

Managing the right ventricular outflow tract for pulmonary regurgitation after tetralogy of Fallot repair

Michael Hauser, Andreas Eicken, Andreas Kuehn, John Hess, Sohrab Fratz, Peter Ewert, Harald Kaemmerer

Department of Pediatric Cardiology and Congenital heart Disease, Deutsches Herzzentrum München, Technische Universität München, Munich, Germany

Correspondence to

Dr Michael Hauser, Department of Pediatric Cardiology and Congenital heart Disease, Deutsches Herzzentrum München, Technische Universität München, Franz-Schrank Strasse 2, Munich 80638, Germany; hauser_kinderkardiologe@yahoo.de

MH, AE and HK contributed equally to this work

Received 16 April 2013
Revised 27 May 2013
Accepted 2 June 2013

ABSTRACT

The long-term outcome of patients with tetralogy of Fallot (TOF) with reconstruction of the right ventricular (RV) outflow tract is often complicated by the sequelae of severe pulmonary regurgitation. Progressive enlargement of the right ventricle, biventricular dysfunction and arrhythmia are apparent in more than 50% of the patients in the fourth decade of life. Pathophysiologic implications, clinical assessment and diagnostic modalities are discussed, whereas CMR imaging seems to be the procedure of choice. Therapeutical options for reconstruction of the RV outflow tract are mentioned, surgical and interventional procedures are explained in detail. The optimal timing of reoperation for significant pulmonary regurgitation after TOF repair is still a matter of controversy given the limited runtime of the lately implanted prostheses and the risk of further reoperation. Early surgery is recommended in these patients before symptoms develop, or RV function has declined. Today we believe that waiting for the patient to become symptomatic is too late. All in all, pulmonary valve replacement is at least indicated in patients developing symptoms due to severe pulmonary regurgitation, particularly if associated with substantial or progressive RV dilatation, tricuspid regurgitation and/or supraventricular or ventricular arrhythmias.

INTRODUCTION

The long-term survival and overall outcome after surgical repair of tetralogy of Fallot (TOF) is favourable.¹ Nevertheless, in many cases, significant residua and sequelae persist or develop, as discussed in detail by Kaemmerer and coworkers.² Pulmonary regurgitation (PR) is one of the most common complications. In the past, PR was regarded as a benign lesion, as many patients tolerate PR well for a considerable time. However, PR can also result in progressive right ventricular (RV) enlargement, RV fibrosis and biventricular dysfunction, and finally, in the fourth decade of life only less than 50% of all patients are free of cardiac symptoms.¹

Mechano-electrical interactions due to PR and RV volume overload with progressive enlargement and stretching of the right atrium and RV may be causal for arrhythmias.

Arrhythmias are reported in up to 35% of TOF patients, and cardiac death in 6% during a follow-up period of 30 years.³ In some studies, moderate or severe PR was the main haemodynamic abnormality in patients with ventricular

tachycardia (VT) and sudden death after TOF repair.³ In order to avoid these—to some extent disastrous sequelae—surgical or interventional pulmonary valve replacement (PVR) is thought of.

PVR may diminish RV size, ameliorate RV function and improve exercise performance, provided that operation is performed in time; if, however, surgery for PR is performed late no significant improvement in RV size and function can be expected.²

However, even today, quantification of PR is difficult, and it is also challenging to decide which group of patients will benefit from PVR. For these reasons, indication and timing for PVR are still controversial issues.

EPIDEMIOLOGIC DATA

The number of patients developing significant PR after TOF repair is undetermined. Long-term follow-up studies up to 20 years after TOF repair give evidence that the number of affected patients is between 1% and 12%, and will increase with a longer follow-up interval.²

PATHOPHYSIOLOGIC IMPLICATIONS

PR is often the consequence of a transannular RV outflow tract patch, that disrupts the integrity of the pulmonary annulus and the PV.⁴ The use of a rigid transannular patch, associated with an increase of PR, will consecutively cause and/or aggravate RV volume overload and RV dilatation, reduction of ejection fraction and finally RV failure.

Thus, in the long term, PR may amplify the RV damage during TOF repair caused by ventriculotomy, by a scar in the RV outflow tract, by a ventricular septum patch, and by myocardial scars from the surrender of small coronary arteries. Moreover, RV function may have been compromised from preoperative cyanosis, pressure overload from early shunt operations prior to repair, and/or deficient myocardial protection.² Because of the drawbacks from transannular patching, today many cardiac surgeons prefer a valve-sparing operation.

