Tetralogy of Fallot

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KEYWORDS

• Repaired tetralogy of Fallot • Congenital heart disease • Pulmonary valve replacement
• Surgical pulmonary valve replacement

KEY POINTS

- Repaired tetralogy of Fallot (rTOF) is one of the most common conditions managed by adult congenital heart disease providers.
- Early studies identified several risk factors for death relating to timing and types of surgical repair, and the major causes of death were sudden and heart failure related.
- Echocardiography is a reliable tool to evaluate for many important late complications of rTOF, including the presence of residual ventricular septal defect, left ventricular systolic dysfunction, aortic root dilation, tricuspid regurgitation severity, and quantification of right ventricular (RV) outflow gradients and RV systolic pressure.
- Cardiac magnetic resonance imaging allows for quantification of right ventricular size and function, pulmonary regurgitation severity, and evaluation of fibrosis.
- Patients with rTOF are at risk for ventricular arrhythmias. Sudden cardiac death remains a leading cause of cardiac death for adults with rTOF, second only to heart failure.

Video content accompanies this article at http://www.cardiology.theclinics.com.

Repaired tetralogy of Fallot (rTOF) is one of the most common conditions managed by adult congenital heart disease providers. Recent comprehensive review articles and book chapters are devoted to this topic. The purpose of this article is to address several common clinical questions encountered in the management of patients with rTOF. These answers are not intended to supplant Practice Guidelines.

WHAT IS THE CONTEMPORARY NATURAL HISTORY OF REPAIRED TETRALOGY OF FALLOT?

The anatomy of tetralogy of Fallot (TOF) was first described by Stetson in 1671, and it was more than a century before Fallot published in 1888.[1] The first management strategies involved establishing a reliable source of pulmonary blood flow with palliative procedures, such as the Blalock-Taussig shunt in the mid 1940s, followed by the first intracardiac repair in 1954. Surgical strategies evolved, and primary neonatal repair began in the 1970s. Innovations over the past several decades have progressed at a much more rapid pace, with the advent of valve-sparing surgical approaches and more recently the widespread application of transcatheter techniques for pulmonary valve replacement (PVR). These advances in management have resulted in improved outcomes. However, the impact of current management strategies will not be fully recognized for several decades.

The mortality for rTOF in the early surgical experience was high, with a hospital mortality of 40% in the initial surgical experience, reported by Lillehei and colleagues.[2] However, survival improved as surgical experience increased. The natural history

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of rTOF has improved over time as well. Initially patients were older at the time of initial repair (median age 10–12 years), and many had undergone prior palliative shunts (23%–40%).[3,4] Early studies identified several risk factors for death relating to timing and types of surgical repair, and the major causes of death were sudden and heart failure related. As the population of rTOF patients has increased and grown older, the mode of death has changed; now patients are more likely to die of noncardiac comorbidities.[5] In 2014, Cuypers and colleagues[6] published results of prospective follow-up of 72 adults repaired between 1968 and 1980; the mean age of repair was 4.6 years. The 40-year survival was 72%. Interestingly, 40% of this cohort had undergone a subsequent PVR, and 50% had been hospitalized in the past decade.

The predominant hemodynamic sequela following repair of TOF is pulmonary regurgitation (PR), although rTOF patients may also have some degree of residual right ventricular outflow tract (RVOT) obstruction. The amount of regurgitation or obstruction is often directly related to the initial anatomy and surgical approach. The surgical approaches have evolved over time to current strategies, which attempt to preserve pulmonary valve function, so-called valve-sparing repairs.[7] Nonetheless, most patients with rTOF have residual PR. The optimal timing of PVR following rTOF remains one of the core challenges in the management of rTOF and is discussed more later. Furthermore, as patients with rTOF age, the incidence of ventricular dysfunction increases.[8] It is unclear at this time how guideline-directed management and therapy might affect the prevalence of heart failure in rTOF patients. In addition, patients with rTOF have an electromechanical cardiomyopathy and are predisposed to both atrial and ventricular arrhythmias. Risk factors for arrhythmia are discussed in greater detail later.[9,10]

Answer: The current late outcomes of TOF patients reflect management strategies performed in a prior era. However, the lessons learned from these patients are extremely important to guide current therapies.

