, mainly for autograft dilation during the second decade after surgery, advancing this observation as worrisome.[6]

The purpose of this study on 25 years of follow-up of the Ross procedure is to anticipate on the long-term fate of the autograft through including a longitudinal analysis of autograft size, in order to identify eventual patient subgroups in need of increased vigilance for later adverse outcome.

Patients and Methods

The Ethical Committee of the University Hospital UCL (Université catholique de Louvain) St Luc-Brussels and University Hospital of Ghent approved this retrospective study (Brussels: B0001530-403, Ghent: B670201732393), waiving the need for informed consent. All patients who underwent a Ross(-Konno) operation at both centers between November 1991 and April 2019 were included into a common database. Patient and operative data were obtained from medical records. To increase the uniformity of the study population between centers, only patients operated at less than or equal to 18 years of age for a congenital aortic valve disease and with the pulmonary autograft implanted via root replacement were included. Patients in whom the pulmonary autograft was wrapped into a vascular prosthesis (n = 4) and patients having a Ross operation for acquired aortic valve disorder (endocarditis, rheumatic valve disease) were excluded.

Regardless of differences in cardiopulmonary bypass and cardioplegia management between centers, the surgical technique of pulmonary autograft implantation as a root was comparable, performed with a single or double running suture and without specific reinforcement of proximal or distal anastomosis. In patients with additional subaortic narrowing, the left ventricular outflow tract was opened by a Konno septal ventriculoplasty. The interventricular septal defect was closed with a prosthetic patch or muscular flap attached to the pulmonary autograft, at the surgeon's discretion. Reconstruction of the right ventricular outflow tract (RVOT) was preferentially performed with cryopreserved pulmonary homografts, but bovine jugular vein conduits were occasionally used in smaller children.

Follow-up consisted of an annual clinical visit and transthoracic echocardiogram performed in hospital by the local cardiologists. For patients followed outside the hospital, echocardiographic reports from the referring cardiologist were considered. Routine echocardiographic examinations available because discharge were reviewed to obtain adequate autograft measurements at 3 levels: (1) the annulus at the leaflet insertion, (2) the sinus of Valsalva at its largest diameter, and (3) the sinotubular junction (STJ). Autograft dimensions were retrieved from parasternal long-axis view acquisitions in systole. At least 4 valid autograft measurements per individual patient during follow-up were required to be considered eligible for longitudinal analysis, using an assessment shortly after surgery and the last visit evaluation as respectively first and last reference. Absolute dimensions were then transformed into z-values to adjust for somatic growth, according to Sluysmans and colleagues.[7] Change of z-value during follow-up was calculated as the ratio of the difference between first and last measurement and the time interval between both measurements, expressed per year time unit.

Assessment of autograft valve function was retrieved from the echocardiographic report at last clinical visit. Aortic regurgitation was graded semiquantitatively on a scale 0 to 4, based on the depth and width of the regurgitant jet.

Clinical and regular echocardiographic follow-up was complete for 96% of the survivors for a median follow-up of 10.1 (interquartile range [IQR], 1.8-17.9) years, resulting in a cumulative follow-up of 1379 patient-years. For the Ross group, the median follow-up time and cumulative follow-up were 11.5 (IQR, 4.1-19.6) years and 1147 patient-years, respectively. The Ross-Konno group had a median follow-up of 7.2 (IQR, 2.2-14.1) years and 333 patient-years cumulative follow-up. Appropriate autograft size data were available for analysis in 86 of 118 (73%) survivors, yielding a total of 867 examinations, or a median of 6 (IQR, 4-14) evaluations per patient. Owing to inadequate image acquisition, only 610 valid STJ measurements were accounted. The serial echo follow-up covered a time lapse of more than 20 years in 19% (n = 16), 15 to 20 years in 20% (n = 17), 10 to 15 in 26% (n = 23), 5 to 10 years in 22% (n = 19), and less than 5 years in 13% (n = 11). In 38 patients, data were incomplete or unavailable, mostly by external follow-up.

Statistical Analysis

Data are reported for the total cohort, and separately for the Ross and Ross-Konno subgroups. Data distribution normality was evaluated by Kolmogorov-Smirnov test and Q-Q plot. Normally distributed data were reported as mean ± SD, and comparison between groups was based on unpaired *t* test. Nonnormally distributed data were given by median and IQR, and compared by Mann-Whitney test. Categorical data were reported as number and frequency, and compared between groups with the chi-square test or Fisher's exact test.

