O R I G I N A L
A R T I C L E

Pulmonary valve replacement after surgical repair of tetralogy of Fallot

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Objective To evaluate the results of pulmonary valve replacement in patients with severe pulmonary regurgitation after tetralogy of Fallot repair in Hong Kong.

Design Retrospective review.

Setting University teaching hospital, Hong Kong.

Patients Consecutive patients undergoing pulmonary valve replacement after repair of tetralogy of Fallot between August 2002 and December 2008.

Main outcome measures Magnetic resonance imaging of right ventricular volume and cardiopulmonary exercise test data before and after the operation were documented and compared.

Results Over a 6-year period, 16 patients underwent pulmonary valve replacement for severe pulmonary regurgitation after prior complete repair for tetralogy of Fallot. There was no in-hospital mortality. The mean time interval between the initial repair and pulmonary valve replacement was 19 (standard deviation, 9) years. In three patients, the indication for pulmonary valve replacement was symptomatic severe pulmonary regurgitation, and asymptomatic progressive right ventricular dilatation in the remaining 13 patients. After pulmonary valve replacement, there was a significant decrease in the mean indexed right ventricular end-diastolic volume from 173 (standard deviation, 44) mL/m^2 to 103 (19) mL/m^2 (P=0.043). After the operation, there was also a tendency for improvement of the right ventricular ejection fraction and the maximum oxygen consumption: from 42% (standard deviation, 9%) to 47% (6%) [P=0.173], and 27 (4) mL/kg/min to 29 (4) mL/kg/min (P=0.208), respectively.

Conclusion Pulmonary valve replacement for severe pulmonary regurgitation after tetralogy of Fallot repair is a safe procedure. However, the indications for such an operation in asymptomatic patients remain controversial. Further studies are required to better delineate the timing of pulmonary valve replacement in this patient group.

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Introduction

With the advances in surgical techniques and peri-operative care, complete repair of tetralogy of Fallot (TOF) is being performed earlier, and in younger age-groups,[1-3] with a view to early elimination of hypoxaemia and thus promotion of normal growth and organ development.[2] The early mortality of TOF repair in patients beyond infancy is low[4] and many survive to adulthood. Many of them, however, present later in life with increasing exercise intolerance and progressive right ventricular dilatation, dysfunction, or failure.[5] It has been suggested that chronic pulmonary regurgitation (PR) after complete repair of TOF together with myocardial scarring contributes to such deteriorating right ventricular performance,[6] many of whom eventually undergo pulmonary valve replacement (PVR), although the timing of such an intervention is still debated. For these patients, benefit from PVR may also extend to improved exercise capacity and right ventricular function.[7,8]

In our centre, the first PVR for severe PR after TOF repair was performed in 2002. With improving survival after complete TOF repair, more patients present with its functional sequelae—severe PR, right ventricular dilatation and dysfunction. In this study, we review the results of PVR in these patients and assess the impact of the operation on functional outcomes.

Methods

All records of consecutive patients undergoing PVR between August 2002 and December 2008 for severe PR after prior TOF repair were reviewed.

Clinical evaluation

All patients had their TOF repair in our centre and were followed up regularly by our paediatric cardiologists for symptom assessment, annual chest X-ray (CXR), electrocardiogram (ECG), and interval echocardiogram. Each patient's functional status, cardiothoracic ratio, and occurrence of arrhythmias were documented in their medical records. Those detected to have severe PR were offered further investigations, including exercise cardiopulmonary tests and magnetic resonance imaging (MRI). Patients were considered for PVR if they were symptomatic (New York Heart Association class >II), defined as having decreased exercise tolerance or heart failure. Asymptomatic patients were offered PVR if they were considered to be at high risk of sudden death,[9] as gauged by right ventricular enlargement or dysfunction, arrhythmias or prolonged QRS duration (>180 ms).

Postoperative out-patient follow-up of the patients entailed documentation of functional status, serial CXR, ECG, and echocardiographic assessment. Cardiopulmonary exercise testing and MRI were performed at a mean of 1 and 2 years, respectively, after discharge from hospital following PVR.

Pulmonary valve replacement

The pericardial cavity was re-entered via the previous median sternotomy incision. Cardiopulmonary bypass was established and cardioplegic arrest of the heart was used according to the surgeon's preference. An incision was made into the right ventricular outflow tract (RVOT), the native pulmonary valve was resected and valvular replacement performed with a bioprosthesis or homograft. After meticulous haemostasis, the wound was closed and the patient sent to the cardiac surgery intensive care unit for postoperative monitoring and further management.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (Windows version 13.0; SPSS Inc, Chicago [IL], US). Data were expressed as means (standard deviations [SDs]). The χ^2 test or the Fisher's exact test were used for comparison of categorical variables. Student's t test or Wilcoxon's signed rank tests were used as appropriate for comparison of parametric and non-parametric variables, respectively. Any P value of less than 0.05 was considered statistically significant.