IS ECHOCARDIOGRAPHY A RELIABLE WAY OF EVALUATING RIGHT VENTRICULAR FUNCTION OR PULMONARY REGURGITATION IN PATIENTS WITH REPAIRED TETRALOGY OF FALLOT?

Despite the high reproducibility and accuracy of CMR, transthoracic echocardiography (TTE) remains the primary imaging modality used to follow patients with rTOF because of advantages of accessibility, comparatively low cost, patient comfort, and practicality in patients with implanted metallic hardware. Echocardiography is a reliable tool to evaluate for many important late complications of rTOF, including the presence of residual ventricular septal defect, left ventricular systolic dysfunction, aortic root dilation, tricuspid regurgitation severity, and quantification of right ventricular (RV) outflow gradients and RV systolic pressure.[11]

Practice guidelines recommend elective PVR for patients with at least moderate PR who have severe RV dilation or RV dysfunction. For this reason, if TTE is to be useful in determining which patients require PVR, it is important to determine whether TTE can reliably measure PR severity, RV size, or RV systolic function.

Transthoracic Echocardiography Evaluation of Pulmonary Regurgitation Severity

Various methods have been proposed to evaluate PR severity by echocardiography, but none has reliably been shown to correlate with cardiac magnetic resonance (CMR) quantification of regurgitation volume or regurgitation fraction. Qualitatively, PR severity can be evaluated by color Doppler. However, in patients with rTOF and free PR, the jet can be low velocity, laminar, and relatively brief, which can make severe PR appear unimpressive by color Doppler. Vena contracta width and proximal isovelocity surface area radius have not been validated in grading of PR and are not typically used. Numerous investigators have attempted to correlate the pressure half-time (PHT) of the PR jet with PR severity. In general, a shorter PHT correlates with more severe PR. However, because PHT is also impacted by ventricular compliance, PHT has modest linear correlation with PR percentage as measured by CMR. Most investigators have found that patients with a long PHT (>100–130 milliseconds) are unlikely to have hemodynamically significant PR.[12–14] Other investigators have studied the correlation between the diastolic-systolic time-velocity integral (DSTVI) and CMR-derived PR severity, with higher DSTVI values correlating with worse PR. Again, the results of these studies have been highly variable in whether this TTE feature can identify severe PR.[12,13,15] An experienced congenital echocardiographer can accurately integrate qualitative data to identify mild, moderate, or severe PR as measured by CMR.[15,16]

Transthoracic Echocardiography Evaluation of Right Ventricular Size and Function

RV volume and ejection fraction (EF) cannot be routinely calculated from 2-dimensional TTE. RV

size is usually determined qualitatively, or from basal dimension. RV function is typically assessed qualitatively or using surrogates for EF, such as fractional area change (FAC), tricuspid annular plane systolic excursion (TAPSE), tissue-Doppler derived tricuspid annulus systolic velocity (S′), and myocardial performance index. These parameters were not developed to evaluate patients with rTOF and do not take into account the aneurysmal and dyskinetic outflow portions of the RV, which are common in patients with rTOF.

Multiple investigators have studied whether echocardiographic measurements of RV size and function correlate with CMR-derived RV volume or RV EF. Overall, the results have been inconsistent. RV end-diastolic area from an apical 4-chamber view seems to have better correlation with CMR-derived RV end-diastolic volume than does the basal RV diameter.[16]

Egbe and colleagues[17] reported that a TAPSE less than 17 mm had the strongest sensitivity and specificity for detecting an RV EF less than 40% and outperformed visual assessment of RV function. However, others have found poor or modest correlation between TAPSE and RV EF, perhaps because patients with rTOF have relatively less functional contribution from the basal portions of the RV and more from the apex.[15,18–21] Correlation between RV FAC% and RV EF has been similarly inconsistent.[16,17] Myocardial performance index is less frequently performed in routine TTE, but has some correlation with RV EF, although misclassification is common.[15,17]

In situations whereby image quality is adequate, software and processing expertise is available, and postprocessing is feasible, 3-dimensional (3D) echocardiography has promise for the determination of RV size and function. However, high-quality analyzable images are uncommon in adult patients and those with multiple sternotomies, limiting the applicability in the adult population with rTOF.[22] Measurement of RV free wall strain may provide additional information, but clinical data remain limited.[23,24]

Answer: Echocardiography remains important for the longitudinal follow-up for patients with rTOF, but no parameters are consistently and strongly associated with PR severity or RV size and function. Qualitative evaluation by experienced congenital imagers is necessary.

