

# The management of tetralogy of Fallot after corrective surgery

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**INTRODUCTION**

Tetralogy of Fallot (TOF) affects approximately 35 per 100 000 live births.<sup>(1)</sup> Its quintessential features result from antero-cephalad displacement of the outlet septum:

- Large anterior malaligned ventricular septal defect (VSD).
- Right ventricular (RV) outflow tract obstruction (RVOT).

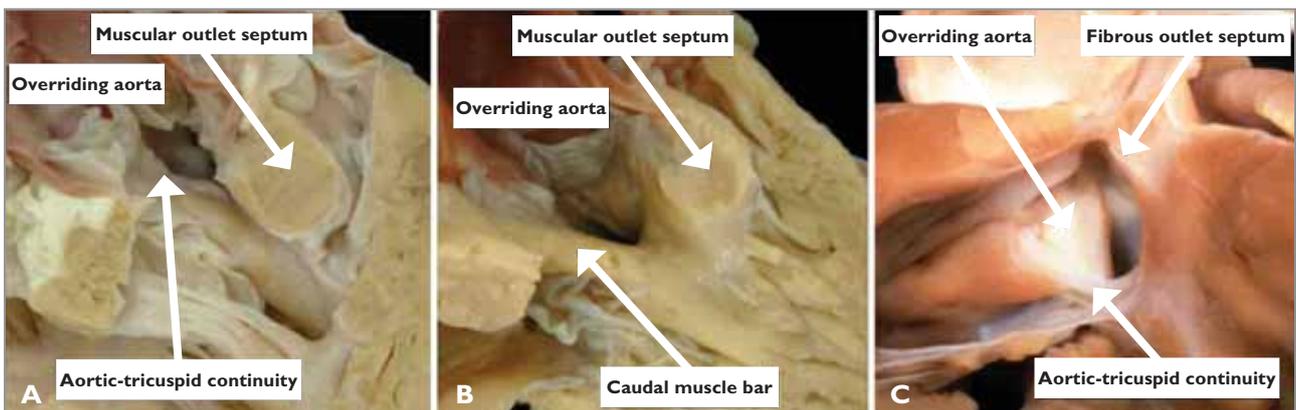
**ABSTRACT**

**With the success of contemporary medical and surgical management in congenital heart disease (CHD), adults with repaired CHD now often outnumber their paediatric equivalents. Tetralogy of Fallot (TOF) has paved the way, not only in the management of native CHD, but also in the management of its repaired form. In this review, we discuss the current surveillance and management of adults with repaired TOF, highlighting outcomes related to these practices.**

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- RV hypertrophy and a rightward positioned overriding aorta.
- Multi-level pulmonary stenosis with its most extreme expression being pulmonary arterial hypoplasia and/or pulmonary atresia (Figure 1).<sup>(2,3)</sup> Other associated anomalies are outlined in Table I.

This anatomic constellation was first described by Etienne-Louis Fallot in 1888.<sup>(2)</sup> However, it was only 5 decades later that progress was made in its physiologic and anatomic treatment. The inspiring history of its surgical management reflects



**FIGURE 1: The 3 common subtypes of anterior malaligned VSDs in tetralogy of Fallot are displayed.**

A: Perimembranous outlet being the most common;

B: Followed by muscular outlet; and

C: Doubly committed with perimembranous extension.

In all types, the outlet septum, whether muscular (A and B) or a fibrous remnant (C), is deviated anteriorly causing subvalvar pulmonary obstruction. In the perimembranous defects, the conduction system resides along the posterior and inferior margins of the defect where there is fibrous continuity between the aortic and tricuspid valves, an important consideration during surgical repair. We are indebted to Professor Robert Anderson for kindly sharing these images.

**TABLE I: Associated anatomic features.**

Anomaly	Prevalence in TOF
Coronary Anomaly (most common - left anterior descending from RCA)	5%
Pulmonary artery origin from the ascending aorta	0.4%
Atrioventricular septal defect	2% - 10%
Absent pulmonary valve syndrome	3% - 6%
Double outlet Right ventricle	4%

the enormous strides that have transformed the intra-cardiac management of all complex congenital cardiac defects over the past 70 years. This article focuses on the late post-surgical management of the condition.

### SURGICAL MANAGEMENT OF TETRALOGY OF FALLOT AND OUTCOMES

The advent of surgical treatment arose from the simple, yet profound, observation that cyanosis was caused by diminished pulmonary blood flow. Helen Taussig, collaborating with Alfred Blalock and Vivien Thomas, created the first successful arterial shunt diverting subclavian arterial flow to the pulmonary artery.<sup>(4)</sup>

Lillehei reported the first complete intracardiac repair of TOF in 1954 utilising a large RV incision and transannular patch.<sup>(5)</sup> This was done under support of the earliest form of cardiopulmonary bypass known as "cross-circulation" between a father and son. Subsequent cardiopulmonary bypass sciences harnessed bubble and membrane oxygenation sciences and made intracardiac repair more feasible.

The late outcomes of Lillehei's original surgical cohort is instructive. It demonstrated persuasively the need for long term follow-up. Among the first 105 successful operations, patient survival at 10, 20 and 30 years were 92%, 80% and 77% respectively. Nine percent required late reoperations for (i) residual VSD, (ii) RV outflow tract malfunction (stenosis or regurgitation), (iii) atrial septal defect and/or (iv) tricuspid regurgitation. Lillehei also demonstrated that sudden death, occurring in 5%, was part of the surgically modified history.

