Circulation

AHA SCIENTIFIC STATEMENT

Long-Term Management of Right Ventricular Outflow Tract Dysfunction in Repaired Tetralogy of Fallot: A Scientific Statement From the American Heart Association

Tal Geva, MD, FAHA, Chair; Rachel M. Wald, MD, Vice Chair; Emily Bucholz, MD, PhD, MPH; James F. Cnota, MD, FAHA; Doff B. McElhinney, MD; Laura M. Mercer-Rosa, MD, FAHA; Carlos M. Mery, MD, MPH; Andrea Leann Miles, APRN, MNSc, CPNP-AC; Jeremy Moore, MD; on behalf of the American Heart Association Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Cardiovascular Surgery and Anesthesia; Council on Clinical Cardiology; and Council on Cardiovascular and Stroke Nursing

ABSTRACT: Right ventricular outflow dysfunction, manifesting as stenosis, regurgitation, or both, is nearly universal in patients with repaired tetralogy of Fallot, precipitating a complex pathophysiological cascade that leads to increasing rates of morbidity and mortality with advancing age. As the number of adolescent and adult patients with repaired tetralogy of Fallot continues to grow as a result of excellent survival during infancy, the need to improve late outcomes has become an urgent priority. This American Heart Association scientific statement provides an update on the current state of knowledge of the pathophysiology, methods of surveillance, risk stratification, and latest available therapies, including transcatheter and surgical pulmonary valve replacement strategies, as well as management of life-threatening arrhythmias. It reviews emerging evidence on the roles of comorbidities and patient-reported outcomes and their impact on quality of life. In addition, this scientific statement explores contemporary evidence for clinical choices such as transcatheter or surgical pulmonary valve replacement, discusses criteria and options for intervention for failing implanted bioprosthetic pulmonary valves, and considers a new approach to determining optimal timing and indications for pulmonary valve replacement.

Key Words: AHA Scientific Statements ■ cardiac surgical procedures ■ diagnostic imaging ■ heart defects, congenital ■ pulmonary valve ■ tetralogy of Fallot

Advances in the diagnosis and management of tetralogy of Fallot (TOF) have led to dramatically improved short- and long-term survival, resulting in a growing population of adults with repaired TOF (rTOF).[1] In parallel, there has been an increase in late morbidity and mortality associated with sequelae of the initial palliation.[2] Residual right ventricular (RV) outflow tract (RVOT) dysfunction, including pulmonary stenosis and pulmonary regurgitation (PR), is the most common lesion after repair and, through a complex pathophysiological cascade, can lead to electromechanical cardiomyopathy and premature death.[2]

Over the past 2 decades, a growing body of literature and an expanding clinical experience have focused on strategies to restore RVOT function through surgical or percutaneous pulmonary valve replacement (PVR) and other medical therapies.[3] Although the effect of PVR on RV remodeling is well documented, the optimal indications for and timing of interventions remain unknown.[4,5] With advances in PVR options and technology, the emergence of novel imaging biomarkers, and advances in risk stratification, there is a compelling need for a comprehensive reassessment of the approach to the diagnosis and therapy of RVOT dysfunction in patients with rTOF. The goal of this scientific statement is to critically evaluate the current state of knowledge and to outline evidence-based suggestions for the management of RVOT dysfunction in this growing patient population.

Supplemental Material is available at https://www.ahajournals.org/journal/doi/suppl/10.1161/CIR.0000000000001291

Circulation is available at www.ahajournals.org/journal/circ

METHODOLOGY

This scientific statement encapsulates the "live-long" objectives of the American Heart Association by reviewing current data guiding long-term RVOT dysfunction in postoperative patients with rTOF. The manuscript was developed according to published American Heart Association processes.[6] The Manuscript Oversight Committee approved statement goals, and a writing committee with established expertise and respect for diversity and inclusion was assembled. After an initial conference call, the writing group was divided into subgroups by topic for comprehensive review of the available literature from English language articles and to summarize content. The co-chairs developed manuscript drafts that were reviewed by the committee before submission. Clinical considerations were made by expert consensus, and gaps in knowledge were identified for future research efforts. The manuscript was reviewed by outside experts not affiliated with the writing group and by the American Heart Association Science Advisory and Coordinating Committee.

EPIDEMIOLOGY AND NATURAL HISTORY

In a systematic review and meta-analysis of articles reporting congenital heart disease prevalence, TOF was found to be the fifth most common congenital heart disease lesion, documented in 34 per 100 000 live births (95% CI, 31–37), and is the most frequently encountered cyanotic congenital heart lesion.[7,8] The cause of TOF is multifactorial, incorporating genetic and nongenetic factors. Up to 25% of patients with TOF will have an identifiable chromosomal abnormality (most commonly trisomy 21 or chromosome 22q11 deletion syndromes).[8] Nongenetic factors reportedly associated with TOF include pregestational diabetes, infections (febrile illnesses or influenza), environmental exposures (specifically, organic solvents), or ingestion of medications (eg, clomiphene). However, it should be noted that observational studies cannot establish cause and effect and may be limited by multiple factors, including chance, bias, and various confounders.[9] Review of temporal trends has revealed stability in the prevalence of TOF over 6 decades (studies spanning 1945–2009).[7] Anomalies of the RVOT, including TOF and pulmonary stenosis, appear to be more prevalent in Asia than in North America or Europe.[7] Of note, data from low-income countries are incomplete, and implications of limited access to care on TOF incidence have not been fully elucidated. Further study is necessary to explore the interplay between the impacts of socioeconomic disparity, genetic modifiers, racial predisposition, and environmental exposures and the epidemiology of TOF.

With the advent of modern-day treatment of TOF, its natural history has transformed from being nearly universally fatal in infancy to a 30-year survival rate of 90%.[1] Initial diagnosis is increasingly made by prenatal ultrasound, although the rate of detection may vary by study and can remain challenging.[10] Contemporary management of infants with TOF generally involves surgical repair during the first several months of life with an effort to preserve RVOT function by minimizing the infundibular incision and sparing the pulmonary valve whenever possible. Interventional catheterization and surgical palliative procedures are considered in patients with additional risk factors (eg, prematurity).[11] Early survival for those undergoing repair during the first year of life is ≈98%, with a 25-year survival of >90%. However, during the third decade of life, the rates of morbidity and mortality begin to rise, with common causes of late death including cardiac arrest, sustained arrhythmia, and congestive heart failure.[1] Genetic abnormalities appear to confer a 3- to 4-fold increase in mortality risk in early and late follow-up.[1]

PATHOPHYSIOLOGY

In patients undergoing TOF repair, reconstruction of the RVOT to relieve obstruction usually involves disruption of pulmonary valve integrity, which leads to immediate PR in most patients. Even with annulus- or leaflet-sparing approaches to TOF repair, significant PR is common, although its onset may be delayed. In addition to PR, some patients experience residual or recurrent RVOT obstruction, resulting in variable degrees of stenosis. Although the regurgitation and obstruction associated with RVOT dysfunction in this population may be tolerated without major clinically apparent implications for many years, it has become clear that chronic PR, with or without associated stenosis, can have a critical impact on long-term outcomes in this population.[12,13] The consequences of PR after TOF repair appear to be a function of both its severity and duration. The severity of PR is determined by (1) regurgitation orifice area; (2) RV compliance; (3) diastolic pressure difference between the main pulmonary artery (PA) and the RV; (4) capacitance and resistance of the PA system; and (5) duration of diastole.[14] Surgical technique influences the PR severity in some respects such as the orifice size of the patched RVOT and the presence and function of residual leaflets, although it is unclear whether the extent or method of RV muscle resection is also important.

The physiological consequences of RVOT dysfunction and the interactions between the various involved structures and processes are depicted in Figure 1. Immediately after TOF repair, some degree of RV enlargement and dysfunction is often evident, but the combination of low RV compliance resulting from hypertrophy, low capacitance of the PA system, and a

 Circulation. 2024;150:e00–e00. DOI: 10.1161/CIR.0000000000001291

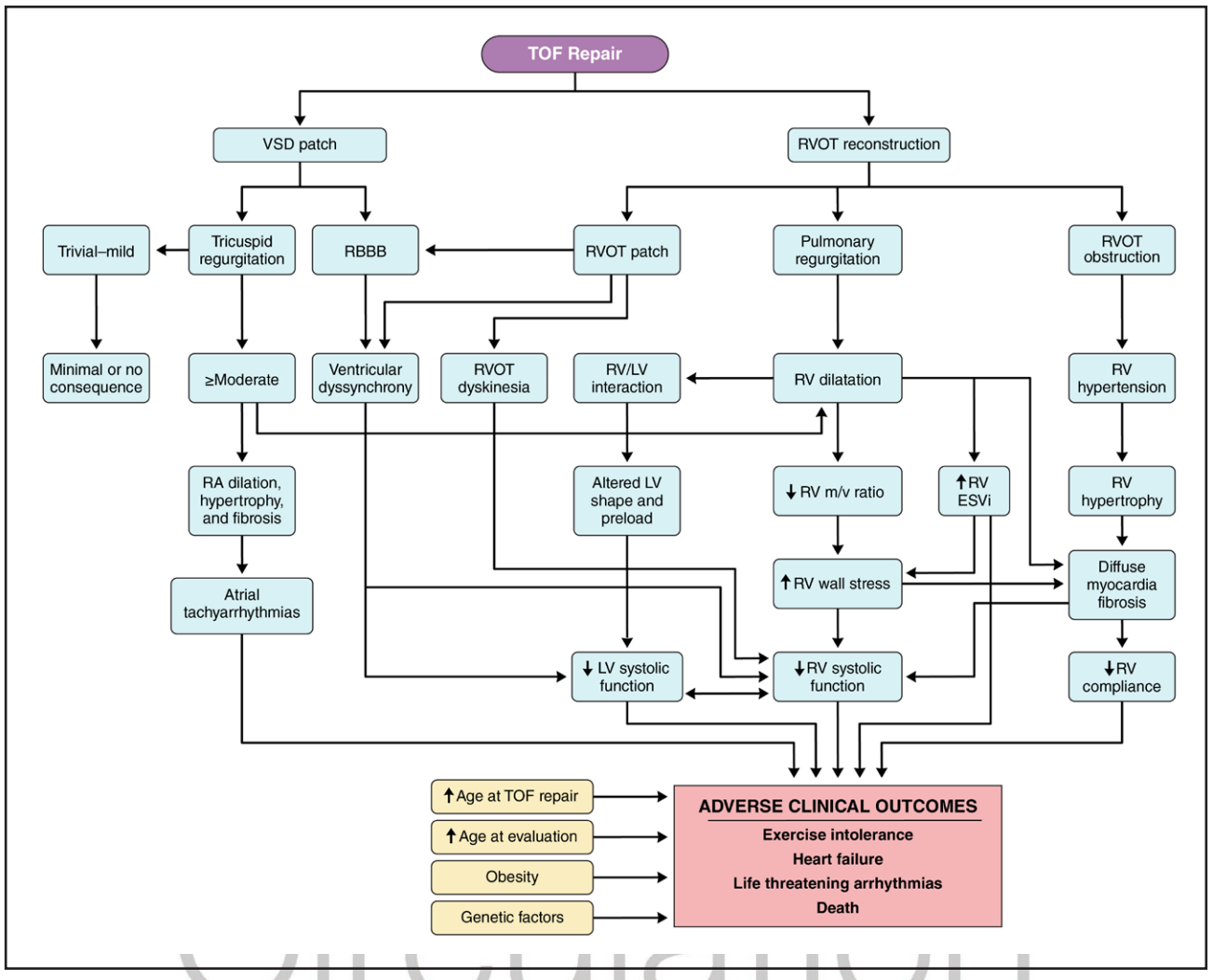

Figure 1. Pathophysiology of RVOT dysfunction after TOF repair.
ESVi indicates end-systolic volume index; LV, left ventricular; m/v, mass/volume; RA, right atrial; RBBB, right bundle-branch block; RV, right ventricular; RVOT, right ventricular outflow tract; TOF, tetralogy of Fallot; and VSD, ventricular septal defect.

short diastolic filling period in young patients limits the impact of PR on the RV even when the PR orifice is large. Over time, the rise in RV stroke volume related to PR and the reduction in RV hypertrophy after relief of the pressure load lead to progressive increases in the size and capacitance of the central PAs and in RV compliance. These changes, along with prolongation of diastole as the heart rate decreases with age, lead to larger PR volume/fraction.[15] As detailed in Figure 1, the consequences of PR revolve around RV dilatation, the changes in RV structure and mechanics, and the implications of these changes on the left ventricle (LV) as a result of ventricular-ventricular interactions.[12,16,17] In conjunction with parallel and overlapping postoperative processes, these changes predispose patients to adverse outcomes over time. Although significant PR is common after TOF repair, the time course of PR progression, concomitant stenosis (when present), and their consequences differ considerably from patient to patient and have not been fully characterized.

