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ORIGINAL ARTICLE

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Results of the Ross procedure in adults: a single-centre experience of 741 operations[†]

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Abstract

OBJECTIVES: Although the Ross procedure provides excellent long-term survival and a high quality of life, only a limited number of centres perform it as an alternative to the standard aortic valve replacement in adults. In the present study, we evaluated our 16-year results of using the Ross procedure in adult patients.

METHODS: Between 1998 and 2014, 741 adult patients underwent the Ross procedure. The mean patient age was 47.4 ± 12.8 years (range, 18–67 years). The total root replacement technique was used in all patients. Right ventricular outflow tract (RVOT) reconstruction was performed with pulmonary allograft in 175 (23.6%) patients, with different types of xenografts in 561 (75.7%) and with polytetrafluoroethylene conduits in 5 (0.7%) patients.

RESULTS: The early mortality rate was 3.0%. The mean follow-up duration was 5.8 ± 2.2 years. The survival rate at 10 years was 90.7% and was comparable with survival of an age- and sex-matched general population. The rate of freedom from autograft reoperations was 94.1 and 88.3% at 5 and 10 years, respectively. The aortic annulus dilatation was the only independent predictor of autograft failure. The 10-year freedom rates from reoperations for allograft, diepoxide- and glutaraldehyde-treated pericardial xenografts as well as porcine aortic root grafts were 100, 94.4, 82.7 and 80.6%, respectively. The use of xenografts and young patient age were associated with increased risk of RVOT conduit failure.

CONCLUSIONS: The Ross operation provides long-term survival rates that are comparable with an age- and gender-matched general population. The dilated aortic annulus is a risk factor for late autograft valve insufficiency. A cryopreserved pulmonary homograft is the best option for RVOT reconstruction. Diepoxide-treated pericardial xenografts can be an alternative to allografts in elderly patients when an allograft is not available.

Keywords: Aortic valve replacement • Ross operation • Xenograft • Outcome

CONGENITAL

INTRODUCTION

The Ross procedure is an attractive alternative to mechanical prosthesis because it provides physiological haemodynamics, prevents the need for anticoagulation with a minimal risk of thromboembolism and results in excellent long-term survival [1–3]. Despite all these advantages, the application of the Ross procedure has been limited to relatively few centres predominantly in the paediatric population [4]. Early mortality and long-term autograft durability significantly differed between series [2]. The reasons for this lie in the technical complexity of the Ross procedure. Moreover, the serious disadvantage of the Ross procedure lies in the need for double-valve intervention. Pulmonary allograft is the gold standard for right ventricular outflow tract (RVOT) reconstruction during the Ross procedure. However, the availability of allografts is limited. Alternative grafts have been proposed, but their use remains controversial [5, 6]. In this observational study, we evaluated the 16-year results of the Ross procedure at a single centre.

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MATERIALS AND METHODS

Patients

Between December 1998 and December 2014, 741 consecutive adult patients (aged ≥18 years) underwent the Ross procedure at our institution. A retrospective analysis of the results was performed. The mean patient age was 47.4 ± 12.8 years (range, 18–67 years). The institutional review board approved our study.

The Ross procedure was discussed and offered as alternative surgical treatment for aortic valve disease to all patients with an active lifestyle and a desire to avoid lifelong anticoagulation therapy. The presence of a primary aortic valve lesion was the main indication

Table 1: Preoperative patient characteristics

Number of patients	741
Age, mean ± SD (years)	47.4 ± 12.8
Sex, *n* (%)	
Male	556 (75)
Female	185 (25)
Aortic valve disease aetiology, *n* (%)	
Bicuspid	281 (37.9)
Rheumatic	220 (29.7)
Endocarditis	134 (18.1)
Degenerative	71 (9.6)
Prosthetic valve dysfunction	14 (1.9)
Other aetiology	21 (2.8)
Aortic valve haemodynamic lesions, *n* (%)	
Stenosis	340 (45.9)
Insufficiency	310 (41.8)
Mixed lesion	91 (12.3)
Previous interventions, *n* (%)	
Aortic valve replacement	13 (1.8)
Bentall-DeBono	1 (0.13)
Aortic valve repair	7 (0.9)
Aortic balloon valvuloplasty	2 (0.27)
Subvalvular aortic membrane resection	2 (0.27)
Coarctation resection	7 (0.9)
PDA ligation	5 (0.7)
Percutaneous coronary intervention	6 (0.8)
NYHA functional class, *n* (%)	
I	15 (2.0)
II	224 (30.2)
III	474 (64.0)
IV	28 (3.8)
Left ventricular ejection fraction, mean ± SD (%)	63.2 ± 11.6

NYHA: New York Heart Association; PDA: patent ductus arteriosus; SD: standard deviation.

