

Long Term Results of Right Ventricular Outflow Tract Reconstruction with Homografts

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Background: Homograft cardiac valves and valved-conduits have been available in our institute since 1992. We sought to determine the long-term outcome after right ventricular outflow tract (RVOT) reconstruction using homografts, and risk factors for reoperation were analyzed. **Materials and Methods:** We retrospectively reviewed 112 patients who had undergone repair using 116 homografts between 1992 and 2008. Median age and body weight at operation were 31.2 months and 12.2 kg, respectively. The diagnoses were pulmonary atresia or stenosis with ventricular septal defect (n=93), congenital aortic valve diseases (n=15), and truncus arteriosus (N=8). Mean follow-up duration was 79.2±14.8 months. **Results:** There were 10 early and 4 late deaths. Overall survival rate was 89.6%, 88.7%, 86.1% at postoperative 1 year, 5 years and 10 years, respectively. Body weight at operation, cardiopulmonary bypass (CPB) time and aortic cross-clamping (ACC) time were identified as risk factors for death. Forty-three reoperations were performed in thirty-nine patients. Freedom from reoperation was 97.0%, 77.8%, 35.0% at postoperative 1 year, 5 years and 10 years respectively. Small-sized graft was identified as a risk factor for reoperation. **Conclusion:** Although long-term survival after RVOT reconstruction with homografts was excellent, freedom from reoperation was unsatisfactory, especially in patients who had small grafts upon initial repair. Thus, alternative surgical strategies not using small grafts may need to be considered in this subset.

Key words: 1. Ventricular outflow tract obstruction, right
2. Homograft
3. Conduit

INTRODUCTION

A number of prosthetic conduits have been used for the correction of congenital heart defects. Homograft cardiac valves and valved-conduits are deemed standing out in terms of durability, easy handling and availability of various sizes [1]. However, somatic outgrowth over small-sized conduit, calcification of the aortic or pulmonary homograft wall, and degeneration of the valve leaflets are the caveats when using

homograft is contemplated. From the time when the first case of heart transplantation was successfully performed in our institute in 1992 [2], we started to use homograft cardiac valves for right ventricular outflow tract (RVOT) reconstruction. In this study, we sought to determine the long-term outcome after the use of homograft cardiac valves for RVOT reconstruction, and risk factor analysis for adverse outcomes was conducted.

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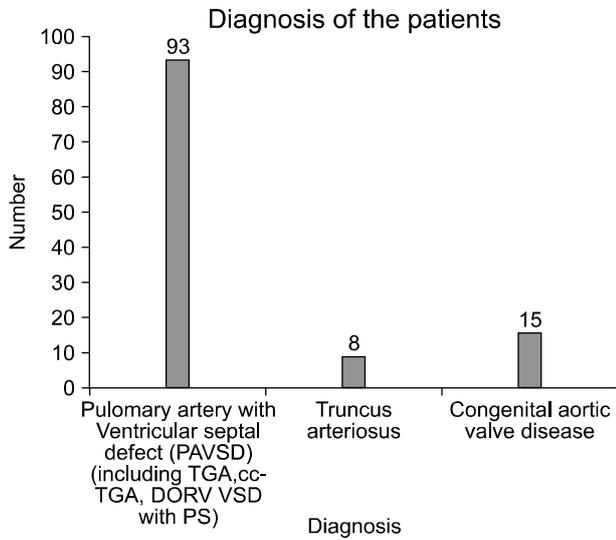


Fig. 1. Distribution of the patients according to the diagnosis. TGA=Transposition of the great arteries; cc-TGA=Congenitally corrected transposition of the great arteries; DORV=Double outlet right ventricle.