BEYOND PULMONARY REGURGITATION VOLUME AND VENTRICULAR FUNCTION, WHAT ELSE CAN WE LEARN FROM CARDIAC MRI?

CMR is ideally suited for assessment of rTOF because it allows comprehensive assessment of cardiovascular morphology and physiology, is independent of acoustic windows, and avoids ionizing radiation, which makes it ideally suited for longitudinal follow-up of rTOF patients.[25] Bokma and colleagues[26] published the use of CMR in the noninvasive risk stratification in 575 adults with rTOF, highlighting thresholds of ventricular dysfunction below which result in worse clinical outcomes. Patient-specific 3D models may be created to facilitate increased understanding of the spatial relationships of the anatomy (**Fig. 1**; Video 1). CMR is useful to determine the geometry of the RVOT and identify potential candidates for percutaneous PVR.[27] Delineation of the coronary artery course is essential before any RVOT intervention, because 5% to 7% of patients with rTOF have an anomalous left coronary artery that may course across the RVOT, which can complicate both surgical and transcatheter pulmonic valve implantation (**Fig. 2**). Cardiac and respiratory-gated magnetic resonance angiogram images have sufficient spatial resolution to assess the origins and proximal coronary artery courses. CMR is also superior to echocardiography to evaluate the branch pulmonary artery anatomy, and with phase-contrast imaging, it is possible to determine the percentage of blood flow to each lung. The ability to quantify blood flow to each lung is particularly important because patients with rTOF may have residual branch pulmonary artery stenosis that may result in unequal pulmonary blood flow distribution. CMR is often able to delineate the mechanism and severity of tricuspid valve regurgitation. Ascending aortic dilation is common in patients with rTOF, and CMR allows for reproducible measurements for longitudinal follow. Late gadolinium enhancement is able to identify areas of nonviable myocardium in these patients,

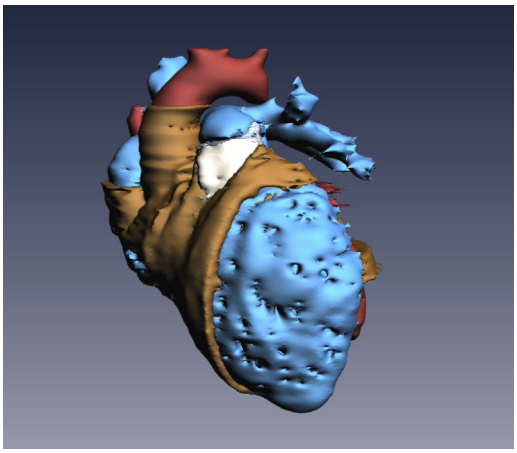

Fig. 1. 3D model of a patient with repaired TOF who has undergone a PVR created from CMR images.