Table 2: Operative data

Cardiopulmonary bypass time, mean ± SD (min)	156.3 ± 38.1
Cross-clamp time, mean ± SD (min)	129.3 ± 25.8
Cardioplegia, *n* (%)	
Crystalloid	717 (96.8)
Blood	24 (3.2)
Ascending aorta dilatation (≥45 mm), *n* (%)	162 (21.9)
Aortic annulus dilatation (≥27 mm), *n* (%)	220 (29.6)
Additional aortic procedures, *n* (%)	
Annulus management	99 (13.4)
Reduction aortoplasty	20 (2.7)
Ascending aortic replacement	10 (1.3)
Autograft wrapping with Dacron prosthesis	2 (0.27)
Aortic arch replacement	2 (0.27)
Konno	1 (0.13)
Concomitant procedures, *n* (%)	
Mitral valve repair	61 (8.2)
Tricuspid valve repair	38 (5.1)
CABG	45 (6.1)
Maze IV	16 (2.2)
ASD/VSD closure	16 (2.2)
RVOT reconstruction, *n* (%)	
Pulmonary allograft	175 (23.6)
Diepoxide-treated pericardial xenograft	375 (50.6)
Glutaraldehyde-treated pericardial xenograft	74 (10.0)
Aortic xenografts	112 (15.1)
PTFE conduit	5 (0.7)

RVOT: right ventricular outflow tract; CABG: coronary artery bypass grafting; ASD: atrial septal defect; VSD: ventricular septal defect; PTFE: polytetrafluoroethylene; SD: standard deviation.

for surgery, in accordance with the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery guidelines for the management of patients with valvular heart disease [7]. A total of 340 patients (45.9%) presented with aortic stenosis, 310 (41.8%) with aortic insufficiency and 91 (12.3%) patients had mixed lesions. Infective endocarditis was a reason of aortic valve disease in 134 (18.1%) patients; among them, 38 patients (5.1%) had acute endocarditis and in the other cases endocarditis was treated.

The contraindications for autograft implantation included the presence of other valve pathologies requiring replacement, pulmonary valve anomalies, connective tissue disorders and multivessel coronary artery diseases. The operations were performed by two surgeons. The preoperative patient characteristics are demonstrated in Table 1.

Operative technique

Cardiopulmonary bypass was established using the standard procedure with aortic and bicaval cannulation, followed by induction of moderate hypothermia (33–34°C). Myocardial protection was performed with antegrade cold crystalloid (Custodiol; Dr Kohler Pharma, Alsbach-Hahnlein, Germany) for cardioplegia in most patients (Table 2). The total root replacement technique was performed in all patients. The pulmonary autograft was enucleated using a 4-mm rim of infundibular muscle below the cusps and implanted inside the aortic annulus using continuous 5/0 polypropylene (Prolene; Ethicon, Inc., Cincinnati, OH, USA and Premilene; B. Braun Melsungen AG, Melsungen, Germany) sutures. The aortic annulus was dilated in 220 patients (29.6%). The indications for annulus reduction included a diameter of ≥27 mm, or greater than the pulmonary annulus by ≥2 mm. Aortic annulus management was performed in 33 (4.5%) patients where the proximal suture line was reinforced with a pericardial strip, in 46 (6.2%) patients where the plication stitches were at the commissures and in 20 (2.7%) patients where the purse-string suture was used subannularly and tied external to the aorta in the area of the non-coronary sinus using the Hegar dilator as described by Elkins *et al.* [1]. The RVOT was reconstructed with cryopreserved pulmonary allografts in 175 (23.6%) patients, with different types of xenografts in 561 (75.7%) and with a factory-made trileaflet polytetrafluoroethylene (PTFE) conduit (Cardiomed, Russia) in 5 (0.7%) patients. The xenografts that were used included the diepoxide-treated (NeoCor, Russia) and glutaraldehyde-treated pericardial xenografts (BioLab, Russia), as well as different types of porcine aortic root grafts (BioLab or NeoCor, Russia). The choice of the conduit size was based on the diameter of the distal portion of the pulmonary artery and was used as much as possible, depending on the patient's needs. The proximal tubular part of the pericardial conduits was adjusted to the RVOT diameter using its oblique cutting. Both the proximal and distal anastomoses were performed with continuous 5/0 polypropylene sutures. In most patients (557; 75.2%), RVOT reconstruction was performed after cross-clamp removal, in order to reduce myocardial ischaemia time (Table 2).

Postoperative management

Oral anticoagulants were prescribed for 3 months postoperatively in patients with the xenografts and the PTFE conduits in the right-side

position and were replaced with low-dose aspirin in patients with sinus rhythm, as documented by 24 h Holter monitoring. In patients with pulmonary allografts only, low-dose aspirin was initially administered postoperatively. Moreover, β-blockers and angiotensin-converting enzyme inhibitors were prescribed for anti-hypertensive treatment. The recommended systolic blood pressure value was ≤110–120 mmHg for 6–12 months postoperatively.