The trans-atrial anatomic repair of 1963,<sup>(6)</sup> was popularised by Roger Mee, reporting a mere 0.5% operative mortality and a 47 month survival of 97.5%.<sup>(7)</sup> The strength of these new approaches lay largely in their minimalist approach to the RV outflow tract, conserving pulmonary valve and infundibular

function in a greater proportion. Adoption of this technique has not, however, been uniform. The European Association of Cardio-Thoracic Surgery Congenital Database showed that only a sixth of surgeons, despite favourable anatomy, use the trans-atrial approach.<sup>(8)</sup>

### LATE ANATOMIC AND PHYSIOLOGIC OUTCOMES

#### Right ventricular and outflow dysfunction

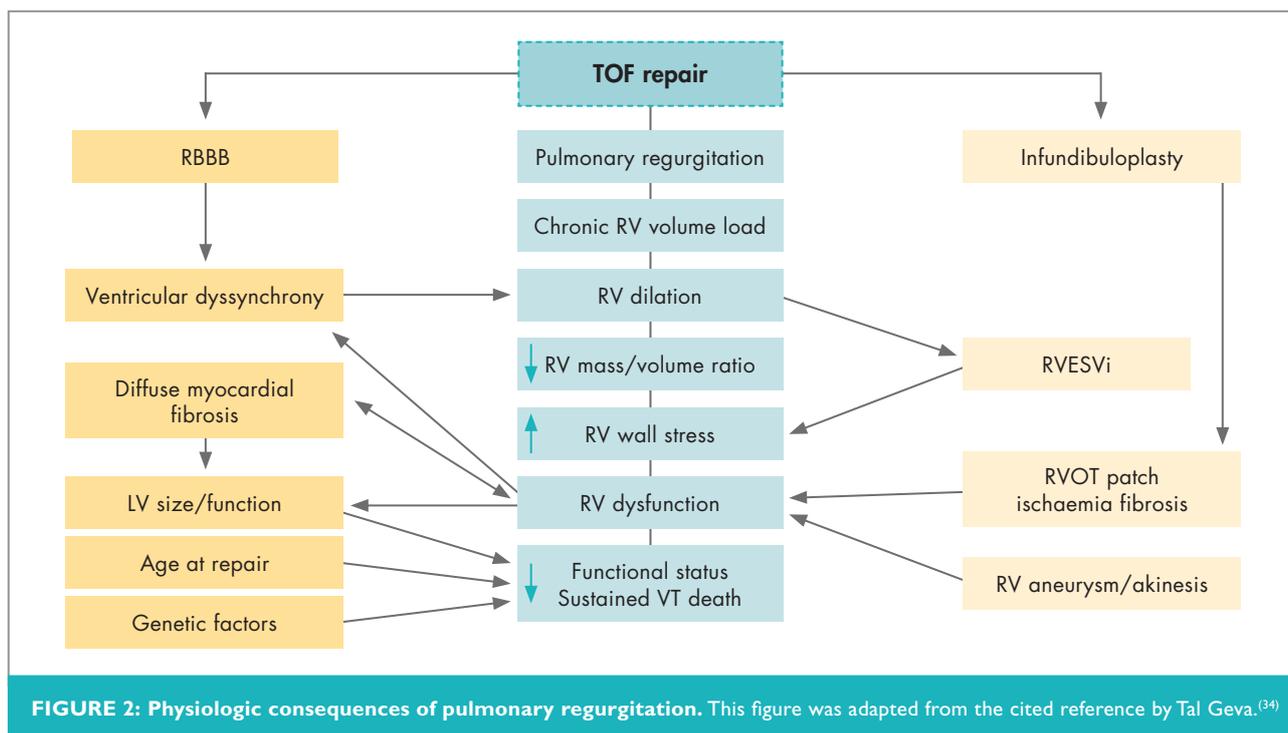
The surgical evolution of intracardiac repair has led to a spectrum of morphologic aberrations in the RV outflow combined with functional impairment. Pulmonary regurgitation, stenosis, or a combination of both, are the most common late manifestations of this RV outflow morphologic derangements. Pulmonary valve replacement therefore has become the most frequent late procedure. In a contemporary cohort, approximately one fifth required pulmonary valve replacement at a mean age of  $20 \pm 13$  years.<sup>(9)</sup> Hickey and colleagues reported the need for additional surgery, as summarised in Table II.<sup>(10)</sup>

Though well tolerated in the childhood years, pulmonary regurgitation usually leads to progressive RV dilation and dysfunction and may affect left ventricular function (Figure 2). Restrictive RV physiology, defined by the presence of end diastolic forward flow in the pulmonary artery coincident with atrial contraction, is most often protective against RV dilation in the presence of PR and tends to promote better exercise capacity.<sup>(11)</sup>

The contractile response to exercise of both the RV (and left ventricle [LV]) are abnormal in repaired TOF, showing marked blunting of isovolumetric contraction as the exercise demand increases.<sup>(12)</sup> There appears to be no significant correlation between these contractile responses and RV or LV volumes.

