The right ventricle in tetralogy of Fallot

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Summary

Surgical repair of tetralogy of Fallot (TOF) may be followed by various conditions and residual findings, early postoperatively or late during follow-up. Most of these conditions affect the right ventricular outflow tract and the pulmonary arteries and thus, indirectly, the right ventricle.

This paper discusses the role of the right ventricle during the natural history of repaired TOF. The different imaging methods used to assess the function of the right ventricle in relation to this congenital heart disease are highlighted. Particular attention is focused on the volume overloaded right ventricle, as this condition is nowadays a subject of intense discussion, particularly regarding the appropriate timing for pulmonary valve replacement. The most recent literature on this topic is briefly reviewed. In summary, preservation of right ventricular function and prevention of right ventricular arrhythmias are crucial for these patients' survival and outcome.

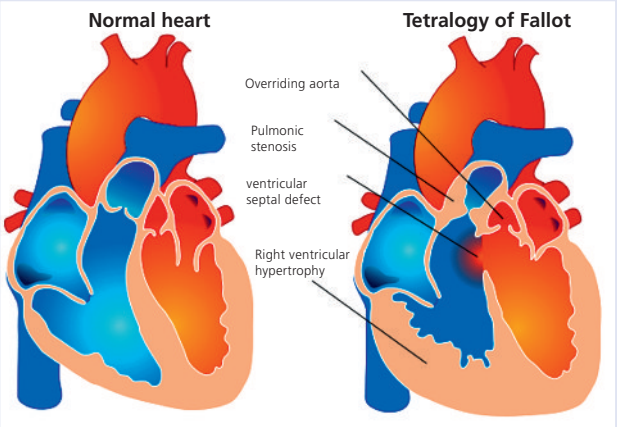
Key words: right ventricle; tetralogy of Fallot; pulmonary regurgitation

Introduction

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease, occurring in 0.04–0.08% of all liveborns [1, 2]. The main feature of TOF is a ventricular septum defect with anterior deviation of the outlet septum, leading to infundibular subpulmonary stenosis and placing the aorta in an overriding position; in addition, valvular pulmonary stenosis with possible hypoplasia of the main pulmonary artery and its side branches occurs, together with hypertrophy of the right ventricle (RV) (fig. 1).

Besides closing the ventricular septal defect, surgical repair consists of reconstruction of the right ventricular outflow tract (RVOT). RVOT reconstruction can be performed by various surgical techniques, some resulting in residual RVOT obstruction (commissurotomy) and others completely relieving the obstruction at the price of causing pulmonary regurgitation (transannular patch). Thus the surgical technique used usually determines the postoperative findings and eventually the patients' long-term outcome. However, the surgical technique providing the best outcome for the patients has not yet been defined, and the type of repair is chiefly determined by the personal strategy of the operating surgeon in each individual centre.

Figure 1
Anatomical features of tetralogy of Fallot.



Surgical repair can be performed during the first months of life, ideally at the age of 3 to 4 months, with low perioperative mortality. Long-term mortality was studied by Nollert et al., who reported a 20-year survival rate of 94% [3]. Nevertheless, the survival curve seems to deteriorate after 25 years post TOF repair [3], and significant residual findings may occur resulting in significant morbidity during follow-up. Similarly, Oechslin et al. reported a cumulative percentage of reinterventions required in TOF patients [4]. The most common indications for reintervention consisted of lesions affecting the (RVOT 75%), including severe pulmonary regurgitation, conduit failure and RVOT obstruction. Due to their anatomical location, all these findings may eventually affect RV function.