Postoperative evaluation

In all patients, transoesophageal echocardiography (Vivid 7; General Electric Healthcare, Little Chalfont, UK and Philips ie33; Philips Healthcare, Cleveland, OH, USA) was performed to evaluate the autograft as well as the right-sided graft function, after the patients were weaned off cardiopulmonary bypass. Transthoracic echocardiography (TTE) was performed before hospital discharge. The transvalvular aortic and pulmonary gradients were measured by continuous-wave Doppler ultrasound, using the Bernoulli equation. The severity of autograft and xenograft regurgitation was evaluated by colour flow Doppler according to the guidelines of the European Association of Echocardiography [8], and was graded as none/trivial, mild, moderate or severe. After discharge, examinations were scheduled annually. In cases when annual clinic visits were unavailable, the follow-up was obtained by contact with the referring cardiologist, the patient or his family (post, e-mail, telephone, etc.). Echocardiograms obtained from outside physicians were reanalysed at our institution by the most experienced echocardiographers. Each period between time of surgery and event or the end of the follow-up period constituted a separate observation. If the contact could not be available, a patient was considered as lost to follow-up, and the date of last communication was defined as the censoring date. The follow-up period was closed in July 2015. The mean clinic follow-up duration was 5.8 ± 2.2 years (range, 0–16 years) and was 91% complete (674 patients) with 3080 patient-years. The echocardiographic data at follow-up were available in 660 patients (89.1% of all operated patients). The mean echocardiographic follow-up was 5.3 ± 2.5 years. Postoperative events were presented in accordance with the 2008 Society of Thoracic Surgeons/American Association for Thoracic Surgery/European Association for Cardio-Thoracic Surgery Guidelines. Early mortality was defined as death from any cause occurring in hospital or during 30 days after operation. Late mortality was considered as death occurring after that period. Reoperation was defined as any surgical procedure performed on the autograft or RVOT conduits or both. Autograft dysfunction was defined as an aortic insufficiency graded as ≥2. A peak systolic gradient of >40 mmHg or the presence of moderate or severe conduit valve insufficiency was determined as RVOT conduit dysfunction.

Statistical analysis

Statistical analysis was performed using the Statistica software, version 10.0 (StatSoft, Inc., Tulsa, USA). Continuous data are presented as the mean ± standard deviation or median (25th; 75th percentile). Categorical data are described as absolute numbers and relative frequencies. Two groups were compared with the independent samples *t*-test (for continuous variables with normal distributions) or the Mann–Whitney *U*-test (non-normal distributions) for unpaired data, and with the paired *t*-test or the Wilcoxon signed-rank test for paired data. The χ^2 test or Fisher's exact test was used to compare two groups for categorical data. The Kaplan–Meier method was used to evaluate survival and freedom from autograft or RVOT graft reoperations. The survival and freedom from events are presented with 95% confidence intervals. Survival and freedom from operations between groups were compared using the log-rank test. The survival of the gender-, age- and calendar year-matched Russian population was calculated based on data published online by the Russian Federal State Statistic Service (www.gks.ru, last accessed 7 March 2016). Risk factor analyses were performed in order to identify the potential predictors of autograft and RVOT graft dysfunctions, using the Cox proportional-hazard regression method. The analysis included factors such as age, gender, body surface area, aortic valve morphology (bicuspid or tricuspid), aortic valve lesion (stenosis or insufficiency), preoperative active endocarditis, previous operations, ascending aortic diameter, aortic annulus diameter, annular reduction, associated procedures, type of RVOT conduit and RVOT conduit size. The constant relative hazard assumption was investigated by correlating sets of scaled Schoenfeld residuals for each covariate with a suitable transformation of time, along with a global test for the model as a whole. Based on the method described above, the proportional hazards assumption was considered as valid. Univariable analysis was performed initially. Variables with a value of $P \leq 0.2$ in the univariable analyses were assessed in the multivariable Cox proportional-hazard regression model. Two-sided *P*-values of <0.05 were considered statistically significant.

RESULTS

Early mortality and morbidity

The early mortality rate was 3.0% (22 patients). The causes of deaths included low cardiac output syndrome (15 patients; 68.2%) due to myocardial infarction (coronary artery angulation or ostial rotation in 5 patients), massive intraoperative bleeding (5 patients; 22.7%) and septic complications (deep sternal wound infection; 2 patients; 9.1%). The most frequent complication in the early postoperative period was atrial fibrillation (115 patients; 15.5%). Reoperations for bleeding were performed in 29 patients (3.9%). Seven patients (0.9%) developed an atrioventricular block and underwent pacemaker insertion. Strokes occurred in 8 patients (1.1%). Non-elective coronary artery interventions (coronary artery bypass grafting or percutaneous coronary intervention) were required in 15 patients (2%).

Late mortality and survival

Eighteen patients died during the follow-up period. The late deaths were sudden and unexplained in 8 patients, and were the result of progression of heart failure in 3 and ischaemic stroke in 1. Two patients died intraoperatively during the reoperations, whereas 4 other deaths were non-cardiac-related (oncology, 2; trauma, 1 and pneumonia, 1). The survival rates at 5 and 10 years were 93.9% (95% confidence interval [CI], 90.5–95.5%) and 90.7% (95% CI, 84.1–92.9%), respectively. This was comparable to the survival rates of an age- and sex-matched general Russian population ($P = 0.182$; Fig. 1).

Late clinical outcome and valve-related complications

At the final follow-up of the examined patients (674), 614 (91.1%) were categorized as NYHA functional class I–II, and 60 (8.9%) were categorized as NYHA class III. Moreover, 30 patients (4.5%) presented with atrial fibrillation at the final follow-up and continued warfarin treatment.

Thromboembolic events occurred in 7 patients, with strokes in 3 patients (1 patient died), transient ischaemic attacks in 3 and retinal artery thrombosis in 1. The linearized rate of thromboembolic events was 0.23%/patient-year. Major bleeding episodes were registered in 3 patients (0.09%/patient-year). All haemorrhagic events occurred in the first 6 months postoperatively, before oral anticoagulant treatment was discontinued. Twenty-five patients had infective endocarditis (22 had autograft and 3 had xenograft endocarditis). In 9 patients, this was identified as late recurrent infective endocarditis.