**TABLE II: The need for late re-intervention.**

Haemodynamic burden	Prevalence
Pulmonary regurgitation	16% - 20%
RV hypertension needing pulmonary arterial intervention	9%
Conduit replacement and/or aneurysm surgery	9%
Tricuspid regurgitation	3%
Residual or recurrent ASD or VSD	9%
Aortic valve replacement	1%



### Diagnostic considerations

Right and left ventricular function can be tracked on echocardiography by tricuspid or mitral annular plane systolic excursion (TAPSE or MAPSE), respectively, RV fractional area change, longitudinal strain and right or left ventricular rate of pressure rise in early systole (dP/dt), as assessed by the tricuspid or mitral regurgitation Doppler envelope, in any combination. Significant pulmonary regurgitation is identified by the presence of a combination of pressure half time (PHT) <100ms and pulmonary regurgitation jet width/annulus ratio  $\geq 1/3$ , and the presence of diastolic reversal of flow in the branch pulmonary arteries.<sup>(13)</sup>

### TRICUSPID REGURGITATION

Some degree of tricuspid regurgitation is common in adults with repaired TOF, often related to annular dilation, especially in those requiring pulmonary valve replacement (PVR). In fact, most major cardiovascular society guidelines include moderate or greater tricuspid regurgitation as an indicator for surgical PVR in the setting of significant pulmonary regurgitation or stenosis,<sup>(14)</sup> as significant tricuspid regurgitation is associated with poor outcomes.<sup>(15,16)</sup> The jury is hung as to what threshold of significant tricuspid regurgitation and annular dilation may warrant the addition of tricuspid valve repair at the time of PVR.<sup>(17)</sup> What has been clearly demonstrated is that in the majority of patients with tricuspid regurgitation, the severity improves after both surgical and percutaneous PVR alone.<sup>(17,18)</sup>

### LEFT VENTRICULAR DYSFUNCTION AND HEART FAILURE

LV dysfunction occurs in up to 20% of repaired TOF patients, with a third of these having moderate or severe dysfunction.<sup>(19)</sup> The underlying etiology is not always evident. Potential causes include: surgical coronary arterial injury or compression, longer arterial shunt duration, poor myocardial protection, LV vents at the time of surgery and acquired coronary vascular disease. LV dysfunction most often coexists with RV dysfunction and dilation, with frank LV systolic and diastolic dysfunction often preceded by abnormal (counterclockwise) rotation of the LV base which is likely secondary to these adverse interventricular interactions.<sup>(20)</sup> In those with RV dilation and dysfunction due to pulmonary regurgitation, when pulmonary competence is restored, LV function often improves.<sup>(21)</sup> This is most marked in those with the worst LV function prior to PVR, in whom LV ejection fraction may improve as much as 15%.

### AORTIC ROOT DILATION

Progressive aortic root dilation is common late after TOF repair. It is likely due to a combination of intrinsic aortopathy (cystic medial degeneration) and haemodynamic factors related to greater stroke volume through the aorta.<sup>(22)</sup> The risk of dissection is small, and has generally prompted more permissive dimensions as surgical thresholds in clinical practice.<sup>(23)</sup>

### CLINICAL ASSESSMENT

Clinical assessment should include a detailed review of the surgical as well as current history and functional capacity. A

history of recurrent arrhythmia should be obtained. Physical examination should elicit signs of 22q11 deletion syndrome on general examination. On cardiovascular examination, signs of RV dilation and/or hypertrophy, congestive right heart failure, pulmonary and tricuspid regurgitation, and the nature of the

second heart sound, i.e. whether a P2 component is present at all, should be sought. Typical CXR and ECG features are demonstrated in Figures 3 and 4.



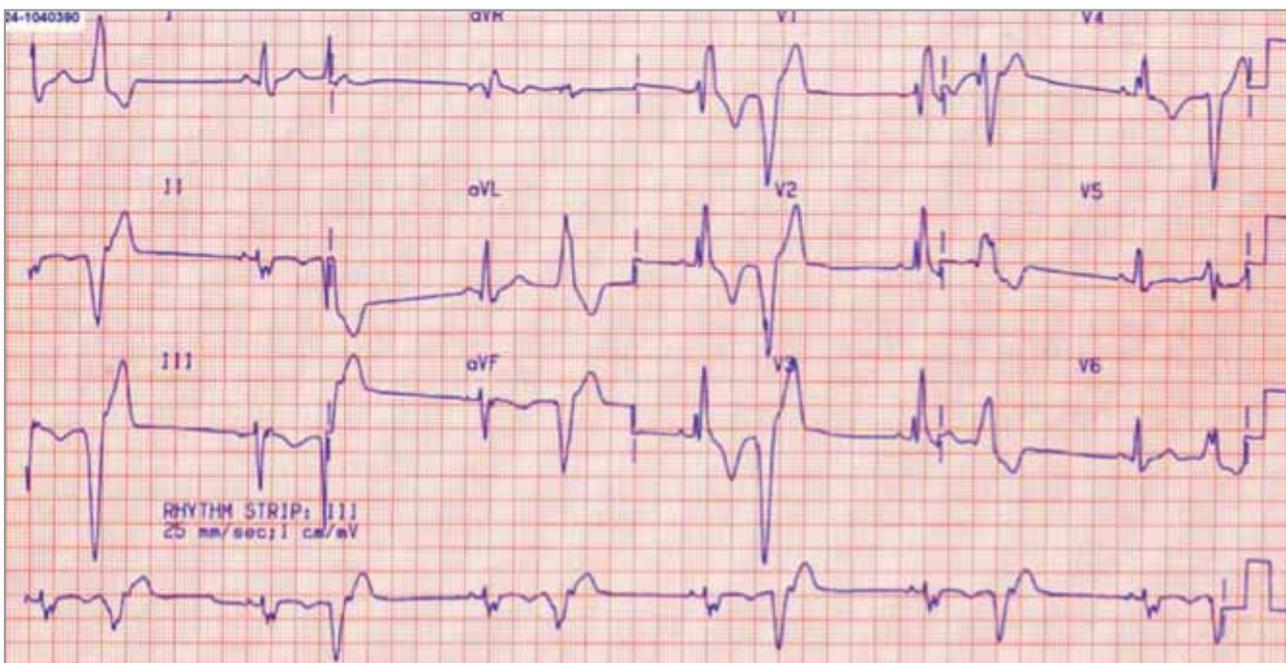
**FIGURE 3: CXR features of tetralogy of Fallot.**  
A prominent pulmonary trunk is evident, with a left aortic arch and normal pulmonary vascularity in this case. Sternal wires are not visible.

