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ORIGINAL ARTICLE

Dilatation and Dysfunction of the Neo-aortic Root and in 76 Patients After the Ross Procedure

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Abstract Pulmonary autograft replacement (Ross procedure) is used as an alternative to prosthetic aortic valve replacement patients with aortic valve disease. There are limited data on incidence and risk factors for dilatation and dysfunction of the neo-aortic after the Ross procedure. Ross procedure was performed in 100 patients at our institution between 1993 and 2011. In 76 patients, complete follow-up data were available. Their median age at surgery was 16 (0.4–58) years (76 % males; 95 % with congenital aortic valve disease). Median follow-up duration was 5.2 years (0.3–16.0 years). We analyzed their clinical and echocardiographic follow-up to identify possible risk factors for neo-aortic root dilatation and dysfunction. Ross procedure included reduction plasty of the native ascending aorta in 25 % of patients. During follow-up, 21 patients (28 %) developed neo-aortic root dilatation, 38 patients (50 %) dilatation oft the native ascending aorta and 7 patients (9 %) at least moderate neo-aortic regurgitation. Univariate risk factors for neo-aortic root dilatation were preoperative aortic regurgitation ($p = 0.04$), concomitant reduction plasty of the ascending aorta ($p = 0.009$) and a longer duration of follow-up ($p = 0.005$). Younger age at surgery was associated with dilatation of the ascending aorta ($p = 0.03$). Reoperation on the neo-aortic root because of severe dilatation was necessary in 6 patients (8 %), where 2 patients had at least moderate neo-aortic root regurgitation. Neo-aortic root and aortic dilatation are common after the Ross procedure. This is often combined with neo-aortic valve dysfunction. Close follow-up of these patients is mandatory.

Keywords Ross procedure · Congenital heart disease · Congenital aortic valve disease · Bicuspid aortic valve disease · Aortic dilatation

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Introduction

The Ross procedure is an accepted surgical option to treat diseases of the left ventricular outflow tract, especially in children and young adults [1, 2]. It involves translocation of the autologous pulmonary valve, including the proximal pulmonary trunk to the aortic position (neo-aortic valve and root) with reimplantation of the coronary arteries and replacement of the pulmonary root with a bioprosthesis [3, 4]. Potential advantages are good durability of the neo-aortic root (autologous tissue) with optimal hemodynamic characteristics of the neo-aortic valve, low risk of endocarditis, no need for anticoagulant therapy and the potential for growth of the neo-aortic root in children [2].

Despite these advantages, the use of the Ross procedure is still controversial [5]. It is technically demanding, and by replacing both the aortic and pulmonary valves, single-valve disease is converted into a double-valve

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disease [3, 6]. Structural failure of both the neo-aortic root and the conduit in the right ventricular outflow tract over time is another concern [7]. Several studies demonstrate the risk of early and late neo-aortic root dilatation, neo-aortic valve insufficiency and dysfunction of the right ventricular outflow tract bioprosthesis. Thus, patients after the Ross procedure are at risk of multiple reinterventions [2, 3, 8].

The need for reoperations, particularly for failure of the neo-aortic root, varies between different centers. Risk factors associated with the need for reintervention of the neo-aortic valve or root are still poorly defined [7].

The purpose of this study was to evaluate the frequency and potential predictors of neo-aortic root dilatation and valve dysfunction at our center.

Materials and Methods

Patients

Patients who underwent a Ross procedure between January 1993 and January 2011 were included in this study, when a clinical and echocardiographic follow-up of at least 30 days was available. The Ross procedure was performed from the same congenital surgical team at the University Hospital Zurich or at the University Children's Hospital Zurich. Both surgical and cardiac databases of the division of cardiac surgery at the University Hospital and the University Children's Hospital, Zurich, were searched for patients. Data were collected by retrospective chart review including review of echocardiography reports and surgical reports.

The institutional review board approved this study.