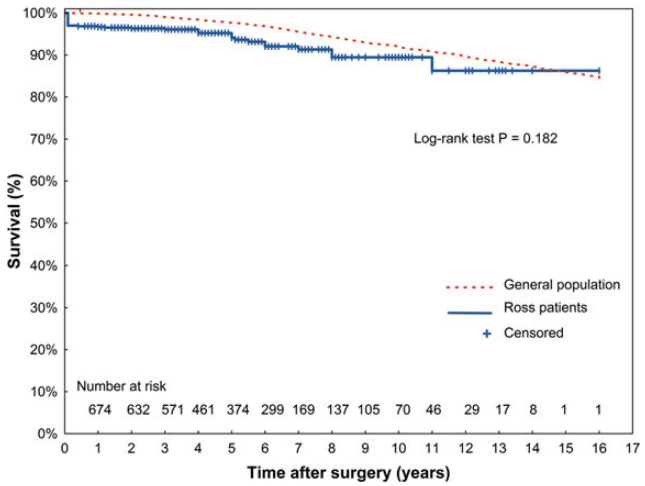

Figure 1: Survival after the Ross procedure compared with survival of an age-, gender- and calendar year-matched general population. *P*-value: comparison of survival between the Ross patients and the general population using a one-sample log-rank test.

The linearized rate of endocarditis was 0.81%/patient-year. Eleven patients with autograft endocarditis required reoperation, whereas others were treated conservatively with resolution of the condition.

One patient with chronic pulmonary embolism had xenograft thrombosis requiring reoperation.

Echocardiographic results

At follow-up, 660 patients underwent TTE. Upon discharge, the peak pressure gradient across the autograft was 5.1 ± 2.5 mmHg with insignificant changes (6.5 ± 3.0 mmHg) at the last follow-up visit ($P = 0.124$). Only 1 patient with autograft endocarditis had stenosis of the autograft valve with a peak gradient of 63 mmHg (combined with severe insufficiency) and needed reoperation. At follow-up, 602 patients (91.2%) did not have or only had mild presentations, whereas 19 (2.9%) developed moderate aortic insufficiency. Thirty-seven (5.6%) patients developed severe aortic insufficiency, necessitating reoperation. Freedom from an aortic insufficiency of ≥2 was identified in 88.3% (95% CI, 84.3–90.3%) and 82.2% (95% CI, 76.8–86.5%) of patients at 5 and 10 years, respectively. Autograft dilatation (≥45 mm) was found in 62 patients (9.4%). The rate of freedom from root dilatation was 76.5% (95% CI, 63.4–85.1%) at 10 years. Only 2 patients had autograft or aortic diameters exceeding 50 mm.

All types of right-sided grafts demonstrated significant increases in the transvalvular gradients during follow-up (Table 3). The use of pulmonary allografts was associated with lower gradients. All types of xenografts had significantly higher gradient at discharge and during the follow-up period, in comparison with the allograft group. Among all the xenografts, patients with the diepoxide-treated graft demonstrated lower peak gradients (22.7 ± 6.1 mmHg) at the last follow-up visit, compared with glutaraldehyde-treated (36.7 ± 15.2 mmHg, $P < 0.001$) and aortic root xenografts (38.8 ± 21.3 mmHg, $P < 0.001$).

Reoperations

Fifty-seven patients underwent reoperations due to failure of the autograft and conduits in the RVOT position (Table 4). Eight

Table 3: Comparison of the different right ventricular outflow tract grafts after the Ross procedure

	PA	dt XG	*P*-value	gt XG	*P*-value	AR XG	*P*-value	PTFE[a]	*P*-value
Patients, *n*	175	375	–	74	–	112	–	5	–
Age (years)	39.6 ± 11.1	52.8 ± 10.6	<0.001	47.4 ± 12.8	<0.001	42.0 ± 13.5	0.112	42.0 (41.0; 48.0)	0.383
Conduit size (mm)	26.1 ± 3.0	26.4 ± 0.9	0.321	26.5 ± 1.2	0.131	26.5 ± 1.3	0.323	25.0 (25.0; 27.0)	0.223
Follow-up (years)	5.1 ± 1.8	5.2 ± 1.7	0.121	5.3 ± 1.9	0.243	7.7 ± 2.1	0.012	1.0 (1.0; 2.0)	0.014
Dysfunction, *n* (%)	0	3 (0.8)	0.555	10 (13.5)	<0.001	15 (13.4)	<0.001	0	–
Freedom from reoperation[b]									
At 5 years	100%	98.2 (91.4–99.5)	0.231	82.7 (69.8–90.2)	<0.001	93.3 (86.5–96.8)	0.049	100%	–
At 10 years		94.4 (74.0–98.4)		82.7 (69.8–90.2)		80.6 (66.3–88.0)			
RVOT peak gradient (mmHg)									
At discharge	8.1 ± 3.7	11.4 ± 3.7	0.013	14.9 ± 6.1	<0.001	17.9 ± 7.4	<0.001	12.8 (11.5; 16.0)	0.144
At follow-up	15.4 ± 4.6	22.7 ± 6.1	0.002	36.7 ± 15.2	<0.001	38.8 ± 21.3	<0.001	21.5 (20.0; 23.5)	0.053
P-value*	0.022	0.003	–	<0.001	–	<0.001	–	0.044	

PA: pulmonary allograft; dt XG: diepoxide-treated xenograft; gt XG: glutaraldehyde-treated xenograft; AR XG: aortic root xenograft; PTFE: polytetrafluoroethylene conduit; RVOT: right ventricular outflow tract.
[a]Data are presented as median (25th; 75th percentile).
[b]Data are presented as percentages (95% confidence interval).
P-values: comparison with the findings for the allograft group; *P*-values*: comparison of gradients at follow-up with gradients at discharge.