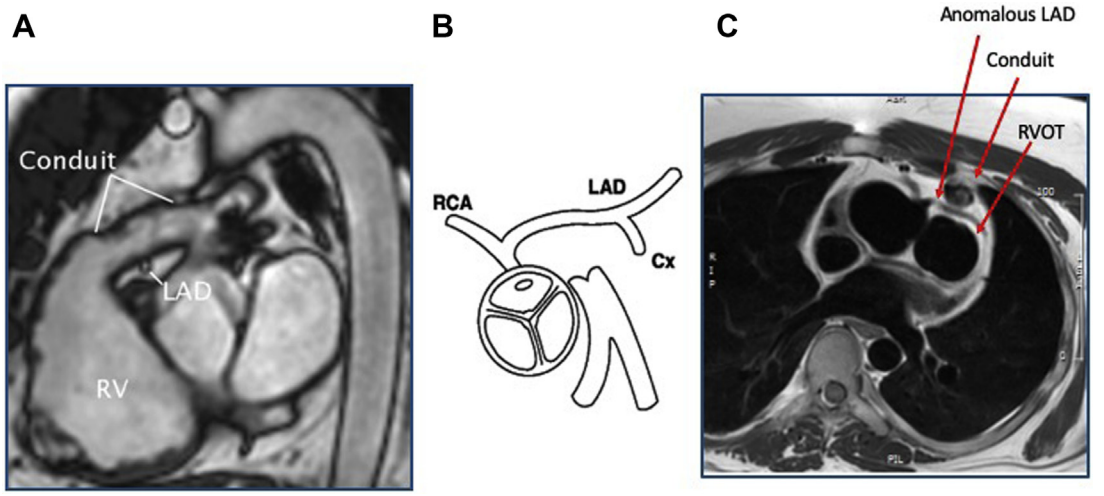

Fig. 2. (*A*) Bright-blood CMR of an rTOF patient with an anomalous left anterior descending artery (LAD) located just posterior to the RV-to-pulmonary artery conduit. (*B*) Short-axis diagram of this coronary anomaly, which is the most common coronary artery anomaly in rTOF. (*C*) Dark-blood axial CMR of an rTOF with the same anatomy, demonstrating the LAD coursing between the conduit and the native RV outflow tract. Cx, circumflex; RCA, right coronary artery.

which occurs at prior surgical sites as well as in areas remote from interventions.

The CMR technique of T1 mapping allows for measurement of the extracellular volume (ECV) fraction, a marker of extracellular matrix remodeling. Several investigators have demonstrated an association between diffuse myocardial fibrosis as measured by this technique in patients with rTOF and ventricular arrhythmias.[28,29] In addition, a linear relationship between left ventricular and RV ECV exists, implying an adverse ventricular-ventricular interaction at the tissue level.[30,31] Yamamura and colleagues[32] reported the association of fibrosis quantified by histologic analysis of RV muscle specimens at the time of PVR in 53 rTOF patients and CMR parameters. PVR patients with a collagen fibrosis volume greater than 11% had increased indexed RV end-systolic volume, increased RV mass, and larger right atrial area than those with less fibrosis.

Answer: In addition to being the gold-standard imaging test for quantification of PR and ventricular volumes in patients with rTOF, CMR provides a complete anatomic assessment of the RVOT, which is necessary for subsequent interventions. It produces accurate and reproducible flow data, including branch pulmonary artery flow distribution. CMR techniques, such as T1 mapping, may also prove to act as prognostic indicators in patients with rTOF.

WHAT CLINICAL AND IMAGING FEATURES DETERMINE TIMING OF PULMONARY VALVE REPLACEMENT?

The indications for PVR in rTOF patients continue to be refined. Historically, the decision to replace a pulmonary valve was driven by symptoms.[33] However, over the past several decades, this practice has been called into question because of the evidence that PVR may be offered to rTOF patients too late.[34] This reasoning was based on the observation that patients with an RV EF less than 40% at the time of PVR had little chance of recovery of RV function following the procedure. Therefore, current guidelines now include considerations for asymptomatic patients who have certain objective imaging or exercise criteria. **Table 1** lists the 2018 American College of Cardiology/American Heart Association Guidelines for PVR in patients with rTOF.[35] It is important to recognize that much of the imaging data used in this decision focuses on identifying a pre-PVR threshold value of RV size that predicts normalization of RV volumes following PVR. Massive RV dilation is unlikely to resolve following PVR and is more likely to be seen in patients with late primary repair and nonwhite race.[36] However, it has been shown that post-PVR RV size is not predictive of adverse clinical outcomes in rTOF patients, and new criteria need to be defined.[37] Although the guidelines suggest RV volumes above which

Table 1
American College of Cardiology/American Heart Association guideline criteria for pulmonary valve replacement in patients with repaired tetralogy of Fallot and at least moderate pulmonary regurgitation[35]