法洛氏四聯症根治術後主肺動脈心瓣替換的臨床分析

目的 回顧法洛氏四聯症根治術後主肺動脈心瓣替換術的臨床資料。

設計 回顧研究。

安排 香港一所大學教學醫院。

患者 2002年8月至2008年12月期間，曾接受法洛氏四聯症根治術及現在須接受主肺動脈心瓣替換的病人。

主要結果測量 分析及比較病人術前和術後用磁共振成像測量右心室容積及心肺運動的數據。

結果 在6年內曾接受法洛氏四聯症根治術並現在接受主肺動脈心瓣替換術的病人共16位。研究期間沒有因手術而死亡的病例。病人接受法洛氏四聯症根治術後須要接受主肺動脈心瓣替換術的時間平均為19年（標準差：9年）。在接受手術的病人當中，3位出現嚴重主肺動脈心瓣倒流的徵兆，另13位沒有出現病徵但有嚴重主肺動脈心瓣倒流的病人均有右心室發大的症狀。在接受主肺動脈心瓣替換術後的右心室舒張末容積指數平均值（標準差）由173（44）mL/m²下降至103（19）mL/m²（P=0.043）。主肺動脈心瓣替換術後，病人的右心室射血分數的平均值（標準差）由42%（9%）增至47%（6%）〔P=0.173〕，而最大氧氣攝取量由27（4）mL/kg/min增至29（4）mL/kg/min（P=0.208）。

結論 在法洛氏四聯症根治術後進行主肺動脈心瓣替換術是安全及可行的。對於無病徵但有嚴重主肺動脈心瓣倒流的病人而言，此項手術的成效及進行手術的最佳時機仍有待確定。

Results

Between August 2002 and December 2008, 16 patients (10 males) underwent PVR after prior complete repair of TOF. Their mean age when they underwent TOF repair was 6 (SD, 5) years, and 24 (SD, 13) years when they underwent PVR. The mean time interval between the initial TOF repair and the subsequent PVR was 19 (SD, 9) years. All patients had severe PR before PVR. Eleven patients had had transannular patch repair of the RVOT at the initial repair of TOF. Three patients had decreased exercise tolerance and progressively worsening shortness of breath on exertion. The remaining 13 patients were asymptomatic and underwent surgery for right ventricular dilatation. The mean preoperative QRS interval was 150 (SD, 36) ms; in three of them it exceeded 180 ms. The mean postoperative QRS interval was 146 (SD, 26) ms (P=0.51). Eleven patients received valve replacement with bioprosthesis and five with homografts. There was no in-hospital mortality. All patients were discharged from the intensive care unit after 1 day. The median duration of hospital stay was 8 (range,

TABLE 1. Preoperative and postoperative cardiovascular parameters of the patients*

Data	Mean±standard deviation		
	Pre-PVR	Post-PVR	P value
Indexed RVEDV (mL/m²)	173±44	103±19	0.043
Indexed RVESV (mL/m²)	102±26	54±11	0.043
RVEF (%)	42±9	47±6	0.173
Indexed LVEDV (mL/m²)	67±13	76±7	0.180
Indexed LVESV (mL/m²)	30±8	32±1	0.180
VO₂ max (mL/kg/min)	27±4	29±4	0.208

* PVR denotes pulmonary valve replacement, RVEDV right ventricular end-diastolic volume, RVESV right ventricular end-systolic volume, RVEF right ventricular ejection fraction, LVEDV left ventricular end-diastolic volume, LVESV left ventricular end-systolic volume, and VO₂ max maximum oxygen consumption

TABLE 2. Surgical mortality of pulmonary valve replacement reported by diverse groups[7,14,15]

Reference	Year	No. of patients	Surgical mortality
Yemets et al,[14] Hospital for Sick Children, Toronto, Canada	1997	85	1.1%
Discigil et al,[15] Mayo Clinic, US	2001	42	2%
Dave et al,[7] University Children's Hospital, Zurich, Switzerland	2005	39	0%
Present study, Queen Mary Hospital, Hong Kong	2010	16	0%

TABLE 3. Suggested indications for pulmonary valve replacement (PVR)[9,16]

Study	Indications for PVR*

Frigiola et al[16]	1. Presence of significant PR (PR fraction ≥35% on MRI) with evidence of progressive RV dilatation and dysfunction
	  i. RV/LV end-diastolic ratio ≥1.5 in symptomatic patients
	  ii. RV/LV end-diastolic ratio ≥ 2 in asymptomatic patients
	2. Reduced exercise capacity with or without documented arrhythmias

Geva[9]	1. Moderate or severe PR (PR fraction ≥25% on MRI) and two or more of the following criteria:
	  i. RV end-diastolic volume index ≥160 mL/m² (Z score >5)
	  ii. RV end-systolic volume index ≥70 mL/m²
	  iii. LV end-diastolic volume index ≥65 mL/m²
	  iv. RV ejection fraction ≤45%
	  v. RV outflow tract aneurysm
	  vi. Clinical criteria: exercise intolerance, symptoms and signs of heart failure, cardiac medications, syncope, sustained ventricular tachycardia
	2. Presence of other haemodynamically significant lesions
	3. Patients who underwent TOF repair at age ≥3 years, PVR may be indicated sooner and in the presence of less severe RV dilatation and dysfunction due to higher risk of adverse clinical outcomes

* PR denotes pulmonary regurgitation, MRI magnetic resonance imaging, RV right ventricular, LV left ventricular, and TOF tetralogy of Fallot

6-34) days. The mean cardiothoracic ratio on CXR before PVR was 0.61 (SD, 0.08; range, 0.50-0.78) and the post-PVR mean cardiothoracic ratio was 0.56 (SD, 0.06; range, 0.50-0.67) [P=0.005]. Preoperative and postoperative MRI data are shown in Table 1. There were significant decreases in the mean indexed right ventricular end-diastolic and end-systolic volumes.