Table 4: Reoperation data

Total number of patients, *N*	57
Autograft reoperations	
Patients, *n* (%)	37 (100)
Time after Ross procedure, mean ± SD (years)	3.5 ± 2.3
Indications, *n* (%)	
Autograft valve insufficiency	33 (89.2)
Insufficiency + stenosis	1 (2.7)
Aortic aneurysm	1 (2.7)
Subvalvular false aneurysm	2 (5.4)
Reasons of autograft valve insufficiency, *n* (%)	34 (100)
Technical	4 (11.8)
Autograft dilatation	18 (52.9)
Endocarditis	6 (17.6)
Autograft dilatation + endocarditis	5 (14.7)
Structural valve deterioration (without annulus dilatation)	1 (2.9)
Type of reoperation, *n* (%)	
Replacement with mechanical prosthesis	31 (83.8)
Autograft valve repair	3 (8.1)
Ascending aortic replacement	1 (2.7)
False aneurysm closure with a xenopericardial patch	2 (5.4)
Concomitant procedures, *n* (%)	
RVOT conduit reoperation	8 (21.6)
Mitral valve repair	2 (5.4)
Tricuspid valve repair	2 (5.4)
RVOT conduit reoperations	
Patients, *n* (%)	28 (100)
Time after Ross procedure, mean ± SD (years)	6.4 ± 2.3
Indications, *n* (%)	
Stenotic structural valve deterioration (mean peak RVOT gradient 67.5 ± 29.0 mmHg)	27 (96.4)
Thrombosis	1 (3.6)
Type of reoperation, *n* (%)	
Replacement with pulmonary allograft	28 (100)
Concomitant procedure, *n* (%)	
Autograft reoperation	8 (28.6)
Mitral valve repair	2 (7.1)
Tricuspid valve repair	5 (17.9)
Peak RVOT gradient at discharge, mean ± SD (mmHg)	13.5 ± 5.6

RVOT: right ventricular outflow tract; SD: standard deviation.

patients underwent both autograft and xenograft interventions. The overall freedom rate from all reoperations was 91.4% (95% CI, 89.9–94.6%) and 80.1% (95% CI, 75.0–86.7%) at 5 and 10 years, respectively.

Thirty-seven patients required reoperations due to autograft dysfunction (7 in the early postoperative period). The rates of freedom from autograft reoperations were 94.1% (95% CI, 92.6–96.6%) and 88.3% (95% CI, 82.5–91.6%) at 5 and 10 years, respectively (Fig. 2). The linearized rate of reoperation was 1.2/patient-year. In patients with aortic annulus dilatation (≥27 mm), the rate of freedom from autograft reoperation at 10 years was 78.4% (95% CI, 65.2–86.2%). In patients with a non-dilated annulus (<27 mm), this rate was 92.6% (95% CI, 86.6–95.7%; $P < 0.001$). The main indication for reoperation was severe autograft valve insufficiency. One patient had ascending aortic aneurysm (55 mm) without haemodynamic autograft disorders and 2 patients had subvalvular false aneurysm (proximal anastomosis line). The main reason for autograft failure was the dilatation predominantly at the annulus level. Infective endocarditis, alone or in combination with autograft dilatation, was identified in 11 patients (29.7%). In 3 patients, autograft valve repair was performed by means of perforation closure with a xenopericardial patch (2 patients) and annuloplasty (1 patient). Univariable analyses identified aortic

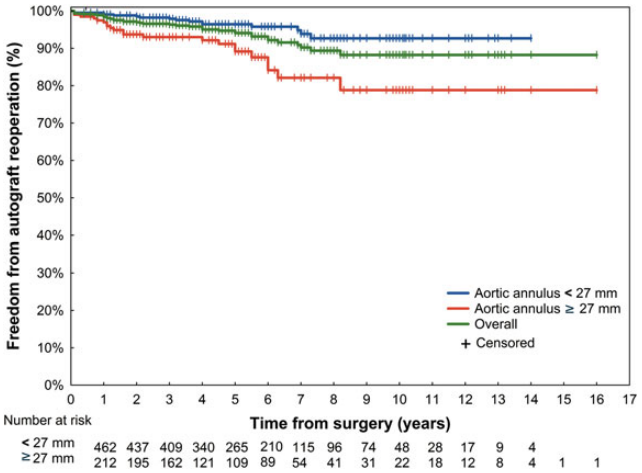

Figure 2: Freedom from autograft reoperations. Comparison between the groups with dilated (≥27 mm) and non-dilated (<27 mm) aortic annulus.

annulus diameter as the only independent predictor of autograft failure (hazard ratio [HR], 1.13/mm; 95% CI, 1.04–1.23; $P = 0.003$; Supplementary Table 1). Predictors of autograft dilatation (≥45 mm) were an aortic annulus diameter (HR, 1.25/mm; 95% CI, 1.12–1.48; $P < 0.001$) and preoperative aortic diameter (HR, 1.11/mm; 95% CI, 1.01–1.19; $P = 0.028$) using multivariable Cox regression analysis.