Early mortality was defined as 30-day mortality. Survival was analyzed by Kaplan-Meier method, with log-rank testing for difference between groups. Cox regression analysis was done to determine risk factors for late mortality. Competing risk analysis was used to estimate the cumulative incidence of all-cause reoperation and autograft or RVOT reoperation, with death as competing event. To provide exact information on the late reoperation rate, 30-day mortality patients were excluded from this analysis. Fine-Gray modeling was performed to estimate the hazard function of risk factors for reoperation, expressed by hazard ratio (HR) and 95% confidence interval (CI).

Analysis of autograft dimensions over time was performed using a linear mixed-effect model. Measurements in patients who required late autograft reoperation were censored from the time of reoperation. In a first analysis,

the evolution of autograft dimensions was compared in between the defined levels, using the autograft level as fixed effect in interaction with follow-up time. Bonferroni correction was used to adjust for multiple comparisons. To account for variability in age at the time of surgery, and in sequence of time intervals of autograft measurements, factors potentially affecting the autograft size evolution were examined in a mixed random-effect model for both intercept and slope, using the defined risk factor in interaction with time. The following factors were investigated: sex, age at the time of Ross operation, Ross vs Ross/Konno subgroup, predominant hemodynamic lesion, associated cardiac disease, and previous or associated aortic arch repair (AAR). Differences between groups were reported for both intercept and slope of the autograft z-values. Assumptions on homoscedasticity and normality of the longitudinal data were tested on the model residuals. Model performance was based on the lowest Akaike information criterion. Graphical presentation of between-group variability of autograft size evolution was based on scatter dot distribution of individual measurements and Loess curve fitting to 90% of the group data. Statistical significance was assumed for $P < .05$. Statistical analysis was performed with SPSS 25.0 (IBM Corporation, Armonk, NY) and R version 3.6.1 (package cmp.rsk) (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient Data

According to the inclusion criteria, 137 patients underwent a Ross procedure at both centers, 73 (53%) patients at the Ghent University Hospital and 64 (47%) at UCL St Luc (Table 1). Of this cohort, 27 (20%) children had a Ross-Konno procedure. The median age at surgery for the whole group was 7.6 (IQR, 2.8-13.2) years. Ross-Konno patients were commonly younger (median age 0.5 [IQR, 0.04-5.2] years vs 10.4 [IQR, 4.7-14.3] years in Ross-patients; $P < .001$); half of them were operated at infant age (Ross-Konno vs Ross: 14 [52%] vs:11 [10%]; $P < .001$). A previous aortic valve procedure was done in 60%, mainly as balloon valvuloplasty in Ross patients (Ross 62%, Ross-Konno 15%; $P = .003$). This procedure was performed at least twice in 28 (20%) patients. The aortic valve disease was isolated in 89 (65%) patients, the majority within the Ross group (77%). Prior or concomitant AAR was performed more frequently in Ross-Konno patients (59% vs 13%; $P < .001$), in accordance with more associated intracardiac defects.

Outcome Data: Survival

Early mortality occurred in 15 (11%) patients, significantly more in Ross-Konno than in Ross patients (n = 9 [33%] vs n = 6 [6%]; $P < .001$). The overall survival was 88.9% ± 2.7%, 86.8% ± 3.0%, and 85.4% ± 3.3% at 1 year, 10 years, and 20 years, respectively, revealing a significant survival difference at the cost of the Ross-Konno group ($P < .001$) (Figure 1). Survival at 10 to 20 years after a simple Ross procedure was 93.1% ± 2.5%. Multivariate analysis of risk factors for late mortality identified age at operation (HR, 0.85; 95% CI, 0.74-0.97; $P = .013$) and the Ross-Konno procedure (HR, 3.59; 95% CI, 1.25-10.33; $P = .018$) as independent determinants (Table 2).

Echocardiographic assessment at last follow-up (excluding 3 patients treated with a mechanical prosthesis during autograft reoperation) revealed an excellent autograft valve function, with aortic regurgitation grade 0 to 1 and grade 2 in 104 (91%) and 10 (9%) patients, respectively. None of the patients had aortic insufficiency grade 3 to 4.