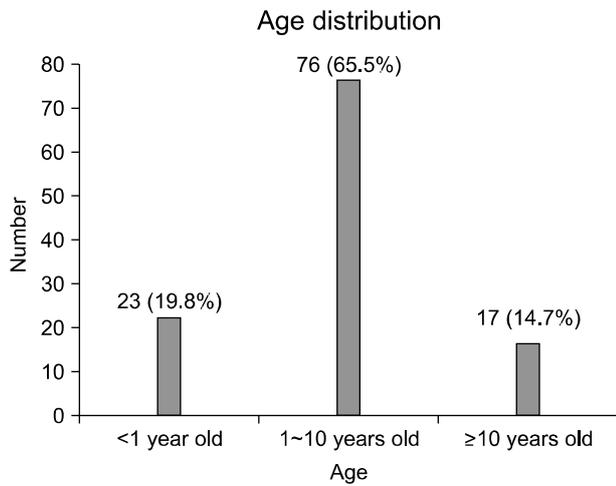


Fig. 2. Distribution of the patients according to the age at operation.

MATERIALS AND METHODS

Retrospective review of the 112 children (younger than 18 years) who had undergone 116 RVOT reconstruction between 1992 and 2008 was performed. Preoperative diagnoses were pulmonary atresia (PA) or stenosis (PS) with ventricular septal defect (VSD) (including transposition of the great arteries with VSD and PS, double outlet right ventricle with VSD

Table 1. Characteristics of the patients

Sex	Male	N: 73 (62.9%)
	Female	N: 43 (37.1%)
Age at operation	Median	31.2 months (6 days to 17 years)
	< 1 year old	N: 23 (19.8%)
	1~10 years old	N: 76 (65.5%)
	≥ 10 years old	N: 17 (14.7%)
Body weight	Median	12.3 kg (2.4 kg to 67.5 kg)
	Diagnosis	PA with VSD (including TGA, cc-TGA, DORV with VSD, PS) N: 93 (80.2%) Truncus arteriosus N: 8 (6.9%) Congenital aortic valve disease N: 15 (12.9%)
CPB time	Median	173 minutes (48 to 858 minutes)
ACC time	Median	76 minutes (0 to 237 minutes)
Type of conduit	Aortic homograft	N: 62 (53.4%)
	Pulmonic homograft	N: 53 (45.7%)
	Missing	N: 1 (0.9%)
Homograft size	Median	19 mm (8 to 29 mm)
	≤ 16 mm	N: 32 (27.6%)
	> 16 mm	N: 72 (62.1%)
	Missing	N: 12 (10.3%)

PA with VSD=Pulmonary atresia with ventricular septal defect; TGA=Transposition of the great arteries (TGA); cc-TGA=Congenitally corrected transposition of the great arteries; DORV=Double outlet right ventricle (DORV); PS=Pulmonary stenosis; CPB=Cardiopulmonary bypass; ACC=Aortic cross clamp.

and PS, and congenitally corrected transposition of great arteries with VSD and PS) in 93, congenital aortic valve diseases in 15 and truncus arteriosus in 8 (Fig. 1). Median age at operation was 31.2 months (6 days~17 years), and median body weight at operation was 12.2 kg (2.4~67.5 kg). Age distribution at repair is illustrated in the Fig. 2. There were 69 males (69/112, 62.9%) and 43 females (43/112, 37.1%). Follow-up duration was 79.2±14.8 months, and follow-up was complete in 98 patients (98/112, 87.5%). Sixty-two aortic homografts (62/116, 53.4%) and fifty-three pulmonary homografts (53/116, 47.5%) were used, and homograft type could not be identified in one (1/116, 0.8%). Median size of homografts was 19 mm (8~29 mm) (Table 1).

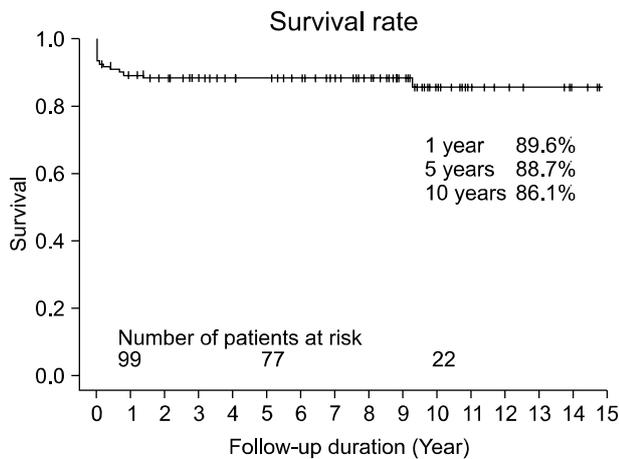


Fig. 3. Overall survival after the use of right ventricular outflow tract reconstruction using homograft conduits.