Twenty-eight patients underwent RVOT reinterventions. Twenty-five patients had severe graft stenosis. In 3 patients, stenosis was moderate, with the main indications for operation being severe aortic insufficiency in 2 and mitral insufficiency in 1. The overall freedom from RVOT reoperations was 95.4% (95% CI, 92.7–97.1%) and 83.5% (95% CI, 72.5–90.4%) at 5 and 10 years, respectively. The linearized rate of RVOT interventions was 0.9/patient-year. Multivariable Cox regression analysis revealed patient age (HR, 0.95/year; 95% CI, 0.93–0.98; $P = 0.008$) and using xenografts (HR, 4.34; 95% CI, 1.50–13.72; $P = 0.016$) as the risk factors for RVOT conduit failure (Supplementary Table 2). There were no reoperations due to pulmonary allograft dysfunction. We also had no reoperations in patients with the PTFE grafts; however, these prostheses had the shortest follow-up (Table 4). The 10-year freedom rates from reoperations for diepoxide- and glutaraldehyde-treated pericardial xenografts as well as porcine aortic root grafts were 94.4% (95% CI, 74.0–98.4%), 82.7% (95% CI, 69.8–90.2%) and 80.6% (95% CI, 66.3–88.0%), respectively (Fig. 3). The reoperation rate varied according to the different age groups. The 10-year freedom rate from xenograft reoperation rates in patients >60 years ($n = 111$) was 100%, while in groups <50 years (202 patients) and 50–59 years (248 patients), these rates were 76.9% (95% CI, 59.8–85.4%; $P = 0.033$) and 92.2% (95% CI, 79.6–97.8%; $P = 0.112$), respectively (Fig. 4).

The reoperative mortality rate was 3.5% (2 patients) and was caused by massive intraoperative bleeding in both patients. Other details of the reoperations are demonstrated in Table 4. Seven patients underwent catheter ablation for atrial fibrillation or flutter during follow-up.

DISCUSSION

The pulmonary autograft is an attractive alternative to prosthetic aortic valve replacement. It was demonstrated that pulmonary autograft in the aortic position preserves its viability during

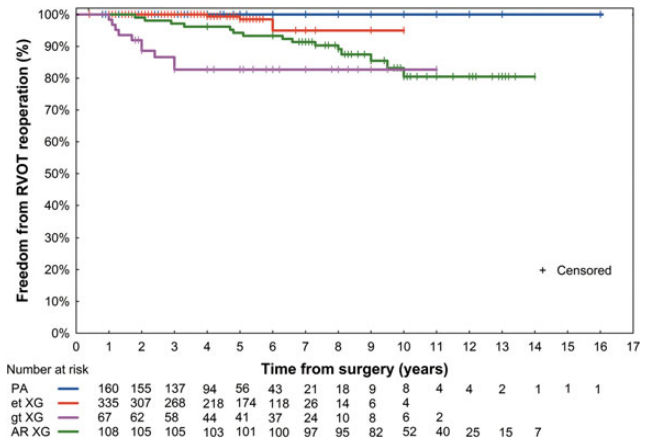

Figure 3: Freedom from reoperations for the different right ventricular outflow tract grafts. PA: pulmonary allograft; dt XG: diepoxide-treated xenograft; gt XG: glutaraldehyde-treated xenograft; AR XG: aortic root xenograft.

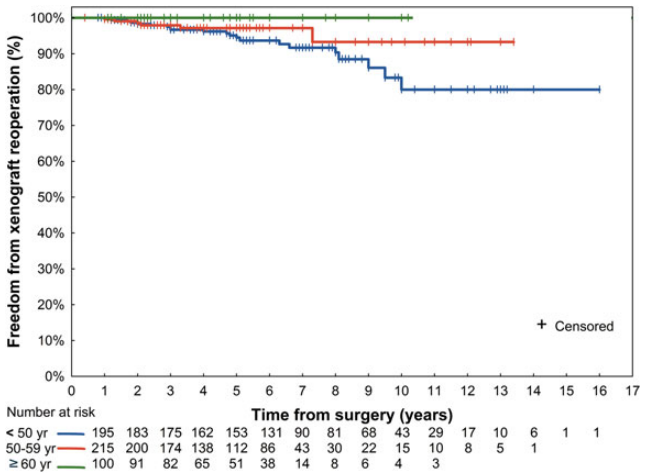

Figure 4: Comparison of the freedom from xenograft reoperations in the different age groups.

long-term follow-up. Several studies with histological examinations of explanted pulmonary autografts demonstrated the presence of preserved viable cells in the autograft wall [2, 9]. Histological and morphological similarity to the native aortic root determines the unique properties of the pulmonary autograft. The autograft's ability to change its shape and size during the cardiac cycle provides excellent haemodynamic characteristics, which makes it superior to mechanical prostheses [10]. Transaortic gradient remains constant in the vast number of patients during the long-term follow-up period [9]. Lower residual transvalvular gradients allow for a more rapid and complete left ventricular mass regression after the Ross procedure that probably has a positive effect on long-term results [9]. The pulmonary autograft provides the minimal risk of thromboembolism and avoidance of anticoagulation. The rate of valve-related complications after the Ross procedure is very low and is less than that with using mechanical prostheses [11, 12]. The quality of life of patients who underwent the Ross population is higher in comparison with those who underwent treatment with mechanical prostheses and allografts [13, 14]. El-Hamamsy *et al.* [13] believe the reason for this lies in the ability of the living autograft valve to rapidly adapt to changing haemodynamic conditions during exercise.