Clinical and experimental evidence suggests important similarities between the RV and LV responses to chronic volume overload. Thus, the LV response to aortic

Table 1. Ventricular Response to Chronic Semilunar Valve Regurgitation

Stage	Characteristics
1	Compensated chronic volume overload: ↑ EDV with eccentric and concentric hypertrophy → normal mass-to-volume ratio, end-systolic fiber stress, and global systolic function, along with cellular elongation, addition of myofibers, and a decrease in collagen content
2	Failure of compensatory mechanisms: progressive ↑ EDV but with inadequate hypertrophy and increased end-systolic stress → reduced systolic function with normal intrinsic myocardial contractility
3	Reduced but reversible impairment of myocardial contractility
4	Irreversible myocardial injury associated with fibrosis and increased interstitial collagen

The duration of each stage is highly variable, but stage 1 may last for many years.
EDV indicates end-diastolic volume.

regurgitation, which has been studied extensively, can inform our understanding of the RV response to PR (Table 1).[18,19] Although the pathophysiology of RV remodeling in response to the altered hemodynamic conditions after TOF repair is strikingly similar to the response of the LV to chronic volume load, important differences include chamber geometry, myofiber architecture, chamber contraction pattern, coronary artery anatomy and flow, disposition of the conduction system, and dependency on LV size and function (ie, ventricular-ventricular interaction).[20,21] In addition, the RV free wall and septum in patients with TOF are independently affected by the surgical repair, including RVOT incision/patch augmentation and ventricular septal defect closure, which contribute to the pathophysiological cascade detailed in Figure 1.[12,22,23] Dilatation of the tricuspid valve annulus, displacement of the free wall papillary muscles, and distortion of the septal attachments by the ventricular septal defect patch can lead to tricuspid regurgitation, further contributing to RV volume overload and to right atrial enlargement.[12]

Because of space limitations, it is not possible to provide a comprehensive review of RV pathophysiology related to postoperative PR in patients with TOF. More thorough reviews have been reported previously.[12,16] However, it is worth elaborating briefly on the impact of TOF repair and PR on the LV, which is one of the most critical pathophysiological considerations in this population, because LV dysfunction is a key predictor of adverse outcome in patients with repaired TOF.[15,17,24,25] Through a complex interplay involving the shared myofibers, septum, pericardium, and coronary flow, RV volume loading causes the ventricular septum to shift toward the LV (especially during diastole), with a consequent leftward shift of the LV pressure-volume loop, reduction in LV functional volumes, and impairment of LV filling.[26] Initially, LV function is preserved, but it deteriorates with progressive RV dysfunction and enlargement. Electromechanical dyssynchrony, both within and between the ventricles, likely contributes to adverse RV-LV interaction as well.[24]

RISK STRATIFICATION

The rising rates of premature death, life-threatening arrhythmias, heart failure symptoms, and exercise intolerance in adolescent and adult patients with rTOF have prompted numerous investigations aimed at identifying those at high risk for mortality and morbidity. The literature, which consists mostly of single-center retrospective or cross-sectional studies with a modest sample size and surrogate outcomes, has identified numerous factors associated with increased risk of selected outcomes. A small number of multicenter cohort studies further characterized patients at higher risk for shorter time to death and for life-threatening arrhythmias.[13,27–30] In general, risk factors for adverse clinical outcomes in patients with rTOF can be broadly categorized as patient characteristics and clinical history (eg, older age at repair, history of a staged palliation with a systemic-to-PA shunt, repair with RV-to-PA conduit, older age at time of risk stratification, obesity) and parameters associated with the complex pathophysiological sequelae of RVOT dysfunction after primary repair (Figure 1), including imaging biomarkers of adverse remodeling (eg, RV hypertrophy, severe RV dilatation, RV or LV dysfunction, RV hypertension) and electrical abnormalities (eg, atrial arrhythmias, nonsustained ventricular tachycardia [VT]). In addition, focal and diffuse myocardial fibrosis, adverse RV-PA coupling, and global biventricular function index[32]—which incorporates biventricular volumes, mass, and function—have been shown to discriminate between patients with low risk and those with high risk for adverse clinical outcomes. More recently, several studies proposed risk stratification algorithms in this patient group (Table 2). In addition, patient-reported outcomes provide invaluable insights into determinants of health status and quality of life in this population, highlighting increasing incidences of pain, discomfort, and reduced mobility with advancing age.[33]

It is notable that current risk stratification models account for only 25% to 30% of the variability in patient outcome.[34] Future work to further refine risk stratification in this population should explore novel imaging biomarkers such as myocardial strain[35], fibrosis by cardiovascular magnetic resonance (CMR) T1 mapping[36]; serum biomarkers such as exosomal cargo, microRNA, or novel proteins[37]; the role of social determinants of health in outcomes[38]; and artificial intelligence–enhanced electrocardiographic and raw CMR image analysis.[39] As with other conditions, these risk stratification algorithms will require validation and continual updating as the aging rTOF population evolves (eg, earlier age at repair, lower rates of staged palliation, advances in myocardial protection, and use of newer and better options for PVR, incorporating percutaneous approaches as alternatives to conventional surgical options).

METHODS OF EVALUATION

Table 3 summarizes suggested frequencies of surveillance tests in patients with rTOF.

History and Physical Examination

Assessment of patients after TOF repair should include a thorough medical history and physical examination. Particular attention should be paid to the operative report and the presence of residual postoperative lesions. Patients who undergo transannular patch repair have obligate severe PR and may experience earlier RV dilation, leading to arrhythmias or sudden death.[1,40–42] Regurgitation may also occur with valved RV-to-PA conduits or monocusp valves in a reconstructed RVOT as they become progressively incompetent over time.

Table 2. Risk Stratification Scoring Algorithms in Patients With rTOF

Brompton, UK[27]		The Netherlands[28]		Congenital Electrophysiology Society[29]			INDICATOR[13]	
Outcome: all-cause mortality		Outcome: all-cause mortality, sustained VT		Outcome: sudden death, sustained VT, ICD discharge			Outcome: all-cause mortality	
n=550; F/U 6.4 y; 27 deaths		n=575; F/U 7.1 y; 35 outcomes		n=288 (case-control); F/U NA; 72 outcomes			n=1552; F/U 9.5 y; 102 deaths	
Risk score validated: no		Risk score validated: no		Risk score validated: no			Risk score validated: yes	
					Surgical Era		**Parameter**	**Parameter estimate**
RV LGE		Prerepair shunt	2		1960–1979	1980–2000	Age at CMR	0.05785
Moderate	24	QRS ≥180 ms	1	Symptoms (e.g., palpitations, syncope)	3	3	Obesity (BMI ≥30 kg/m^2)	0.53076
Severe	40	Ventriculotomy	2	Moderate to severe LV dysfunction	3	3	Repair type	
LV LGE: yes	6	History of VT	2	Moderate to severe RV dysfunction	2	1	Transannular patch	Reference
RV EF		LV EF <45%	2	Moderate to severe RV hypertension	1	1	RV-PA conduit	1.08807
36-47%	4	RV EF <30%	3	Moderate to severe RV volume load	1	1	Other/unknown	0.66857
≤35%	10	**Total score**	12	Age at repair <6.5 y	2	0	RV ESVi	0.00883
LV EF		**Risk categories**		Prerepair shunt	2	1	BVGFI[32]	−0.06769
>55%	0	Low	0-1	Complex repair	1	2	**Risk score**=0.05785×age at CMR+0.53076 (if BMI ≥30 kg/m^2)+1.08807 (if RV-PA conduit repair type)+0.66857 (if repair type other than transannular patch or RV-PA conduit)+0.00883×RVESVi−0.06769×(BVGFI−48)	
36–55%	4	Moderate	2-3	QRS ≥180 ms	1	1		
≤35%	12	High	4-6	VT (any)	1	1		
Peak Vo_2		Very high	≥7	**Total score**	17	14		
>17 mL·kg^{-1}·m^{-2}	0			**Risk categories**				
≤17 mL·kg^{-1}·m^{-2}	6			Low	<3			
BNP				Moderate	3–6		**Risk categories**	
<127 ng/L	0			High	7–9		Low	≤4
≥127 ng/L	12			Very high	>9		High	>4
Atrial arrhythmias	8							
Age >50 y	6							
Total score	100							
Low risk	0–20							
Medium risk	21–50							
High risk	≥51							

BMI indicates body mass index; BNP, brain natriuretic peptide; BVGFI, biventricular global function index; CMR, cardiac magnetic resonance; EF, ejection fraction; ESVi, end-systolic volume index; F/U, follow-up; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LV, left ventricular; NA, not available; PA, pulmonary artery; rTOF, repaired tetralogy of Fallot; RV, right ventricular; and VT, ventricular tachycardia.

Residual lesions such as branch PA stenosis or tricuspid regurgitation may increase the degree of PR by placing added pressure or volume load on the RV.

The classic murmur of PR is a low-frequency early diastolic murmur that can be best heard with the bell of the stethoscope along the left sternal border. A systolic ejection murmur can be related to residual stenosis or to PR-induced increased stroke volume. When a pulmonary valvotomy or transannular patch is performed, the pulmonary component of the second heart sound may be absent. The presence of an RV heave suggests RV volume overload, and prominent jugular venous pulsations may be observed in the setting of elevated right atrial pressure or tricuspid regurgitation. Signs of RV failure may include elevated jugular venous pressure, liver enlargement, ascites, and peripheral edema.

ECG, Holter, and Invasive Electrophysiology

Atrial and ventricular tachyarrhythmias are the principal electrophysiological complications in rTOF, with an estimated cumulative incidence of severe ventricular arrhythmias of 6% to 14%, that increases rapidly in the third and fourth decades after repair.[40,44] Risk assessment of severe ventricular arrhythmias includes a thorough evaluation of the clinical history (eg, palpitations, syncope), 12-lead ECG, ambulatory rhythm monitor (including implantable loop recorder when indicated), and invasive electrophysiological study in selected patients. The ECG

Table 3. Surveillance Testing in Patients With rTOF

Test	Childhood (≤12 y of age)	Adolescence (13-18 y of age)	Adulthood (>18 y of age)*
Outpatient visit with physical examination	Every 12 mo	Every 12 mo	Stage A: 12–24 mo Stage B: 12 mo Stage C: 6–12 mo Stage D: 3–6 mo
ECG	Every 12 mo	Every 12 mo	Stage A: 24 mo Stage B: 12 mo Stage C: 12 mo Stage D: 6–12 mo
Echocardiogram	Every 12–24 mo	Every 12–24 mo	Stage A: 24–36 mo Stage B: 24 mo Stage C: 12 mo Stage D: 6–12 mo
Holter	Directed by symptoms	Directed by symptoms	Stage A: Directed by symptoms Stage B: Directed by symptoms Stage C: 12–24 mo Stage D: 12–24 mo
Bloodwork: BNP, renal and liver function	Directed by clinical data	Directed by clinical data	Directed by clinical data
Cardiopulmonary exercise test	Baseline at 12 y of age	Every 4–5 y	Stage A: 36–60 mo Stage B: 24–60 mo Stage C: 12–24 mo Stage D: 12–24 mo
CMR	Baseline at 12 y of age	Every 4–5 y	Stage A: 36 mo Stage B: 24–36 mo Stage C: 12–24 mo Stage D: 12 mo
Cardiac CT	As needed	As needed	As needed
Cardiac catheterization	Directed by clinical data	Directed by clinical data	Directed by clinical data

BNP indicates brain natriuretic peptide; CMR, cardiac magnetic resonance; CT, computed tomography; and rTOF, repaired tetralogy of Fallot.

*Physiological stages in adult patients with congenital heart disease as defined by Stout et al.[39a] Physiological stages A through D incorporate factors such as severity of symptoms (New York Heart Association classification), lesion complexity, arrhythmia status, and end-organ function (renal/hepatic/pulmonary) such that physiological stage A is a reflection of optimal physiology and stage D reflects the most deranged physiology.

is evaluated for morphology,[45] fragmentation, duration of the QRS complex, prolongation of the PR interval,[46] and repolarization abnormality.[47] Ambulatory monitoring may link arrhythmic symptoms to nonsustained VT.[27] Last, findings from invasive electrophysiological study may inform the likelihood of future ventricular arrhythmia risk and may be considered before RVOT interventions, particularly in patients considered to be at elevated risk.[48,49]

Exercise Testing

Diminished exercise capacity is a prevalent and potentially debilitating morbidity in patients with rTOF. Even those who are subjectively asymptomatic often exhibit low oxygen consumption and restrictive lung physiology on cardiopulmonary exercise testing.[50] The determinants of exercise capacity after rTOF are multifactorial and include, in addition to RVOT dysfunction, chronotropic impairment, abnormal pulmonary vasculature, diminished lung volumes, genetic syndromes, and physical deconditioning.[50,51] Exercise is generally safe in patients with rTOF; however, as a whole, they tend to exercise less than their healthy peers.[52,53] Evidence indicates that exercise training programs result in improvement in exercise capacity and oxygen consumption.[53] Thus, an active lifestyle and physical activity are strongly encouraged in this population because they positively affect cardiovascular health and quality of life.[53]

Echocardiography

Echocardiography, including 2-dimensional, 3-dimensional, Doppler, and myocardial deformation imaging, is a key modality in the assessment of RVOT dysfunction and its sequelae, being the primary imaging tool in childhood and complementary in adolescents and adults.[54] RV-focused imaging is challenging but essential for the analysis of RV systolic function, including fractional area change, tricuspid annular velocity, and free-wall longitudinal strain.[55,56] More than a

3-percentage-point change in peak RV longitudinal strain is considered clinically meaningful and should prompt further investigation by CMR.[57,58] Key diagnostic elements include RV systolic pressure by tricuspid regurgitation jet velocity, tricuspid regurgitation grade and mechanism, RVOT pressure gradient, PR grade, RV systolic function, PAs, LV size and function, and aortic dimensions.

CMR and Computed Tomography

CMR is considered the reference standard for assessment of ventricular function, measurement of chamber dimensions, quantification of intracardiac and extracardiac flows, and evaluation of myocardial viability.[12,59] CMR is routinely incorporated into clinical care pathways of adolescents and adults with rTOF. This modality is particularly well suited for the characterization of residual lesions and hemodynamic sequelae, risk stratification, and longitudinal follow-up. Beginning in the second decade of life, CMR is indicated for routine surveillance of adverse cardiac remodeling, valve dysfunction, blood flow measurements, and extent and location of scar tissue.[12,60] In addition, CMR can aid in the determination of timing of and planning for reintervention, as well as the frequency of diagnostic testing. Goals of the CMR study in patients with rTOF include some or all of the following: (1) quantification of biventricular volumes, function, and mass; (2) characterization of regional wall motion abnormalities; (3) assessment of RVOT and PA morphology; (4) measurement of PR volume and fraction; (5) measurement of tricuspid regurgitation if mild or more; (6) identification of residual shunts; (7) delineation of proximal coronary arteries; and (8) assessment of myocardial viability for presence of focal scar (with late gadolinium enhancement) and diffuse fibrosis (with parametric imaging). Although CMR is successful in the vast majority of patients with rTOF, cardiac computed tomography can be considered in select circumstances such as the presence of indwelling metal, which can produce susceptibility artifacts on CMR, need to confirm coronary artery anatomy/patency, or limited ability of a subject to comply with motionless breath holding as necessary for adequate CMR imaging. Computed tomography is also used for preprocedural modeling because of its superior spatial resolution.

Nuclear Imaging

Radionuclide imaging, a physiological diagnostic modality that uses radioisotope-labeled compounds, has been used in patients with congenital heart disease, including those with rTOF, for evaluation of RV size and function[61] and lung perfusion[62] and for assessment of myocardial perfusion and viability.[63] However, because most of these indications are now more readily evaluated with CMR, which provides superior anatomic delineation and does not expose patients to the ionizing radiation inherent to nuclear scintigraphy, this modality has been used in modern clinical practice almost exclusively to assess lung perfusion in patients who are unable to undergo CMR.