Data are presented as frequencies, medians with ranges or means with standard deviations. Survival analysis was performed by the Kaplan-Meier method, and unadjusted comparison of the survival data between the variables of interest was conducted using log-rank test. All statistical analyses were performed using SPSS 11.0 (SPSS Inc, Chicago, IL), and a p-value of 0.05 was defined as being significant. Early mortality was defined as a death within 30 days after the operation, regardless of hospitalization or discharge.

RESULTS

There were 10 early deaths (10/112, 8.9%) and 4 late deaths (4/112, 3.6%). Causes of early mortality were low cardiac output in 8, sepsis in 1 and brain death in 1, and causes of late deaths were pneumonia in 2, right heart failure in 1, and sudden death at home in 1. Preoperative diagnoses of the patients with early or late mortality were pulmonary atresia with VSD in 7, truncus arteriosus in 3, transposition of the great arteries with VSD and PS in 1, congenitally corrected transposition with VSD and PS in 1, double outlet right ventricle with VSD and PS in 1, and aortic valve disease in 1. Age at operation was younger than 12 months in 5 and between 1 and 10 years in 9. Overall postoperative survival at 1 year, 5 years, and 10 years were 89.6%, 88.7%, 86.1%, respectively (Fig. 3) Fig. 4 illustrates age-stratified survival, which shows better survival in patients with older age at

repair.

Univariate analysis revealed that body weight and age at repair, cardiopulmonary bypass time, and the diagnosis of truncus arteriosus were associated with the increased risk of death. There was no difference in survival between Ross and non-Ross operation groups (Table 2). Thirty-nine patients underwent 43 reoperations. Freedom from reoperation at 1 year, 5 years and 10 years after the operation was 97.0%, 77.8%, and 35.0%, respectively (Fig. 5). Age-stratified freedom from reoperation is plotted in Fig. 6, which also shows better outcome in patients who were older at repair. The mean interval between initial repair and reoperation was 5.6 ± 2.8 years. Univariate analysis for reoperation revealed that aortic homograft and small-sized conduit were associated with an increased risk of reoperation. By multivariate analysis, however, only the size of the homograft remained significant (Table 3). Freedom from reoperation stratified by the size of the homografts is plotted in Fig. 7, which shows that small sized conduit is associated with a higher risk of reoperation ($p=0.08$ by log rank test, $p=0.022$ by multivariate analysis). There was no difference in the risk of reoperation between Ross and non-Ross operation groups.

DISCUSSION

In the current practice of right ventricular outflow tract (RVOT) reconstruction for patients with various congenital heart diseases, strenuous efforts have been made to minimize the risk of conduit stenosis, valve regurgitation and right ventricular dysfunction, which may lead to improvements in freedom from reoperation on long-term follow-up. A number of biologic and prosthetic conduits, such as homografts, heterografts and synthetic conduits, have been developed to this end. Although homograft cardiac valves were introduced for clinical application in early 1960s, the use of homograft cardiac valves became popular again in 1980s, thanks to the development of cryopreservation technique. Dearani et al. [3] reported that surgical mortality after RVOT reconstruction using homograft decreased from 23.5% to 3.7% after 1980s, which, he claimed, could be attributed to the development of cryopreservation technique. Homograft cardiac valves are easy to handle and hemostatic, and various sizes are available. Given