Surgical Technique of the Ross Procedure at Our Institutions

After instituting cardiopulmonary bypass and cardioplegic arrest, the neo-aortic root was harvested using standard techniques. Pulmonary autograft insertion was performed in aortic position using a root replacement technique. A 15-degree anticlockwise rotation is often effected so as to put the left sinus in an anatomically posterior position. The proximal anastomosis is performed using continuous suture. The left coronary button is sutured into the posterior sinus of the pulmonary neo-aortic root, with the aim of eliminating most of the sinus tissue. The distal anastomosis is performed with continuous sutures except the anterior sinus (the prospective site of right coronary button) where interrupted sutures are placed. The aortic clamp is temporarily opened to see the optimal location for the right coronary button, which is usually higher than that of the left coronary button. The aorta is clamped again and the right coronary button is sutured often straddling the distal suture line, again with the aim of removing as much neo-aortic root tissue as possible, thus reducing the substrate for root dilatation. The non-coronary sinus is subjected to circular purse-string sutures with the aim of strengthening the wall and avoiding late dilatation. Since 2009, the neo-aortic root is additionally covered with a Mersilene mesh. The mesh is incorporated into the proximal and distal suture line as a preventive step against late neo-aortic root dilatation.

Implantation technique of the bioprosthetic valve in pulmonary position has been previously reported [9, 10]. Our preferred choice for the reconstruction of the right ventricular outflow tract is the pulmonary homograft, although bovine jugular vein grafts (Contegra; Medtronic Inc, Minneapolis, MN) were implanted in the early part of the series. Generally, the bioprosthetic valves in right ventricular outflow tract were not oversized [11].

Blood Pressure Management

We do not have specific protocols for blood pressure control in patients after the Ross operation but aim to keep blood pressure within the normal range. We have a low threshold to start medical blood pressure therapy, even in patients with high-normal blood pressures, preferably with Losartan or a beta-blocker or both.

Echocardiographic Examination

The following data were obtained from the transthoracic echocardiographic examination: left ventricular size and function (biplane ejection fraction; Simpson's method); aortic dimensions (aortic root, mid-ascending aorta at the height of the right pulmonary artery) normalized for age and body surface area; and degree of aortic and pulmonary regurgitation and stenosis as recommended by guidelines [12–15]. Aortic root dimensions were obtained at end diastole according to Roman et al. [14]. The diameter of the neo-aortic root or sinus was recorded at the last echocardiographic examination. *Z* score for each patient's aorta that objectively defines the extent of dilatation in relation to the norm for a given body surface area (according to Dubois [16]) was calculated. For calculation of the *Z* score, the formula provided by Colan et al. [17] was used for the aortic root and the formula provided by Mary Roman for the ascending aorta [14]. As the aortic root diameters after the Ross procedure are often slightly dilated and not comparable to a normal aortic root dilation in a normal population, "severe" dilatation was arbitrary defined as a *Z* score of more than +4 compared with an age- and gender-matched population as defined above.

Table 1 Baseline characteristics

	Data of the 76 patients
Median age, years	15.9 (0.4–58.4)
Age <2 years	4 (5 %)
Age 2–18 years	40 (53 %)
Age >18 years	32 (42 %)
Male gender	58 (76 %)
Congenital aortic valve disease	72 (95 %)
Bicuspid (%)	53 (70 %)
Monocuspid (%)	11 (15 %)
Quadricuspid (%)	2 (3 %)
Tricuspid dysplastic aortic valve	6 (8 %)
Indeterminate number of cusps	4 (5 %)
Aortic valve endocarditis	6 (8 %)
Type aortic valve dysfunction	
Predominant AR	30 (40 %)
Predominant AS	20 (26 %)
Mixed AR/AS	25 (33 %)
None, but aortic aneurysm after BAV	1 (1 %)
Subaortic stenosis	3 (4 %)
Associated coarctation of the aorta	7 (9 %)
Associated ventricular septal defect	2 (3 %)
Any previous cardiac surgery	28 (37 %)
Previous surgical aortic valve repair	22 (29 %)
Previous aortic balloon valvuloplasty	17 (22 %)
Previous surgery/intervention for coarctation of the aorta	8 (11 %)

AS aortic stenosis, *AR* aortic regurgitation, *BAV* bicuspid aortic valve

Endpoints

The goal of our analysis was to define the frequency of neo-aortic root dilatation, neo-aortic regurgitation, dilatation of the native ascending aorta and their association with demographic and baseline echocardiographic parameters. Secondary endpoints were the occurrence of major averse cardiovascular events and reoperations of the neo-aortic root or the native ascending aorta.