Cardiac Catheterization

The role of catheterization in evaluating PR is related primarily to hemodynamic assessment because catheter angiography is inferior to other methods for the assessment of PR severity and right-sided heart volumes. Both hemodynamic catheterization and angiography are useful for evaluation of RVOT obstruction and are performed as part of transcatheter PVR (TPVR) procedures. Catheterization may also be useful in assessing patients before surgical intervention to clarify whether concomitant interventions are indicated (eg, branch pulmonary arterioplasty) or to ascertain hemodynamic conditions that may be associated with procedural risk or merit preoperative or perioperative therapy (eg, heart failure or pulmonary hypertension). Selective coronary angiography is performed to assess the feasibility of TPVR procedures and to detect associated coronary artery disease in adults with rTOF.[64]

RATIONALE FOR PVR

As detailed in the Pathophysiology section, surgical repair of TOF often results in hemodynamically significant PR, which, along with other contributing factors, leads to a pathophysiological cascade, resulting in increasing long-term rates of morbidity and mortality.[65,66] PVR is highly effective at eliminating or greatly reducing PR and has been shown to improve clinical outcomes in rTOF.[67] In selected patients with rTOF and PR, leaflet and annular repair procedures may provide an alternative to PVR for restoring pulmonary valve competence.[68] Appropriately timed PVR has been associated with improved RV dimensions and function, biventricular mechanics, symptoms, and clinical outcomes, including freedom from death and sustained VT.[67,69,70] Studies using CMR have demonstrated reductions of up to 30% to 40% in RV end-diastolic and end-systolic volumes as early as 4 to 6 months after PVR in both children and adults.[69,71] By restoring pulmonary valve function, PVR improves ventricular loading conditions and decreases septal shift toward the LV, thereby augmenting LV volumes.[12] Studies evaluating recovery of RV and LV systolic function after PVR have been inconsistent, with some reporting no change and others finding improvement in regurgitation volume–adjusted RV function,[70–72] although empirical evidence supporting such adjustment is lacking. Furthermore, depressed pre-PVR RV ejection fraction <40% (without adjustment for volume load) has been shown to be an independent predictor of adverse clinical outcomes after PVR.[31]

Clinically, many patients report fewer cardiac symptoms after PVR, and studies have consistently demonstrated improvement in New York Heart Association functional class.[70] In contrast, data on changes in

exercise capacity, QRS duration, and arrhythmia risk after PVR are conflicting. Some studies have noted improvements in objective measures of aerobic capacity (eg, peak Vo_2, ventilatory aerobic threshold) after PVR[73,74] whereas others have not.[71,75] Similarly, some studies have found a reduction in the incidence of VT after PVR,[76] whereas others have found no significant change in the frequency of arrhythmias.[77,78]

The variability in these outcomes after PVR across studies and patients suggests that preoperative factors affect the extent of ventricular remodeling and symptom improvement. Investigations into preoperative ventricular volumes and mechanics, RVOT anatomy, electrocardiographic parameters, and cardiorespiratory fitness, among other variables, have emphasized the importance of PVR timing.[79,80] Studies on the pathophysiology and outcomes of patients with rTOF have shown that delaying PVR until the occurrence of irreversible mechanoelectrical cardiomyopathy is associated with poor clinical outcomes.[31,81] At the same time, evidence exists that prematurely implanting a pulmonary valve is associated with risks of morbidity and reinterventions.[82] Currently, there is a lack of rigorous information on the optimal timing of PVR before irreversible myocardial damage occurs. A recent multicenter study of 1143 patients with rTOF observed death or sustained VT in 7.2% of individuals (n=82) at a mean follow-up of 8.3±5.2 years. A propensity score was used to match patients with PVR to patients without PVR. Compared with patients without PVR, those with PVR had a 59% decrease in risk of death or sustained VT (hazard ratio, 0.41 [95% CI, 0.21–0.81]; $P<0.01$). Furthermore, the benefits of PVR were greatest in patients with RV end-systolic volume index >80 mL/m^2 (hazard ratio, 0.32 [95% CI, 016–0.62]).[67]

TECHNICAL CONSIDERATIONS FOR SURGICAL PVR

Various prostheses have been used for surgical PVR (SPVR). These include stented and stentless bioprostheses, biological conduits, mechanical valves, and surgeon-fashioned expanded polytetrafluoroethylene valves and conduits. Stented bioprostheses created from bovine pericardium (eg, CE PERIMOUNT Magna, Magna Ease, and Inspiris Resilia from Edwards Lifesciences) or mounted porcine valves (eg, Hancock II and Mosaic from Medtronic, Epic and Epic Plus from Abbott) are the most used valves because of their availability and durability, no absolute need for anticoagulation, and the ability to provide a landing zone for future transcatheter valves. Biological conduits include pulmonary and aortic homografts, bovine jugular valve conduits (Contegra from Medtronic), and bioprosthetic conduits with porcine or bovine pericardial valves.

SPVR is a relatively safe procedure with a perioperative mortality rate of 0% to 4.1%, with most series reporting rates of 1% to 2%.[84–91] Older age at reoperation, a greater number of previous sternotomies, and the need for urgent surgical intervention are risk factors for higher mortality and longer length of stay.[86,87,89] On average, pulmonary valve deterioration in bioprostheses and biological conduits (defined as peak Doppler velocity >4 m/s or severe regurgitation) tends to occur after 10 to 15 years after implantation.[85] Long-term freedom from reintervention has been shown to be 99% at 1 year, 94% to 98% at 5 years, 83% to 96% at 10 years, and 52% to 89% at 15 years, depending on age at implantation and valve size.[84,85,88–90,92–94] In general, reintervention rates are higher with younger age, smaller valves, worse postimplantation hemodynamics, and lack of a native RVOT (ie, pulmonary atresia).[84,91,92,94,96] The performance and durability of the different types of biological valves and conduits appear to be relatively similar, although some studies suggest that bovine pericardial valves,[91,97] in particular Mitroflow valves,[94] are associated with worse durability. Antiplatelet therapy is commonly used after implantation, although some studies have suggested that the use of vitamin K inhibitors for anticoagulation may decrease the rate of pulmonary valve deterioration.[85,91] The use of bovine jugular conduits has been associated with a higher risk of late endocarditis.[98]

Mechanical valves require anticoagulation, have potential thromboembolic risks, and preclude the use of transcatheter valves in the future. These valves should be considered only in highly selected adult patients such as those who require anticoagulation for other reasons and have had accelerated deterioration of other tissue prostheses.[99] There are limited data on long-term results of handmade expanded polytetrafluoroethylene valves and conduits; thus, they continue to be experimental at this time.

Selection of the optimal valve for SPVR should be individualized according to availability, patient characteristics, and an overall lifelong strategy that aims to minimize the number of reoperations. It is important to optimize valve hemodynamics to decrease the long-term risk of reintervention. Young children or those with a prior conduit may benefit from placement of a new biological conduit, although in older patients, bioprosthetic valves can also be placed within a previous conduit. For older patients, an appropriately stented bioprosthetic valve may provide the optimal solution and allow future placement of transcatheter valves. In certain patients, a conduit may be considered instead if thought to provide better hemodynamics.

TECHNICAL CONSIDERATIONS FOR PERCUTANEOUS PVR

TPVR was initially described in 2000 and has become a mainstay in the treatment of postoperative RVOT dysfunction in patients with TOF and other conditions.[100–102] The first available TPVR devices, The

Melody valve (Medtronic Inc, Minneapolis, MN) and several years later the Sapien valve (Edwards Lifesciences, Irvine, CA), are stent-mounted balloon-expandable valves that were designed to treat RVOT conduit dysfunction and acquired aortic valve stenosis, respectively. Accordingly, their initial role in management of postoperative RVOT dysfunction was to treat stenosis, regurgitation, or mixed dysfunction of conduits or surgical bioprosthetic valves, for which they are generally reliable and successful.[100–102] However, the substantial anatomic heterogeneity of the patched RVOT,[103] along with considerable dynamic variation in many cases, poses unique challenges for which these balloon-expandable valves are not ideally suited. Although several series have reported outcomes of Melody valve implantation for PR or mixed disease after nonconduit RVOT repair,[104,105] this valve (which has a maximum intended diameter of 22 mm and a maximum effective diameter of ≈24 mm) is suitable primarily for younger/smaller patients and those with RVOT obstruction or mixed obstruction and PR. With the introduction of larger-diameter (29 mm) second- and third-generation Sapien valves, treatment became feasible in a larger subset of patients with TOF with predominant PR and a native/patched RVOT,[102] although many were still not candidates for anatomic reasons. Although preliminary outcomes in patients with PR after surgical RVOT augmentation have been favorable with Melody and Sapien valves, longer-term data are limited.

The emergence of self-expanding transcatheter pulmonary valve prostheses designed expressly for patients with larger patched RVOT anatomy, particularly those with rTOF, has expanded the population eligible for TPVR substantially. The Harmony valve was approved by the US Food and Drug Administration for the treatment of postoperative PR in early 2022,[106] followed soon thereafter by the Alterra adaptive prestent, which is configured as a landing platform for a Sapien S3 valve.[107] Other conceptually similar valves, including the Venus P (Venus Medtech, Shanghai, China),[108] Pulsta (TaeWoong Medical Co, Gyeonggi-do, South Korea),[109] and MedZenith PT (Beijing Med-Zenith, Beijing, China)[110] valves, have been used outside the United States in the same population. Experience with these valves is limited, so it would be premature to offer conclusions about efficacy, but they all appear to be technically straightforward to implant and to perform well in the short term. Midterm data for the Harmony, Pulsta, and Venus P valves are encouraging.[100,111,112] Between them, currently available self-expanding and balloon-expandable transcatheter pulmonary valves seem to be suitable for a majority of patients with rTOF with a patched/native RVOT, although there remain patients with anatomy that is not appropriate for various reasons (RVOT too large, too short, unfavorable shape). If the promise of these technologies holds up beyond the current early adoption stage, they will likely become established as suitable alternatives to SPVR in many patients with rTOF and PR through a large native/patched RVOT and may be preferable in others, particularly those deemed to be at relatively high risk for open heart surgery.

HOW TO CHOOSE BETWEEN TRANSCATHETER AND SURGICAL PVR?

Many patients with an indication for PVR will be eligible for either SPVR or TPVR. Unbiased comparisons between both techniques are not possible because of differing indications and patient populations in the few retrospective and observational studies available.[113–119] Before expanded application of the newer-generation Sapien valves to treat PR after RVOT patch repair and, more recently, the emergence of self-expanding transcatheter pulmonary valves, SPVR and TPVR experiences were not necessarily comparable. The TPVR experience has consisted predominantly of transcatheter valve–in–conduit and transcatheter valve–in–bioprosthetic valve implantations, with a smaller, albeit growing, contingent of patients who undergo TPVR into a native, patched RVOT with PR.

There are some obvious differences between techniques and some areas that require further clarification. TPVR does not involve sternotomy or thoracotomy, as SPVR does, which inevitably entails differences in the recovery time. In general, postprocedural mortality rate is similar and low for both techniques (0.5%–≤2%).[113,114,118,120,121] Postprocedural hospitalization tends to be longer with SVPR,[117,118,120,122] although the cost in both the short term[118,122] and long term[121] is similar between both techniques. Complications are unique to one therapy or the other (eg, embolization of a transcatheter valve or sternal wound infection after surgery), making comparisons between techniques difficult.[120]

As noted, impartial long-term data comparing SPVR and TPVR are not yet available. One frequently raised difference is that transcatheter devices are a newer technology, whereas SPVR has been performed for several decades and has been studied extensively. Although this is true for overall SPVR, it is not necessarily true for every surgical prosthesis type, and the literature is inconclusive when it comes to durability and complications based on specific valve type. Both SPVR and TPVR seem to have a similar incidence of repeat interventions in the midterm.[113,114,117] Although some studies have shown similar rates of endocarditis between the 2 techniques,[114,116] others[120,123] have shown a higher incidence of endocarditis in patients after TPVR. The long-term survival is similar with both techniques.[114]

Patients with RVOT dysfunction will likely require many procedures throughout their lifetime. A coordinated approach between the patient's primary cardiologist, surgeon, and interventionalist incorporating

both modalities throughout the patient's lifetime likely provides the optimal strategy to reduce long-term morbidity. Several patient-, clinician-, and technology-related considerations should be taken into account in the selection of a valve implantation approach for a particular patient and setting (Table 4).[124] These considerations include, among others, age, body size, particular anatomy of the RVOT and adjacent structures, prior implantation of valves or conduits, presence of coexisting abnormalities needing to be addressed, number of previous sternotomies, expected number of future PVRs, presence of endocarditis, presence of pacemaker leads, comorbidities, surgical risk, and institutional experience. A multidisciplinary approach with shared decision-making will likely ensure the best short- and long-term results in each setting. Of course, therapeutic options are continually evolving, and it will be important in the future to consider the role of other emerging technologies such as living allogenic heart valve transplantation or other new surgical or transcatheter prosthetic valves.[125]

INDICATIONS FOR PVR

The overarching goals of PVR are to prolong life and to minimize morbidity. Research over the past 30 years has led to our current understanding of the pathophysiology and natural history of rTOF, which informs our thinking about the optimal timing of PVR. Patients with rTOF experience 3 pathophysiological phases: (1) a compensated phase during which the postrepair hemodynamic burdens are well tolerated with few or no cardiac symptoms, RV enlargement and hypertrophy are compensated, systolic function is preserved, and the risk of major adverse outcomes is low; (2) transition from compensated RV volume or pressure overload to irreversible adverse RV remodeling, during which the potential for reversal of ventricular remodeling is possible but the risk of adverse outcomes remains low; and (3) development of irreversible electromechanical cardiomyopathy with an exponential increase in the risk of adverse outcomes, including death, heart failure, and major arrhythmias.[12] Given that PVR is associated with risk of complications and that all replacement bioprosthetic valves undergo time-related degeneration requiring repeat intervention, indications for PVR aim to identify patients during phase 2, when the risk-benefit balance is most favorable. PVR during phase 1 might expose patients to unwarranted risks while affording minimal benefit, whereas delaying PVR until patients reach phase 3 exposes them to risks of poor clinical outcomes and adverse RV remodeling may be too advanced to realize the full benefit of the procedure. Therefore, published indications for PVR have generally aimed to identify biomarkers of the transition from phase 2 to phase 3.