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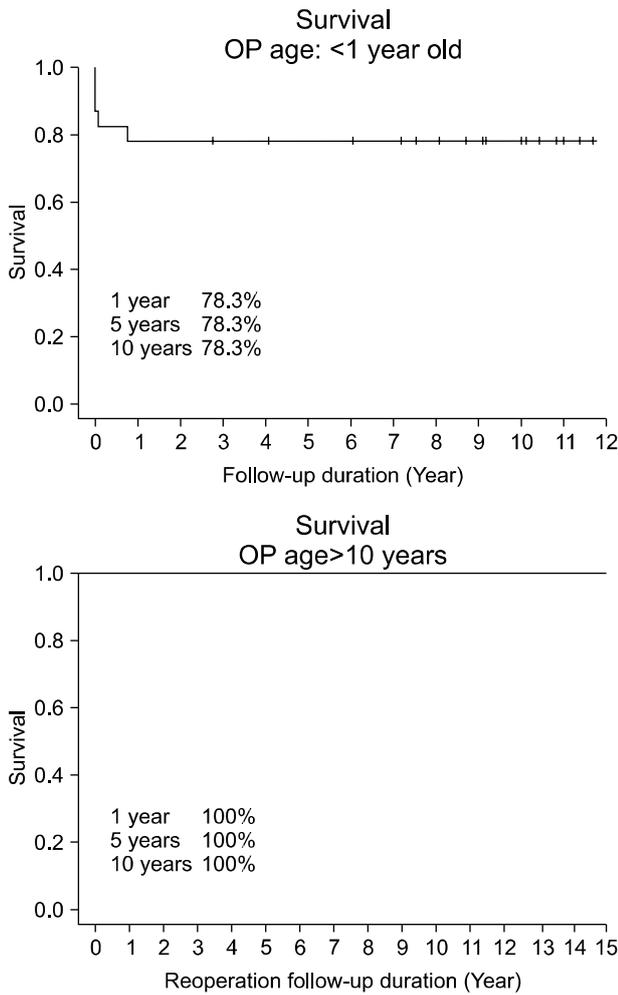


Fig. 4. Age stratified survival after the use of right ventricular outflow tract reconstruction using homograft conduits.

Table 2. Risk factors for mortality

Variables	Univariate p-value	Multivariate		
		p-value	HR	95% CI
Sex	0.271			
Body weight	0.004	0.0042	0.817	0.711, 0.938
OP age	0.040			
Truncus arteriosus	0.018			
Non-Ross OP	0.547			
CPB time	<0.001	<0.0001	1.009	1.005, 1.012
ACC time	0.091	0.0397	0.988	0.977, 0.999
Type of conduit	0.199			
Conduit size	0.167			

CPB=Cardiopulmonary bypass; ACC=Aortic cross clamp.

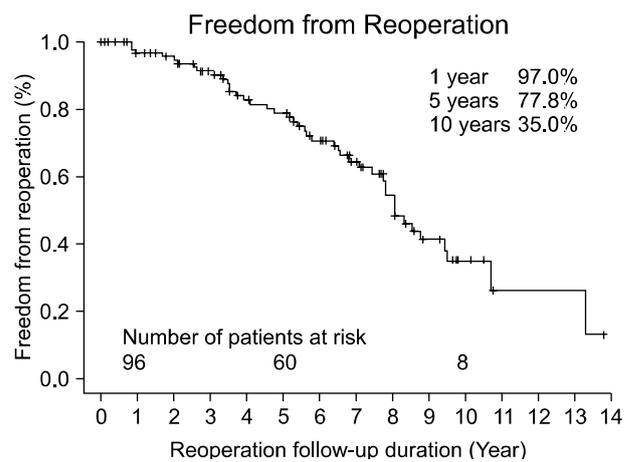


Fig. 5. Freedom from reoperation after the use of right ventricular outflow tract reconstruction using homograft conduits.