Statistics

Continuous data are presented as mean ± standard deviation and median with range as appropriate and compared between groups using the Mann–Whitney test. Categorical data are presented as number with percentage and compared between groups using the Fisher's exact test. Univariate analysis was used to determine possible risk factors for severe dilation of the aortic root. Multivariate analysis was not carried out as many possible risk factors had small numbers of events. Early death was defined as occurring within 30 days postoperatively. The two-sided p values <0.05 were considered statistically significant.

Results

Hundred patients underwent a Ross procedure at our institutions between 1993 and 2011. One 18-year old patient died perioperatively from multiple cerebral infarctions and ventricular fibrillation. A clinical follow-up at least 30 days postoperatively including a complete echocardiographic examination was available in 76 (77 %) patients of 99 surviving patients.

Median age of the 76 patients within the study cohort was 15.9 (0.4–58.4) years (Table 1). The majority of the patients had congenital aortic valve disease. Aortic regurgitation or mixed aortic valve disease were more common than isolated aortic stenosis. Nearly half of the patients had previous aortic valve interventions: aortic valve surgery in 22/76 (29 %) patients (29 %) and/or balloon valvuloplasty in 17/76 (22 %) patients.

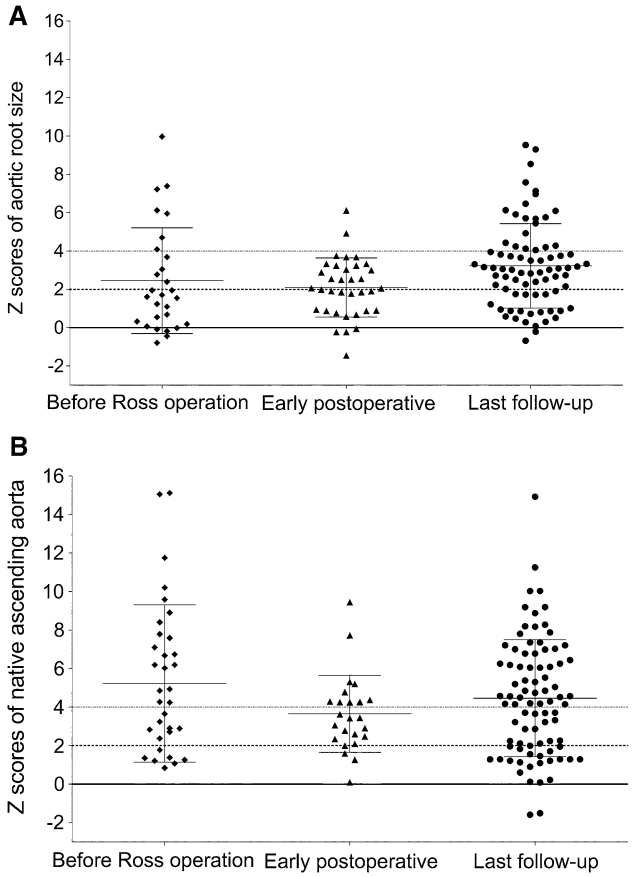

Fig. 1 **a** Aortic root size before Ross procedure (29 patients), after Ross procedure (28 patients) and at last follow-up before any aortic root surgery (76 patients). **b** Ascending aortic size before Ross procedure (41 patients), after Ross procedure (26 patients) and at last follow-up before any aortic root surgery (67 patients)

Detailed pre-operative data on aortic root and native ascending aortic dimensions were not available in all patients. In patients with available preoperative echocardiographic data ($n = 32$), 17 % had dilatation of the aortic root >2 *Z* scores and 9 % had severe dilatation of >4 *Z* scores (Fig. 1a). Mid-ascending aortic dilatation >4 *Z* scores was present in 25 % (Fig. 1b).

Operative Data

Operative data are given in Table 2. Pulmonary homograft was used in the majority of patients for reconstruction of the right ventricular outflow tract. Additional surgical procedures at the time of the Ross operation are summarized in Table 2 and included most commonly reduction plasty of the ascending aorta or the neo-aortic root and resection of subaortic stenosis. Average aortic cross-clamp time was 126 ± 39 min and average aorto-pulmonary bypass time 215 ± 55 min.