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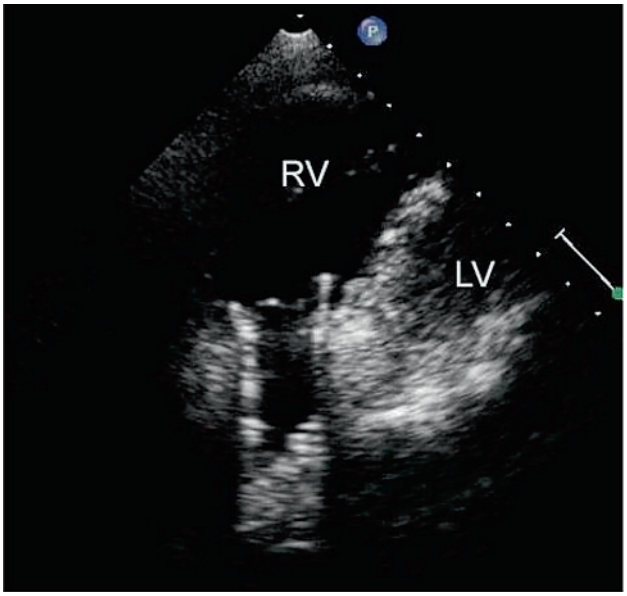
Restrictive physiology of the right ventricle

Restrictive RV physiology has been described in up to 50% of patients during the immediate postoperative period after TOF repair. Restrictive physiology correlated with the use of a transannular patch for RVOT reconstruction, and was identified as a cause of a postoperative low output status and a prolonged ICU stay (7 versus 2 days) [5]. Echocardiography readily demonstrates the presence of restrictive RV physiology. Doppler echocardiographic signs of RV diastolic dysfunction are an increased retrograde flow in the vena cava inferior and in the hepatic veins, a shortened E wave deceleration time at the tricuspid valve inflow, and an antegrade diastolic flow in the main pulmonary artery, corresponding to the atrial systole [6]. Early postoperative restrictive physiology is predictive of late restriction. However, in contrast to the immediate postoperative phase, during long-term follow-up restrictive physiology may favourably influence the secondary effects of pulmonary regurgitation by delaying RV dilatation. In fact, patients presenting with pulmonary regurgitation and restrictive physiology present a shorter QRS duration in the ECG, a lower cardiothoracic ratio on x-ray and better exercise test performance [7, 8].

Pressure overload

Pressure overload is usually well tolerated by the RV. Pressure overload induces RV hypertrophy, which initially may protect the RV from dilatation and dysfunction. Intervention is recommended when the RV pressure rises higher than ⅔ times the pressure in the left ventricle, since there is an increased risk of progressive deterioration in RV function above this cutoff value [9]. Depending on the patient's clinical history and RVOT geometry, balloon angioplasty is now considered to be the intervention of choice for relief of isolated residual pulmonary valve stenosis. In the presence of combined pulmonary valve disease, i.e. stenosis and regurgitation, percutaneous insertion of a new pulmonary valve, such as Melody®, should be considered [10] (fig. 2). However, even though this does indeed represent an intriguing technique, several strict selection criteria need to be fulfilled for successful percutaneous pulmonary valve insertion (table 1). At present therefore, percutaneous pulmonary valve replacement represents only a real alternative to surgery in a restricted number of patients. The future development of other techniques allowing insertion of larger valves may overcome these limitations.

Figure 2
Transcutaneous pulmonary valve replacement.
2a. Echocardiography showing the stent with the valve in the right ventricular outflow tract
2b. The Melody valve® consists of a fresh bovine jugular vein containing a native valve sutured into a vascular stent.



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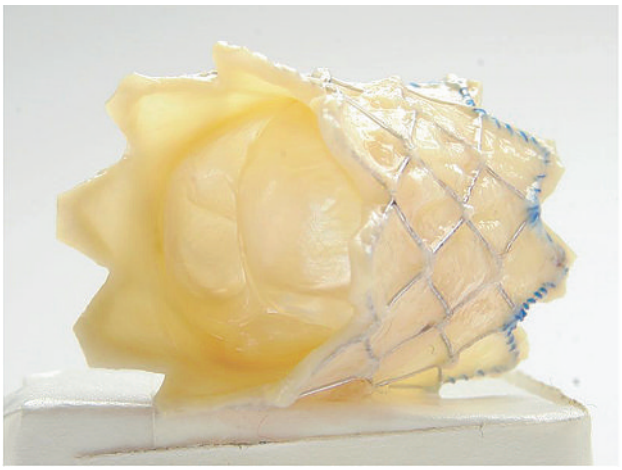

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Table 1
Patient's selection for percutaneous pulmonary valve replacement with Melody.