Outcome Data: Reoperation Rate

The all-cause reoperation rate of the whole cohort was 25.9%, resulting in a cumulative reoperation incidence of 24.5% ± 2.9% and 39.7% ± 5.3% at 10 years and 20 years, respectively. Ross-Konno patients required more frequently a reoperation over time than Ross patients, revealing a significant difference in cumulative reoperation incidence of 36.0% ± 6.7% vs 11.8% ± 1.4% at 10 years ($P < .001$).

Autograft-related reoperation was performed in 14 (10.7%) patients at a median interval of 14 (IQR, 9-16) years. The majority of autograft reoperations were performed in Ross patients (n = 13 [12.1%]), but 1 was performed in a Ross-Konno patient, showing no difference in autograft reoperation rate between groups (log-rank $P = .736$) (Figure 2). Reasons for autograft reoperation were critical autograft dilation (root diameter >55 mm) with or without valve insufficiency (11 Ross patients, 1 Ross-Konno patient) and primary valve dysfunction due to autograft distortion in 2 Ross patients. Reoperation consisted of isolated AVR with mechanical prosthesis (n = 1), a Bentall procedure (n = 2), and valve-sparing root replacement by David (n = 10) or Yacoub (n = 1) technique. The low number of events precluded to identify risk factors for autograft reoperation.

RVOT conduit replacement was required in 26 (20.3%) patients and significantly more often in Ross-Konno patients ($P = .013$) (Figure 3). This was achieved by redo-surgery in 10 patients and percutaneous valve implantation in 16 patients. The median interval to RVOT reoperation was overall 10.2 (IQR, 4.0-16.9) years, and was significantly shorter for Ross-Konno patients (3.3 (IQR, 1.7-10.2) years vs 11.2 (IQR, 6.2-18.3) years; $P = .001$). Univariate analysis revealed age (HR, 0.88; 95% CI, 0.81-0.96; $P = .004$), Ross-Konno operation (HR, 5.86; 95% CI, 2.22-15.44; $P < .001$) and associated complex cardiac disease (HR, 3.78; 95% CI, 1.86-8.49; $P = .001$) as significant predictors for RVOT reoperation, and retained age (HR, 0.91; 95% CI, 0.83-0.99; $P = .037$) and complex cardiac defects (HR, 3.12; 95% CI, 1.26-7.75; $P = .014$) at multivariate analysis.

Other reinterventions were balloon dilation (n = 4) or redo-aortic arch enlargement (n = 1) for recurrent coarctation, closure of residual VSD (n = 2) and pacemaker implantation (n = 5).

Table 1. Patient Data

Variable	Total (N = 137)	Ross (110)	Ross-Konno (n = 27)	*P* Value
Center				.550
Ghent	73	60 (82)	13 (18)	
UCL-Brussels	64	50 (78)	14 (22)	
Male	97 (71)	82 (75)	15 (56)	.102
Age, y	7.6 (2.8-13.2)	10.4 (4.7-14.3)	0.5 (0.04-5.2)	<.001
Previous AoV procedure	82 (60)	72 (66)	10 (37)	.031
Balloon dilation	72 (53)	68 (62)	4 (15)	.003
Number previous procedures				
1	65 (47)	54 (49)	11 (41)	.664
≥2	28 (20)	22 (20)	6 (22)	.732
Isolated AoV disease	89 (65)	85 (77)	4 (15)	<.001
Associated cardiac disease	48 (35)	25 (23)	23 (85)	<.001
VSD	18 (13)	6 (5)	12 (44)	
cAVSD	1 (0.7)	-	1 (4)	
CoA/IAA	23 (17)/8 (6)	14 (13)/…	10 (37)/7 (26)	
Shone	14 (10)	3 (3)	11 (41)	
Type of valve dysfunction				.004
Stenosis	72 (53)	50 (45)	22 (82)	
Regurgitation	18 (13)	16 (15)	2 (7)	
Mixed	47 (34)	44 (40)	3 (11)	
Associated aortic arch surgery	31 (23)	14 (13)	17 (59)	<.001
Patch repair	17 (12)	5 (5)	12 (44)	<.001
Simple CoA resection	14 (10)	9 (8)	5 (14)	.097

Values are n (%) or median (interquartile range).

AoV, aortic valve; cAVSD, complete atrioventricular septal defect; CoA, coarctation; IAA, interrupted aortic arch; UCL, Université Catholique de Louvain; VSD, ventricular septal defect.