Table 2 Operative information of the 76 patients

Allograft type	
Homograft	54 (71 %)
Contegra graft	19 (25 %)
Other	3 (4 %)
Allograft size, mm	22 (15–29)
Reduction plasty ascending aorta	19 (25 %)
Reduction plasty neo-aortic root	13 (17 %)
Resection subaortic stenosis ± myectomy	8 (11 %)
Ross Konno procedure	8 (11 %)
Other adjunctive procedures	
Mitral valve repair or replacement	4 (5 %)
CABG	1 (1 %)

Allograft for right ventricular outflow tract; *CABG* coronary artery bypass grafting

Table 3 Echocardiographic findings in the 76 patients at last follow-up prior to any cardiac reintervention

Age echo (years)	22.1 (1.4 to 64.1)
Time of follow-up since RP (years)	5.2 (0.3 to 16.0)
Body weight (kg)	70.0 (7.5 to 105.0)
Body surface area (m^2)	1.85 (0.4 to 2.3)
LVEF (%)	59.0 (41.0 to 78.0)
Aortic root (mm)	38 (20 to 58)
Z score aortic root	3.0 (−1.7 to 9.5)
Z score aortic root >2	54 pts (71 %)
Z score aortic root >4	21 pts (28 %)
Mid-ascending aorta (mm) ($n = 67$)	34 (16 to 57)
Z score mid-ascending aorta	4.3 (−1.6 to 14.9)
Z score mid-ascending aorta >2	47 pts (62 %)
Z score mid-ascending aorta >4	38 pts (50 %)
Neo-aortic root regurgitation	
No AR	39 (51 %)
Mild AR	30 (40 %)
Moderate AR	5 (7 %)
Severe AR	2 (3 %)
Neo-aortic root stenosis	1 (1 %)
RV-PA graft; mean systolic gradient (mmHg)	11.0 (2.0–63.0)

LVEF left ventricular ejection fraction, *AR* aortic regurgitation, *RV-PA graft* right ventricular-pulmonary artery, *graft* allograft

Follow-up of the Neo-aortic Root and Native Ascending Aorta

Median follow-up duration until the last echocardiographic examination before any aortic reintervention was 5.2 years (0.3–16.0 years). Echocardiographic findings at the last follow-up are summarized in Table 3. In 54 patients

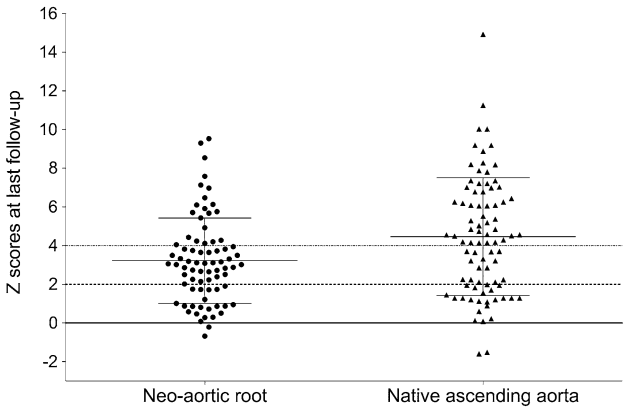

Fig. 2 *Z* scores in 76 patients after Ross procedure at their last follow-up prior to any reintervention

(71 %), mild dilatation of the neo-aortic root with a *Z* score of >2 was observed. Severe dilatation of the neo-aortic root and dilatation of the native ascending aorta (*Z* score of >4) was found in 21 patients (28 %) and in 38 patients (50 %), respectively (Fig. 2). While mild stenosis of the neo-aortic valve was found in only one patient, moderate or severe neo-aortic regurgitation was found in 7 patients (9 %).

Factors Associated with Neo-aortic Root Dilatation

Table 4 shows factors associated with neo-aortic root dilatation and dilatation of the native ascending aorta (defined as *Z* score >4.0). On univariate analysis, neo-aortic root dilatation was more common in patients with preoperative isolated aortic regurgitation ($p = 0.044$) and those who required already concomitant reduction plasty of the ascending aorta at the time of Ross operation ($p = 0.009$). In addition, a longer follow-up duration was significantly associated with neo-aortic root dilatation ($p = 0.005$) and native ascending aortic dilation ($p = 0.002$) illustrated in Fig. 3a, b. In this line, younger age at Ross surgery was associated with native ascending aortic dilatation in univariate analysis ($p = 0.030$).

