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ORIGINAL ARTICLE

CME

Mid-term results of bioprosthetic pulmonary valve replacement in pulmonary regurgitation after tetralogy of Fallot repair

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CONGENITAL

Abstract

OBJECTIVES: Pulmonary valve replacement (PVR) is performed to reduce right ventricular (RV) volume overload, resulting in improved ventricular function and clinical status. Significant pulmonary regurgitation (PR) after tetralogy of Fallot (TOF) repair could result in RV dysfunction, exercise intolerance, arrhythmia and sudden death. The present study was conducted to investigate the mid-term clinical outcomes of PVR after TOF repair.

METHODS: Between 2001 and 2010, we retrospectively reviewed the outcomes of 131 (89 males and 42 females) PVRs with PR or pulmonary steno-insufficiency after TOF repair. PVR was performed at a mean age of 14.8 ± 6.7 years. The mean interval from total correction of TOF to PVR was 12.5 ± 5.2 years. Surgical indications of PVR were more than moderate PR with/without pulmonary stenosis, right ventricle dilatation, right ventricle dysfunction and reduced exercise capacity. Hancock II ($n = 58$), Carpentier–Edwards Perimount ($n = 49$) and St Jude Biocor ($n = 35$) bioprosthetic valves were used. The mean z-score at implantation was 1.1 ± 0.8. The mean valve size implanted was 25.1 ± 1.5 mm.

RESULTS: There was no early or late mortality in this study. RV end-diastolic and end-systolic volume indices (from 111.3 ± 34.7 to 64.6 ± 23.6, $P < 0.01$) (preoperative $n = 70$, postoperative n = 17) were markedly decreased PVR during the 13.2 ± 16.1 months follow-up period. Eleven patients (male = 10, female = 1) required a repeat PVR operation due to prosthetic valve failure. The rate of freedom from reoperation at 10 years was 66.4 ± 4.4%. Implanted valve type (Carpentier–Edwards bovine valve), young age, and large-sized valve implantation (z-score > 2.0) were risk factors for a repeat PVR in the univariate analysis. There was no risk factor in the multivariable analysis.

CONCLUSIONS: PVR reduced the RV volume and improved the RV function within the first postoperative year. The rate of freedom from reoperation during the 10-year follow-up period in our series was acceptable. However, a longer follow-up will be necessary to determine the long-term outcomes of bioprosthetic valves in PVR.

Keywords: Pulmonary valve replacement • Bioprosthetic valve • Tetralogy of Fallot

INTRODUCTION

A total correction of tetralogy of Fallot (TOF) via a transannular incision is often required to relieve right ventricular (RV) outflow stenosis in patients whose annulus is too small. Such a repair may lead to progressive pulmonary regurgitation (PR) over long-term periods. There have also been some reports that PR after a TOF repair induces late sudden cardiac death and ventricular arrhythmias. In addition, RV dilatation, ventricular dysfunction and poor exercise intolerance may develop after TOF repair. Previously established risk factors for such complications include repair at an old age, previous use of a transannular patch and QRS duration >180 ms after TOF repair [1–4]. Thus, pulmonary valve replacement (PVR) has been performed to reduce RV volume overload, resulting in improved ventricular function and clinical status. Bioprosthetic PVRs are commonly used, although other valve types are also available. However, surgical results with a bioprosthetic PVR after TOF repair have not been well documented, and there is still some degree of controversy regarding the appropriate surgical timing as well as the overall efficacy of PVR [1, 4–6]. The duration of valve regurgitation, the degree of ventricular dilatation, type of valve implantation, patient age at operation and valve haemodynamics may affect both the long-term durability of the repair and the clinical outcome. Thus, the present study was conducted to investigate the mid- and long-term results of such repairs and to identify the risk factors and advantages of a bioprosthetic PVR in TOF repair patients.

MATERIALS AND METHODS

The study protocol was approved by the Institutional Review Board of the University of Seoul National University Hospital (No. H-1107-004-366). The procedures were in accordance with institutional guidelines for the protection of patient confidentiality. The requirement for patient consent was waived due to the retrospective nature of the study.