The early mortality rate significantly varies in different studies [2]. In our series, early mortality was higher in comparison with those after conventional aortic valve replacement procedures that were performed in our institute. Most deaths occurred in the initial period of the Ross procedure in our clinic. With additional experience, the mortality rates after the Ross procedure became comparable with those from a conventional aortic valve replacement procedure, which demonstrates the need for a learning curve. One of the reasons why the Ross procedure is not widely used is the considerable experience needed in order to obtain acceptable results [15].

The most significant advantage of the Ross procedure is its excellent long-term survival rates. In recent years, numerous studies have demonstrated that survival after the Ross procedure is comparable to that with the age- and gender-matched general populations in different countries [12, 15–19]. Some authors believe that this is the result of the careful selection of patients for the Ross procedure [20]. However, several studies have demonstrated the superiority of the Ross procedure in achieving long-term survival compared with mechanical prostheses and aortic allografts [11, 13]. In the present study, survival rates after the Ross procedure was also comparable with the age- and gender-matched general population, but was slightly lower than in other studies. This can be explained by the relatively short follow-up period in our study, and possibly by the demographic features of the Russian population. The incidence of valve-related events was low. However, the rate of endocarditis in the long-term postoperative period was slightly higher in our series, compared with previous studies. This is explained by the fact that a significant proportion of patients had active endocarditis as an indication for the initial Ross operation in comparison with the other studies [16, 19].

The freedom from autograft reoperations differs significantly between the series [4, 12, 17, 18]. In the German-Dutch Ross registry, the rates of freedom from reoperation at 10 years for the root replacement technique, with and without a reinforcement procedure, were 95.9 and 87.3%, respectively [21]. The root dilatation is the main cause of autograft dysfunction in long-term follow-up [21]. Infective endocarditis leads to autograft failure in 20–22% patients [17, 21]. In our series, the rate of freedom from autograft reintervention was 88.3 ± 2.2% at 10 years. The main reason for early autograft failure in our study was the early technical mistakes that occurred with the Ross procedure in our institution and also confirms the need for a learning curve with this procedure. Although autograft dilatation was the leading cause, endocarditis was also a significant reason in the 29.7% of patients who underwent autograft reoperations in our study. Similar results were reported recently by Weimar *et al.* [12]. The authors concluded that the Ross procedure is not superior in preventing recurrent endocarditis compared with other types of aortic valve replacement procedures and they had abandoned using the pulmonary autograft in patients with active endocarditis. The analysis of the patients with autograft endocarditis in our series revealed inadequate antibiotic prophylaxis during the different procedures after discharge, resulting in mucosal injury in most of these patients. Although autologous tissues are used for aortic valve replacement during the Ross procedure, lifelong antibiotic prophylaxis is needed, as recommended for patients with prosthetic heart valves. This approach can reduce the rate of autograft failure in the long-term period.

The most frequently reported risk factors for autograft failure are preoperative aortic insufficiency [1, 3, 12, 16, 19], aortic

annulus dilatation [1, 3, 19], the total root replacement technique [21], bicuspid aortic valve [22], young age [2], male sex [1, 19] and arterial hypertension in the postoperative period [2, 13]. Our study confirms that preoperative aortic annulus dilatation is an independent risk factor for autograft reoperation, while the presence of a bicuspid valve and aortic preoperative insufficiency were not associated with autograft failure. A significant proportion of the patients in our study (162 patients; 21.9%) had concomitant aortic aneurysm. Although preoperative aortic dilatation was a predictor of autograft dilatation at follow-up, it was not associated with autograft dysfunction. At follow-up, only 2 patients had an aortic diameter exceeding 50 mm in our study. However, our study had a relatively short follow-up period and it is currently unknown whether reoperation will be necessary in the future.

It is unclear whether annulus reduction prevents autograft dysfunction in the long-term period. Some believe that the dilated annulus is a sign of a connective tissue disorder. Thus, aortic annulus reduction and reinforcement does not protect the affected autograft from dilatation [3]. Conversely, the reoperation rate was low in some series involving the annulus reduction [1]. In our study, annulus management did not have any effects on the prevention of aortic insufficiency. Among the patients who underwent annulus reduction, only 2 required autograft reoperations. However, the mean follow-up period for these patients was only 2.1 ± 2.1 years, whereas the mean time for autograft reoperations in our study was 3.5 ± 2.3 years.