Notably, the degree of PR can be augmented by a pulmonary artery stenosis, or by an increased pulmonary artery pressure. The latter originates most often from pulmonary vascular disease, from a longstanding aorto-pulmonary shunt prior to repair, from a residual ventricular septal defect, from left heart failure, or from lung disease.²

To cite: Hauser M, Eicken A, Kuehn A, et al. *Heart Asia* Published Online First: [please include Day Month Year] doi:10.1136/heartasia-2013-010319

Moreover, RV dilation as well as dilation of the tricuspid valve annulus can induce progression of tricuspid regurgitation (TR) and further RV volume overload.

There are similarities in the pathophysiological response of a volume-loaded left ventricle (LV) and RV.

In chronic aortic regurgitation, after a variable period of time during which LV dilatation is potentially reversible, the volume-loaded LV will develop irreversible ventricular dilatation with myocardial scarring, fibrosis and increased interstitial collagen; in these patients, myocardial dysfunction persists even after aortic valve replacement.⁵

In a volume-loaded RV, however, significant differences exist concerning chamber geometry, myofibre architecture, myocardial contraction pattern, coronary perfusion and the conduction system.

The degree of pulmonary regurgitation after TOF repair is dependent on the regurgitation orifice area, the compliance of the right ventricle and the duration of diastole.

CLINICAL ASSESSMENT

Patient history

Patients with preserved systolic RV function are free of symptoms for years or even decades. However, it has to be kept in mind, that patients with congenital heart anomalies often adapt themselves and underestimate their disability.

If PR deteriorates to a significant degree, the compensatory mechanisms of the RV fail, the RV afterload increases, and the ejection fraction of the RV declines.⁶ At that stage, patients usually present with diminished exercise tolerance, fatigue, dyspnoea on exertion and sometimes with palpitations due to supraventricular or ventricular arrhythmias.

An impaired clinical status in long-term survivors after TOF repair is not only associated with the degree of PR. Also, a low left ventricular ejection fraction is a strong, independent factor associated with impaired clinical status, perhaps by means of ventricular–ventricular interaction, where one ventricle influences the other adversely.⁷

Physical examination

Physical examination reveals a jugular venous pulse that is normal without right heart failure, or mild to moderate systemic venous pressure elevation with a prominent 'a' wave. In TR, the jugular venous pressure may be elevated, showing a large 'v' wave.

A parasternal lift from the right ventricle is palpable in almost all patients, while the left ventricular apical impulse is usually absent due to a posterior displacement.

At the left upper sternal border, a prominent main pulmonary artery impulse may be present.

On auscultation, some adults have an early systolic pulmonary ejection sound, and a fourth heart sound. The aortic component of the second heart sound is loud, because of the anterior position of the aorta, while the pulmonary component of the widely and fixed split second heart sound is usually diminished in PR.

There is usually a spindle-shaped systolic murmur in the pulmonary area, indicating some degree of RV outflow tract obstruction or pulmonary valve or pulmonary artery stenosis.

An isodynamic, holosystolic murmur of TR, increasing its intensity after inspiration, may occur at the left lower parasternal border.

Pathognomonic for PR is a diastolic decrescendo murmur at the left upper parasternal border. The murmur starts immediately after the (diminished) pulmonary component of the

second heart sound, and is medium to low pitched. The duration of the murmur is variable, depending on the degree of PR. With mild PR it is usually short, with moderate degree nearly holodiastolic, and, again shorter with severe PR. As PR is associated with a low pulmonary artery pressure, the intensity of the murmur is usually low.

A third heart sound, as well as hepatosplenomegaly, a pulsatile liver, ascites, or peripheral oedema occur with right heart failure.

ECG

A right bundle branch block pattern almost always follows TOF repair, even if no ventriculotomy has been performed. There are only few exceptions to this rule.

QRS duration may increase over years, often associated with increased RV size. The RV volume and mass are positively correlated with the duration of the QRS complex.