Between January 2001 and August 2011, we retrospectively reviewed the outcomes of 131 patients (89 males and 42 females) with PR or pulmonary steno-insufficiency after TOF total correction. There is still no consensus regarding the indications for PVR. Initially, at our institution, the surgical indications were greater than moderate PR with or without pulmonary stenosis and one of the following: (a) decreased RV function on echocardiography, (b) standardized RV end-diastolic volume index (RVEDVI) >170 ml/m^2 in cardiac magnetic resonance imaging (MRI) or (c) reduced exercise capacity. Patients who had pulmonary atresia with a ventricular septal defect, a double-outlet right ventricle, a TOF with a unilateral absent pulmonary artery as well as patients who had undergone valved conduit or homograft implantations were excluded. Prosthetic valve failure (PVF) after a PVR was defined as a peak pressure gradient ≥50 mmHg or at least a moderate amount of PR on the most recent echocardiography.

Statistical analysis

Categorical variables were expressed as frequencies and percentages. Continuous variables were expressed as the mean ± standard deviation. Comparisons between preoperative and postoperative continuous variables were performed using Student's *t*-tests. Matched preoperative and postoperative data were compared via paired *t*-tests.

Freedom from reoperation was analysed using life-table methods. We used the log-rank test to analyse the difference between the two groups using the life-table method. A logistic regression model was used to assess the multivariable risk factors. A *P*-value of <0.05 was considered statistically significant, and all analyses were performed using the SPSS statistical package (SPSS version 17.0, SPSS Inc., Chicago, IL, USA).

RESULTS

Patient profiles

PVR was performed for both dominant pulmonary insufficiency (*n* = 113, 86.3%) and steno-insufficiency (*n* = 18, 13.7%). There was no early or late mortality in this study. Fourteen postoperative complications occurred (Table 1). One patient had postoperative sinus node dysfunction with ventricular escape beats and non-sustained junctional ectopic tachycardia; thus, we implanted a permanent pacemaker during the outpatient follow-up period.

PVR was performed at a mean age of 14.8 ± 6.7 years (range: 2.2–40.0 years). The mean interval from total correction of TOF to PVR was 12.5 ± 5.2 years (range: 1.1–28.8 years). The mean follow-up duration was 4.2 ± 2.6 years (range: 0.03–9.65 years). The mean body weight at operation was 44.1 ± 16.9 kg (range: 12.2–89.7 kg). Before the total correction, a modified Blalock–Taussig shunt was created in 20 (20/131, 15.3%) patients as an initial palliative procedure, and transannular patch widening was performed in 84 (84/131, 64.1%) patients to relieve pulmonary stenosis during the total correction of TOF.

Table 1: Postoperative complications

Complications	*n*
Significant bleeding	5
Reintubation due to respiratory problems	2
Infective endocarditis	2
Wound dehiscence and infection	2
Pneumonia	1
Postoperative arrhythmia	1
Vocal cord palsy	1
Total	14

The valve types used in this population included the porcine Hancock II (Medtronic Heart Valve Division, Irvine, CA, USA, *n* = 58), Carpentier–Edwards Perimount (CE valve, Edwards Lifesciences, Irvine, CA, USA, *n* = 49) and St Jude Biocor (St Jude Medical, MN, USA, *n* = 35) bioprosthetic heart valves. The choice of valve materials was based on the preference of the surgeons. A repeat PVR was performed in 11 patients. The valve types found to have PVF resulting in repeat PVRs were the Carpentier–Edwards Perimount (*n* = 10) and the Hancock II (*n* = 1) bioprosthetic valves. Thus, the Hancock II (*n* = 6) and the St Jude Biocor (*n* = 5) valves were employed for repeat PVR operations.

The mean valve size implanted in the patients was 25.1 ± 1.5 mm (range: 21–27 mm). The implanted valve mean *z*-score was 1.1 ± 0.8 (range: 0.4–3.7). The valve sizes and types used for both PVR and repeat PVR are illustrated in Fig. 1.

The mean cardiopulmonary bypass time was 146.0 ± 49.9 min, and the mean time to hospital discharge was 11.0 ± 7.2 days.

Additional procedures

One hundred and eighty-nine additional procedures were performed in 104 patients (104/131, 79.4%) during PVR. Pulmonary artery angioplasty was the most common additional procedure and was performed in 63 patients (63/131, 48.1%), followed by right ventricular outflow tract patch widening in 37 patients (37/131, 28.2%) (Table 2).