It is known that the pulmonary autograft adapts to the system haemodynamics for a short time postoperatively [23]. We believe that adequate anti-hypertensive treatment may potentially increase autograft root durability. We recommend strict anti-hypertensive therapy, especially in the first 6–12 months after the Ross procedure, as previously recommended by other authors [12, 13].

The Ross procedure has serious limitations, including the need for a double-valve intervention. The cryopreserved pulmonary allograft is the most widely used graft for RVOT reconstruction. Several reports have demonstrated excellent late results when using pulmonary allografts in the Ross procedure. In the German Ross registry (1779 adult patients), freedom from reoperation when using pulmonary allografts was 92.3% at 15 years [15]. In a meta-analysis of the Ross operation by Takkenberg *et al.* [2], the allograft deterioration rate in adults was 0.55% per patient-year. David *et al.* [3] also reported that the rate of freedom from allograft reoperation was 93.6% after 20 years.

Despite the fact that the allograft is the gold standard for RVOT reconstruction, limited availability restricts its widespread use. Thus, alternative grafts have been proposed.

Hechadi *et al.* [5] compared long-term results between patients who received the Medronic Freestyle grafts (17 patients) and pulmonary allografts (37 patients). Over a mean follow-up period of 8.2 years, the authors observed no differences in haemodynamics, and concluded that the Freestyle grafts can be an acceptable alternative for RVOT reconstruction when a pulmonary homograft is not available. In a recent study, Juthier *et al.* [24] also reported good early and mid-term results using different stentless porcine root models in 61 patients.

However, contrary results using xenografts have also been reported [6, 21, 25]. Miskovic *et al.* [6] and Weimar *et al.* [25] both reported that patients with bioprostheses in the RVOT position (Medtronic Freestyle) demonstrated a significantly higher risk of reintervention due to pulmonary conduit dysfunction. In the German Ross registry, the durability of bioprostheses (149 patients) implanted in the RVOT was unacceptably low [15].

Hence, experience with xenografts in the Ross procedure is limited and controversial. We presented the largest study on the use of xenografts for RVOT reconstruction during the Ross procedure. The reason for using the xenografts was the limited availability of allografts in our country. Haemodynamic performance of all types of xenografts was worse compared with allografts. Glutaraldehyde-treated pericardial and porcine aortic root xenografts demonstrated an unacceptable level of dysfunction due to fast calcium degeneration, which is the reason they are no longer used. At the midterm follow-up, diepoxide-treated pericardial xenografts demonstrated acceptable haemodynamic characteristics, but long-term follow-up is needed. We conclude that the use of xenografts during the Ross procedure should be restricted. However, the diepoxide-treated pericardial xenografts can be an alternative to allografts in elderly patients, when allografts are not available. In our institution, allografts remain the substitute of choice. We applied PTFE conduits for RVOT conduits in 5 patients and observed no dysfunctions. However, the limited number of patients and short follow-up period did not allow us to make conclusions about their durability.

Study limitations

The present study has some limitations. It was a retrospective analysis. The mean follow-up was relatively short (5.8 ± 2.2 years) and long-term follow-up results are needed. The xenografts used in this study is not available in the EC and other countries, and were not compared with the xenografts that are widely used for right ventricular tract reconstruction.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: none declared.

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APPENDIX. CONFERENCE DISCUSSION

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Dr J. Pepper *(London, UK)*: Can you tell me how the 741 that you have reported were chosen from the total number of 868? Are these the patients over 18, or was there some other method in which you selected the 741 you reported on? Overall there were 868.

Dr Bogachev-Prokophiev: We analysed patients over 18 year old only and that's why there was 741, but not 868.

Dr Pepper: Did you use a consistent technique of a total root that was free-standing or was this a supported root inclusion? I wasn't quite clear.

Dr Bogachev-Prokophiev: It was only total root replacement technique, without any support, but in the last 5 years we do support only the aortic annulus in patients with a previous dilatation more than 26 cm or 27 cm. We did not have experience with the root inclusion technique.

Dr Pepper: One more question based really on your manuscript. Is there a problem obtaining pulmonary homografts in Siberia? Is this why you used a variety of different substitutes in the right outflow tract?

Dr Bogachev-Prokophiev: Yes. It's the same problem as told by the previous speaker, Professor H. Sievers. We have a real problem with homografts. In our own clinic we produce these type of grafts and if we have homografts at the operation time, we use it.

Dr I. El-Hamamsy *(Montreal, Canada)*: A very nice result and an elegant presentation. What is the aortic annuloplasty technique that you use?

Dr Bogachev-Prokophiev: Aortic root or aortic valve?

Dr El-Hamamsy: For the annulus, when you have a dilated annulus

Dr Bogachev-Prokophiev: We have done two techniques. We use a pericardial patch, and the other variant—it's 3 plication stitches on the commissures and use a Hegar dilator to achieve 22 or 23 mm annulus comparable with the autograft diameter.

Dr El-Hamamsy: You showed that an annulus above 27 was a risk factor for autograft reoperation. The patients who came back, were those patients who had an annuloplasty or the ones who were before you started doing annuloplasties?

Dr Bogachev-Prokophiev: We have done this procedure only for the last 4 or 5 years. All patients who came to our clinic with aortic insufficiency and dilatation of the aortic annulus were patients without any aortic annulus management, without any support. We didn't do any redo operation in patients in whom we perform this management, but follow-up is not long enough.