Prior published guidelines for PVR in this population have relied mostly on single-center retrospective studies with surrogate outcome measures.[39a,127,128] Furthermore, it is unclear whether the emphasis these suggestions place on identifying an RV end-diastolic volume index threshold (usually 150–160 mL/m^2) that optimizes return to normal range after PVR are associated with appreciable clinical benefit. Pastor et al,[129] in a study of 189 young adults with rTOF, noted that mild or moderate RV dilatation after PVR was not associated with adverse clinical outcomes, questioning whether there is undue emphasis on RV end-diastolic volume index in PVR guidelines. More recent guidelines also emphasized RV end-systolic volume index (end-systolic volume index ≥80 mL/m^2), which reflects both RV size and function. However, despite evidence that pre-PVR ventricular dysfunction is associated with adverse outcomes after PVR,[31] several recent guidelines have been vague on thresholds for RV or LV dysfunction that warrant consideration of PVR (Supplemental Table).

Figure 2 proposes a framework for considering PVR in patients with rTOF. This framework is informed by recent evidence from large multicenter cohort studies, including CORRELATE (Comprehensive Outcomes Registry Late After Tetralogy of Fallot Repair),[33] CONCOR (Congenital Corvitia),[28] and INDICATOR (International Multicenter TOF Registry).[13,67,130] A notable addition to the proposed framework is the INDICATOR risk calculator,[13,131] which incorporates patient age at evaluation, obesity (body mass index ≥30 kg/m^2), type of TOF repair, RV end-systolic volume index, and biventricular global function index, a recently described measure incorporating LV and RV volume, mass, and function.[32] The risk prediction utility

Table 4. Factors Potentially Favoring SPVR or TPVR in Patients With RVOT Dysfunction

Factors favoring SPVR	Factors favoring TPVR
Coexisting abnormalities requiring surgical intervention (eg, tricuspid regurgitation, aortic disease, residual shunting)	Isolated RVOT lesion that can be adequately addressed with a transcatheter valve
Arrhythmias that can be addressed surgically	Appropriate RVOT anatomy for implantation of a transcatheter valve
Inability to place adequately sized transcatheter valve because of the anatomy of RVOT or nonfracturable prosthesis	Palliation for pediatric patients requiring frequent interventions
Concerns for coronary compression with transcatheter valve	High surgical risk (eg, severe cardiac dysfunction, multiple prior sternotomies, hazardous surgical reentry, comorbidities)
Presence of pseudoaneurysm	Institutional experience in safely performing transcatheter procedures
Multilevel obstruction not addressable with transcatheter techniques	
Active endocarditis	

RVOT indicates right ventricular outflow tract; SVPR, surgical pulmonary valve replacement; and TPVR, transcatheter pulmonary valve replacement.

Adapted from Stephens et al.[124] Copyright © 2022, with permission from Elsevier.

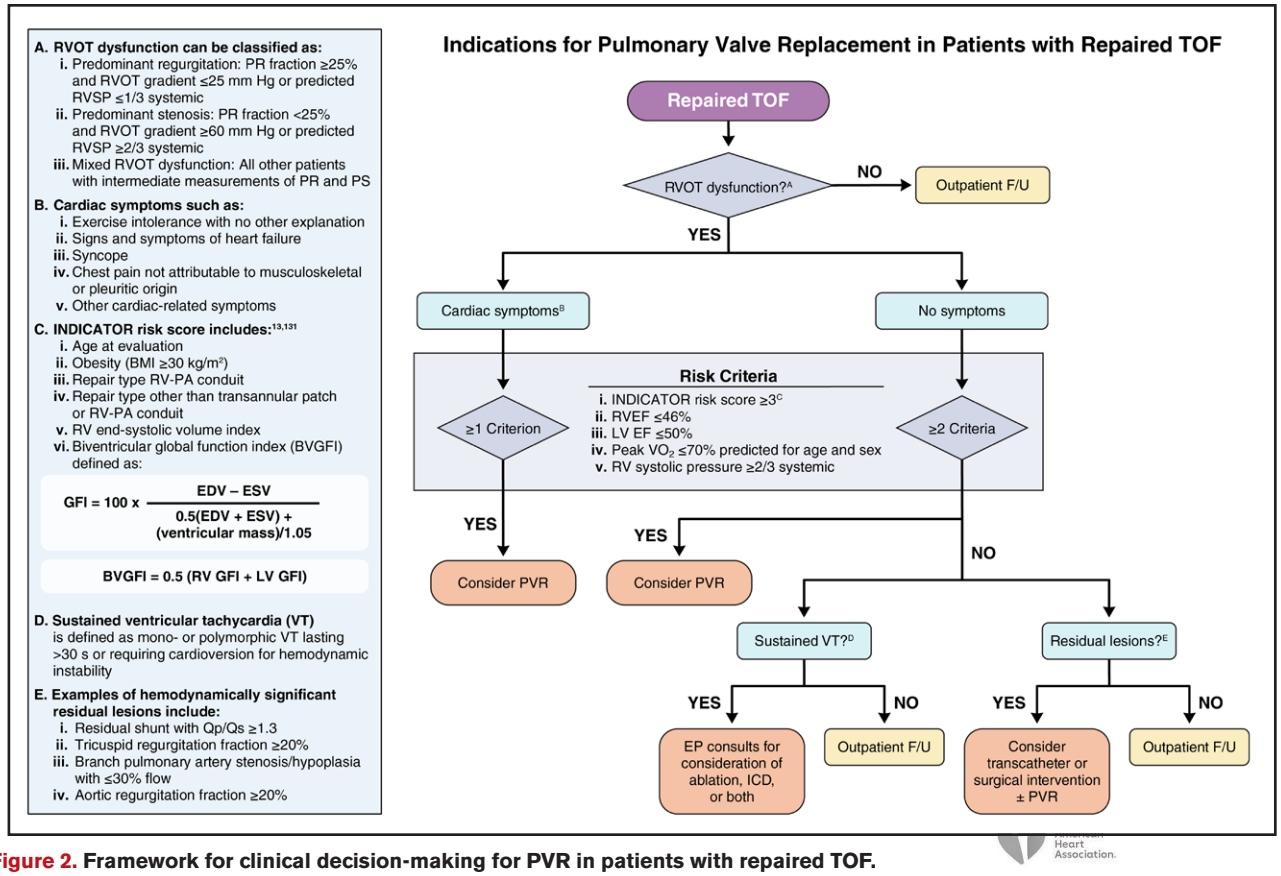

Figure 2. Framework for clinical decision-making for PVR in patients with repaired TOF.
Pressure measurements are by Doppler echocardiography or cardiac catheterization. Volume measurements are by cardiovascular magnetic resonance (CMR) or computed tomography. Flow measurements are by CMR. Peak Vo_2 (oxygen consumption) was obtained by exercise stress test with gas analysis; values are percent expected for age and sex. An online calculator for the INDICATOR risk score is available at https://github.com/rTOF-INDICATOR/Mortality-Risk-Score.[131] BMI indicates body mass index; EDV, end-diastolic volume; EP, electrophysiology; ESV, end-systolic volume; F/U, follow-up; ICD, implantable cardioverter defibrillator; INDICATOR, International Multicenter TOF Registry; LV, left ventricular; LVEF, left ventricular ejection fraction; PA, pulmonary artery; PR, pulmonary regurgitation; PS, pulmonary stenosis; PVR, pulmonary valve replacement; RV, right ventricular; RVEF, right ventricular ejection fraction; RVOT, right ventricular outflow tract; RVSP, right ventricular systolic pressure; and TOF, tetralogy of Fallot.

of the biventricular global function index has been demonstrated in patients with various acquired and congenital heart conditions, including rTOF.[32,132–135] Given that biventricular global function index incorporates RV volumes and mass, these parameters are not listed separately in the proposed framework. Although Mayourian et al[13] identified an INDICATOR risk score ≥4 as optimally discriminating between patients with low risk and those with high risk for 10- and 15-year mortality, the framework in Figure 2 proposes a risk score ≥3 for considering PVR. The rationale for this and other progressive criteria is to identify patients well before transition to pathophysiology phase 3. Last, as with all clinical pathways, this framework will undoubtedly evolve as knowledge expands, new biomarkers are refined, and the longevity of valves used for surgical or TPVR continues to improve.

INDICATIONS FOR REPEAT PVR

TPVR within a previously implanted surgical bioprosthesis, or valve-in-valve TPVR, can be performed successfully with Melody and Sapien balloon-expandable devices. When considering whether to replace a dysfunctional bioprosthesis with a catheter valve or a new surgical valve, we should consider several factors, including the size of the surgical valve and the ability to implant a sufficiently large transcatheter valve, surgical risk, and what each option will confer with respect to future interventions. In some patients, it might be preferable to implant a larger surgical bioprosthesis with the expectation of performing valve-in-valve TPVR when the new surgical valve develops dysfunction, whereas in others, a TPVR would yield a good hemodynamic and procedural result with little downside. In other words, when decisions are being made about TPVR or SPVR for bioprosthetic valve failure, it is critical to have a multidisciplinary approach considering the lifetime management of the patient. However, it is important to recognize that attempts to shift risk earlier or later are only speculative; new valve technologies continue to emerge, and projections about options available in 10 to 20 years in the future may not be accurate.

Guidelines and suggested criteria for intervention in patients with rTOF typically focus on the circumstance of PR, RV volume overload, RVOT obstruction, and RV systolic function. After PVR, whether surgical or transcatheter, dysfunction of the bioprosthesis can involve stenosis, regurgitation, or mixed disease, and criteria for intervention in such situations are not always clear. Among the important mitigating circumstances that can complicate such decisions is declining RV or LV function, and further research is warranted to determine whether the threshold for repeat valve implantation should be more proactive than the initial PVR.

MANAGEMENT OF ARRHYTHMIAS

Supraventricular arrhythmias develop in ≈30% of patients with rTOF and are attributed to anatomic and hemodynamic postoperative sequelae.[136] The most common form is intra-atrial reentrant tachycardia, a consequence of repetitive wavefront propagation through regions of slow conduction.[137] Catheter ablation has emerged as the first-line treatment modality for elimination of intra-atrial reentrant tachycardia among patients with rTOF given the improved outcomes associated with 3-dimensional mapping and irrigated catheter ablation technology in the modern era.[138] Beyond intra-atrial reentrant tachycardia, atrial fibrillation becomes common in the aging TOF population, particularly after the fifth decade of life, in whom catheter-based pulmonary vein isolation is increasingly used. For patients referred for SPVR, concomitant arrhythmia surgery with modified Cox-maze IV procedure with or without ligation of the left atrial appendage is often performed.[139]

Sustained monomorphic VT is the most common form of life-threatening arrhythmia in rTOF, making up between 70% and 86% of ventricular arrhythmia episodes.[44] Histological and endocardial mapping data suggest that adjacent ventricular myocardium in the RVOT undergoes progressive degenerative remodeling in the decades after repair, ultimately establishing the slowly conducting anatomical isthmuses that support reentrant VT.[49,140]

Risk assessment strategies for the primary prevention of sudden cardiac death in patients with rTOF continue to evolve. Currently, calculation relies on a constellation of clinical and imaging biomarkers supplemented by invasive electrophysiology testing when an intermediate risk for sudden cardiac death is suspected.[141] In patients with sustained VT, the 2020 European guidelines suggest invasive electrophysiology testing before PVR (Level of Evidence IIB).[127] Radiofrequency catheter ablation is increasingly used to eliminate VT circuit pathways in these patients.[142,143] Clear documentation of bidirectional block after catheter ablation is essential and can achieve an acceptably low risk of ventricular arrhythmia recurrence.[143] A recent multicenter observational study evaluating the utility of routine pre-PVR invasive electrophysiology testing identified inducible sustained VT in 23% of patients, prompting catheter ablation in 15%, surgical cryoablation during PVR in 3%, and implantable cardioverter defibrillator (ICD) implantation in 8%.[49] Intraoperative cryoablation of VT substrate is an adjunct treatment during SPVR in selected patients.[144] In some patients, pre-PVR invasive electrophysiology testing may inform the choice between SPVR and TPVR.

For patients with rTOF and resuscitated sudden cardiac death or sustained monomorphic VT, ICD placement is indicated.[141] Although highly effective for the prevention of sudden cardiac death, adverse outcomes after ICD placement in patients with rTOF, including device-related infections and inappropriate shocks, negatively affect quality of life.[145] Recently, subcutaneous ICD has been shown to be associated with equivalent defibrillation efficacy and may circumvent many limitations of lead failure and intravascular infection.[146] A major disadvantage, however, is the absence of antitachycardia pacing for monomorphic VT.[147] Therefore, a subcutaneous ICD may be appropriate for patients in whom polymorphic VT or VF constitutes the primary implantation indication.