Requirements
Bodyweight >20 kg
Native graft diameter ≥16 mm and ≤22 mm
Circular conduit
Contraindications / Limitations
Native right ventricular outflow tract / pulmonary artery
Severely dilated conduit >22 mm
Transannular patch
Severe right ventricular outflow obstruction, which cannot be dilated by high-pressure balloon
Obstruction of the central veins / venous anatomy unable to accommodate a 22 Fr size introducer sheath (contraindication for percutaneous approach)

Volume overload

Pulmonary valve regurgitation is a frequent residual finding after TOF repair with insertion of a transannular patch and/or of a monocusp homograft in the pulmonary position. These surgical techniques have been used in the past since smaller grafts, such as the bovine jugular vein Contegra®, were not available at the time. Pulmonary regurgitation represents the main cause of chronic volume overload, RV dilatation and RV dysfunction. The natural course of the disease may lead to life-threatening ventricular arrhythmias and possibly sudden death [11]. Echocardiography may help to depict RV dilatation and dysfunction. However, echocardiography allows only qualitative and semiquantitative assessment of RV size and function and of the severity of pulmonary regurgitation. Moreover, the reproducibility of the measurements during follow-up appears to be very poor. For these reasons, thanks to the excellent reproducibility of its measurements, cardiovascular magnetic resonance (CMR) is nowadays considered "the gold standard" for assessment of right ventricular volumes and function [12].

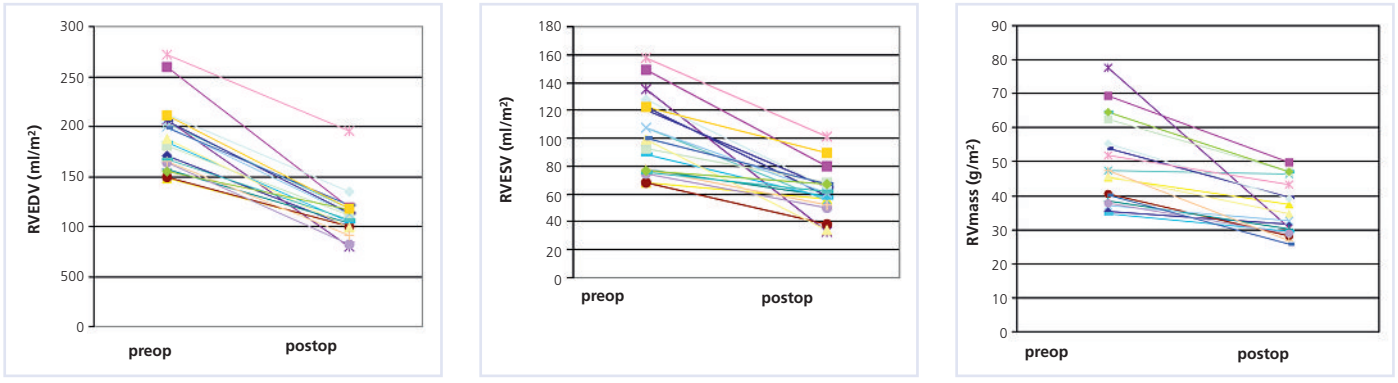
ECG is the crucial investigative tool for risk stratification of arrhythmias; progressive prolongation of the QRS complex can be observed at the same time as RV dilatation. A QRS duration longer than 180 msec has been shown to be a risk factor for life-threatening ventricular arrhythmias [11]. Moreover, abnormal QT dispersion has been recognised as an additional risk factor for arrhythmias [13]. On the other hand, by comparing several functional residual findings, including pulmonary stenosis, tricuspid valve regurgitation and pulmonary valve regurgitation, the group of Gatzoulis demonstrated that pulmonary regurgitation correlated closely with ventricular tachycardia and sudden death [11].