Outcome Data: Evolution of Autograft Dimensions

The evolution of diameters and z-values at the autograft annulus, sinus and STJ in the whole cohort is shown in figure 4. The intercept z-values were significantly higher at the sinus and STJ than at the annulus (annulus = 1.8 ± 0.9, sinus = 3.3 ± 3.1, STJ = 3.8 ± 2.9; $P < .001$), whereas the slope evolution remained stable for the annular z-values in contrast to both other levels (annulus = 0.05 ± 0.38/y, sinus = 0.14 ± 0.25/y, STJ = 0.17 ± 0.34/y; $P = .015$).

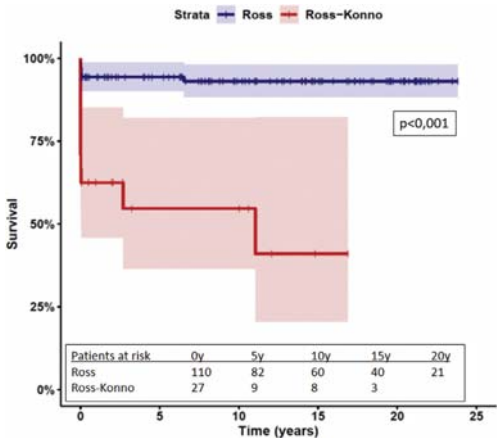

Figure 1. Survival plot of Ross and Ross-Konno patients.

The mixed random-effect investigation of autograft measurements over time identified a significantly different evolution between Ross and Ross-Konno patients, and in children with associated AAR. Adequate autograft measurements were available in 75 Ross and 11 Ross-Konno patients. At the index operation, the annulus z-value at the intercept was in average 2.24 ± 0.42 ($P < .001$) higher in Ross than in Ross-Konno patients, while the z-value slope was steeper in Ross-Konno patients (mean difference 0.05 ± 0.13/y, $P = .029$). Similar observations were made for the sinus z-values (mean intercept difference 2.85 ± 0.50, $P < .001$ in favor of Ross; mean slope difference 0.12 ± 0.17/y, $P < .001$ in favor of Ross-Konno), and for the STJ z-values (mean intercept difference 2.69 ± 0.58, $P < ,001$ in favor of Ross; mean slope difference 0.10 ± 0.16/y, $P = .012$) in favor of Ross-Konno) (Figure 5A-C).

Autograft size evolution was also significantly influenced by previous or concomitant AAR, represented by data of 16 patients. The mean z-value difference at the intercept was higher at all levels in patients without AAR (annulus = 1.56 ± 0.48, $P = .012$; sinus = 2.90 ± 0.54, $P < .001$; STJ = 2.96 ± 0.90, $P < .001$). However, the z-value slope expressed as z-value change/year was higher in patients with AAR at the sinus ($P = .038$) and STJ ($P = .024$) but not at the annulus ($P = .113$) (Figure 6).

Table 2. Univariate and Multivariate Risk Factor Analysis for Late Mortality

	Univariate Analysis			Multivariate Analysis		
Variable	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Age	0.79	0.70-0.90	<.001	0.85	0.74-0.97	.013
Sex(female to male)	0.84	0.32-2.24	.727			
Ross-Konno vs Ross	8.20	3.15-21.31	<.001	3.59	1.25-10.33	.018
Associated cardiac disease	5.40	1.92-15.18	.001			
Genetic syndrome	2.37	0.68-8.17	.174			
Aortic arch surgery	3.29	1.29-8.36	.012			

CI, confidence interval; HR, hazard ratio.

Other factors like age, gender, type of valve dysfunction and associated cardiac disease had no significant effect on autograft size evolution.

Comment

In children and young adolescents presenting with aortic valve dysfunction unamenable to successful repair is the Ross procedure the preferred option for aortic valve replacement (AVR). The survival after a Ross operation is exceeding 90% at 10 years to 20 years in experienced centers, yielding generally few deaths beyond the early postoperative period.[4,6,8] This study confirmed the excellent survival perspective in patients after a simple Ross operation, but revealed younger age at the time of surgery and the need of a Ross-Konno procedure as independent risk factors for late mortality. This finding has been identified by other groups also.[9-11] The need for AVR in early infancy is usually a surrogate for the precarious hemodynamic condition or the complexity of the underlying cardiac malformation requiring early intervention, which might be particularly the case for the Ross-Konno subgroup.