LONG-TERM SURVEILLANCE

Patients with rTOF require lifelong surveillance to detect preclinical onset of mechanoelectrical cardiomyopathy, prompting consideration of medical, electrophysiologic, catheter-based, or surgical interventions. Surveillance consists of clinical and multimodality testing tailored to patient age and clinical status (Table 3). In general, imaging surveillance in children relies primarily on echocardiography, whereas CMR and exercise testing are suggested beginning at 12 years of age.[148] CMR or computed tomography is indicated in children only when clinical, electrocardiographic/rhythm monitor, and echocardiography are concerning for changes in RV size or function that may warrant catheter-based or surgical intervention such as PVR. Echocardiographic surveillance should use a comprehensive imaging protocol[54] because evidence from routine clinical practice has demonstrated that key diagnostic elements remain underreported or unreported.[149]

Surveillance in adolescents and adults with rTOF encompasses regular clinical evaluations in an adult congenital heart disease clinic along with diagnostic testing tailored to the severity of illness as outlined by the American College of Cardiology/American Heart Association management guidelines for adult congenital heart disease care.[39a] Frequency of testing varies according to age, diagnostic modality, and acuity of illness as designated by physiological stage (A through D) (Table 3).[54] For example, CMR can be considered

every 60 months for stage A, every 24 to 36 months for stage B, every 24 months for stage C, and every ≤12 months for stage D. Several studies have demonstrated that interval deterioration is relatively uncommon in adults,[150,151] with 1 study of 339 patients with rTOF with 849 CMR studies demonstrating that the optimal surveillance frequency for the detection of clinically important disease progression (defined as an increase in RV end-diastolic volume index of ≥30 mL/m^2, RV ejection fraction decline ≥10%, or LV ejection fraction decline ≥10%) was 36 months.[151]

FUTURE RESEARCH

There are many important unanswered questions related to the pathophysiology, management, and outcomes of RVOT dysfunction after TOF repair. The most important future research related to this area should aim to determine how to improve outcomes and prevent harmful consequences of the deleterious pathophysiology in this population. Potential areas of focus include a deeper understanding and early detection of subclinical myocardial disease; methods of identifying or anticipating pathophysiological transformation from reversible to irreversible cardiomyopathy; the development of less invasive and more durable, safe, and effective therapies to eliminate or mitigate the consequences of RVOT dysfunction; and methods of promoting right-sided heart recovery from the accumulated insult of chronic RVOT dysfunction. In particular, additional research is needed to better understand (1) the ideal timing for PVR, including whether there are accessible clinical metrics, imaging biomarkers, or other data (eg, exercise, electrophysiological, serum biomarkers, social determinants of health) corresponding to the progression of adverse remodeling or that can anticipate changes in potential for therapeutic benefit of PVR; (2) patient-related, procedural, or other factors associated with the variable RV geometric and functional response to PR; (3) whether there are medical therapies that can ameliorate or mitigate the adverse impacts of PR, RVOT obstruction, or both; (4) factors associated with and how to mitigate or prevent deterioration of LV function in this population; and (5) whether it is possible to provide better protection at the time of initial repair against the anatomic, electrical, and hemodynamic sequelae of the repair leading to RV and LV deterioration over time (eg, further refinements of the initial TOF repair with development of novel techniques to preserve or restore pulmonary valve function). Additional research will also aid in the (1) development of longer-lasting PVR options (eg, allogenic valve transplantation,[125] improved transcatheter options) and research into risk factors and outcomes of endocarditis complications after TPVR or SPVR; (2) establishment of new prospective multicenter registries to gain new insights into the evolving natural history and pathophysiology of repaired TOF and to inform future interventional trials; and (3) exploration of the potential impact of genetic anomalies on risk stratification and the potential for patient-specific therapies. Of course, there are many other important areas of research related to this population, but these topics offer the potential for some of the highest clinical impact.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on August 20, 2024, and the American Heart Association Executive Committee on September 23, 2024. A copy of the document is available at https://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com

The American Heart Association requests that this document be cited as follows: Geva T, Wald RM, Bucholz E, Cnota JF, McElhinney DB, Mercer-Rosa LM, Mery CM, Miles AL, Moore J; on behalf of the American Heart Association Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Cardiovascular Surgery and Anesthesia; Council on Clinical Cardiology; and Council on Cardiovascular and Stroke Nursing. Long-term management of right ventricular outflow tract dysfunction in repaired tetralogy of Fallot: a scientific statement from the American Heart Association. *Circulation*. 2024;150:e•••–e•••. doi: 10.1161/CIR.0000000000001291

The expert peer review of AHA-commissioned documents (eg, scientific statements, clinical practice guidelines, systematic reviews) is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit https://professional.heart.org/statements. Select the "Guidelines & Statements" drop-down menu, then click "Publication Development."

Acknowledgment

The authors acknowledge and thank Barbara Entl, MD, Science and Medicine Advisor, American Heart Association, and Julie Eisele, Assistant Managing Editor, American Heart Association for their expert assistance with this AHA scientific statement.

Disclosures

Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Tal Geva	Boston Children's Hospital	None	None	None	None	None	None	None
Rachel M. Wald	University of Toronto, Peter Munk Cardiac Centre (Canada)	None	None	None	None	None	None	None
Emily Bucholz	Children's Hospital of Colorado	None	None	None	None	None	None	None
James F. Cnota	Cincinnati Children's Hospital Medical Center Heart Institute	None	None	None	None	None	None	None
Doff B. McElhinney	Stanford University	None	None	None	None	None	Medtronic†	None
Laura M. Mercer-Rosa	Children's Hospital of Philadelphia	None	None	None	None	None	None	None
Carlos M. Mery	University of Texas Dell Medical School/Dell Children's Medical Center	None	None	None	None	None	None	None
Andrea Leann Miles	Children Mercy Hospital Ward Family Heart Center	None	None	None	None	None	None	None
Jeremy Moore	UCLA Medical Center	None	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Emile Bacha	New York Presbyterian Hospital–Columbia University College of Physicians and Surgeons	None	None	None	None	None	None	None
Natasja M.S. de Groot	Erasmus Medical Center (Netherlands)	None	None	None	None	None	None	None
Pirooz Eghtesady	Washington University School of Medicine	None	None	None	None	None	None	None
Kenan W.D. Stern	Mount Sinai Children's Heart Center	None	None	None	None	None	None	None
Emanuela R. Valsangiacomo Buechel	University Children's Hospital Zurich (Switzerland)	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

REFERENCES

1. Smith CA, McCracken C, Thomas AS, Spector LG, St Louis JD, Oster ME, Moller JH, Kochilas L. Long-term outcomes of tetralogy of Fallot: a study from the Pediatric Cardiac Care Consortium. *JAMA Cardiol*. 2019;4:34–41. doi: 10.1001/jamacardio.2018.4255
2. Cuypers JA, Menting ME, Konings EE, Opic P, Utens EM, Helbing WA, Witsenburg M, van den Bosch AE, Ouhlous M, van Domburg RT, et al. Unnatural history of tetralogy of Fallot: prospective follow-up of 40 years after surgical correction. *Circulation*. 2014;130:1944–1953. doi: 10.1161/CIRCULATIONAHA.114.009454
3. Mongeon FP, Ben Ali W, Khairy P, Bouhout I, Therrien J, Wald RM, Dallaire F, Bernier PL, Poirier N, Dore A, et al. Pulmonary valve replacement for pulmonary regurgitation in adults with tetralogy of Fallot: a meta-analysis: a report for the Writing Committee of the 2019 Update of the Canadian Cardiovascular Society Guidelines for the Management of Adults With Congenital Heart Disease. *Can J Cardiol*. 2019;35:1772–1783. doi: 10.1016/j.cjca.2019.08.031
4. Tretter JT, Friedberg MK, Wald RM, McElhinney DB. Defining and refining indications for transcatheter pulmonary valve replacement in patients with repaired tetralogy of Fallot: contributions from anatomical and functional imaging. *Int J Cardiol*. 2016;221:916–925. doi: 10.1016/j.ijcard.2016.07.120
5. Geva T. Indications for pulmonary valve replacement in repaired tetralogy of Fallot: the quest continues. *Circulation*. 2013;128:1855–1857. doi: 10.1161/CIRCULATIONAHA.113.005878
6. American Heart Association. Guideline and statement development. Accessed September 1, 2021. https://professional.heart.org/en/guidelines-and-statements/policies-development
7. van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, Roos-Hesselink JW. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2011;58:2241–2247. doi: 10.1016/j.jacc.2011.08.025

8. Villafane J, Feinstein JA, Jenkins KJ, Vincent RN, Walsh EP, Dubin AM, Geva T, Towbin JA, Cohen MS, Fraser C, et al; Adult Congenital and Pediatric Cardiology Section, American College of Cardiology. Hot topics in tetralogy of Fallot. *J Am Coll Cardiol*. 2013;62:2155–2166. doi: 10.1016/j.jacc.2013.07.100
9. Jenkins KJ, Correa A, Feinstein JA, Botto L, Britt AE, Daniels SR, Elixson M, Warnes CA, Webb CL; American Heart Association Council on Cardiovascular Disease in the Young. Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young. *Circulation*. 2007;115:2995–3014. doi: 10.1161/CIRCULATIONAHA.106.183216
10. Quartermain MD, Pasquali SK, Hill KD, Goldberg DJ, Huhta JC, Jacobs JP, Jacobs ML, Kim S, Ungerleider RM. Variation in prenatal diagnosis of congenital heart disease in infants. *Pediatrics*. 2015;136:e378–e385. doi: 10.1542/peds.2014-3783
11. Miller JR, Stephens EH, Goldstone AB, Glatz AC, Kane L, Van Arsdell GS, Stellin G, Barron DJ, d'Udekem Y, Benson L, et al; Expert Consensus Panel:. The American Association for Thoracic Surgery (AATS) 2022 expert consensus document: management of infants and neonates with tetralogy of Fallot. *J Thorac Cardiovasc Surg*. 2023;165:221–250. doi: 10.1016/j.jtcvs.2022.07.025
12. Geva T. Repaired tetralogy of Fallot: the roles of cardiovascular magnetic resonance in evaluating pathophysiology and for pulmonary valve replacement decision support. *J Cardiovasc Magn Reson*. 2011;13:9. doi: 10.1186/1532-429X-13-9
13. Mayourian J, Sleeper LA, Lee J, Lu M, Geva A, Mulder B, Babu-Narayan SV, Wald RM, Sompolinsky T, Valente AM, et al. Development and validation of a mortality risk score for repaired tetralogy of Fallot. *J Am Heart Assoc*. 2024;13:e034871. doi: 10.1161/JAHA.123.034871
14. Kilner PJ, Balossino R, Dubini G, Babu-Narayan SV, Taylor AM, Pennati G, Migliavacca F. Pulmonary regurgitation: the effects of varying pulmonary artery compliance, and of increased resistance proximal or distal to the compliance. *Int J Cardiol*. 2009;133:157–166. doi: 10.1016/j.ijcard.2008.06.078
15. Kuehne T, Saeed M, Gleason K, Turner D, Teitel D, Higgins CB, Moore P. Effects of pulmonary insufficiency on biventricular function in the developing heart of growing swine. *Circulation*. 2003;108:2007–2013. doi: 10.1161/01.CIR.0000092887.84425.09
16. Alipour Symakani RS, van Genuchten WJ, Zandbergen LM, Henry S, Taverne Y, Merkus D, Helbing WA, Bartelds B. The right ventricle in tetralogy of Fallot: adaptation to sequential loading. *Front Pediatr*. 2023;11:1098248. doi: 10.3389/fped.2023.1098248
17. Sjoberg P, Toger J, Hedstrom E, Arvidsson P, Heiberg E, Arheden H, Gustafsson R, Nozohoor S, Carlsson M. Altered biventricular hemodynamic forces in patients with repaired tetralogy of Fallot and right ventricular volume overload because of pulmonary regurgitation. *Am J Physiol Heart Circ Physiol*. 2018;315:H1691–H1702. doi: 10.1152/ajpheart.00330.2018
18. Bekeredjian R, Grayburn PA. Valvular heart disease: aortic regurgitation. *Circulation*. 2005;112:125–134. doi: 10.1161/CIRCULATIONAHA.104.488825
19. Tornos MP, Olona M, Permanyer-Miralda G, Evangelista A, Candell J, Padilla F, Soler J. Heart failure after aortic valve replacement for aortic regurgitation: prospective 20-year study. *Am Heart J*. 1998;136:681–687. doi: 10.1016/s0002-8703(98)70016-x
20. Tverskaya MS, Mishnev OD, Raksha AP, Karpova VV, Sukhoparova VV, Izmailova NS, Virganskii AO, Kadyrova M, Abdulkerimova NZ. Comparative pathomorphological study of contractile myocardium under conditions of increased left and right ventricular afterload. *Bull Exp Biol Med*. 2004;138:616–620. doi: 10.1007/s10517-005-0140-6
21. Dragulescu A, Friedberg MK. A tale of two ventricles: ventricular-ventricular interactions and LV dysfunction after surgical repair of tetralogy of Fallot. *Eur Heart J Cardiovasc Imaging*. 2014;15:498–499. doi: 10.1093/ehjci/jet260
22. Davlouros PA, Kilner PJ, Hornung TS, Li W, Francis JM, Moon JC, Smith GC, Tat T, Pennell DJ, Gatzoulis MA. right ventricular function in adults with repaired tetralogy of Fallot assessed with cardiovascular magnetic resonance imaging: detrimental role of right ventricular outflow aneurysms or akinesia and adverse right-to-left ventricular interaction. *J Am Coll Cardiol*. 2002;40:2044–2052. doi: 10.1016/s0735-1097(02)02566-4
23. Wald RM, Haber I, Wald R, Valente AM, Powell AJ, Geva T. Effects of regional dysfunction and late gadolinium enhancement on global right ventricular function and exercise capacity in patients with repaired tetralogy of Fallot. *Circulation*. 2009;119:1370–1377. doi: 10.1161/CIRCULATIONAHA.108.816546
24. Ortega M, Triedman JK, Geva T, Harrild DM. Relation of left ventricular dyssynchrony measured by cardiac magnetic resonance tissue tracking in repaired tetralogy of Fallot to ventricular tachycardia and death. *Am J Cardiol*. 2011;107:1535–1540. doi: 10.1016/j.amjcard.2011.01.032
25. Tzemos N, Harris L, Carasso S, Subira LD, Greutmann M, Provost Y, Redington AN, Rakowski H, Siu SC, Silversides CK. Adverse left ventricular mechanics in adults with repaired tetralogy of Fallot. *Am J Cardiol*. 2009;103:420–425. doi: 10.1016/j.amjcard.2008.09.101
26. Miyake M, Abe R, Matsutani H, Sakamoto J, Kondo H, Iwakura A, Doi H, Tamura T. Relationship between right and left ventricular diastolic dysfunction assessed by 2-dimensional speckle-tracking echocardiography in adults with repaired tetralogy of Fallot. *Int J Cardiovasc Imaging*. 2021;37:569–576. doi: 10.1007/s10554-020-02045-7
27. Ghonim S, Gatzoulis MA, Ernst S, Li W, Moon JC, Smith GC, Heng EL, Keegan J, Ho SY, McCarthy KP, et al. Predicting survival in repaired tetralogy of Fallot: a lesion-specific and personalized approach. *JACC Cardiovasc Imaging*. 2022;15:257–268. doi: 10.1016/j.jcmg.2021.07.026
28. Bokma JP, de Wilde KC, Vliegen HW, van Dijk AP, van Melle JP, Meijboom FJ, Zwinderman AH, Groenink M, Mulder BJM, Bouma BJ. Value of cardiovascular magnetic resonance imaging in noninvasive risk stratification in tetralogy of Fallot. *JAMA Cardiol*. 2017;2:678–683. doi: 10.1001/jamacardio.2016.5818
29. Atallah J, Gonzalez Corcia MC, Walsh EP; Participating Members of the Pediatric and Congenital Electrophysiology Society. Ventricular arrhythmia and life-threatening events in patients with repaired tetralogy of fallot. *Am J Cardiol*. 2020;132:126–132. doi: 10.1016/j.amjcard.2020.07.012
30. Deleted in proof
31. Geva T, Mulder B, Gauvreau K, Babu-Narayan SV, Wald RM, Hickey K, Powell AJ, Gatzoulis MA, Valente AM. Preoperative predictors of death and sustained ventricular tachycardia after pulmonary valve replacement in patients with repaired tetralogy of Fallot enrolled in the INDICATOR cohort. *Circulation*. 2018;138:2106–2115. doi: 10.1161/CIRCULATIONAHA.118.034740
32. Alsaied T, Geva T, Graf JA, Sleeper LA, Marie Valente A. Biventricular global function index is associated with adverse outcomes in repaired tetralogy of Fallot. *Circ Cardiovasc Imaging*. 2021;14:e012519. doi: 10.1161/CIRCIMAGING.121.012519
33. Kovacs AH, Lebovic G, Raptis S, Blais S, Caldarone CA, Dahdah N, Dallaire F, Drolet C, Grewal J, Hancock Friesen CL, et al. Patient-reported outcomes after tetralogy of Fallot repair. *J Am Coll Cardiol*. 2023;81:1937–1950. doi: 10.1016/j.jacc.2023.03.385
34. Valente AM, Gauvreau K, Assenza GE, Babu-Narayan SV, Schreier J, Gatzoulis MA, Groenink M, Inuzuka R, Kilner PJ, Koyak Z, et al. Contemporary predictors of death and sustained ventricular tachycardia in patients with repaired tetralogy of Fallot enrolled in the INDICATOR cohort. *Heart*. 2014;100:247–253. doi: 10.1136/heartjnl-2013-304958
35. Orwat S, Diller GP, Kempny A, Radke R, Peters B, Kuhne T, Boethig D, Gutberlet M, Dubowy KO, Beerbaum P, et al; German Competence Network for Congenital Heart Defects Investigators. Myocardial deformation parameters predict outcome in patients with repaired tetralogy of Fallot. *Heart*. 2016;102:209–215. doi: 10.1136/heartjnl-2015-308569
36. Chen CA, Dusenbery SM, Valente AM, Powell AJ, Geva T. Myocardial ECV fraction assessed by CMR is associated with type of hemodynamic load and arrhythmia in repaired tetralogy of Fallot. *JACC Cardiovasc Imaging*. 2016;9:1–10. doi: 10.1016/j.jcmg.2015.09.011
37. Jadli AS, Parasor A, Gomes KP, Shandilya R, Patel VB. Exosomes in cardiovascular diseases: pathological potential of nano-messenger. *Front Cardiovasc Med*. 2021;8:767488. doi: 10.3389/fcvm.2021.767488
38. Sengupta A, Gauvreau K, Bucholz EM, Newburger JW, Del Nido PJ, Nathan M. Contemporary socioeconomic and childhood opportunity disparities in congenital heart surgery. *Circulation*. 2022;146:1284–1296. doi: 10.1161/CIRCULATIONAHA.122.060030
39. Siontis KC, Noseworthy PA, Attia ZI, Friedman PA. Artificial intelligence-enhanced electrocardiography in cardiovascular disease management. *Nat Rev Cardiol*. 2021;18:465–478. doi: 10.1038/s41569-020-00503-2