Particularly, a progressive QRS duration >180 ms may be a warning sign of ventricular arrhythmias and sudden death.⁸ QRS duration >180 ms has a 100% sensitivity for sustained VT and sudden death, while a QRS duration <180 ms has a negative predictive value of 100% for these events.⁸

The change in QRS duration over time (mean 3.5 ms/year) is an additional predictor of increased risk of sudden death.⁹

The clinical relevance of these data for the individual, however, should be interpreted with caution. Some even believe that QRS prolongation is rather a marker of RV dysfunction but not for sudden death.

QT dispersion or heart rate turbulence as an expression of an impaired cardiac autonomic nervous activity may be adjuvant methods of risk assessment.⁹

The ECG may also show right atrial enlargement (P-dextroatriale), right axis deviation and RV hypertrophy.

Atrial or ventricular arrhythmias may be present and need to be further evaluated in detail.

Chest x-ray

The cardiothoracic ratio (CTR) largely depends on the RV volume load. Depending on the amount of RV dilatation due to significant PR, the CTR is usually increased to more than 0.55.

Echocardiography

Transthoracic echocardiographic (TTE) and Doppler assessment of the RV, pulmonary artery and PR is the first-line imaging modality in the follow-up of TOF patients. Additionally, residual RV outflow obstruction, pulmonary artery stenosis, residual shunts and TR can be evaluated.

Because of the complex RV geometry, the transthoracic echocardiographic evaluation of RV volumes, function and mass has several limitations, and surrogate markers, such as fractional area shortening, tricuspid annular plane systolic excursion and tissue Doppler velocities, have to be applied.¹⁰

Three-dimensional TTE will elude some limitations in the volumetric assessment of the RV at some point. Current echocardiographic techniques to assess RV volume are highly feasible and reproducible in postoperative Fallot patients. When compared with CMR measurements, three-dimensional reconstruction of the right ventricle is the most accurate technique.¹¹

In patients with moderate to severe pulmonary regurgitation, colour flow depicts a flow-reversed blood flow from the right or left pulmonary artery to the RV body in diastole (figure 1A). However, Doppler assessment may easily overestimate pulmonary regurgitation.

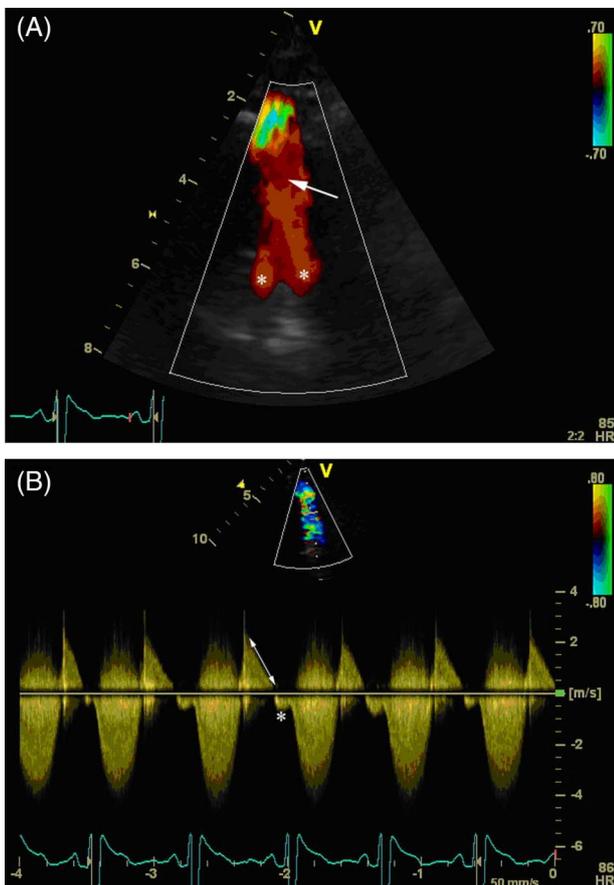


Figure 1 (A) Colour Doppler flow map showing broad diastolic back flow (red coded) in the main (arrow) and in the proximal part of the left and right pulmonary artery (asterisks) as usually seen in higher grade pulmonary regurgitation. (B) Doppler trace of a patient after tetralogy of Fallot repair showing moderate residual outflow tract obstruction with a peak jet velocity of 3.8 m/s and a rapid flow deceleration during diastole as a sign of severe pulmonary regurgitation (arrow). Antegrade diastolic flow in the pulmonary artery after the p-wave indicates restrictive right ventricular physiology (asterisk).