### FUNCTIONAL CAPACITY

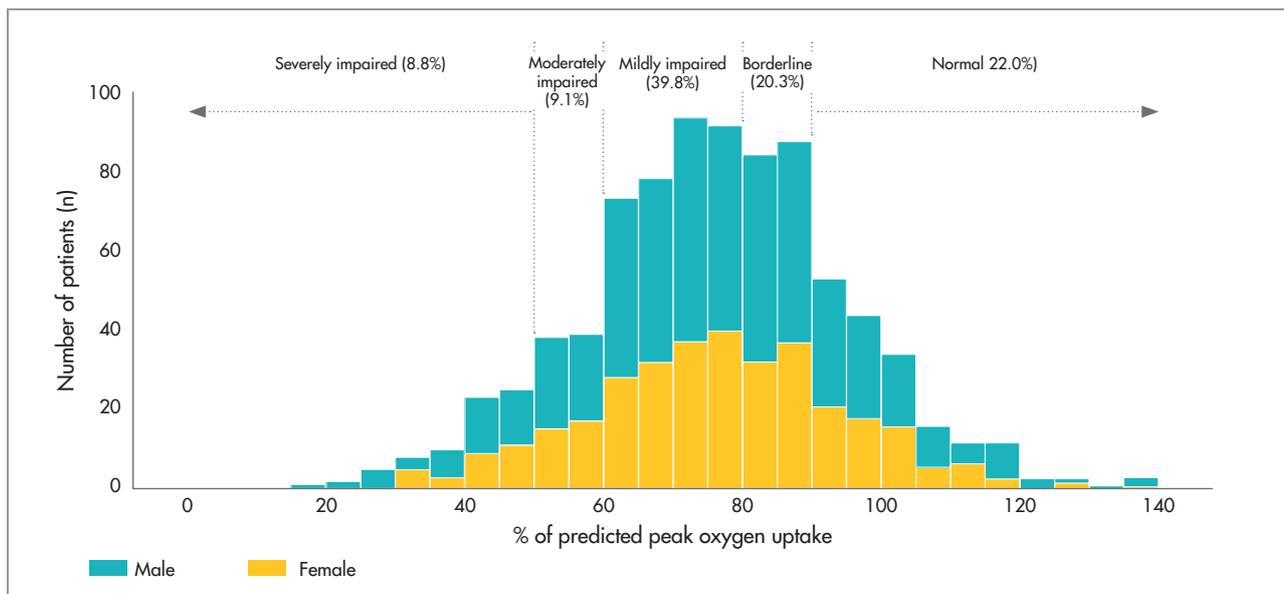
Cardiopulmonary exercise capacity is usually only mildly reduced in 40% of TOF patients during late follow-up. Less than one tenth have severe limitation in exercise capacity (Figure 5).<sup>(24)</sup> This reduction in percent of predicted exercise capacity is a powerful and independent predictor of mortality or ventricular tachycardia (VT). Functional decline over time seems to parallel that of the normal population.