39a. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in *Circulation*. 2019;139:e833–e834]. *Circulation*. 2019;139:e698–e800. doi: 10.1161/CIR.0000000000000603

40. Khairy P, Aboulhosn J, Gurvitz MZ, Opotowsky AR, Mongeon FP, Kay J, Valente AM, Earing MG, Lui G, Gersony DR, et al; Alliance for Adult Research in Congenital Cardiology (AARCC). Arrhythmia burden in adults with surgically repaired tetralogy of Fallot: a multi-institutional study. *Circulation*. 2010;122:868–875. doi: 10.1161/CIRCULATIONAHA.109.928481

41. Possner M, Tseng SY, Alahdab F, Bokma JP, Lubert AM, Khairy P, Murad MH, Ben Ali W, Prokop LJ, Czosek RJ, et al. Risk factors for mortality and ventricular tachycardia in patients with repaired tetralogy of Fallot: a systematic review and meta-analysis. *Can J Cardiol*. 2020;36:1815–1825. doi: 10.1016/j.cjca.2020.01.023
42. Gatzoulis MA, Balaji S, Webber SA, Siu SC, Hokanson JS, Poile C, Rosenthal M, Nakazawa M, Moller JH, Gillette PC, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. *Lancet*. 2000;356:975–981. doi: 10.1016/S0140-6736(00)02714-8
43. Deleted in proof
44. Mouws E, Roos-Hesselink JW, Bogers A, de Groot NMS. Coexistence of tachyarrhythmias in patients with tetralogy of Fallot. *Heart Rhythm*. 2018;15:503–511. doi: 10.1016/j.hrthm.2017.11.021
45. Moore JP, Shannon KM, Khairy P, Waldmann V, Bessiere F, Burrows A, Su J, Shivkumar K. Sinus rhythm QRS morphology reflects right ventricular activation and anatomical ventricular tachycardia isthmus conduction in repaired tetralogy of Fallot. *Heart Rhythm*. 2023;20:1689–1696. doi: 10.1016/j.hrthm.2023.08.020
46. Kimura Y, Fukuda K, Nakano M, Hasebe Y, Fukasawa K, Chiba T, Miki K, Tatebe S, Miyata S, Ota H, et al. Prognostic significance of PR interval prolongation in adult patients with total correction of tetralogy of Fallot. *Circ Arrhythm Electrophysiol*. 2018;11:e006234. doi: 10.1161/CIRCEP.118.006234
47. Koyak Z, Harris L, de Groot JR, Silversides CK, Oechslin EN, Bouma BJ, Budts W, Zwinderman AH, Van Gelder IC, Mulder BJ. Sudden cardiac death in adult congenital heart disease. *Circulation*. 2012;126:1944–1954. doi: 10.1161/CIRCULATIONAHA.112.104786
48. Krieger EV, Zeppenfeld K, DeWitt ES, Duarte VE, Egbe AC, Haeffele C, Lin KY, Robinson MR, Sillman C, Upadhyay S; on behalf of the American Heart Association Adults With Congenital Heart Disease Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young and Council on Clinical Cardiology. Arrhythmias in repaired tetralogy of Fallot: a scientific statement from the American Heart Association. *Circ Arrhythm Electrophysiol*. 2022;15:e000084. doi: 10.1161/HAE.0000000000000084
49. Waldmann V, Bessiere F, Gardey K, Bakloul M, Belli E, Bonnet D, Chaussade AS, Cohen S, Delasnerie H, Dib N, et al. Systematic electrophysiological study prior to pulmonary valve replacement in tetralogy of Fallot: a prospective multicenter study. *Circ Arrhythm Electrophysiol*. 2023;16:e011745. doi: 10.1161/CIRCEP.122.011745
50. Powell AW, Mays WA, Knecht SK, Chin C. Pulmonary effects on exercise testing in tetralogy of Fallot patients repaired with a transannular patch. *Cardiol Young*. 2019;29:133–139. doi: 10.1017/S1047951118001920
51. Goldmuntz E, Cassedy A, Mercer-Rosa L, Fogel MA, Paridon SM, Marino BS. Exercise performance and 22q11.2 deletion status affect quality of life in tetralogy of Fallot. *J Pediatr*. 2017;189:162–168. doi: 10.1016/j.jpeds.2017.06.049
52. Takken T, Giardini A, Reybrouck T, Gewillig M, Hovels-Gurich HH, Longmuir PE, McCrindle BW, Paridon SM, Hager A. Recommendations for physical activity, recreation sport, and exercise training in paediatric patients with congenital heart disease: a report from the Exercise, Basic & Translational Research Section of the European Association of Cardiovascular Prevention and Rehabilitation, the European Congenital Heart and Lung Exercise Group, and the Association for European Paediatric Cardiology. *Eur J Prev Cardiol*. 2012;19:1034–1065. doi: 10.1177/1741826711420000
53. Schuermans A, Boerma M, Sansoni GA, Van den Eynde J, Takkenberg JJM, Helbing WA, Geva T, Moons P, Van De Bruaene A, Budts W. Exercise in patients with repaired tetralogy of Fallot: a systematic review and meta-analysis. *Heart*. 2023;109:984–991. doi: 10.1136/heartjnl-2022-321850
54. Valente AM, Cook S, Festa P, Ko HH, Krishnamurthy R, Taylor AM, Warnes CA, Kreutzer J, Geva T. Multimodality imaging guidelines for patients with repaired tetralogy of Fallot: a report from the American Society of Echocardiography: developed in collaboration with the Society for Cardiovascular Magnetic Resonance and the Society for Pediatric Radiology. *J Am Soc Echocardiogr*. 2014;27:111–141. doi: 10.1016/j.echo.2013.11.009
55. Fujiwara J, Tatebe S, Nochioka K, Ota H, Funamizu Y, Miki T, Saiki Y, Yasuda S, Saijo Y. Usefulness of right ventricular free wall strain obtained with two-dimensional speckle-tracking echocardiography in patients with repaired tetralogy of Fallot and pulmonary regurgitation. *Tohoku J Exp Med*. 2022;257:7–15. doi: 10.1620/tjem.2022.J011
56. Carluccio E, Biagioli P, Lauciello R, Zuchi C, Mengoni A, Bardelli G, Alunni G, Gronda EG, Ambrosio G. Superior prognostic value of right ventricular free wall compared to global longitudinal strain in patients with heart failure. *J Am Soc Echocardiogr*. 2019;32:836–844.e1. doi: 10.1016/j.echo.2019.02.011
57. Scherptong RW, Mollema SA, Blom NA, Kroft LJ, de Roos A, Vliegen HW, van der Wall EE, Bax JJ, Holman ER. Right ventricular peak systolic longitudinal strain is a sensitive marker for right ventricular deterioration in adult patients with tetralogy of Fallot. *Int J Cardiovasc Imaging*. 2009;25:669–676. doi: 10.1007/s10554-009-9477-7
58. Arroyo-Rodriguez C, Fritche-Salazar JF, Posada-Martinez EL, Arias-Godinez JA, Ortiz-Leon XA, Calvillo-Arguelles O, Ruiz-Esparza ME, Sandoval JP, Sierra-Lara D, Araiza-Garaygordobil D, et al. Right ventricular free wall strain predicts functional capacity in patients with repaired tetralogy of Fallot. *Int J Cardiovasc Imaging*. 2020;36:595–604. doi: 10.1007/s10554-019-01753-z
59. Geva T. Is MRI the preferred method for evaluating right ventricular size and function in patients with congenital heart disease? MRI is the preferred method for evaluating right ventricular size and function in patients with congenital heart disease. *Circ Cardiovasc Imaging*. 2014;7:190–197. doi: 10.1161/CIRCIMAGING.113.000553
60. Fratz S, Chung T, Greil GF, Samyn MM, Taylor AM, Valsangiacomo Buechel ER, Yoo SJ, Powell AJ. Guidelines and protocols for cardiovascular magnetic resonance in children and adults with congenital heart disease: SCMR expert consensus group on congenital heart disease. *J Cardiovasc Magn Reson*. 2013;15:51. doi: 10.1186/1532-429X-15-51
61. Caresia-Aroztegui AP, Aguade-Bruix S, Castell-Conesa J, Pifarre-Montaner P, Cuberas-Borros G, Casaldaliga J, Girona J, Romero-Farina G, Candell-Riera J. Gated-SPECT equilibrium radionuclide angiography in right ventricular assessment of patients with repaired tetralogy of Fallot. *Nucl Med Commun*. 2007;28:159–164. doi: 10.1097/MNM.0b013e328013ebb1
62. Wu MT, Huang YL, Hsieh KS, Huang JT, Peng NJ, Pan JY, Huang JS, Yang TL. Influence of pulmonary regurgitation inequality on differential perfusion of the lungs in tetralogy of Fallot after repair: a phase-contrast magnetic resonance imaging and perfusion scintigraphy study. *J Am Coll Cardiol*. 2007;49:1880–1886. doi: 10.1016/j.jacc.2007.01.077
63. Cusimano RJ, Guest C. Coronary artery disease following repair of tetralogy of Fallot: implications and management. *Can J Cardiol*. 1996;12:172–174.
64. Morray BH, McElhinney DB, Cheatham JP, Zahn EM, Berman DP, Sullivan PM, Lock JE, Jones TK. Risk of coronary artery compression among patients referred for transcatheter pulmonary valve implantation: a multicenter experience. *Circ Cardiovasc Interv*. 2013;6:535–542. doi: 10.1161/CIRCINTERVENTIONS.113.000202
65. Therrien J, Marx GR, Gatzoulis MA. Late problems in tetralogy of Fallot: recognition, management, and prevention. *Cardiol Clin*. 2002;20:395–404. doi: 10.1016/s0733-8651(02)00010-3
66. Knauth AL, Gauvreau K, Powell AJ, Landzberg MJ, Walsh EP, Lock JE, del Nido PJ, Geva T. Ventricular size and function assessed by cardiac MRI predict major adverse clinical outcomes late after tetralogy of Fallot repair. *Heart*. 2008;94:211–216. doi: 10.1136/hrt.2006.104745
67. Bokma JP, Geva T, Sleeper LA, Lee JH, Lu M, Sompolinsky T, Babu-Narayan SV, Wald RM, Mulder BJM, Valente AM. Improved outcomes after pulmonary valve replacement in repaired tetralogy of Fallot. *J Am Coll Cardiol*. 2023;81:2075–2085. doi: 10.1016/j.jacc.2023.02.052
68. Adamson GT, McElhinney DB, Lui G, Meadows AK, Rigdon J, Hanley FL, Maskatia SA. Secondary repair of incompetent pulmonary valves after previous surgery or intervention: patient selection and outcomes. *J Thorac Cardiovasc Surg*. 2020;159:2383–2392.e2. doi: 10.1016/j.jtcvs.2019.06.110
69. Buechel ER, Dave HH, Kellenberger CJ, Dodge-Khatami A, Pretre R, Berger F, Bauersfeld U. 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;26:2721–2727. doi: 10.1093/eurheartj/ehi581
70. Ferraz Cavalcanti PE, Sa MP, Santos CA, Esmeraldo IM, de Escobar RR, de Menezes AM, de Azevedo OM Jr, de Vasconcelos Silva FP, Lins RF, de Carvalho Lima R. Pulmonary valve replacement after operative repair of tetralogy of Fallot: meta-analysis and meta-regression of 3,118 patients from 48 studies. *J Am Coll Cardiol*. 2013;62:2227–2243. doi: 10.1016/j.jacc.2013.04.107
71. Geva T, Gauvreau K, Powell AJ, Cecchin F, Rhodes J, Geva J, del Nido P. Randomized trial of pulmonary valve replacement with and without right ventricular remodeling surgery. *Circulation*. 2010;122:S201–S208. doi: 10.1161/CIRCULATIONAHA.110.951178
72. van Straten A, Vliegen HW, Lamb HJ, Roes SD, van der Wall EE, Hazekamp MG, de Roos A. Time course of diastolic and systolic function improvement after pulmonary valve replacement in adult patients with tetralogy of Fallot. *J Am Coll Cardiol*. 2005;46:1559–1564. doi: 10.1016/j.jacc.2005.07.030
73. Frigiola A, Tsang V, Bull C, Coats L, Khambadkone S, Derrick G, Mist B, Walker F, van Doorn C, Bonhoeffer P, et al. Biventricular response after pulmonary valve replacement for right ventricular outflow tract dysfunction: is age a predictor of outcome? *Circulation*. 2008;118:S182–S190. doi: 10.1161/CIRCULATIONAHA.107.756825