The type of underlying aortic valve disease, other associated congenital heart disease and the presence of preoperative aortic dilatation were not associated with later neo-aortic root dilatation in our cohort. In 3 patients, the neo-aortic root was reinforced with a Mersilene mesh. After a median follow-up of 28.6 months, in one of these patients neo-aortic root dilatation was found despite this technique (*Z* score: postoperative −1.5, at last follow-up 4.1).

Adverse Cardiovascular Events and Reoperations During Follow-up

During follow-up, 6 patients needed a reintervention of the neo-aortic root. The details are summarized in Table 5. The reasons for reoperation included dilatation of the neo-aortic root and the native ascending aorta (6 patients) or neo-aortic regurgitation (2 patients).

Discussion

In this analysis of a single-center cohort of patients after the Ross procedure, severe neo-aortic root dilatation (*Z* score of >4) was found in more than a forth and dilatation of the native ascending aorta in half of all patients. Both neo-aortic root and native ascending aorta showed a progressive, time-dependent dilatation with a *Z* score of >4. Younger age at surgery was a risk factor for dilatation of the ascending aorta. Other possible risk factors such as technique, aortic valve morphology or associated congenital heart disease was not significantly associated with dilatation of the aortic root or the need for neo-aortic root intervention in our cohort.

Aortic Dilatation After the Ross procedure

In a study by Valeske et al. [18] including a similar cohort of patients (mean age: 11 years) with a comparable follow-up of 60 ± 37 months, neo-aortic dilatation (defined as *Z* score of at least 2.4) occurred in 10 % of patients and 2 needed neo-aortic root reoperations. In a recent study by Tan Tanny et al. [19], 100 children who had Ross procedure were studied. During a follow-up time of 7.0 ± 4.8 years, neo-aortic root dilatation (*Z* score of >4) was observed in 23 % of patients at the level of the sino-tubular junction and in 14 % of patients at the level of the neo-aortic sinus. Data on the size of the ascending aorta were not available.

Fortunately, despite a high frequency of neo-aortic root dilatation after the Ross operation, aortic dissections seem to be exceedingly rare in patients after the Ross operation. To our knowledge, only a single case has been reported in the literature so far (Venkataraman et al. [20]).

In our patients, dilatation of the neo-aortic root and the native ascending aorta were common. The latter likely reflects the natural history of bicuspid aortic valve disease, which is commonly associated with ascending aortic dilatation. In contrast, dilatation of the neo-aortic root (anatomically the former pulmonary root) is not unlikely caused by the different vessel wall structure of pulmonary artery tissue [21].

Reoperations After the Ross Procedure

It has been described in a series by Stulak et al. [2] that among reoperations after Ross procedure, neo-aortic root problems are common; these authors found that neo-aortic

Table 4 Univariate analysis of risk factors for neo-aortic dilatation and native ascending dilation with *Z* score >4