As the end-diastolic, RV pressure is often only a few mm Hg lower than the diastolic pulmonary artery pressure, and it can be difficult to reliably grade the severity of the PR. In adults, pulmonary pressure half-time <100 ms has been proposed as a good indicator of haemodynamically significant PR.¹²

Some postoperative patients have a restrictive RV function that is consistent with a lesser degree of pulmonary regurgitation. This type of diastolic dysfunction is marked by an antegrade diastolic flow in the pulmonary artery (figure 1B), and also a flow reversal in the superior vena cava during atrial systole. The tricuspid E-wave deceleration time is short.

Even if a restrictive RV haemodynamic is adverse in the early postoperative period, it has emerged as advantageous in the long term, and may preclude RV dilatation in spite of significant PR.¹³

Exercise test

It is well known that PR after tetralogy repair may cause, beside malignant ventricular arrhythmia and sudden death, reduced exercise performance.⁸

Exercise studies with determination of maximum oxygen consumption (VO_{2max}) and anaerobic threshold are helpful to assign symptomatology, objectively graduate exercise capacity,

and to unmask exercise limitations secondary to PR. Exercise parameters are also important for an appropriate decision making on timely replacement of the pulmonary valve.

MRI, CT and nuclear cardiology

Cardiac Magnetic Resonance (CMR) is an ideal tool for serial assessment of RV volumes and systolic function in the longitudinal follow-up after TOF repair, providing not only important anatomic details of both ventricles, pulmonary arteries and the aorta with good accuracy and reproducibility, but also functional data about right and left ventricular size, function and muscle mass, ventricular-ventricular interaction, as well as flow and regurgitant volumes¹⁴ (figure 2). CMR is regarded as the gold standard for the evaluation of RV size and function, as well as for the quantitative assessment of PR. Hereby, the deficiency of older studies, lacking of reproducible data regarding the severity of PR and RV size and function have been overcome. Age-related and gender-related reference values for RV volumes and systolic function have been published.¹⁵

Furthermore the amount of blood flow to each lung in patients with right or left pulmonary stenosis can be quantified reliably by CMR.¹⁶

A recent CMR study could determine that RV dilatation and systolic RV dysfunction or LV dysfunction were independent predictors of major adverse clinical outcomes at a median of 21 years after TOF repair. High-risk CMR parameters in this study included a preoperative RV end-diastolic volume Z score of 7 (corresponding to 172 cc/m² in women, and 185 cc/m² in men), or a global systolic dysfunction (ejection fraction <45%).¹⁷

Modern CT provides excellent imaging, in patients with pacemakers, or other contraindications for CMR however without haemodynamic information.

Because of the overwhelming developments of CMR, nuclear cardiology studies have become largely obsolete for longitudinal follow-up studies after TOF repair.

Cardiac catheterisation

The main purpose of cardiac catheterisation in patients with PR is to determine ventricular physiology, RV or pulmonary artery obstruction, or residual shunts. It is particularly indicated if the haemodynamic status is not clarified by non-invasive procedures or in the planning of a transcatheter intervention.

THERAPEUTICAL OPTIONS

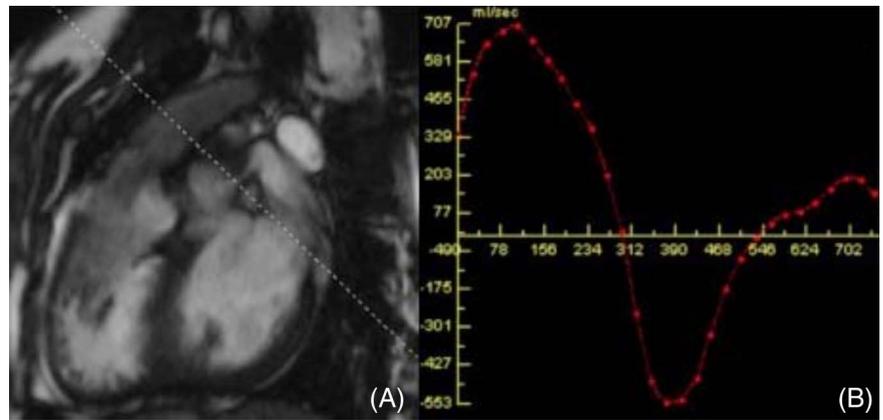
There are no data to show that medical treatment is able to slow the progression of PR. Currently, no sufficient reliable data are available regarding the influence of selective pulmonary vasodilators on the outcome of patients with PR after TOF repair.