### ARRHYTHMIA, SUDDEN CARDIAC DEATH AND RISK STRATIFICATION

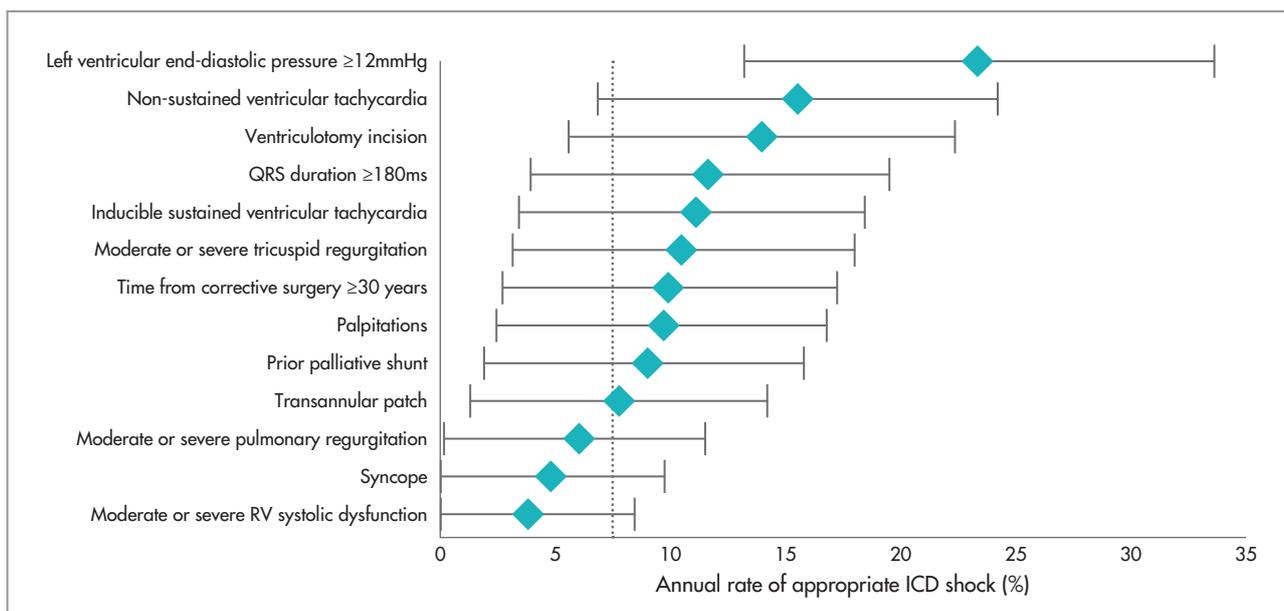
Arrhythmia and sudden cardiac death are recognised late sequelae of surgically repaired TOF individuals, occurring at approximately 0.2% per year with a late overall prevalence of up to 10%.<sup>(25)</sup> Risk stratification is therefore an important part of meaningful late follow-up and management (Table III).<sup>(26)</sup> The strongest independent predictor of late sudden events, however, seems to be LV dysfunction and a high LV end-diastolic pressure (Figure 6). Those at highest risk should be considered for invasive haemodynamic assessment with programmed ventricular stimulation to identify sustained VT (Table IV). The positive and negative predictive value of inducible ventricular tachycardia and/or ventricular fibrillation (VF) is reported to be 55% and 91% respectively.<sup>(27)</sup> VT/VF



**FIGURE 4: ECG features of repaired tetralogy of Fallot.**  
Broad right bundle branch block with ventricular ectopy. Sometimes RV hypertrophy and right atrial enlargement coexist.



**FIGURE 5: Cardiopulmonary exercise capacity in patients with repaired TOF, as assessed by percentage of predicted peak oxygen uptake.** Although many patients will have some degree of exercise intolerance, less than one tenth will have severely impaired exercise tolerance.<sup>(26)</sup>



**FIGURE 6: Mean actuarial annualised rates of appropriate implantable cardioverter-defibrillator shocks in primary prevention according to clinical characteristics, with elevated left ventricular end-diastolic pressure being the most predictive for appropriate shocks. The mean is represented by the black diamonds, bound by the lower and upper 95% confidence limits. The vertical dotted line represents the actuarial annualised rate of appropriate shocks in all primary prevention patients. RV; right ventricle.<sup>(28)</sup>**

risk in high risk populations occurs at 3.6% per year.<sup>(28)</sup> VT often arises from the RV outflow in the region of the RV outflow patch and the VSD. The anterior wall of the RV outflow forms a critical part of the VT circuit, as well as the septal surface of the RV free wall through the outlet (infundibular or

conal) septum. Scar burden may extend well beyond these areas, especially in more diseased RVs.<sup>(29)</sup> Atrial arrhythmias have an overall prevalence of 20% (including atrial re-entrant tachycardia and atrial flutter) in repaired TOF patients, with atrial fibrillation occurring in approximately 7%.<sup>(30)</sup>



**TABLE III: Risk stratification of arrhythmia and sudden cardiac death.**

Risk Factor	Hazard Ratio OR Exp (B)
Prior palliative shunt	HR, 2.6 mortality
Inducible sustained VT	HR, 2.1 mortality
QRS duration >180ms	HR, 2.0 mortality
Ventriculotomy incision	HR, 2.4 mortality
LVEDP ≥12 mmHg	HR, 1.5 mortality
Non-sustained VT	HR, 2.7 mortality
RV hypertension per 1mmHg	HR, 1.06 mortality
Pulmonary hypertension per 1mmHg	HR, 1.16 mortality
LVEDP per 1mm Hg above 12mmHg	HR, 1.34 mortality or VT
Peak VO <sub>2</sub> <63% of predicted	Sensitivity 82%, specificity 63% for predicting 5 year mortality
Combination QRS >170 + Peak VO <sub>2</sub> <65%	HR 11.4, mortality
Combination of QRS >170ms +Peak VO <sub>2</sub> <65% + VE/CO <sub>2</sub> ratio >31	HR 5.4 of combined endpoint Mortality, VT, or hospitalisation
Transannular patch	1.08

LV = left ventricle, LVEDP = LV end-diastolic pressure, PVC = premature ventricular contraction, RV = right ventricle, VE/CO<sub>2</sub> = minute ventilation/carbon dioxide production, VO<sub>2</sub> = oxygen consumption, VT = ventricular tachycardia.

Late survival is also influenced by the original anatomic subtype. For example, those with atrioventricular septal defects and TOF, or TOF and pulmonary atresia, appear to have the poorest late survival outcomes.<sup>(10)</sup>

**Management considerations**

Ventricular tachycardia management now generally includes AICD as part of the strategy in addition to ablation where possible. Arrhythmia surgery is another strategy and can be performed at the time of PVR. See below for recommendation from PACE/HRS expert consensus statement.<sup>(31)</sup>

**MANAGEMENT OPTIONS**

**Indications for surgical and transcatheter pulmonary valve replacement**

The major cardiovascular society guidelines for timing of surgical PVR are summarised in Table V. The focus has historically been on RV systolic function and volumetric criteria.<sup>(23,32,33)</sup> More recent treatment strategies favour earlier intervention in an attempt to improve RV functional recovery, and perhaps late patient survival.<sup>(14,34-36)</sup> Summarised in Table VI on page 14 is our own criteria for intervention.