Characteristics	Neo-aortic root dilatation >4 *Z* scores ($n = 21$)	Neo-aortic root dilatation >4 *Z* scores *p* value	Native ascending aortic dilatation ($n = 38$)	Native ascending aortic dilatation $Z > 4$ *p* value
Male gender	16 (76 %)	1.00	29 (76 %)	0.78
Ross Konno	1 (5 %)	0.44	5 (13 %)	1.00
History of aortic coarctation	4 (19 %)	0.080	4 (11 %)	0.47
Preoperative endocarditis	1 (5 %)	1.00	3 (8 %)	1.00
Preoperative AR (>mild)	17 (81 %)	0.66	28 (74 %)	0.99
Preoperative isolated AS	2 (10 %)	0.45	6 (16 %)	1.00
Preoperative isolated AR	9 (43 %)	0.044	10 (26 %)	1.00
Preoperative predominant				
Aortic stenosis	4 (19 %)	0.32	9 (24 %)	0.84
Aortic regurgitation	11 (52 %)		16 (42 %)	
Mixed stenosis/regurgitation	6 (29 %)		13 (34 %)	
Congenital aortic valve disease				
Bicuspid	16 (76 %)	0.77	26 (68 %)	0.67
Monocuspid	2 (10 %)		3 (8 %)	
Quadricuspid	0		7 (18 %)	
Isolated aortic valve disease	20 (95 %)	0.43	32 (84 %)	0.13
Age at Ross operation, years	15.9 (0.9–31.5)	0.50	14.2 (0.9–34.6)	0.030
Follow-up time since Ross operation (years)	6.7 (0.5–16.0)	0.005	5.9 (0.3–15.9)	0.002
Preoperative aortic root dilatation ($Z > 4$)	4/13 (31 %)	0.67	13/19 (68 %)	0.11
Age at Ross operation				
<2 years	1 (5 %)	0.41	3 (8 %)	0.33
2–18 years	12 (57 %)		21 (55 %)	
18–30 years	7 (33 %)		12 (32 %)	
>30 years	1 (5 %)		2 (5 %)	
Underlying aortic valve disease				
Congenital	19 (91 %)	0.67	35 (92 %)	0.93
Endocarditis	0		1 (3 %)	
Congenital + endocarditis	1 (5 %)		2 (5 %)	
Concomitant reduction plasty of ascending aorta at time of Ross operation	1 (5 %)	0.009	9 (24 %)	1.00
Systemic arterial hypertension	4 (19 %)	0.48	5 (13 %)	1.00

AR aortic regurgitation, *AS* aortic stenosis, *RP* Ross procedure

root problems were the reason for reoperations in 45 % of patients and neo-aortic valve replacement and aortic root replacement were quite frequent also including ascending aortic/arch reconstruction. In our own experience, during a follow-up of only 5.2 years, 8 % of patients required a reoperation on the neo-aortic root. The most likely explanation is that in a significant proportion of patients, the pulmonary autograft may not be able to withstand the forces of the systemic circulation given its different tissue architecture. Mixed intrinsic abnormalities of the connective tissue, which lead to the aortic valve disease, may be additionally involved in this process. Pees et al. [22] have shown that neo-aortic root dilatation after the Ross procedure is much more common than after the arterial switch procedure. This cannot be explained by the older age at surgery alone. It has been shown in the past that medial abnormalities are common in patients with congenital heart disease not only in the aorta but also in the pulmonary trunk, which then makes its more prone for dilatation and aneurysm formation [21]. So far it is

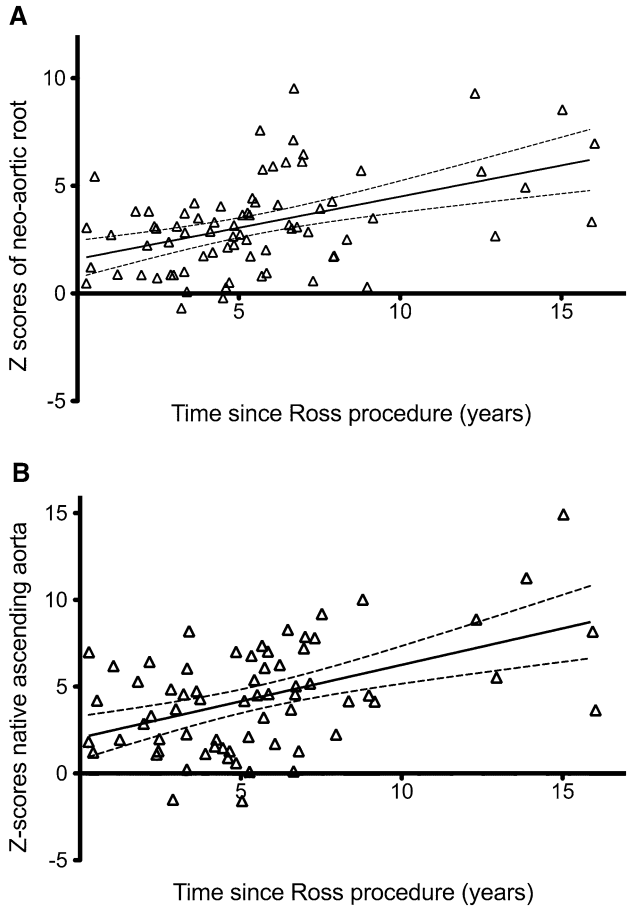

Fig. 3 **a** *Z* scores along their time of follow-up in the neo-aortic root. **b** *Z* scores along their time of follow-up in the native ascending aorta

unknown whether there are underlying genetic differences; it has just been shown in the literature that aortic dilatation in bicuspid aortic valve disease is not due to TGFBR1 or 2 mutations [23]. Therefore, these differences are open for study and may lead to a better understanding of the underlying congenital abnormality, which leads to the Ross procedure.