Pathology of deteriorated valves

Tissue from the deteriorated valves of selected patients was immunohistochemically stained. We performed macrophage immunohistochemical staining for the detection of macrophage infiltration, Masson trichrome staining for the detection of fibrosis and von Kossa staining to identify calcium deposits.

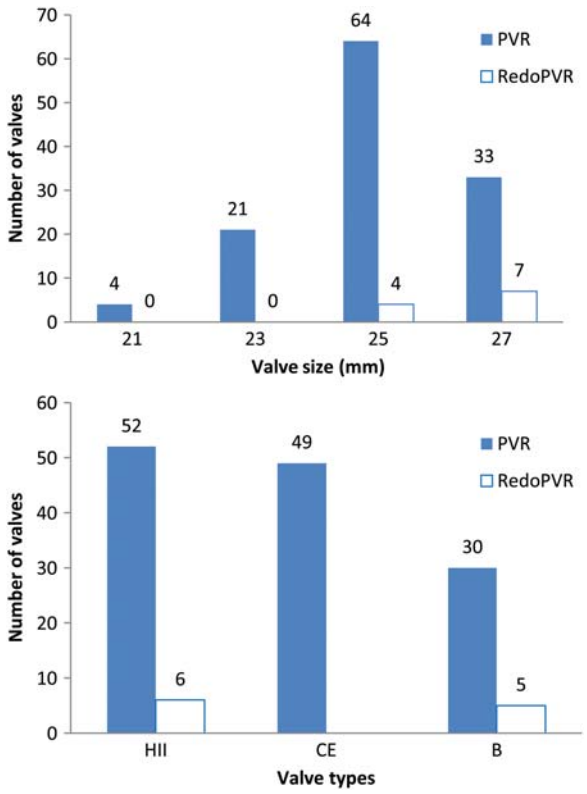

Figure 1: Implanted valve sizes and types in PVR. PVR: pulmonary vale replacement; HII: Hancock II porcine valve; CE: Carpentier–Edwards bovine valve; B: St Jude Biocor valve.

Table 2: Additional procedures

Procedures	Number
RVOT patch or angioplasty	100
TVP or TAP	28
Hypertrophied RV muscle resection	18
RVOT aneurysmectomy or plication	9
Residual VSD closure	8
Right side cryoablation	8
Ascending aorta reduction plasty	4
AVP or AVR	4
Permanent pacemaker insertion	2
Others	8
Total	189

RVOT: right ventricle outflow tract; TVP: tricuspid valvuloplasty; TAP: tricuspid annuloplasty; RV: right ventricle; VSD: ventricular septal defect; AVP: aortic valvuloplasty; AVR: aortic valve replacement.

Changes in haemodynamic parameters after pulmonary valve replacement

Postoperative parameters were compared by cardiac MRI. For the cohort as a whole, there was no significant interval change in RV ejection fraction (EF), but a significant volume reduction after PVR was observed (mean interval: 13.2 ± 16.1 months). RVEDVI and RV end-diastolic systolic volume index (RVESVI) were markedly decreased from 178.0 ± 37.8 to 100.7 ± 19.9 and 111.3 ± 34.7 to 64.6 ± 23.6, respectively, after PVR ($P < 0.01$). Matched preoperative and postoperative MRIs in 15 patients showed markedly reduced ventricular volumes from 170.9 ± 42.0 to 100.0 ± 20.4 and 112.6 ± 31.4 to 64.8 ± 24.5, respectively, following PVR ($P < 0.001$). Although there was no statistically significant difference, the overall EF after PVR showed an increase on matched MRI data (39.7 ± 6.2–42.8 ± 7.5%, $P = 0.23$).

We compared two groups: one with RVEDVI > 180 ml/body surface area (BSA) and RVESVI > 100 ml/BSA, and the other with figures below these to determine whether this volume index was predictive of recovery. The volume change in RVEDVI after operation was 96.4 ± 27.1 in the >180 ml/BSA group ($n = 8$) and 58.4 ± 20.1 in the <180 ml/BSA group ($n = 7$) ($P = 0.009$). The volume change in RVESVI after operation was 50.0 ± 34.2 in the >100 ml/BSA group ($n = 8$) and 28.7 ± 20.5 in the <100 ml/BSA group ($n = 7$) ($P = 0.176$). There was no difference in the EF between the two groups ($P = 0.49$).