Percutaneous treatment has emerged as a vital and readily accessible treatment for patients with pulmonary regurgitation and/or stenosis, meeting criteria for intervention. Treatment of RVOT outflow diameter ≥16mm and up to 31mm is now feasible including the treatment of both native RVOT substrates, and undersized homografts.<sup>(14)</sup> Medtronic’s new Harmony valve promises to extend that spectrum even further, allowing treatment of much larger RVOT diameters (Figure 7).<sup>(37)</sup>

**MEDICAL MANAGEMENT OF TETRALOGY OF FALLOT DURING LATE FOLLOW-UP**

TOF, not unlike other forms of congenital heart disease, demonstrates neurohormonal activation, prompting conventional heart failure approaches to pulmonary regurgitation and/or tricuspid regurgitation. In a double-blinded, placebo-controlled study, Ramipril taken over a 6 month period in clinically stable patients with repaired TOF and associated moderate, to severe, pulmonary regurgitation failed to demonstrate improved values of ANP, BNP nor CMR – derived RV ejection fraction.<sup>(38)</sup> RV and LV long-axis function did, however, improve significantly. Those with restrictive RV physiology showed lower LV end-systolic volume indices and an increase in LV ejection fraction. Beta-blockers, specifically Bisoprolol, in

**TABLE IV: Arrhythmia surveillance.**

Heart Rhythm Society ACHD 2014
Coronary artery evaluation is indicated in assessing life threatening ventricular arrhythmias or resuscitated SCD in adults with CHD over 40 years of age and in those with CHD associated with a higher risk of coronary ischaemia, such as (i) congenital anomalies of the coronary arteries, (ii) coronary arteriovenous fistulae, (iii) a history of coronary surgery or (iv) the potential for coronary compression by vascular conduits or stents (IB).
EP testing is indicated in adults with unexplained syncope and “high-risk” CHD substrates associated with primary ventricular arrhythmias or poorly tolerated atrial tachyarrhythmias, such as (i) tetralogy of Fallot, (ii) transposition of the great arteries with atrial switch surgery or (iii) significant systemic or single ventricular dysfunction (IC).
Surveillance for adults with moderate or severe CHD should include a standard 12-lead ECG at least once per year (IC).
Periodic Holter monitoring can be beneficial as part of routine follow-up in adults with (i) transposition of the great arteries and atrial switch surgery, (ii) Fontan palliation and (iii) tetralogy of Fallot over 35 years of age (IIA-B).
Programmed ventricular stimulation can be useful in risk stratifying adults with TOF who have additional risk factors for SCD such as (i) LV systolic or diastolic dysfunction, (ii) non-sustained ventricular tachycardia, (iii) QRS duration >80ms and (iv) extensive RV scarring (IIA-B).
ICD therapy is reasonable in selected adults with TOF and multiple risk factors for SCD, such as (i) LV systolic or diastolic dysfunction, (ii) non-sustained ventricular tachycardia, (iii) QRS duration >180 ms, (iv) extensive right ventricular scarring or (v) inducible sustained ventricular tachycardia at EP study (IIA-B).

CHD = congenital heart disease, ECG = electrocardiogram, EP = electrophysiology, LV = left ventricle, RV = right ventricle, SCD = sudden cardiac death.

TABLE V: Summary of current guidelines for the late surveillance and management.