Through including a longitudinal analysis of autograft dimensions over a longer time span, the principal focus of this study was to address the long-term fate of the

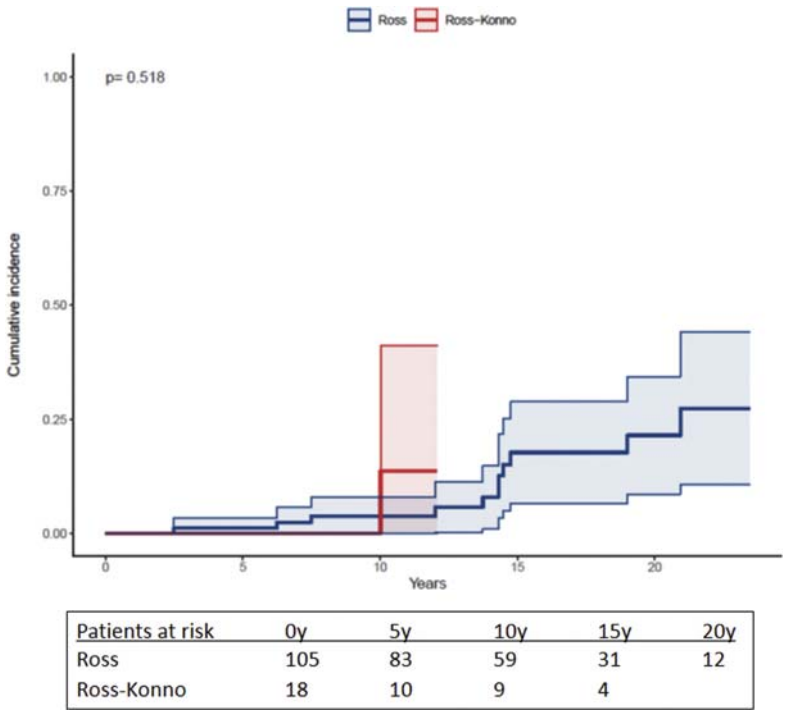

Figure 2. Cumulative incidence of autograft reoperation for Ross an Ross-Konno patients.

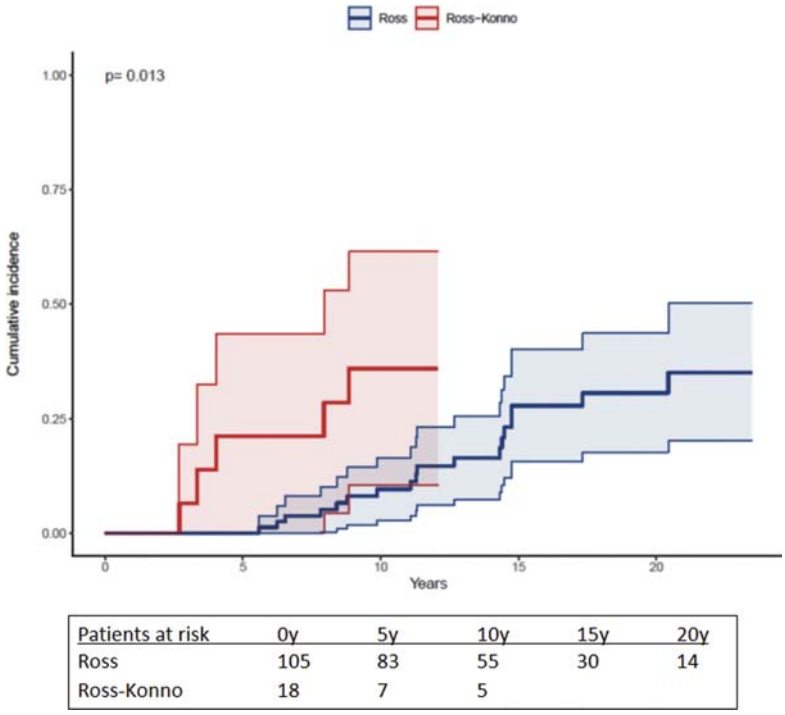

Figure 3. Cumulative incidence of right ventricular outflow tract reoperation for Ross and Ross-Konno patients.

Patients at risk	0y	5y	10y	15y	20y
Ross	105	83	55	30	14
Ross-Konno	18	7	5		

pulmonary autograft in a pediatric population. To improve the uniformity of the study cohort, inclusion was restricted to patients of 18 years of age or younger, all treated by a root replacement technique. Congenital aortic valve stenosis was the main predisposing disease, commonly presenting recurrent stenosis or mixed hemodynamic lesions after previous attempts of balloon dilation or occasionally surgical valvuloplasty.