On the preoperative electrocardiogram, 94.4% (117/124) of patients had a complete right bundle branch block (cRBBB), but there was no interval change in the incidence of cRBBB after PVR (91.9%, 114/124) during the 4.7 ± 2.5 year mean interval period ($P > 0.99$). There was also no interval change in the QRS duration (from 147.8 ± 30.3 to 149.0 ± 27.3, $n = 123$, $P = 0.74$) or the QTc interval (from 474.7 ± 38.2 to 469.8 ± 35.4, $n = 124$, $P = 0.29$) following PVR.

The preoperative mean cardiothoracic (CT) ratio ($n = 128$) was 56.7 ± 6.2, and the postoperative CT ratio was decreased to a mean of 53.4 ± 5.8 at 6 months postoperatively ($P < 0.001$). However, a further decrease in the CT ratio (53.0 ± 9.5) could not be found after 6 months over a mean follow-up period of 4.7 ± 0.3 years ($n = 115$, $P = 0.33$).

Exercise pulmonary function tests (PFTs) were also checked. The preoperative maximal oxygen consumption (MVO_2) was 31.1 ± 5.3 (range: 20.1–41.7, $n = 41$), and the minute ventilation/production of CO_2 (VE/VCO_2) slope was 30.4 ± 3.7 (range: 26–39, $n = 41$). The exercise MVO2 increased to 32.2 ± 5.5 (range: 20.1–45.0, $n = 89$) postoperatively, while the VE/VCO_2 slope decreased to 28.8 ± 3.2 (range: 22–39, $n = 89$) compared with preoperative exercise PFTs. The mean follow-up interval was 2.2 ± 1.0 years, and there was no significant interval change in MVO_2 or the VE/VCO_2 slope after matched patients ($n = 12$) ($P = 0.25$, $P = 0.90$, respectively). The changes in the haemodynamic parameters are illustrated in Table 3.

When the subgroup analysis was performed to assess transannular widening at the time of TOF total correction, the QRS duration was the only parameter that had increased in the transannular widening group compared with the non-transannular widening group ($P = 0.006$) (Table 4).

Among 131 patients, 11 (male = 10, female = 1) required a repeat PVR operation due to PVF. Indications for reoperation were pulmonary steno-insufficiency ($n = 9$) and prosthetic valve endocarditis ($n = 1$). The mean age at reoperation was 15.5 ± 3.0 years (range: 11.0–21.3). The mean interval from the initial PVR to the repeat PVR was 5.9 ± 2.5 years (range: 1.8–10.0 years). The mean peak pressure gradient across the pulmonary valve at preoperative echocardiography was 62.5 ± 13.4 mmHg (range: 48–88 mmHg). Valve sizes at the initial PVR and repeat PVR were 25.2 ± 1.40 mm (range: 23–27 mm) and 26.0 ± 1.1 mm (range: 25–27 mm), respectively.

During the long-term follow-up, rates of freedom from reoperation from total TOF correction to PVR at 5, 10 and 15 years during a mean follow-up period of 13.1 ± 5.1 years were 96.5 ±

Table 3: Changes in haemodynamic parameters

Parameters	Preoperation	*n*	Mean interval	Postoperation	*n*	*P*-value
MRI		70	13.2 ± 16.1 mo.		17	
PR (%)	40.2 ± 11.7			Trivial (<5%)		
RVEF (%)	39.8 ± 7.7			42.9 ± 7.2		0.15
RVEDV (ml/BSA)	178.0 ± 37.8			100.7 ± 19.9		<0.001
RVESV (ml/BSA)	111.3 ± 34.7			64.6 ± 23.6		<0.001
Matched MRI		15	13.6 ± 15.3 mo.		15	
RVEF (%)	39.7 ± 6.2			42.8 ± 7.5		0.23
RVEDV (ml/BSA)	170.9 ± 42.0			100.0 ± 20.4		<0.001
RVESV (ml/BSA)	112.6 ± 31.4			64.8 ± 24.5		<0.001
ECG		124	4.7 ± 2.5 yrs		124	
QRS duration (ms)	147.8 ± 30.3			149.0 ± 27.3		0.74
QTc (ms)	474.7 ± 38.2			469.8 ± 35.4		0.29
cRBBB	94.4% (117/124)			91.9% (114/124)		1.00
Chest X-ray		128	4.6 ± 0.3 yrs		128	
CT ratio	56.7 ± 8.6			53.4 ± 7.6		<0.001
Exercise PFT		41	2.2 ± 1.0 yrs		89	
MVO_2	31.1 ± 5.3			32.2 ± 5.5		0.25
VE/VCO_2 slope	30.4 ± 3.7			28.8 ± 3.2		0.90