	ACC/AHA ACHD 2008	CCS 2009	GUCH 2010
<b>General Management</b>	Annual (at least) follow up recommended with an ACHD cardiologist (I-C).	Patients who require <b>surgery</b> for TOF should be operated on by congenital heart surgeons (I-C).	
	Catheterisation should be performed in regional centres with expertise in ACHD (IC).	Patients who require <b>reoperation</b> for TOF should be operated on by congenital heart surgeons (IIA-B).	
	Surgeons with training/expertise in CHD should perform operations (IC).		
	Genetic screening (i.e. 22q11 deletion) should be offered to all patients (I-C).		
<b>Indications for intervention</b>	<b>PVR is indicated</b> for <b>severe PR</b> and symptoms or decreased exercise tolerance (I-B).	The following situations <b>may warrant intervention</b> after repair:	<b>AVR</b> should be performed in patients with <b>severe AR</b> with symptoms or signs of LV dysfunction (I-C).
	<b>PVR is reasonable</b> in the setting of <b>severe PR</b> and any of the following: A. Moderate to severe RV dysfunction (IIA-B). B. Moderate to severe RV enlargement (IIA-B). C. Symptomatic or sustained atrial and/or ventricular arrhythmia (IIA-C). D. Moderate to severe TR (IIA-C).	<b>I. Free PR</b> associated with: <b>A.</b> Progressive or moderate to severe RV enlargement (RVDEV greater than 170mL/m <sup>2</sup> ). <b>B.</b> Moderate to severe RV dysfunction. <b>C.</b> Important TR. <b>D.</b> Atrial or ventricular arrhythmias. <b>E.</b> Symptoms such as deteriorating exercise performance (IIA-C).	<b>PVR</b> should be performed in symptomatic patients with <b>severe PR</b> and/or <b>PS</b> (RV systolic pressure >60mmHg, TR velocity >3.5 m/s) (I-C).
	Coronary artery anatomy (specifically the possibility of an anomalous anterior descending coronary artery across the RVOT) should be ascertained before surgery (I-C).	<b>II. Residual VSD</b> with a shunt greater than 1.5:1 (IIA-C). <b>III. Residual PS</b> with RV pressure at least two-thirds the systemic pressure (either the native RV outflow or valved conduit if one is present) (IIA-C).	<b>PVR</b> should be <b>considered</b> in asymptomatic patients with <b>severe PR</b> and/or <b>PS</b> when at least one of the following is present: <b>A.</b> Decrease in objective exercise capacity. <b>B.</b> Progressive RV dilation. <b>C.</b> Progressive RV systolic dysfunction. <b>D.</b> Progressive TR (at least moderate). <b>E.</b> RVOT obstruction with RV systolic pressure >80mmHg (TR velocity >4.3 m/s). <b>F.</b> Sustained atrial/ventricular arrhythmias (IIA-C for all).
	<b>Surgery is reasonable</b> for <b>residual RVOT</b> obstruction (valvar or subvalvar) and any of the following: <b>A.</b> Peak RVOT gradient on echo greater than 50mmHg (IIA-C). <b>B.</b> RV/LV pressure ratio greater than 0.7 (IIA-C). <b>C.</b> Progressive and/or severe RV dilatation with RV dysfunction (IIA-C). <b>D.</b> Residual VSD with a left-to-right shunt greater than 1.5:1 (IIA-B). <b>E.</b> Severe AR with associated symptoms or more than mild LV dysfunction (IIA-C). <b>F.</b> Combination of multiple residual lesions (i.e. VSD and RVOT obstruction) leading to RV enlargement or dysfunction (IIA-C).	<b>IV. Significant AI</b> associated with symptoms and/or progressive LV systolic dysfunction (IIA-C). <b>V. Aortic root enlargement</b> of at least 5.5cm in diameter (IIA-C). <b>VI.</b> A large <b>RVOT aneurysm</b> or evidence of infection or false aneurysm (IIA-C). <b>VII. Sustained clinical arrhythmias</b> , (most commonly atrial flutter or fibrillation and sustained monomorphic ventricular tachycardia). When any of these occur; the patient should also be evaluated for a treatable hemodynamic cause of the arrhythmia (IIA-C).	<b>VSD closure</b> should be considered in patients with residual VSD and significant LV volume overload or if the patient is undergoing pulmonary valve surgery (IIA-C).
	<b>Interventional catheterisation is indicated</b> for: <b>A.</b> Elimination of residual native or palliative systemic – pulmonary artery shunts (I-B). <b>B.</b> Management of coronary artery disease (I-B).	<b>VIII.</b> The combination of <b>residual VSD</b> and residual <b>PS</b> or <b>PR</b> that are all <b>mild-moderate</b> in severity but leading to substantial RV enlargement, RV dysfunction or symptoms (IIA-C).	
	<b>Interventional catheterisation is reasonable</b> for: <b>A.</b> Elimination of residual ASD or VSD with a left-to-right shunt greater than 1.5:1. It at an appropriate anatomic location (IIA-C).		
	<b>Arrhythmia Assessment</b>	Periodic Holter monitoring can be beneficial. Frequency should be individualised depending on haemodynamics and clinical suspicion of arrhythmia (IIA-C).	Patients who have experienced ventricular tachyarrhythmias and/or have been resuscitated from sudden cardiac death of no clearly identified reversible cause <b>should</b> undergo ICDs for <b>secondary prevention</b> (I-B).
		Patients deemed to be at particularly high risk for sudden cardiac death <b>may benefit</b> from ICDs for <b>primary prevention</b> (IIA-B).	

\* AHA and CCS guidelines require the listed degree of pulmonary regurgitation or stenosis and one additional listed criterion.

33 TOF patients with residual pulmonary regurgitation or pulmonary stenosis and NYHA class I-II heart failure symptoms over 6 months showed no significant effect on NYHA class, exercise capacity, RV or LV volumes nor ejection fraction by CMR.<sup>(39)</sup> BNP and ANP levels increased when compared to patients receiving placebo. This preliminary data discourages systematic use of beta-blockers in this population.

**THE ROLE OF BNP IN LATE FOLLOW-UP**

BNP may be helpful in late surveillance of TOF. In a recently published prospective study of patients with repaired TOF,

**TABLE VI: Suggested criteria for Intervention.** We have adopted the following criteria for PVR (both surgical and/or percutaneous) in our clinical practice: Interventional criteria are fulfilled when there is more than moderate pulmonary regurgitation or stenosis and 2 additional criteria.

Criteria	Value
Pulmonary regurgitation	>= 25%
RVEDVi	>150cc/m <sup>2</sup>
RVSEVi	>80cc/m <sup>2</sup>
RV EF	<45% or >= moderate dysfunction
RVOT obstruction	RVSP >=2/3 systemic pressure
Tricuspid regurgitation	>= moderate
QRS duration	>160ms
Arrhythmia	New onset atrial flutter, atrial tachycardia or fibrillation, or ventricular tachycardia
Exercise capacity	<17ml/kg/min
LV EF	<50%
Branch PA stenosis	<30% flow to affected side
Large RVOT aneurysm	