Surgical Technique and Follow-up

We preferred to use the free-standing root replacement technique with adequate buttressing of the neo-aortic root using the remnants of the native aortic root. This tried to achieve both the advantages of the free-standing root replacement and those of the cylinder inclusion technique. We are aware that the cylinder inclusion technique is robust in stabilizing the aortic root, but can lead to distortion of the fine geometric architecture of the aortic valve leaflets sometimes leading to early aortic valve insufficiency. We concentrated on achieving good competence of the neo-aortic valve as well as retaining advantages of the inclusion technique by buttressing and reinforcing the neo-aortic root with the native root remnants as well as strengthening sutures. Unfortunately, progressive dilatation of the neo-aortic sinus was time dependent in our cohort. This rises the question of whether we have to expect a high proportion of these patients to need a reintervention after a longer median follow-up, which strengthens the need for a systematic follow-up in these patients. The results have made us even more critical toward the Ross procedure: Apart from its transformation into a two-valve disease, it also does also not solve the problem of management of aortic dilatation. The optimal management of aortic valve disease in young adults remains difficult. Nevertheless, the Ross operation remained a valuable option at our institutions for infants and small children.

Table 5 Summary of the 6 patients needing reintervention on the neo-aortic root

Pt ♯, gender	Age at reoperation (yr)	Time since RP	Etiology	Reoperation	Aortic root before reoperation, mm	Ascending aorta before reoperation, mm
♯1, M	20.5	6.7 yr	Aortic dilatation	TD, plication of right aortic sinus	54 (*Z* score +7.1)	37 (*Z* score +4.6)
♯2, M	10.2	7 m	Aortic dilatation, severe AR	Aortic valve replacement	34 (*Z* score +7.0)	22 (*Z* score +3.6)
♯3, F	39.7	10.9 yr	Aortic dilatation, moderate AR	TD, aortic valve reconstruction	53 (*Z* score +9.3)	42 (*Z* score +8.9)
♯4, M	20.6	10.4 yr	Aortic dilatation, mild AR	Yacoub procedure	55 (*Z* score +8.5)	57 (*Z* score +14.9)
♯5, M	27.0	5.2 yr	Aortic dilatation, mild AR	Aortic valve replacement, Dacron graft ascending aorta	53 (*Z* score +7.6)	43 (*Z* score +7.4)
♯6, M	17.6	9.3 yr	Aortic dilatation, mild AR	TD, aortic valve reconstruction	41 (+4.9)	41 (+11.3)

Pt ♯ patient number, *M* male, *F* female, *yr* years, *m* months, *AR* aortic regurgitation, *TD* Tirone David operation

Limitations

This cohort contains a higher proportion of pediatric patients than other series. Therefore, in these patients cardiac magnetic resonance imaging was rarely performed and these data were not included.

This series is not the largest series published, but it is a very homogenous patient group as almost all patients were operated by the same team of 2 surgeons, and thus, no major difference in surgical technique is likely to have caused differences on outcome. The age distribution is less homogenous but appeared to us a typical mixed distribution of patients we follow in a mixed pediatric and grown up clinical setting.

The main caveat of this series is that preoperative exact measurements of the aortic root were only available in 43 patients (57 %). However, the data in the patients in whom the data are available show that preoperative native ascending aortic dilatation did not predict late aortic root dilatation.

Conclusions

Neo-aortic root dilatation is a frequent problem after the Ross procedure and is related to the length of follow-up. The need for reoperation on the neo-aortic root was common and related to dilatation and/or neo-aortic regurgitation. This underscores the need for careful patient selection for the Ross procedure, as alternative surgical approaches with a lower risk of later reintervention are available.

Compliance with Ethical Standards

Conflicts of interest None.

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