PFT: pulmonary function test; MVO_2: maximal oxygen consumption; VE: minute ventilation; VCO_2: production of CO_2; PR: pulmonary regurgitation; RVEF: right ventricular ejection fraction; RVEDV: right ventricular end-diastolic volume; RVESV: right ventricular end-systolic volume; BSA: body surface area; CT ratio: cardiothoracic ratio; yrs: years; mo: months.

Table 4: Comparison of ventricular parameters according to transannular widening

	Transannular widening (–)		Transannular widening (+)		*P*-value
	n	Mean ± SD	*n*	Mean ± SD	
QRS duration (ms)	44	142.5 ± 25.5	79	155.0 ± 23.0	0.006
QTc duration (ms)	44	468.4 ± 35.5	79	478.3 ± 39.5	0.161
PVR age (years)	47	13.6 ± 5.8	83	15.5 ± 7.1	0.126
Preop PR (%)	22	40.2 ± 10.8	46	40.8 ± 12.6	0.838
Preop RVEF (%)	23	38.5 ± 7.6	47	40.5 ± 7.8	0.333
Pre RVEDV (ml/BSA)	23	187.3 ± 37.6	47	173.5 ± 37.5	0.151
Pre RVESV (ml/BSA)	23	116.6 ± 29.2	47	111.0 ± 33.7	0.496

PVR: pulmonary valve replacement; PR: pulmonary regurgitation; RVEF: right ventricular ejection fraction; RVEDV: right ventricular end-diastolic volume; RVESV: right ventricular end-systolic volume; BSA: body surface area.

1.7, 66.4 ± 4.4 and 21.2 ± 3.8%, respectively. When we performed the subgroup analysis, freedom from reoperation at 7 years varied with age at PVR, although the difference failed to reach statistical significance at a baseline of 15 years (<15 years group (76.4 ± 7.1%) vs 100% in the >15 years group) ($P = 0.165$). In the analysis of the freedom from reoperation rate according to the valve type at 7 years, the Hancock II valve showed 97.5 ± 2.5% durability, the Carpentier–Edwards valve showed 74.7 ± 7.4% durability and the Biocor valve showed 100 ± 0.0% durability. Although the difference was not statistically significant, the Carpentier–Edwards valve had a higher repeat PVR rate compared with the Hancock II and Biocor valves ($P = 0.324$, $P = 0.368$). Freedom from reoperation at 7 years according to *z*-score was 87.8 ± 5.9% for the *z*-score < 2.0 group and 52.1 ± 15.6% for the *z*-score > 2.0 group ($P = 0.005$) (Fig. 2).

The implanted valve type, duration of chronic regurgitation, young age and implantation of large valves (large *z*-score) were identified as the risk factors for repeat PVR in a univariate analysis. However, no risk factors for repeat PVR were identified in the multivariable analysis (Table 5).

Pathological findings in deteriorated valves

We performed a pathological staining of deteriorated valves in five patients. Macrophage infiltration, fibrotic tissue deposits and calcium deposits were observed in the deteriorated valves (Fig. 3).

DISCUSSION

This study was designed to establish the surgical results of PVR in TOF patients and to identify the benefits of PVR as well as the