Discussion

In this review of PVR at our centre, there was a significant reduction in the indexed right ventricular end-diastolic volume and also a tendency for improvement of cardiopulmonary exercise tolerance.

With the advances in surgical techniques and peri-operative care, early mortality of complete TOF repair beyond infancy has become very low.[10] Thus, increasing numbers survive to adulthood and present with adverse functional sequelae from their operation, namely severe PR. Pulmonary regurgitation can be tolerated for years, due to compensatory mechanisms in the right ventricle. However, studies have shown that chronic PR correlates with decreased exercise performance[11,12] and right ventricular dysfunction.[5,13] Owing to the low surgical mortality of PVR (Table 2[7,14,15]), currently most symptomatic patients are offered PVR. For asymptomatic patients, early intervention has also been suggested as a means of reducing right ventricular volume overload.[9] Table 3 lists the suggested criteria for PVR in different centres.[9,16] As per these criteria, our centre offers PVR to anyone who is symptomatic due to severe PR, as well as asymptomatic individuals at high risk of sudden death. The latter include: patients with right ventricular enlargement or dysfunction, arrhythmias or a prolonged QRS duration (>180 ms). A significant reduction in the mean indexed right ventricular end-diastolic and end-systolic volumes can be achieved with this PVR protocol. However, in our study there was only a marginal improvement in exercise capacity in terms of the change in maximum oxygen consumption. Studies have shown that early restoration of pulmonary valve competence can result in restoration of the right ventricular function[7,8] and exercise capacity,[17] but the exact timing of such intervention remains controversial. It has been suggested that right ventricular volumes were not reversible in patients with preoperative right ventricular end-diastolic volumes exceeding 170 mL/m² or end-systolic volumes of more than 85 mL/m².[18] Other studies have suggested potential of normalisation of right ventricular volume if PVR is performed, with the right ventricular end-diastolic volume index becoming less than 150 mL/m².[7]

The traditional method for restoration of pulmonary valve competence is by surgical PVR, using a mechanical or bioprosthetic valve, jugular vein valved conduit or homograft. Pulmonary homografts have the advantage of providing low transvalvular gradients, and good long-term outcomes without the need for anticoagulation.[19,20] In many centres, however, their cost and availability may deter their use. A mechanical prosthesis has the advantages of a low re-operation rate,[21] but the need for long-term anticoagulation and potential thrombo-embolic

complications and risk of bleeding are drawbacks. The majority of our patients had bioprosthetic PVRs. These valves are readily available and require only short-term anticoagulation.

Recently, in selected patients, percutaneous pulmonary valve implantation (PPVI) has been introduced as an alternative to open PVR.[22,23] Khambadkone and Bonhoeffer[22] claim that its efficacy is likely to be comparable to surgery, but entails a lower morbidity and mortality. However, the longevity of such a device is not yet proven.[24] Hopefully, this method can prolong the life of the RVOT conduit and reduce the number of repeated open-heart interventions in the future. With the currently available technology, another drawback of PPVI is that it can only be used for patients with certain types of RVOT morphology, such as in those with right ventricle to pulmonary artery conduits in situ. Moreover, accurate pre-implantation assessment of the RVOT anatomy is essential for its success.[25,26] Aneurysmal RVOTs that often ensue after transannular patch repair for complete repair of TOF also pose problems for the percutaneous approach.[8,24] Complications of PPVI are well documented and include: dislodgement of the stent graft, stent fracture, rupture of the RVOT conduit, and occlusion of adjacent structures (coronary and pulmonary arteries) by the stent graft.[8,27,28]

The main limitations of the present study were its retrospective design, and the small patient sample. Larger study populations might enable demonstration of statistically significant post-PVR improvements in cardiopulmonary exercise capacity and right ventricular ejection fraction.

Pulmonary valve replacement for severe PR after prior complete repair of TOF was a safe procedure; there being no in-hospital mortality or morbidity in our patient cohort. Our results concur with those reported in the literature and confirm restoration of right ventricular volume after PVR for severe PR following prior complete repair of TOF. In our patients, however, only a marginal improvement in maximum oxygen consumption was demonstrated. We believe that patient selection and the timing of referral for surgical intervention is of paramount importance. The optimal timing for this operation remains controversial. Further studies are required to better delineate when PVR should be performed in this patient group. Although PPVI is an attractive option, surgical PVR is still the gold standard, whilst further studies to evaluate the long-term results of this new technique are awaited.

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