PVR is at present the only option to reduce RV size and to improve RV function in the long term.

Surgical or interventional replacement of the regurgitant PV can stop PR, and may even reverse the progression of complications developed from PR, including RV dysfunction and TR. It remains controversial, however, whether ventricular arrhythmias can be remediated.¹⁸ Notably, in a large cohort of patients, late PVR alone for symptomatic PR and RV dilation did not reduce the incidence of ventricular arrhythmias and sudden death.¹⁸

Therefore, at the time of PVR, patients with known arrhythmias should be considered for intraoperative ablative treatment.

Figure 2 Diastolic still frame of a patient with corrected Fallot's tetralogy (A). The dotted line depicts the slice where forward and backward flow were measured by phase-contrast magnetic resonance (B).



Surgical replacement of pulmonary valve

Surgical PVR can either be performed as biological valve (preserved homografts or porcine bioprosthesis), or as a mechanical valve.

In experienced centres, the surgical risk of reoperation after TOF repair is low and the long-term outcome favourable.¹ However, the morbidity of repeated cardiothoracic operations is significant, and these operations become technically more demanding with every consecutive procedure due to adhesions and progressive scarring.

Long-term survival rates after TOF reoperation with PVR were 95% after 5 years, and 76% after 10 years. Freedom from pulmonary valve re-replacement was 70% after 10 years.¹⁹ In another recent series, the survival probability of PVR was 92% at 5 years, and 86% at 10 years.¹⁸

Even so, the risk of irreversible RV dysfunction must be weighted against the surgical risk and emerging complications. Moreover, the durability of a biological or mechanical pulmonary valve prosthesis is not perfect. Bioprosthetic valves will degenerate in due course, while mechanical prostheses have other disadvantages, including thrombosis, and requirement of lifelong anticoagulation.²⁰

Many, but not all patients benefit from PVR. Functional class and exercise tolerance, ventricular volumes and biventricular function improve by eliminating the chronic volume overload from PR.¹⁹

However, conflicting data also exist. After PVR, a step-up of a preliminary reduced RV ejection fraction could not be verified in all series, even if PVR could reduce RV volumes.²¹

Interventional replacement of PV-percutaneous pulmonary valve implantation (PPVI)

Percutaneous pulmonary valve implantation (PPVI) was introduced by Bohnoeffler *et al*²² in 2000 aiming to reduce the number of reoperations in patients with complex congenital heart disease, who needed a valved biological conduit.

The currently available Melody valve consists of a 34 mm bare metal Cheatham Platinum stent, into which a contegra bovine jugular venous valve has been sewn (figure 3).

The Edwards Sapien transcatheter valve is made of three bovine pericardial leaflets sewn inside a stainless steel stent (figure 3).

Meanwhile, PPVI has emerged to be the preferred treatment for selected patients with conduit dysfunction in the pulmonary position at some centres. PPVI is feasible at a relatively low risk, and mid-term follow-up shows a sustained haemodynamic improvement.²³

The intervention is relatively safe with only two published periprocedural deaths—both due to coronary arterial compression. The gradient in the right ventricular outflow tract (RVOT) was reduced significantly, pulmonary regurgitation was abolished and the reintervention rate in the recent series was low.²³

If valvular function deteriorates, the valve-in-valve concept proved to be feasible.

Initially, PPVI was only suggested if a biological conduit was present in the RVOT, and the patient's body weight was at least 25 kg. However, in selected patients, PPVI is possible also in patients with a 'native' RVOT, and was possible even in pre-school children with body weight below 20 kg.²³ In conclusion, PPVI is feasible, safe, with good and sustained haemodynamic results at mid-term follow-up. Yet, long-term results are missing after this intervention.

INDICATIONS FOR PULMONARY VALVE REPLACEMENT

In prevailing stenosis (RV systolic pressure >60 mm Hg, TR velocity >3.5 m/s) selecting patients for therapy is relatively straightforward.