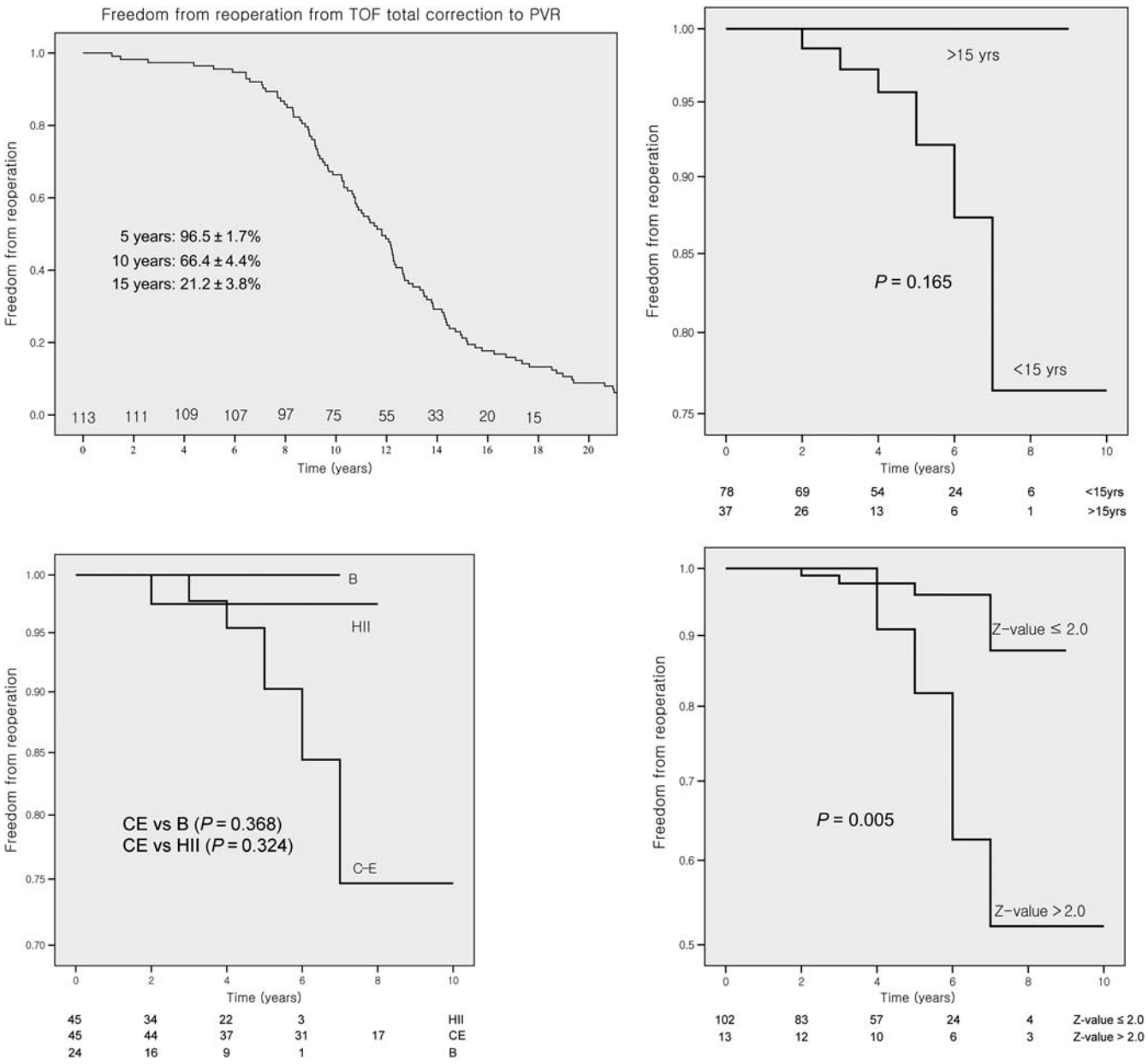

Figure 2: Fifteen-year freedom from reoperation from total TOF correction to PVR. Freedom from reoperation according to age, valve type and *z*-value. TOF: tetralogy of Fallot; PVR: pulmonary valve replacement; HII: Hancock II porcine valve: CE: Carpentier–Edwards bovine valve; B: St Jude Biocor valve.

risk factors for PVF in TOF patients. There is still a debate in the medical community regarding the optimal timing for PVR in TOF. Late ventricular arrhythmias have been identified as a major risk factor for sudden cardiac death after TOF repair, and PR, RV dilatation and RV dysfunction may induce such ventricular arrhythmias [2, 3, 7]. In this study, we demonstrated marked right-sided ventricular diastolic and systolic volume reduction on cardiac MRI within 1 year. Notably, we found that the CT ratio was markedly reduced within 6 months postoperatively. This observation suggests that PVR may decrease the chance of a sudden cardiac death and improve the haemodynamic parameters and clinical symptoms of TOF repair patients.