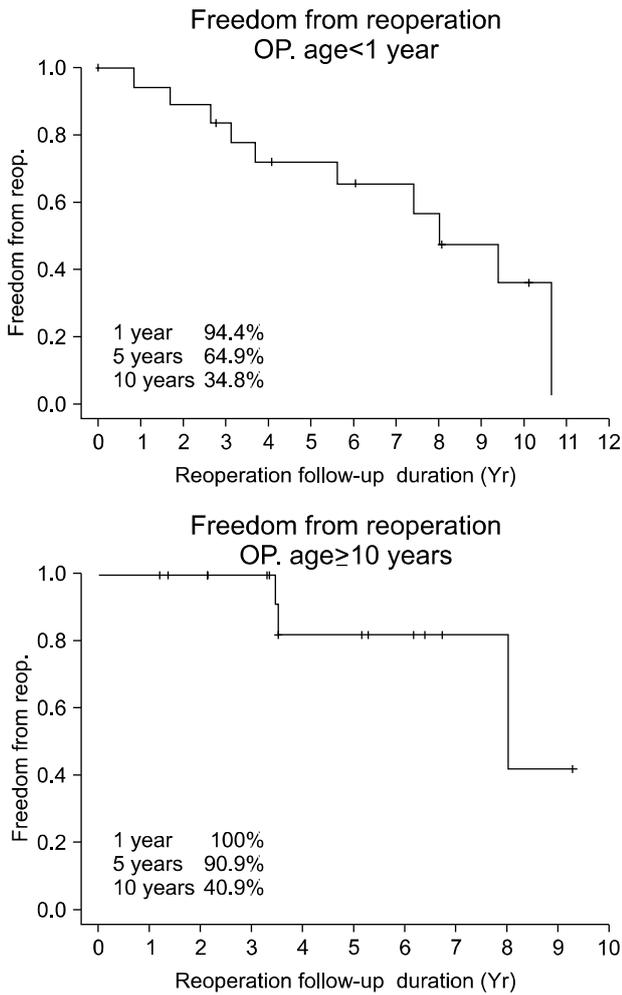


Fig. 6. Age-stratified freedom from reoperation after the use of right ventricular outflow tract reconstruction using homograft conduits.

Table 3. Risk factors for reoperation

Variables	Univariate	Multivariate		
	p-value	p-value	HR	95% CI
Sex	0.785			
Body weight	0.393			
OP age	0.447			
Truncus arteriosus	0.457			
Non-Ross OP	0.455			
CPB time	0.820			
ACC time	0.216			
Type of conduit	0.018			
Conduit size	0.022	0.022	0.913	0.845~0.987

CPB=Cardiopulmonary bypass; ACC=Aortic cross clamp.

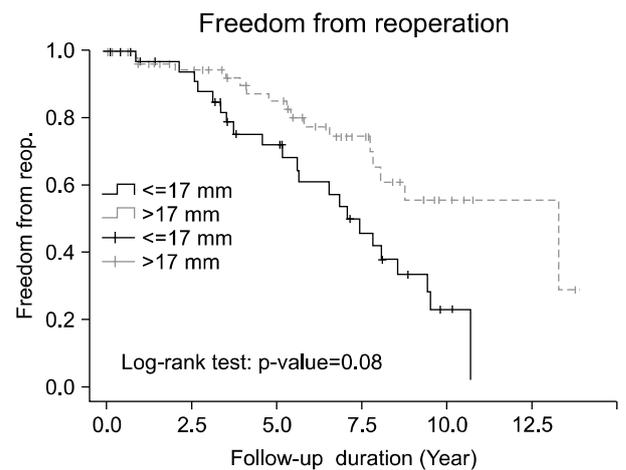


Fig. 7. Freedom from reoperation after the use of right ventricular outflow tract reconstruction using homograft conduits stratified by conduit size.

the fact that homografts lack growth potential, small-sized homograft conduits used for young patients may well fail very soon. Forbess et al. [1] stratified patients with RVOT reconstruction using homografts according to their age at operation (infants, 1~10 years, and older than 10 years), and freedom from conduit failure at postoperative 5 years was 25%, 61% and 81%, respectively. In his study, risk factors for homograft failure were identified as small homograft size, young age and the diagnosis of Truncus arteriosus. Brown et al. [4] also reported that freedom from reoperation after RVOT reconstruction using homografts at postoperative 5 and 15 years was 60% and 43%, respectively, even though survival at postoperative 15 years was up to 80%. Risk factors for graft failure in our study were identified as small body weight, the diagnosis of truncus arteriosus (which necessitate early Rastelli-type operation), small-sized graft and longer aortic cross-clamping time, which is comparable to previous reports. Even though small sized conduit tends to fail early, the availability of small sized conduit is one of the advantages of the use of homograft conduits. Lange et al. [5] claimed that there was no difference in conduit failure between homografts and bioprosthetic valved conduit when the size of the conduit was smaller than 15 mm, while the outcome of the latter was better than that of the former when the size of the conduit was larger than 15 mm. Our study also revealed that freedom from reoperation after RVOT reconstruction using homografts smaller than 17 mm at postoperative 5 and 10 years was 67.7% and 21.4%, respectively, while freedom from reoperation of the patients who had homografts larger than 17 mm at postoperative 5 and 10 years was 85.5% and 54.8%, respectively, which signifies that smaller size of the grafts was a risk factor for reoperation. Boething et al. [6] reported almost the same results when the patients were stratified according to the size (19 mm) and age (10 years), speculating that homograft failure may be related to graft degeneration. In this regard, alternative conduits, such as bovine jugular vein graft (Contegra[®], 12~22 mm) [7-9], No-React treated porcine pulmonary valved conduit (Shellhigh[®], 10~24 mm) [10], freestyle porcine aortic root (Medtronic[®], 19~29 mm) [11], have been developed to overcome the shortcomings of homograft conduits. These relatively new conduits are thought to be superior to homografts in terms of the superb availability of various sized conduits,