Comparison of the autograft evolution amongst studies is hindered by several factors. Many studies are mixing up pediatric and adult Ross patients, and are thereby frequently contaminated by acquired valve pathologies as

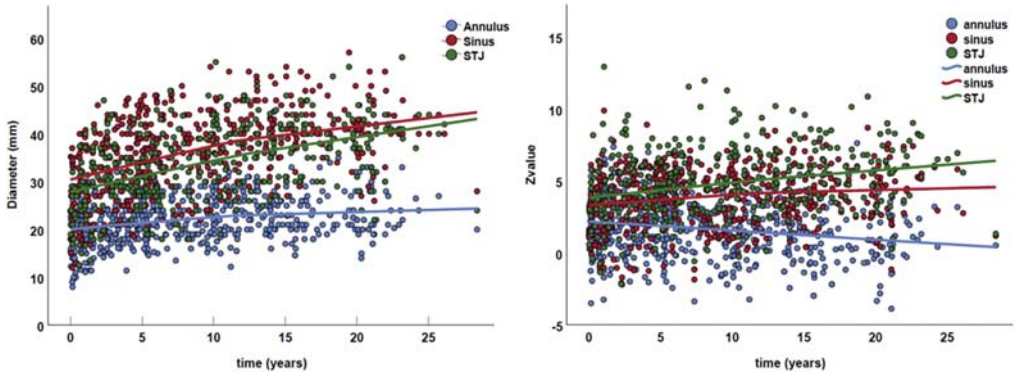

Figure 4. (Left panel) Evolution of autograft diameters at annulus, sinus, and sinotubular junction (STJ). (Right panel) Evolution of autograft z-values at annulus, sinus, and STJ. Lines represent the Loess curve with 90% fit to the data, according to annulus (blue), sinus (red), and STJ (green).