74. Sabate Rotes A, Johnson JN, Burkhart HM, Eidem BW, Allison TG, Driscoll DJ. Cardiorespiratory response to exercise before and after pulmonary valve replacement in patients with repaired tetralogy of Fallot: a retrospective study and systematic review of the literature. *Congenit Heart Dis*. 2015;10:263–270. doi: 10.1111/chd.12207
75. Lurz P, Giardini A, Taylor AM, Nordmeyer J, Muthurangu V, Odendaal D, Mist B, Khambadkone S, Schievano S, Bonhoeffer P, et al. Effect of altering pathologic right ventricular loading conditions by percutaneous pulmonary valve implantation on exercise capacity. *Am J Cardiol*. 2010;105:721–726. doi: 10.1016/j.amjcard.2009.10.054
76. Therrien J, Siu SC, Harris L, Dore A, Niwa K, Janousek J, Williams WG, Webb G, Gatzoulis MA. Impact of pulmonary valve replacement on arrhythmia propensity late after repair of tetralogy of Fallot. *Circulation*. 2001;103:2489–2494. doi: 10.1161/01.cir.103.20.2489
77. Harrild DM, Berul CI, Cecchin F, Geva T, Gauvreau K, Pigula F, Walsh EP. Pulmonary valve replacement in tetralogy of Fallot: impact on survival and ventricular tachycardia. *Circulation*. 2009;119:445–451. doi: 10.1161/CIRCULATIONAHA.108.775221
78. Gengsakul A, Harris L, Bradley TJ, Webb GD, Williams WG, Siu SC, Merchant N, McCrindle BW. The impact of pulmonary valve replacement after tetralogy of Fallot repair: a matched comparison. *Eur J Cardiothorac Surg*. 2007;32:462–468. doi: 10.1016/j.ejcts.2007.06.009
79. Oosterhof T, van Straten A, Vliegen HW, Meijboom FJ, van Dijk AP, Spijkerboer AM, Bouma BJ, Zwinderman AH, Hazekamp MG, de Roos A, et al. Preoperative thresholds for pulmonary valve replacement in patients with corrected tetralogy of Fallot using cardiovascular magnetic resonance. *Circulation*. 2007;116:545–551. doi: 10.1161/CIRCULATIONAHA.106.659664
80. Therrien J, Provost Y, Merchant N, Williams W, Colman J, Webb G. Optimal timing for pulmonary valve replacement in adults after tetralogy of Fallot repair. *Am J Cardiol*. 2005;95:779–782. doi: 10.1016/j.amjcard.2004.11.037
81. Therrien J, Siu SC, McLaughlin PR, Liu PP, Williams WG, Webb GD. Pulmonary valve replacement in adults late after repair of tetralogy of Fallot: are we operating too late? *J Am Coll Cardiol*. 2000;36:1670–1675. doi: 10.1016/s0735-1097(00)00930-x
82. Bokma JP, Geva T, Sleeper LA, Babu Narayan SV, Wald R, Hickey K, Jansen K, Wassall R, Lu M, Gatzoulis MA, et al. A propensity score-adjusted analysis of clinical outcomes after pulmonary valve replacement in tetralogy of Fallot. *Heart*. 2018;104:738–744. doi: 10.1136/heartjnl-2017-312048
83. Deleted in proof
84. McKenzie ED, Khan MS, Dietzman TW, Guzmán-Pruneda FA, Samayoa AX, Liou A, Heinle JS, Fraser CD. Surgical pulmonary valve replacement: a benchmark for outcomes comparisons. *J Thorac Cardiovasc Surg*. 2014;148:1450–1453. doi: 10.1016/j.jtcvs.2014.02.060
85. Egbe AC, Connolly HM, Miranda WR, Dearani JA, Schaff HV. Outcomes of bioprosthetic valves in the pulmonary position in adults with congenital heart disease. *Ann Thorac Surg*. 2019;108:1410–1415. doi: 10.1016/j.athoracsur.2019.05.068
86. Dos L, Dadashev A, Tanous D, Ferreira-González IJ, Haberer K, Siu SC, Van Arsdell GS, Oechslin EN, Williams WG, Silversides CK. Pulmonary valve replacement in repaired tetralogy of Fallot: determinants of early postoperative adverse outcomes. *J Thorac Cardiovasc Surg*. 2009;138:553–559. doi: 10.1016/j.jtcvs.2009.02.042
87. Khanna AD, Hill KD, Pasquali SK, Wallace AS, Masoudi FA, Jacobs ML, Jacobs JP, Karamlou T. Benchmark outcomes for pulmonary valve replacement using the Society of Thoracic Surgeons databases. *Ann Thorac Surg*. 2015;100:138–145. doi: 10.1016/j.athoracsur.2015.03.025
88. Van den Eynde J, Sá MPBO, Vervoort D, Roever L, Meyns B, Budts W, Gewillig M, Ruhparwar A, Zhigalov K, Weymann A. Pulmonary valve replacement in tetralogy of Fallot: an updated meta-analysis. *Ann Thorac Surg*. 2022;113:1036–1046. doi: 10.1016/j.athoracsur.2020.11.040
89. Dorobantu DM, Sharabiani MTA, Taliotis D, Parry AJ, Tulloh RMR, Bentham JR, Caputo M, van Doorn C, Stoica SC. Age over 35 years is associated with increased mortality after pulmonary valve replacement in repaired tetralogy of Fallot: results from the UK National Congenital Heart Disease Audit database. *Eur J Cardiothorac Surg*. 2020;58:825–831. doi: 10.1093/ejcts/ezaa069
90. Larsen SH, Dimopoulos K, Gatzoulis MA, Uebing A, Shore DF, Alonso-Gonzalez R, Kempny A. Surgical and percutaneous pulmonary valve replacement in England over the past two decades. *Heart*. 2019;105:932–937. doi: 10.1136/heartjnl-2018-314102
91. Patel PM, Zapata D, Qu W, Callahan M, Rao N, Kelleman M, Kanter KR, Chai PJ, Shaw FR, Shashidharan S, et al. Bioprosthetic pulmonary valve dysfunction in congenital heart disease. *Ann Thorac Surg*. 2022;115:641–648. doi: 10.1016/j.athoracsur.2021.12.025
92. Lee C, Park CS, Lee C-H, Kwak JG, Kim S-J, Shim W-S, Song JY, Choi EY, Lee SY. Durability of bioprosthetic valves in the pulmonary position: long-term follow-up of 181 implants in patients with congenital heart disease. *J Thorac Cardiovasc Surg*. 2011;142:351–358. doi: 10.1016/j.jtcvs.2010.12.020
93. Babu-Narayan SV, Diller G-P, Gheta RR, Bastin AJ, Karonis T, Li W, Pennell DJ, Uemura H, Sethia B, Gatzoulis MA, et al. Clinical outcomes of surgical pulmonary valve replacement after repair of tetralogy of Fallot and potential prognostic value of preoperative cardiopulmonary exercise testing. *Circulation*. 2014;129:18–27. doi: 10.1161/CIRCULATIONAHA.113.001485
94. Baird CW, Chavez M, Sleeper LA, Borisuk MJ, Bacha EA, Burchill L, Guleserian K, Ilbawi M, Nguyen K, Razzouk A, et al. Reintervention rates after bioprosthetic pulmonary valve replacement in patients younger than 30 years of age: a multicenter analysis. *J Thorac Cardiovasc Surg*. 2021;161:345–362.e2. doi: 10.1016/j.jtcvs.2020.06.157
95. Deleted in proof
96. Bokma JP, Winter MM, Oosterhof T, Vliegen HW, van Dijk AP, Hazekamp MG, Koolbergen DR, Groenink M, Mulder BJM, Bouma BJ. Individualised prediction of pulmonary homograft durability in tetralogy of Fallot. *Heart*. 2015;101:1717–1723. doi: 10.1136/heartjnl-2015-307754
97. Jang W, Kim YJ, Choi K, Lim HG, Kim WH, Lee JR. Mid-term results of bioprosthetic pulmonary valve replacement in pulmonary regurgitation after tetralogy of Fallot repair. *Eur J Cardiothorac Surg*. 2012;42:e1–e8. doi: 10.1093/ejcts/ezs219
98. Mery CM, Guzmán-Pruneda FA, De León LE, Zhang W, Terwelp MD, Bocchini CE, Adachi I, Heinle JS, McKenzie ED, Fraser CD. Risk factors for development of endocarditis and reintervention in patients undergoing right ventricle to pulmonary artery valved conduit placement. *J Thorac Cardiovasc Surg*. 2016;151:432–439, 441.e1. doi: 10.1016/j.jtcvs.2015.10.069
99. Stulak JM, Mora BN, Said SM, Schaff HV, Dearani JA. Mechanical pulmonary valve replacement. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2016;19:82–89. doi: 10.1053/j.pcsu.2015.12.003
100. McElhinney DB, Zhang Y, Levi DS, Georgiev S, Biernacka EK, Goldstein BH, Shahanavaz S, Qureshi AM, Cabalka AK, Bauser-Heaton H, et al. Reintervention and survival after transcatheter pulmonary valve replacement. *J Am Coll Cardiol*. 2022;79:18–32. doi: 10.1016/j.jacc.2021.10.031
101. Jones TK, McElhinney DB, Vincent JA, Hellenbrand WE, Cheatham JP, Berman DP, Zahn EM, Khan DM, Rhodes JF Jr, Weng S, et al. Long-term outcomes after Melody transcatheter pulmonary valve replacement in the US Investigational Device Exemption Trial. *Circ Cardiovasc Interv*. 2022;15:e010852. doi: 10.1161/CIRCINTERVENTIONS.121.010852
102. Shahanavaz S, Zahn EM, Levi DS, Aboulhousn JA, Hascoet S, Qureshi AM, Porras D, Morgan GJ, Bauser Heaton H, Martin MH, et al. Transcatheter pulmonary valve replacement with the Sapien prosthesis. *J Am Coll Cardiol*. 2020;76:2847–2858. doi: 10.1016/j.jacc.2020.10.041
103. Schievano S, Coats L, Migliavacca F, Norman W, Frigiola A, Deanfield J, Bonhoeffer P, Taylor AM. Variations in right ventricular outflow tract morphology following repair of congenital heart disease: implications for percutaneous pulmonary valve implantation. *J Cardiovasc Magn Reson*. 2007;9:687–695. doi: 10.1080/10976640601187596
104. Meadows JJ, Moore PM, Berman DP, Cheatham JP, Cheatham SL, Porras D, Gillespie MJ, Rome JJ, Zahn EM, McElhinney DB. Use and performance of the Melody transcatheter pulmonary valve in native and post-surgical, nonconduit right ventricular outflow tracts. *Circ Cardiovasc Interv*. 2014;7:374–380. doi: 10.1161/CIRCINTERVENTIONS.114.001225
105. Martin MH, Meadows J, McElhinney DB, Goldstein BH, Bergersen L, Qureshi AM, Shahanavaz S, Aboulhosn J, Berman D, Peng L, et al. Safety and feasibility of Melody transcatheter pulmonary valve replacement in the native right ventricular outflow tract: a multicenter Pediatric Heart Network Scholar study. *JACC Cardiovasc Interv*. 2018;11:1642–1650. doi: 10.1016/j.jcin.2018.05.051
106. Benson LN, Gillespie MJ, Bergersen L, Cheatham SL, Hor KN, Horlick EM, Weng S, McHenry BT, Osten MD, Powell AJ, et al. Three-year outcomes from the Harmony Native Outflow Tract Early Feasibility Study. *Circ Cardiovasc Interv*. 2020;13:e008320. doi: 10.1161/CIRCINTERVENTIONS.119.008320
107. Shahanavaz S, Balzer D, Babaliaros V, Kim D, Dimas V, Veeram Reddy SR, Leipsic J, Blanke P, Shirali G, Parthiban A, et al. Alterra adaptive prestent and SAPIEN 3 THV for congenital pulmonic valve dysfunction: an early feasibility study. *JACC Cardiovasc Interv*. 2020;13:2510–2524. doi: 10.1016/j.jcin.2020.06.039
108. Morgan G, Prachasilchai P, Promphan W, Rosenthal E, Sivakumar K, Kappanayil M, Sakidjan I, Walsh KP, Kenny D, Thomson J, et al. Medium-term