The treatment indication in patients with predominant pulmonary regurgitation, or a combination of stenosis and regurgitation, is not as simple. In fact, most patients with RV outflow tract dysfunction show a combination of obstruction and regurgitation.²³

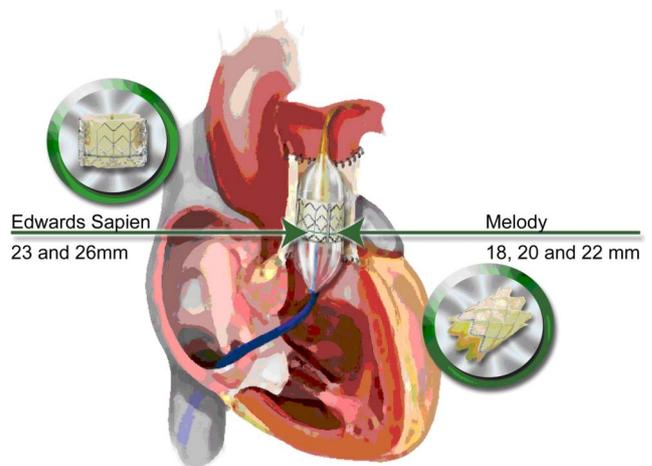


Figure 3 The Melody valve is delivered over the superstiff guidewire on an 18, 20, or 22 mm double balloon into the right ventricular outflow tract. The Sapien valve is available in two sizes (external diameter 23 and 26 mm, respectively).

Table 1 Recommendations regarding pulmonary valve replacement in adults with previous tetralogy of Fallot according to the current American, Canadian and European guidelines

ACC/AHA guidelines (2008) ²⁷	PVR is indicated for severe pulmonary regurgitation and symptoms or decreased exercise tolerance. PVR is reasonable in adults with previous tetralogy of Fallot, severe pulmonary regurgitation, and any of the following: Moderate to severe RV dysfunction. Moderate to severe RV enlargement. Development of symptomatic or sustained atrial and/or ventricular arrhythmias. Moderate to severe TR.
Canadian guidelines (2009) ²⁸	The following situations may warrant intervention following repair: Free pulmonary regurgitation associated with progressive or moderate to severe RV enlargement (RV end-diastolic volume of greater than 170 mL/m ²), moderate to severe RV dysfunction, important TR, atrial or ventricular arrhythmias, or symptoms such as deteriorating exercise performance.
European guidelines (2010) ²⁹	PVRep should be performed in symptomatic patients with severe PR and/or stenosis (RV systolic pressure >60 mm Hg, TR velocity >3.5 m/s) PVRep should be considered in asymptomatic patients with severe PR and/or PS when at least one of the following criteria is present: Decrease in objective exercise capacity Progressive RV dilation Progressive RV systolic dysfunction Progressive TR (at least moderate) RVOTO with RV systolic pressure >80 mm Hg (TR velocity >4.3 m/s) Sustained atrial/ventricular arrhythmias

PVR, pulmonary valve replacement; RV, right ventricular; RVOTO, right ventricular outflow tract obstruction; TR, tricuspid regurgitation.

The optimal timing of reoperation for significant PR after TOF repair is a matter of controversy given the limited runtime of the lately implanted prostheses and the risk of a further reoperation.

Currently, more and more experts recommend early surgery in these patients before symptoms develop, or RV function has declined.²⁴ Today we believe that waiting for the patient to become symptomatic is too late. By contrast, some believe that PVR should be performed only if RV dysfunction is existent.

Unfortunately, currently no randomised controlled studies are available to help in the decision for timing therapy in presence of significant pulmonary regurgitation.

A CMR-study in adults with repaired TOF revealed after PVR, a significant decrease in RV volumes, while the RV systolic function remained unchanged. However, in patients with a RV end-diastolic volume >170 mL/m² or a RV end-systolic volume >85 mL/m² before PVR, the RV volumes did not return to normal after PVR.²⁵

However, in a study including younger patients with TOF and pulmonary regurgitation RV remodelling after PVR could be shown at even higher right ventricular enddiastolic (RVED) volume indices.²⁴

A threshold beyond which RV function is unlikely to decrease to normal after surgery is difficult to specify at all. However, there seems to be an age and volume index-dependent potential of the volume-loaded right ventricle to remodel after adequate therapy for severe pulmonary regurgitation. Normalisation of RV volumes has been described when PVR was performed before the end-diastolic RV volume reached 160 mL/m² or the end-systolic RV volume reached 82 mL/m².²⁵

Frigola *et al* studied 71 consecutive patients (mean age 22 years, 72% TOF) before and 1 year after PVR by CMR.²⁶ They concluded that treating patients with an end-diastolic volume <150 mL/m² leads to normalisation of RV volumes, improvement in biventricular function, and submaximal exercise capability. Normalisation of the ventilatory response to carbon dioxide production was most likely to occur when surgery was performed at an age <=17.5 years.