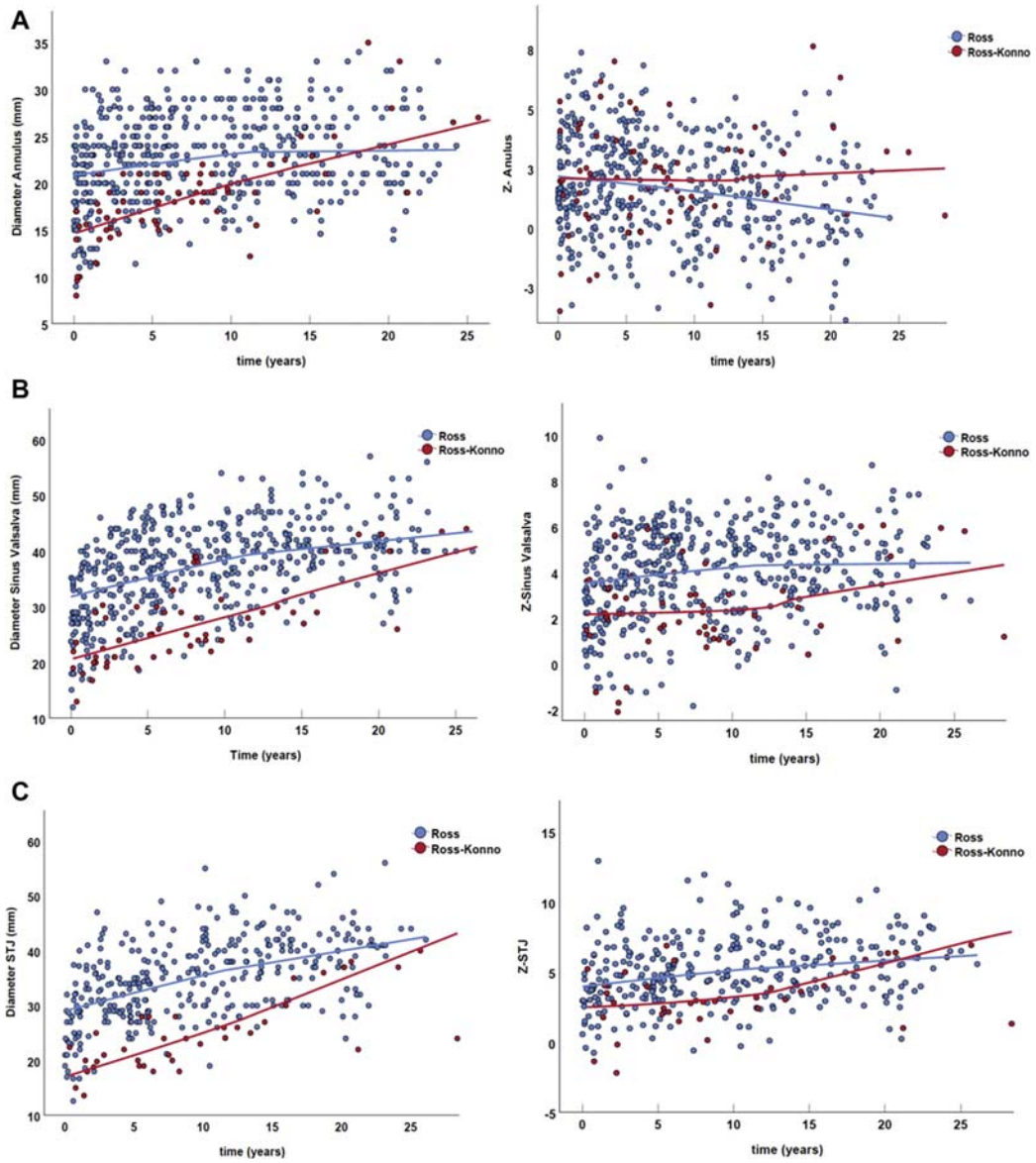

Figure 5. (A) Evolution of annulus diameters (left) and z-values (right): comparison between Ross and Ross-Konno patients. (B) Evolution of sinus diameters (left) and z-values (right): comparison between Ross and Ross-Konno patients. (C) Evolution of sinotubular junction (STJ) diameters (left) and z-values (right): comparison between Ross and Ross-Konno patients. Lines represent the Loess curve with 90% fit to the data, according to Ross (blue) and Ross-Konno (red).

endocarditis. Such series are consequently including a larger proportion of patients with primary aortic regurgitation, a hemodynamic burden known to enhance the risk of autograft dilation.[12,13] Our serial analysis of autograft size showed that (1) the autograft has a higher z-value at the sinus and STJ compared with the annulus directly after implantation, and (2) the autograft appears to dilate disproportionally to the somatic growth at the

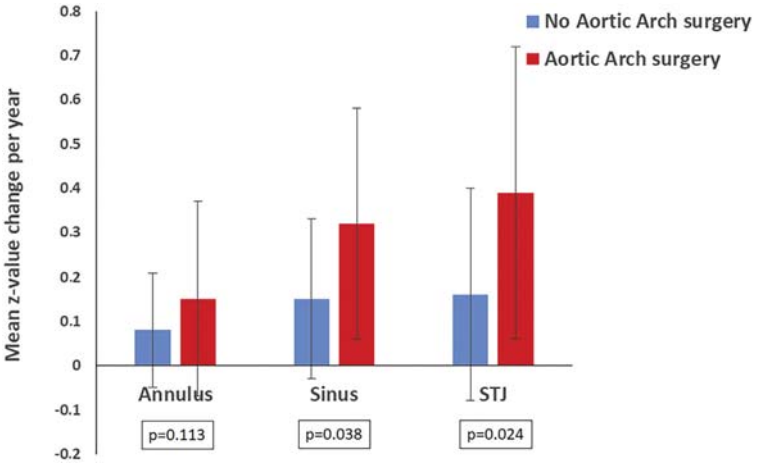

Figure 6. Mean z-value change per year for annulus, sinus, and sinotubular junction (STJ): comparison between patients with (red) and without aortic arch surgery (blue).

sinus and STJ, in contrast to a more stable evolution of the annulus. Horer and colleagues[14] made similar observations in 48 children with a mean age of 10 years during a shorter follow-up time of 5.1 years. Accordingly, the first observation is attributed to the originally larger size of the pulmonary root compared with the aortic one, and to the immediate adaptive remodeling of the pulmonary root exposed to systemic pressures. However, the dilation progress at the sinus and STJ in their analysis appeared to be faster, yielding an annual z-value increase of 0.5 and 0.7, respectively. Compared with the respective slopes of 0.14 and 0.17 at the sinus and STJ, respectively, our data are favoring a more optimistic perspective on the autograft progression over 20 years.