especially very small sized conduits for neonates and young infants. With respect to the intermediate-term outcome of these alternative bio-prosthetic materials, Shellhigh[®] has been reported to have a higher risk of graft stenosis by peel formation [12]. To the contrary, Brown et al. [7] asserted that freedom from reoperation after the use of Contegra[®] at postoperative 2, 5 and 7 years are 88.9%, 87.6% and 81.3%, respectively, which is comparable to the outcome of homograft conduits, and Fiore et al. [13] showed better outcome after the use of Contergra[®] compared to that of pulmonary homografts. Rastan et al. [14], however, pointed out that the risk of reoperation after this new conduit is as high as homografts in patients with risk factors, such as young age at operation, diagnosis of truncus arteriosus, small sized conduit (12 mm), high postoperative right ventricular pressure, which could be regarded as caveats for the use of Contegra[®].

Synthetic prosthetic conduits comprises valveless grafts for temporary use to facilitate the growth of the peripheral pulmonary artery, and valved conduits composed of Dacron or Polytetrafluoroethylene (PTFE) conduit and bioprosthetic or mechanical valves. Belli et al. [15] reported long term outcome of porcine-valve seated Dacron conduit (Hancock conduit), which showed freedom from reoperation at postoperative 1, 5 and 10 years was 98%, 81% and 32%, respectively. He insisted that this valved conduit is the most appropriate material for patients with pulmonary hypertension, but it seems hard to say that this material is superior to other valved conduits, given relatively low 10-year freedom from reoperation.

With respect to the materials to substitute for the function of the pulmonary valve, Brown et al. [16] supported the use of PTFE membrane due to its chemical inertness, which leads to lower risk of degeneration or calcification. Ando and Takahashi [17] reported that freedom from reoperation and freedom from significant pulmonary regurgitation at 10 years after three-leaflet formation using PTFE membrane were 88.0±6.8% and 75.0%, respectively. Despite this promising outcome in adults, Koh et al. [18] delineated that three-leaflet formation using PTFE membrane for children is associated with high prevalence of reoperation.

Durability is the most important aspect in selecting the types of conduits in the pulmonary position. In this regard, mechanical valve seated conduits are also a potential alter-

natives for selected subset. Haas et al reported excellent mid-term results in 14 patents with multiple RVOT reconstruction procedures, showing that mechanical valve function was normal in all patients while trans-valvar gradient was minimal [19]. He asserted that in a subset of patients, such as older patients with a history of multiple operations without contraindications for coumadinization, could be good candidates for receiving mechanical valve-seated conduits. Hörer et al. [20] also pointed out that this type of valved conduits have benefits of excellent hemodynamic profiles with slow development of valve regurgitation, and, thus, could be indicated for patients with multiple operations and arrhythmias.

CONCLUSION

The long-term outcome after the use of homograft in the pulmonary position was excellent, although freedom from reoperation sharply deteriorates as time passes. The high incidence of reoperation at 10 years may be attributed to the use of small-sized conduits. Therefore, efforts should be made to seek alternative small-sized conduit materials for young children, which could complement a number of benefits from medium or large-sized homograft conduits.

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