results of percutaneous pulmonary valve implantation using the Venus P-valve: international experience. *EuroIntervention*. 2019;14:1363–1370. doi: 10.4244/EIJ-D-18-00299
109. Lee SY, Kim GB, Kim SH, Jang SI, Choi JY, Kang IS, Kim YH. Mid-term outcomes of the Pulsta transcatheter pulmonary valve for the native right ventricular outflow tract. *Catheter Cardiovasc Interv*. 2021;98:E724–E732. doi: 10.1002/ccd.29865
110. Shang X, Dong N, Zhang C, Wang Y. The clinical trial outcomes of Med-Zenith PT-Valve in the treatment of patients with severe pulmonary regurgitation. *Front Cardiovasc Med*. 2022;9:887886. doi: 10.3389/fcvm.2022.887886
111. Gillespie MJ, Bergersen L, Benson LN, Weng S, Cheatham JP. 5-Year outcomes from the Harmony Native Outflow Tract Early Feasibility Study. *JACC Cardiovasc Interv*. 2021;14:816–817. doi: 10.1016/j.jcin.2021.01.046
112. Jin Q, Long Y, Zhang G, Pan X, Chen M, Feng Y, Liu J, Yu S, Pan W, Zhou D, et al. Five-year follow-up after percutaneous pulmonary valve implantation using the Venus P-valve system for patients with pulmonary regurgitation and an enlarged native right ventricular outflow tract. *Catheter Cardiovasc Interv*. 2024;103:359–366. doi: 10.1002/ccd.30916
113. Caughron H, Kim D, Kamioka N, Lerakis S, Yousef A, Maini A, Reginauld S, Sahu A, Shashidharan S, Jokhadar M, et al. Repeat pulmonary valve replacement. *JACC: Cardiovasc Interv*. 2018;11:2495–2503. doi: 10.1016/j.jcin.2018.07.042
114. Georgiev S, Ewert P, Eicken A, Hager A, Hörer J, Cleuziou J, Meierhofer C, Tanase D. Munich comparative study: prospective long-term outcome of the transcatheter Melody Valve versus surgical pulmonary bioprosthesis with up to 12 years of follow-up. *Circ Cardiovasc Interv*. 2020;13:e008963. doi: 10.1161/CIRCINTERVENTIONS.119.008963
115. Li WF, Pollard H, Karimi M, Asnes JD, Hellenbrand WE, Shabanova V, Weismann CG. Comparison of valvar and right ventricular function following transcatheter and surgical pulmonary valve replacement. *Congenital Heart Dis*. 2018;13:140–146. doi: 10.1111/chd.12544
116. Lluri G, Levi DS, Miller E, Hageman A, Sinha S, Sadeghi S, Reemtsen B, Laks H, Biniwale R, Salem M, et al. Incidence and outcome of infective endocarditis following percutaneous versus surgical pulmonary valve replacement. *Catheter Cardiovasc Interv*. 2018;91:277–284. doi: 10.1002/ccd.27312
117. Sharma V, Griffiths ER, Eckhauser AW, Gray RG, Martin MH, Zhang C, Presson AP, Burch PT. Pulmonary valve replacement: a single-institution comparison of surgical and transcatheter valves. *Ann Thorac Surg*. 2018;106:807–813. doi: 10.1016/j.athoracsur.2018.04.002
118. Steinberg ZL, Jones TK, Verrier E, Stout KK, Krieger EV, Karamlou T. Early outcomes in patients undergoing transcatheter versus surgical pulmonary valve replacement. *Heart*. 2017;103:1455–1460. doi: 10.1136/heartjnl-2016-310776
119. Zablah JE, Misra N, Gruber D, Kholwadwala D, Epstein S. Comparison of patients undergoing surgical versus transcatheter pulmonary valve replacement: criteria for referral and mid-term outcome. *Pediatr Cardiol*. 2017;38:603–607. doi: 10.1007/s00246-016-1554-9
120. Ribeiro JM, Teixeira R, Lopes J, Costa M, Pires A, Gonçalves L. Transcatheter versus surgical pulmonary valve replacement: a systemic review and meta-analysis. *Ann Thorac Surg*. 2020;110:1751–1761. doi: 10.1016/j.athoracsur.2020.03.007
121. Daily JA, Tang X, Angtuaco M, Bolin E, Lang SM, Collins RT. Transcatheter versus surgical pulmonary valve replacement in repaired tetralogy of Fallot. *Am J Cardiol*. 2018;122:498–504. doi: 10.1016/j.amjcard.2018.04.028
122. O'Byrne ML, Gillespie MJ, Shinohara RT, Dori Y, Rome JJ, Glatz AC. Cost comparison of transcatheter and operative pulmonary valve replacement (from the Pediatric Health Information Systems database). *Am J Cardiol*. 2016;117:121–126. doi: 10.1016/j.amjcard.2015.10.011
123. Zhou Y, Xiong T, Bai P, Chu C, Dong N. Clinical outcomes of transcatheter versus surgical pulmonary valve replacement: a meta-analysis. *J Thorac Dis*. 2019;11:5343–5351. doi: 10.21037/jtd.2019.11.64
124. Stephens EH, Dearani JA, Taggart NW, Anderson JH, Miranda WR. Team approach to decision-making in pulmonary valve replacement. *Semin Thorac Cardiovasc Surg*. 2022;34:963–971. doi: 10.1053/j.semtcvs.2022.02.008
125. Kalfa D, Rajab TK, Cordoves E, Emani S, Bacha E, Jaggers J, Goldstone A, Eghtesady P, Turek J. Living allogenic heart valve transplantation: relative advantages and unanswered questions. *J Thorac Cardiovasc Surg*. 2024;167:1543–1546. doi: 10.1016/j.jtcvs.2023.09.036
126. Deleted in proof
127. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller GP, Lung B, Kluin J, Lang IM, Meijboom F, et al. 2020 ESC guidelines for the management of adult congenital heart disease. *Eur Heart J*. 2021;42:563–645. doi: 10.1093/eurheartj/ehaa554
128. Marelli A, Beauchesne L, Colman J, Ducas R, Grewal J, Keir M, Khairy P, Oechslin E, Therrien J, Vonder Muhll IF, et al. Canadian Cardiovascular Society 2022 guidelines for cardiovascular interventions in adults with congenital heart disease. *Can J Cardiol*. 2022;38:862–896. doi: 10.1016/j.cjca.2022.03.021
129. Pastor TA, Geva T, Lu M, Duarte VE, Drakeley S, Sleeper LA, Valente AM. Relation of right ventricular dilation after pulmonary valve replacement to outcomes in patients with repaired tetralogy of Fallot. *Am J Cardiol*. 2020;125:977–981. doi: 10.1016/j.amjcard.2019.12.017
130. Majeed A, Geva T, Sleeper LA, Graf JA, Lu M, Babu-Narayan SV, Wald RM, Mulder BJM, Valente AM. Cardiac MRI predictors of good long-term outcomes in patients with repaired TOF. *Am Heart J*. 2022;245:70–77. doi: 10.1016/j.ahj.2021.11.015
131. Mayourian J, Sleeper LA, Lee JH, Lu M, Geva A, Mulder B, Babu-Narayan SV, Wald RM, Sompolinsky T, Valente AM, et al. Online calculator: the INDICATOR mortality risk score in repaired tetralogy of Fallot. 2024. Accessed August 26, 2024. https://github.com/rTOF-INDICATOR/Mortality-Risk-Score
132. Ta HT, Critser PJ, Alsaied T, Germann J, Powell AW, Redington AN, Tretter JT. Modified ventricular global function index correlates with exercise capacity in repaired tetralogy of Fallot. *J Am Heart Assoc*. 2020;9:e016308. doi: 10.1161/JAHA.120.016308
133. Doganay B, Celebi OO. Prognostic role of the left ventricular global function index in predicting major adverse cardiovascular events in acute coronary syndrome patients. *Biomark Med*. 2023;17:5–16. doi: 10.2217/bmm-2023-0063
134. Liu T, Zhou Z, Bo K, Gao Y, Wang H, Wang R, Liu W, Chang S, Liu Y, Sun Y, et al. Association between left ventricular global function index and outcomes in patients with dilated cardiomyopathy. *Front Cardiovasc Med*. 2021;8:751907. doi: 10.3389/fcvm.2021.751907
135. Alsaied T, Critser PJ, Azcue N, St Clair N, Powell AJ, Rathod RH. CMR-derived ventricular global function index in patients late after the Fontan operation. *JACC Cardiovasc Imaging*. 2020;13:2686–2687. doi: 10.1016/j.jcmg.2020.06.011
136. Kido T, Ueno T, Taira M, Kanaya T, Okuda N, Toda K, Kuratani T, Sawa Y. Clinical significance of right atrial volume in patients with repaired tetralogy of Fallot. *Interact Cardiovasc Thorac Surg*. 2020;30:296–302. doi: 10.1093/icvts/ivz254
137. Kahle AK, Gallotti RG, Alken FA, Meyer C, Moore JP. Electrophysiological characteristics of intra-atrial reentrant tachycardia in adult congenital heart disease: implications for catheter ablation. *J Am Heart Assoc*. 2021;10:e020835. doi: 10.1161/JAHA.121.020835
138. Triedman JK, Alexander ME, Love BA, Collins KK, Berul CI, Bevilacqua LM, Walsh EP. Influence of patient factors and ablative technologies on outcomes of radiofrequency ablation of intra-atrial re-entrant tachycardia in patients with congenital heart disease. *J Am Coll Cardiol*. 2002;39:1827–1835. doi: 10.1016/s0735-1097(02)01858-2
139. Houck CA, de Groot NMS, Kardys I, Niehot CD, Bogers A, Mouws E. Outcomes of atrial arrhythmia surgery in patients with congenital heart disease: a systematic review. *J Am Heart Assoc*. 2020;9:e016921. doi: 10.1161/JAHA.120.016921
140. Kapel GF, Sacher F, Dekkers OM, Watanabe M, Blom NA, Thambo JB, Derval N, Schalij MJ, Jalal Z, Wijnmaalen AP, et al. Arrhythmogenic anatomical isthmuses identified by electroanatomical mapping are the substrate for ventricular tachycardia in repaired tetralogy of Fallot. *Eur Heart J*. 2017;38:268–276. doi: 10.1093/eurheartj/ehw202
141. Khairy P, Van Hare GF, Balaji S, Berul CI, Cecchin F, Cohen MI, Daniels CJ, Deal BJ, Dearani JA, de Groot N, et al. PACES/HRS expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease: executive summary. *Heart Rhythm*. 2014;11:e81–e101. doi: 10.1016/j.hrthm.2014.05.008
142. Kawada S, Chakraborty P, Downar E, Sanchez AP, Sathananthan G, Bhaskaran A, Kugamoorthy P, Albertini L, Oechslin EN, Silversides C, et al. The role of ablation in prevention of recurrent implantable cardioverter defibrillator shocks in patients with tetralogy of Fallot. *CJC Open*. 2021;3:619–626. doi: 10.1016/j.cjco.2021.01.005
143. Kapel GF, Reichlin T, Wijnmaalen AP, Piers SR, Holman ER, Tedrow UB, Schalij MJ, Stevenson WG, Zeppenfeld K. Re-entry using anatomically determined isthmuses: a curable ventricular tachycardia in repaired congenital heart disease. *Circ Arrhythm Electrophysiol*. 2015;8:102–109. doi: 10.1161/CIRCEP.114.001929
144. Nevvazhay T, Zeppenfeld K, Brouwer C, Hazekamp M. Intraoperative cryoablation in late pulmonary valve replacement for tetralogy of Fallot. *Interact Cardiovasc Thorac Surg*. 2020;30:780–782. doi: 10.1093/icvts/ivaa013

145. Waldmann V, Bouzeman A, Duthoit G, Koutbi L, Bessiere F, Labombarda F, Marquie C, Gourraud JB, Mondoly P, Sellal JM, et al; DAI-T4F Investigators. Long-term follow-up of patients with tetralogy of Fallot and implantable cardioverter defibrillator: the DAI-T4F nationwide registry. *Circulation*. 2020;142:1612–1622. doi: 10.1161/CIRCULATIONAHA.120.046745
146. Waldmann V, Marquie C, Bouzeman A, Duthoit G, Thambo JB, Koutbi L, Maltret A, Pasquie JL, Combes N, Marijon E. Subcutaneous vs transvenous implantable cardioverter-defibrillator therapy in patients with tetralogy of Fallot. *J Am Coll Cardiol*. 2022;80:1701–1703. doi: 10.1016/j.jacc.2022.08.761
147. Henmi R, Ejima K, Yagishita D, Iwanami Y, Nishimura T, Takeuchi D, Toyohara K, Shoda M, Hagiwara N. Long-term efficacy of implantable cardioverter defibrillator in repaired tetralogy of Fallot: role of anti-tachycardia pacing. *Circ J*. 2017;81:165–171. doi: 10.1253/circj.CJ-16-0932
148. Wernovsky G, Lihn SL, Olen MM. Creating a lesion-specific "roadmap" for ambulatory care following surgery for complex congenital cardiac disease. *Cardiol Young*. 2017;27:648–662. doi: 10.1017/S1047951116000974
149. Annavajjhala V, Valente AM, Lopez L, Sachdeva R, Glickstein JS, Natarajan SS, Buddhe S, Altmann K, Soriano BD, Colquitt JL, et al. Echocardiographic surveillance in children after tetralogy of Fallot repair: adherence to guidelines? *Int J Cardiol*. 2020;307:31–35. doi: 10.1016/j.ijcard.2019.09.075
150. Quail MA, Frigiola A, Giardini A, Muthurangu V, Hughes M, Lurz P, Khambadkone S, Deanfield JE, Tsang V, Taylor AM. Impact of pulmonary valve replacement in tetralogy of Fallot with pulmonary regurgitation: a comparison of intervention and nonintervention. *Ann Thorac Surg*. 2012;94:1619–1626. doi: 10.1016/j.athoracsur.2012.06.062
151. Wald RM, Valente AM, Gauvreau K, Babu-Narayan SV, Assenza GE, Schreier J, Gatzoulis MA, Kilner PJ, Koyak Z, Mulder B, et al. Cardiac magnetic resonance markers of progressive RV dilation and dysfunction after tetralogy of Fallot repair. *Heart*. 2015;101:1724–1730. doi: 10.1136/heartjnl-2015-308014