On the basis of these observations reported in the last decade, the previous common opinion that pulmonary regurgitation may be well tolerated by the RV has recently been revised [14]. The observation reported by Therrien et al., that RV with an enddiastolic volume larger than 170 mL/m² may not regress to normal size after pulmonary valve replacement, provided more evidence in favour of a different approach to this problem [15]. Hence a more aggressive treatment for pulmonary regurgitation is now being adopted in most congenital cardiology centres and pulmonary valve replacement is being performed earlier, with the goal of preserving RV function and preventing the deleterious complications mentioned above. Nevertheless, the ideal timing for pulmonary valve replacement remains unclear. The fact that the ideal graft for pulmonary valve replacement has not yet been found, and that the available grafts have a half-life of 10 years, needs to be borne in mind as a factor prompting caution when discussing pulmonary valve replacement [16].

Several groups have recently used CMR to investigate the optimal RV size cutoff values for performance of pulmonary valve replacement [17, 18]. We evaluated 22 young patients with severe pulmonary valve regurgitation and RV dilatation after TOF repair, and demonstrated that, if pulmonary valve replacement is performed when the RV enddiastolic volume is larger than 150 mL/m², RV remodelling, i.e. a significant reduction of RV volume and mass, can be expected [17] (fig. 3 and 4). Similar findings were obtained in Boston [18], by applying a cutoff value of 160 mL/m², and in Toronto, by applying a cutoff of 170 mL/m² [14]. Interestingly, remodelling in RV size did not correspond to an improvement in global right ventricular function, expressed as ejection fraction, in either report.

Hence the current indication (class IIa) for pulmonary valve replacement, as reported in the most recently published international guidelines, is the presence of severe pulmonary regurgitation and any of the following findings: moderate to severe RV dysfunction, moderate to severe RV enlargement (i.e. enddiastolic

Figure 3
Remodelling of the right ventricle 6 months after pulmonary valve replacement expressed as reduction of enddiastolic volume (3a), endsystolic volume (3b), and RV mass (3c).



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volume 150–170 mL/m²), development of arrhythmias, and moderate to severe tricuspid regurgitation [9].

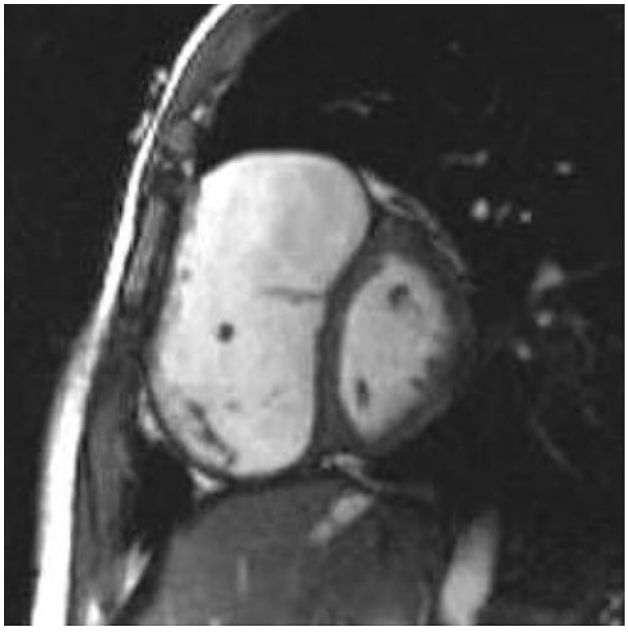
Advanced echocardiographic assessment of RV function, including measurements of myocardial velocities, strain and strain rate, may provide new insight into RV function under abnormal loading conditions [19, 20]. Decreased myocardial velocities and strain rate have been reported in patients after TOF repair compared to normal subjects, not only in the right ventricular free wall but also in the septum and in the left ventricular lateral wall [12, 20, 21]. This important observation suggests that patients after TOF repair may have decreased intrinsic myocardial contractility, not only of the RV, but also of the left ventricle. Several causes can be postulated, including chronic cyanosis before repair, intrinsic myocardial fibrosis, scars after open-heart surgery, and interventricular interactions. Frigiola et al., testing the parameters of RV myocardial contractility in different degrees of pulmonary valve regurgitation (mild, moderate, severe), identified the isovolumetric acceleration time of the right and the left ventricle, the size of the tricuspid valve ring and QRS duration as correlating with the degree of pulmonary regurgitation; in contrast, load-dependent myocardial velocities and strain were not influenced by the severity of pulmonary regurgitation [20].