To date, it is indefinite, whether a full normalisation of RV volumes is required for improving the outcome on a long-term course.

Altogether, even if the RV volume is very high and RV dysfunction exists, PVR can reduce RV size substantially, and improve RV function, even if these parameters may not decrease to the normal range. Apparently, regarding reverse remodelling, no threshold is present above which RV volumes do not decrease after PVR.

In the last few years, several international guidelines have been published focusing on the management of adults with TOF comprising certain discrepancies (table 1).^{27–29}

The recommendations of our institution are listed in table 2.

CONCLUSION

All in all, PVR is at least indicated in patients developing symptoms due to severe pulmonary regurgitation, particularly if associated with substantial or progressive RV dilatation, TR, and/or supraventricular or ventricular arrhythmias.

Finally, the long-term outcome of patients treated according to the current guidelines has to be evaluated.

Table 2 Contemporary inclusion criteria for pulmonary valve replacement as used at the German Heart Centre Munich

German Heart Centre Munich (2011)	<ul style="list-style-type: none"> ▶ Increased RV pressure (>2/3 systemic pressure, echo peak gradient >80 mm Hg) ▶ Pulmonary regurgitation leading to a CMR-RVED-volume index >150 mL/m², reduced and declining RV function in cardiac MRI ▶ A combination of stenosis and regurgitation with RV dysfunction and dilatation ▶ Symptomatic (?) patients with declining exercise tolerance (<65% of normal) ▶ No clear lower age limit, looping of stiff delivery system is limited in small patients ▶ Conduits or RV outflow tracts which can accommodate a covered stent to be dilated to at least 18 mm
-----------------------------------	---

RV, right ventricle; RVED, right ventricular enddiastolic.