To compare the valve durability according to the valve material, the rate of freedom from reoperation was investigated. The bioprosthetic valve made from stented bovine pericardium was observed to have an early PVF, although the rate of such a failure did not reach statistical significance in our population. Kwak *et al.* [8] reported that the Hancock II porcine valve is superior to the Carpentier–Edwards bovine valve in terms of the rate of freedom from reoperation; however, Carpentier–Edwards bovine valves have shown more favourable freedom from reoperation rates in other reports [9, 10]. Thus, the question of which valve has the greatest long-term durability is still controversial. In our population, the age at valve implantation, implantation of large valves [10] and turbulent flow due to an angulated valve or leaflet distortion could be considered as confounding factors. Thus, long-term follow-up was needed.

MVO_2 and the relationship of VE/VCO_2 slope were measured as parameters of exercise intolerance, which is known to be

Table 5: Risk factors for repeat PVR

Variable	Univariate analysis			Multivariable analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Sex						
Male						
Female	0.208	0.025–1.704	0.109	0.143	0.013–1.537	0.108
RVOT widening	0.575	0.157–2.104	0.399	0.678	0.137–3.359	0.634
Valve type						
HII	Reference					
CE	11.077	1.345–91.251	0.007*	5.892	0.611–56.790	0.125
B	0.980	0.941–1.020	0.463	0		0.998
z-value	11.78	2.864–48.439	<0.001*	4.779	0.620–36.813	0.133
PreEDV	0.448	0.337–0.596	0.272			
PreESV	0.439	0.327–0.588	0.263			
PVR Age			0.019			
0	Reference		Reference	Reference		
1	0.420	0.110–1.604	0.195	1.225	0.175–8.570	0.838
2	0.800	0.658–0.973	0.003*	0.000		0.997

HR: hazard ratio; CI: confidence interval; RVOT: right ventricle outflow tract; HII: Hancock II porcine valve; CE: Carpentier–Edwards bovine valve; B: St Jude Biocor valve; EDV: end-diastolic volume; ESV: end-systolic volume; PVR: pulmonary valve replacement. *$P < 0.05$.