Transcutaneous pulmonary valve insertion can be considered the ideal model for the study of functional RV parameters before and after pulmonary valve replacement, since this technique eliminates all the possible confounding factors introduced by open-heart surgery. Isovolumetric acceleration time was shortened in patients with pulmonary regurgitation before intervention, and did not change significantly immediately after transcutaneous pulmonary valve replacement, one month and three months later [22]. This observation supports the data suggesting that RV function remains impaired in spite of normalised loading conditions after valve replacement and remodelling of RV size.

The natural course of right ventricular dilatation: how fast does it progress?

What is the natural course of right ventricular dilatation in the presence of severe pulmonary regurgitation? Our group analysed the CMR volumetric data of 22 patients, age range 5–26 years, with severe pulmonary regurgitation and significant RV dilatation, who for different reasons did not undergo pulmonary valve replacement. A second CMR examination for assessment of RV volume and function was performed after a mean interval of 2 years (range 9 months to 4 years). Right ventricular volume showed no significant progression of dilatation independently of the degree of regurgitation [23]. Similar findings have recently been reported by Meijbom et al., who analysed the clinical course of 28 patients with severe pulmonary regurgitation [24]. Patients were examined by echocardiography, ECG and exercise testing, 15 and 26 years after TOF repair. QRS duration was the only parameter showing a significant progression, mean value from 123 ±27 msec to 145 ±29 msec. Echocardiographic measurements of RV dilatation, such as RVOT diameter and tricuspidal inlet, showed no significant progression; exercise performance remained unchanged. These observations may re-

Figure 4
MRI short-axis images of the right ventricle before (4a) and after (4b) pulmonary valve replacement.



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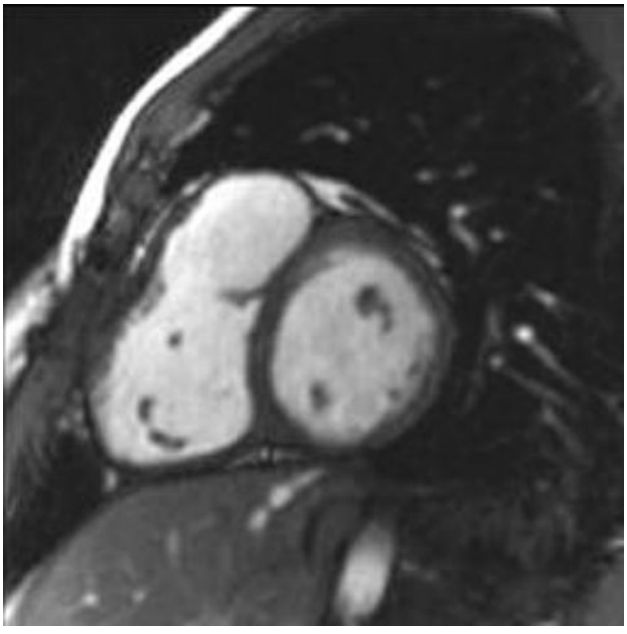

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open the debate surrounding the ideal timing for pulmonary valve replacement.

Conclusion

Among several abnormal loading conditions to which the right ventricle may be exposed after TOF repair, volume overload due to severe pulmonary regurgitation is the most common and gives cause for most concern, due to its potentially deleterious complications. Even though this appears to be one of the most investigated topics in congenital cardiology, no generally accepted recommendations exist yet concerning treatment. In fact, the ideal solution, regarding both the correct timing for pulmonary valve replacement and the ideal graft to insert as pulmonary valve, is far from having been found. So "deciphering the effect of pulmonary regurgitation on right ventricular function and deciding on timing for valve replacement seems like cracking the 'Da Vinci code'" [25].

Future clinical research focusing on the natural course of the disease and on the effects of pulmonary valve replacement on RV function may provide the answer. Several validated and other new advanced techniques, including myocardial Doppler velocities, strain and strain rate, as well as CMR, are available for this purpose, but some need further validation; moreover, their results need to be better understood. Follow-up of TOF may represent the ideal model for this.

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