Contributors MH, AE, AK, JH, SF, PE and HK had substantial contribution to conception, acquisition and interpretation of the data. MH, AE, AK, JH, SF, PE and HK had substantial contribution in preparation of the manuscript. MH, AE, AK, JH, SF, PE and HK gave final approval to the version to be published. MH, AE, AK, JH, SF, PE and HK take public responsibility for appropriate parts of the content of the manuscript.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- Hickey EJ, Veldtman G, Bradley TJ, *et al.* Late risk of outcomes for adults with repaired tetralogy of Fallot from an inception cohort spanning four decades. *Eur J Cardiothorac Surg* 2009;35:156–64.
- Kaemmerer H, Eicken A, Hess J. Managing the right ventricular outflow tract for pulmonary regurgitation after TOF. In: Chessa M, Gamberti A, eds. *The right ventricle in adults with tetralogy of Fallot*. Springer, 2012:113–24.
- Gatzoulis MA, Balaji S, Webber SA, *et al.* Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. *Lancet* 2000;356:975–81.
- Cheung MM, Konstantinov IE, Redington AN. Late complications of repair of tetralogy of Fallot and indications for pulmonary valve replacement. *Semin Thorac Cardiovasc Surg* 2005;17:155–9.
- Borer JS, Truter S, Herrold EM, *et al.* Myocardial fibrosis in chronic aortic regurgitation: molecular and cellular responses to volume overload. *Circulation* 2002;105:1837–42.
- Geva T. Indications and timing of pulmonary valve replacement after tetralogy of Fallot repair. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu* 2006:11–22.
- Tobler D, Crean AM, Redington AN, *et al.* The left heart after pulmonary valve replacement in adults late after tetralogy of Fallot repair. *International journal of cardiology*. *Int J Cardiol* 2012;160:165–70.
- Gatzoulis MA, Till JA, Somerville J, *et al.* Mechano-electrical interaction in tetralogy of Fallot. QRS prolongation relates to right ventricular size and predicts malignant ventricular arrhythmias and sudden death. *Circulation* 1995;92:231–7.
- Steeds RP, Oakley D. Predicting late sudden death from ventricular arrhythmia in adults following surgical repair of tetralogy of Fallot. *QJM* 2004;97:7–13.
- Lang RM, Bierig M, Devereux RB, *et al.* Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440–63.
- Dragulescu A, Grosse-Wortmann L, Fackoury C, *et al.* Echocardiographic assessment of right ventricular volumes: a comparison of different techniques in children after surgical repair of tetralogy of Fallot. *Eur Heart J Cardiovasc Imaging* 2012;13:596–604.
- Silversides CK, Veldtman GR, Crossin J, *et al.* Pressure half-time predicts hemodynamically significant pulmonary regurgitation in adult patients with repaired tetralogy of fallot. *J Am Soc Echocardiogr* 2003;16:1057–62.
- Lu JC, Cotts TB, Agarwal PP, *et al.* Relation of right ventricular dilation, age of repair, and restrictive right ventricular physiology with patient-reported quality of life in adolescents and adults with repaired tetralogy of fallot. *Am J Cardiol* 2010;106:1798–802.
- Kilner PJ, Geva T, Kaemmerer H, *et al.* Recommendations for cardiovascular magnetic resonance in adults with congenital heart disease from the respective working groups of the European Society of Cardiology. *Eur Heart J* 2010;31:794–805.
- Maceira AM, Prasad SK, Khan M, *et al.* Reference right ventricular systolic and diastolic function normalized to age, gender and body surface area from steady-state free precession cardiovascular magnetic resonance. *Eur Heart J* 2006;27:2879–88.
- Fratz S, Hess J, Schwaiger M, *et al.* More accurate quantification of pulmonary blood flow by magnetic resonance imaging than by lung perfusion scintigraphy in patients with fontan circulation. *Circulation* 2002;106:1510–13.
- Knauth AL, Gauvreau K, Powell AJ, *et al.* Ventricular size and function assessed by cardiac MRI predict major adverse clinical outcomes late after tetralogy of Fallot repair. *Heart* 2008;94:211–16.
- Therrien J, Siu SC, Harris L, *et al.* Impact of pulmonary valve replacement on arrhythmia propensity late after repair of tetralogy of Fallot. *Circulation* 2001;103:2489–94.
- Discigil B, Dearani JA, Puga FJ, *et al.* Late pulmonary valve replacement after repair of tetralogy of Fallot. *J Thorac Cardiovasc Surg* 2001;121:344–51.
- Pibarot P, Dumesnil JG. Prosthetic heart valves: selection of the optimal prosthesis and long-term management. *Circulation* 2009;119:1034–48.
- Vliegen HW, van Straten A, de Roos A, *et al.* Magnetic resonance imaging to assess the hemodynamic effects of pulmonary valve replacement in adults late after repair of tetralogy of fallot. *Circulation* 2002;106:1703–7.
- Bonhoeffer P, Boudjemline Y, Saliba Z, *et al.* Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. *Lancet* 2000;356:1403–5.
- Eicken A, Ewert P, Hager A, *et al.* Percutaneous pulmonary valve implantation: two-centre experience with more than 100 patients. *Eur Heart J* 2011;32:1260–5.
- Buechel ER, Dave HH, Kellenberger CJ, *et al.* Remodelling of the right ventricle after early pulmonary valve replacement in children with repaired tetralogy of Fallot: assessment by cardiovascular magnetic resonance. *Eur Heart J* 2005;26:2721–7.
- Therrien J, Provost Y, Merchant N, *et al.* Optimal timing for pulmonary valve replacement in adults after tetralogy of Fallot repair. *Am J Cardiol* 2005;95:779–82.
- Frigiola A, Tsang V, Bull C, *et al.* Biventricular response after pulmonary valve replacement for right ventricular outflow tract dysfunction: is age a predictor of outcome? *Circulation* 2008;118:182–90.
- Warnes CA, Williams RG, Bashore TM, *et al.* ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to develop guidelines on the management of adults with congenital heart disease). *Circulation* 2008;118:714–833.
- Silversides CK, Kiess M, Beauchesne L, *et al.* Canadian Cardiovascular Society 2009 Consensus Conference on the management of adults with congenital heart disease: outflow tract obstruction, coarctation of the aorta, tetralogy of Fallot, Ebstein anomaly and Marfan's syndrome. *Can J Cardiol* 2010;26:80–97.
- Baumgartner H, Bonhoeffer P, De Groot NM, *et al.* ESC Guidelines for the management of grown-up congenital heart disease. *Eur Heart J* 2010;31:2915–57.