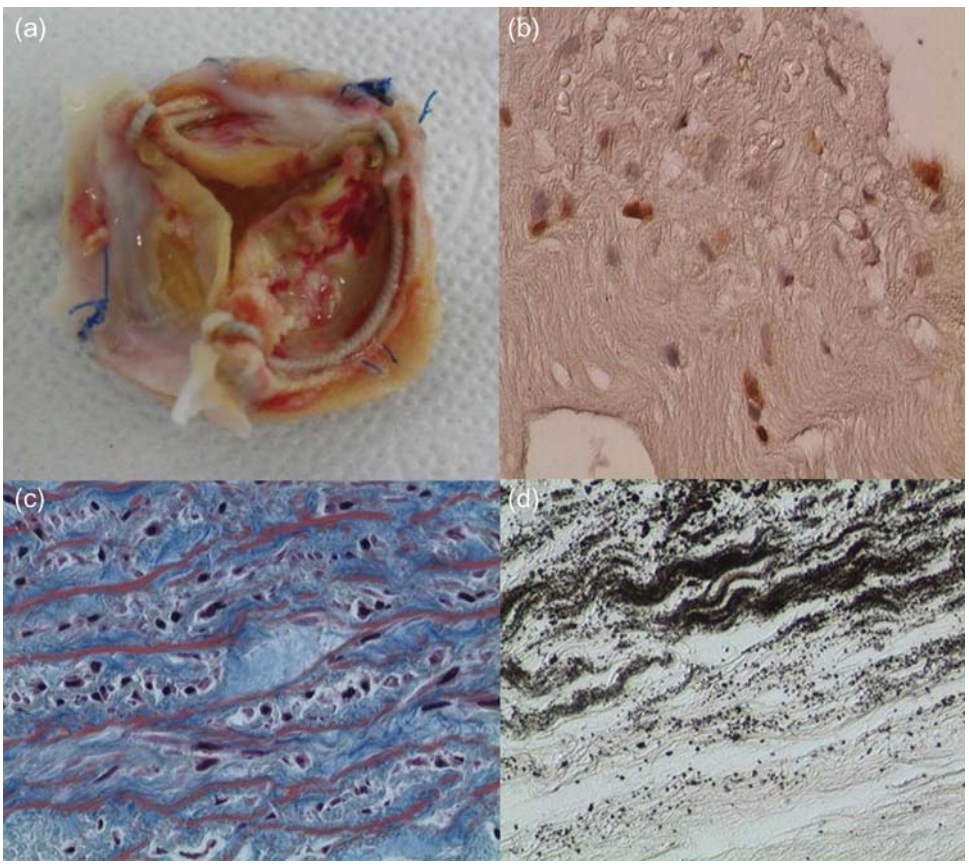

Figure 3: Pulmonary valve deterioration (a). Gross morphology of deterioration (b). Macrophage immunohistochemical staining (c). Masson trichrome staining for fibrosis (d). von Kossa staining for calcium deposit.

strongly correlated with survival rates and quality of life in heart failure patients [11, 12]. There was no improvement in exercise PFTs overall, although the VE/VCO_2 slope decreased following PVR in our study. However, we speculated that the preoperative exercise pulmonary function did not accurately reflect the patient's decreased exercise capacity within the normal range of values of preoperative exercise PFTs. Interestingly, although the QRS duration did not show an interval change over our follow-

up period, the QTC duration was found to decrease. The results of the present study correspond well with those of an earlier study that reported that QRS prolongation is associated with inducible ventricular tachycardia after a TOF repair [13]. Several studies have also described associations between hypertrophy and prolonged repolarization [14–16]. The reversibility of the prolongation of repolarization during the regression of hypertrophy implies a reduction of ventricle muscle hypertrophy, which can also be expected to reduce the risk of arrhythmias. Lim *et al.* [17] reported that early replacement of the pulmonary valve after PVR had multiple clinical benefits, including symptomatic improvement. In addition, Harrild *et al.* [18] found that late PVR for symptomatic PR and RV dilatation did not reduce the incidence of ventricular tachycardia or death. Thus, decisions regarding the appropriate timing of operation must be made carefully. Our results correspond well with previous studies, as we have found that late PVR does not produce clinical improvement nor reduce the incidence of ventricular arrhythmias.

A young age at valve replacement is associated with a higher risk of PVF [19–21]. The current hypothesis for young age as a risk factor is based on the fixed size of the implant during a period of rapid somatic growth, active calcium metabolism and increased immune response [22, 23]. The pathology of deteriorated bioprosthetic valves has recently become a target of study. In the present report, we identified macrophage infiltration, calcium deposits and fibrosis in deteriorated valves despite our limited sample size. We also identified that young age at valve replacement decreases the durability of the valves. Further examination of the differences between young and old age groups will be necessary in future studies.

Karamlou *et al.* [24] reported that an oversized homograft implant does not reduce the rate of pulmonary valve failure, which is compatible with our findings. We speculated that the implantation of large valves may interfere with the laminar flow, thus leading to accelerated valve failure due to a turbulent flow.

We investigated several parameters related to transannular widening during TOF surgery. Only the QRS duration was prolonged in the transannular widening group compared with the non-transannular widening group. However, RV volume measurements on cardiac MRI did not match between the preoperative and postoperative patients; thus, it is difficult to conclude that the transannular widening procedure does not only affect the RV volume index change and the degree of PR.

CONCLUSIONS

PVR reduced the RV volume and improved the RV function within the first postoperative year. Thus, the decision to initiate surgery within the reversibility period is important. The rate of freedom from reoperation during the 10-year follow-up period in our series was acceptable. However, a longer follow-up will be necessary to determine the long-term outcomes of bioprosthetic valves in PVR.

Limitations of the study

This study is limited by its retrospective review and short mean follow-up duration. Moreover, the number of preoperative and postoperative matched parameters on cardiac MRI and exercise PFT was too small. Transannular resection may increase PR and RV dysfunction. However, the small number of matched cardiac MRI parameters made it difficult to determine the risk factors between the non-transannular and transannular groups.

Upon pathological examination, deteriorated valves showed calcification, valve thickening, fibrosis and macrophage infiltration. We suspect that calcification, valve thickening and the degree of macrophage infiltration were severe in the younger age group. However, we were unable to compare the differences between the two age groups. Further studies will be required to elucidate the pathophysiology of valve deterioration in the younger population.

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