Two subgroups at risk for enhanced dilation have been identified: children who had a Ross-Konno procedure and those after previous AAR. To our knowledge, such information has yet not been revealed. Ross-Konno patients demonstrated a higher z-value progression not only at the sinus and STJ, but also at the annulus. Although speculative, partial absence of a fixed annular support at the region of the interventricular septal enlargement might possibly explain this finding. However, confounding with the other promoting factor, aortic arch surgery, is not excluded, as Ross-Konno patients have more frequently associated aortic arch malformations. The effect of aortic stiffening after prior AAR, even for a simple localized coarctation, on vascular remodeling of the proximal aorta has already been shown, especially when the extracellular matrix is abnormal or weakened—as in the pulmonary autograft.[15-17] Hence, the low number of patients and the shorter follow-up of maximal 15 years in both subgroups asks for cautious interpretation and further validation by close surveillance.

Lo Rito and colleagues[18] found a significant effect of age at the time of Ross surgery on autograft size progression. The autograft size stability was better in children operated at less than 18 months of age, compared with older peers, which they attributed to an improved natural adaptation through intrinsically identical histological features of the fetal pulmonary and aortic root. In our analysis, integrating age as continuous variable, the autograft size evolved independently of the children's age at surgery.

Preoperative aortic regurgitation is also associated with pathological autograft dilation but is mainly documented in series comprising adult patients.[5,12,13] It is conceivable that the effect of this factor in our series is attenuated by the obviously higher proportion of stenosis or mixed lesions in this pediatric cohort.

Late autograft reoperation was required in 11%, mainly for progressive root dilation, resulting in a cumulative incidence for autograft reoperation of 21.5 $\pm$ 7.2% at 20 years. Despite comparable results during the first decade, the autograft reoperation rate in our series competes favorably with the 62% freedom from reoperation at 18 years in the Rotterdam study,[12] and the cumulative incidence of autograft reoperation of 31% at 20 years by Schneider and colleagues.[6] The former study concerned equally younger patients operated before 18 years of age, whereas the latter study comprised 26% adult patients. Considering that autograft dilation is the principal opponent of the long-term durability of the Ross operation, and that this process seems constant at the level of the sinus and STJ, the expectation for late autograft reoperation might achieve a significant magnitude beyond the second decade after the Ross procedure. Therefore, adopting root reinforcing techniques like

inclusion into a vascular prosthesis or subcoronary autograft implantation are advisable in the teenaged Ross candidates.[19] Solutions for smaller infants are less evident, but in this specific cohort, the advantage of the Ross operation in terms of survival and valve-related complications needs to be outweighed with the risk of later autograft reoperation.

Study Limitations

Despite the representative sample size and the use of linear mixed models, a statistical method robust to missing values for repeated measurements over a long time span, this study would have been better served by a prospective design including the systematic measurement of autograft dimensions during serial follow-up. Hence, the limitations inherent to the retrospective design are minimized by the completeness of clinical follow-up, concentrated on a purely pediatric population treated uniformly by autograft root implantation. Nonetheless, longer-term data on specific subgroups characterized by a lower number of patients at risk such as those with complex cardiac malformations requiring a Ross-Konno procedure are mandatory.

Because this study was mainly focused on the autograft outcome, specific information on RVOT conduit characteristics as size and type was lacking. Therefore, analysis of risk factors for RVOT conduit replacement included only available clinical data.

Conclusion

In this pediatric population up to 18 years of age, the Ross operation is an excellent option for AVR, offering a 94% survival during the first 2 decades of life, with a very low risk of death beyond the early postoperative period. However, the prognosis is poorer for infants with more complex cardiac malformations in whom relief of the left ventricular outflow tract requires a Ross-Konno procedure.

The issue of treating a single-valve disease by inducing potentially a double-valve problem is pertinent as over 20 years, half of the patients had a reintervention, dominated by the need for RVOT conduit replacement. Although approximately 80% of this pediatric cohort remained free from autograft reoperation within this time frame, progressive autograft dilation remains a concern. As this study demonstrated a constant increase of autograft dimensions, particularly at the level of the sinus and sinotubular junction, the expectancy regarding freedom from autograft reoperation during the third decade or beyond might look worrisome, and justifies additional technical measures at the time of autograft implantation aiming to control this pathological process. Moreover, serial follow-up of autograft size revealed a tendency for enhanced autograft dilation in children after previous Ross-Konno surgery and aortic arch reconstruction, warranting close surveillance during follow-up.

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