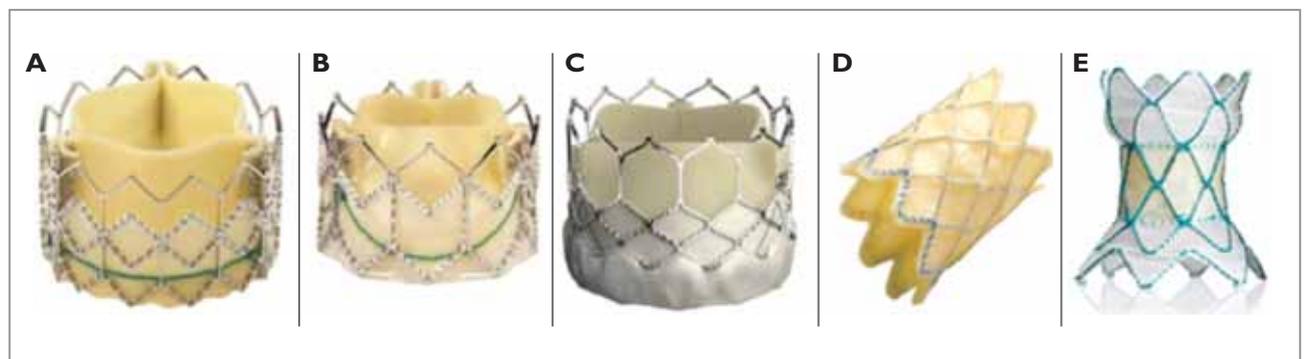
EF = ejection fraction, LV = left ventricle, PA = pulmonary artery, RV = right ventricle, RVEDVi = right ventricular end diastolic volume indexed, RVSEVi = right ventricular systolic volume indexed, RVOT = right ventricular outflow tract.

compared to a smaller group of age- and gender-matched controls, elevated BNP was common in repaired TOF patients independent of the degree of pulmonary regurgitation, CMR-derived metrics or exercise capacitance, being significantly related to increased mortality as well as a predictor of sustained arrhythmia. A BNP value ≥15pmol/L was associated with a fivefold increased risk in death.<sup>(40)</sup> This data suggests that the monitoring of BNP may be helpful in risk stratification during late follow-up.

**SURGICAL AND transcatheter OUTCOMES**

Improved surgical management during the initial repair in infancy has led to remarkable outcomes, minimal if any morbidity or mortality in the first 2 decades of life. However, the incidence of impaired functional status, heart failure, arrhythmias and death nearly triples during the third post-operative decade.<sup>(10,34,41,42)</sup> This period is when patients are commonly considered for either surgical or percutaneous PVR using the general guidelines for determining the proper timing as highlighted above. Considering the short-term outcomes following surgical PVR, a recent review of The Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD) (median age of 17 years) and Adult Cardiac Surgery Database (STS-ACSD) (median age of 41 years) reported a low risk of in-hospital death (<1%) and major complications (~2%) in the younger cohort. The patients in the STS-ACSD were older with a higher prevalence of pre-operative risk factors and, not surprisingly, had a higher incidence of major complications (21%) and in-hospital mortality (4%).<sup>(41)</sup>

Following surgical PVR there is often a reduction in RV volumes and a subjective improvement in functional status.<sup>(43-46)</sup> Discouragingly, RV systolic dysfunction tends not to improve, and more importantly, an improvement in outcomes has not been demonstrated.<sup>(36)</sup> Intermediate- to long-term follow-up



**FIGURE 7: Valves used for percutaneous PVR.**  
A: Sapien valve. B: Sapien XT valve. C: Sapien 3 valve. D: Melody valve. E: Harmony valve.

has now demonstrated that although there may be early improvement in RV volume, pre-operative volumes often return by approximately 7 to 10 years following surgical PVR. These findings should not dissuade providers from recommending surgical or transcatheter PVR as recommended by the current guidelines, but should instead highlight that guidelines may be missing important variable(s) that should be considered. Recent reports have highlighted that factors, such as the important role of the LV, diastolic function, subclinical systolic dysfunction as assessed by deformation imaging, exercise imaging and assessment of ventricular fibrosis (both replacement and interstitial) may be important considerations in better determining the timing for PVR.<sup>(14)</sup>

Transcatheter PVR has emerged as a feasible alternative to surgical PVR in a large proportion of patients. Initially instated as a procedure to prolong the need for surgical PVR, and only intended to be used in patients with RV to pulmonary artery conduits, it is now often pitted against surgical PVR as an alternative therapy, and more commonly being used in native outflow tracts. The appeal of avoiding cardiopulmonary bypass and a repeat thoracotomy may lend to a more aggressive approach, although surgical PVR guidelines for timing are often applied.<sup>(14)</sup> Intermediate outcomes (up to 7 years following implant) in the Melody PVR Investigational Device Exemption trial has reported good outcomes, with low procedure-related morbidity, symptomatic improvement and excellent freedom from re-intervention or explant.<sup>(47)</sup> Short-term complications are rare, but may include complications related to vascular access, coronary artery compression and aortic root compression, the latter 2 which are reduced with balloon compliance testing prior to valve implantation. Long-term adverse outcomes of stent fracture and endocarditis have raised some concerns,<sup>(47)</sup> however, pre-stenting the conduit has reduced the first issue, with appropriate patient selection with adherence to antibiotic prophylaxis potentially reducing the second.<sup>(14,47)</sup>

## CONCLUSION

TOF, once a lethal condition, can now be successfully treated during early childhood, and late surveillance and management is now well established, resulting in excellent outcomes. Emerging data suggests multiple factors past the commonly used RV volumetric and functional criteria that should be used in surveillance and risk stratification of these patients.

**Conflict of interest: none declared.**

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