Class I	Class IIa (Any 2 of the Following)	Class IIb
Symptoms	RV or LV dysfunction RVEDVi $\geq$160 mL/m^2, RVESVi $\geq$80 mL/m^2, or RVEDVi $\geq$LVEDVi RVSP (due to RVOT obstruction) $\geq$2/3 systemic pressure Objective reduction in exercise tolerance	Sustained tachyarrhythmias Residual lesions requiring surgery

Abbreviations: EDV, end-diastolic volume; ESV, end-systolic volume; LV, left ventricular; LVEDVi, left ventricular end-diastolic volume index; RVEDVi, right ventricular end-diastolic volume index; RVESVi, right ventricular end-systolic volume index; RVSP, right ventricular systolic pressure.

patients could be considered for PVR, there is not a clear consensus that has been reached regarding the absolute values.[38–40] Ventricular dysfunction remains a strong criterion for consideration of PVR. In rTOF patients with severe right or left ventricular dysfunction, consultation with an advanced heart disease team for considerations of mechanical support following PVR should be addressed before the procedure.[41]

The goal of timing of PVR should be to do the intervention at a time before deleterious effects of residual disease, yet not so premature that it would lead to recurrent procedures in the future. This "sweet spot" for timing of PVR is a moving target and may be different for individualized patients whether they have a more volume-loading (PR) or pressure-loading (residual RVOT obstruction) lesion.[42] Separate criteria may also need to be defined for transcatheter versus surgical PVR in TOF patients.

Answer: Indications for timing of PVR now include considerations for the asymptomatic rTOF patient with significant ventricular dilation, any degree of ventricular dysfunction, and exercise limitations. There are increasing data that suggest an individualized approach to PVR is advisable.

HOW DOES PULMONARY VALVE REPLACEMENT AFFECT VENTRICULAR FUNCTION AND CLINICAL STATUS?

Although there are many studies relating to various clinical outcomes in rTOF patients, no randomized studies have been performed comparing PVR with conservative medical therapy. In a metaanalysis of 657 adults with rTOF who underwent PVR in 10 studies, the pooled incidence rate of death was 1% per year (95% confidence interval [CI]: 0% to 1% per year), and the pooled incidence rate of sustained ventricular arrhythmias was 1% per year (95% CI: 1% to 2% per year).

PVR results in beneficial reverse remodeling of the RV.[43,44] Although there is a significant reduction in RV volumes following PVR, there is evidence that RV volumes gradually return to near preoperative values 7 to 10 years following PVR.[45] Despite gains in RV size early after PVR, there is no beneficial effect on ventricular function.[43,44,46]

Most adults with rTOF experience symptomatic improvement following PVR. A systematic review showed that New York Heart Association (NYHA) functional class improves by nearly 1 functional class following PVR, but this benefit was attenuated in patients with very large preoperative RV volumes.[43] However, most studies included in the analysis were retrospective studies and all were unblended, so bias may contribute to the perceived improvement in functional status following PVR. A metaanalysis that accompanied the Canadian Cardiovascular Society guidelines confirmed that PVR did improve symptoms as reported by NYHA class (odds ratio: 0.08; 95% CI: 0.03–0.24).[44] A separate metaanalysis found no significant improvement in peak oxygen consumption (V_{O_2}) following PVR.[47]

There is no evidence that PVR lessens mortality or reduces the risk of ventricular arrhythmias in rTOF patients.[48] Geva and colleagues[49] identified pre-PVR risk factors that are associated with a shorter time to postoperative death and sustained ventricular tachycardia (VT) in 452 rTOF patients from 4 centers. These predictors included age at PVR $\geq$28 years, preoperative RV mass-to-volume ratio $\geq$0.45 g/mL, and an RV EF less than 40%. The threshold of age at PVR at which there may be a mortality benefit has been confirmed by a retrospective study of 707 patients in the National Institute for Outcomes Research in the United Kingdom, which reported a 5.6-fold increase in 10-year mortality following PVR in rTOF patients who were older than 35 years at the time of PVR.[50]

Answer: PVR results in improved symptomatic status and reduced RV size. However, there is no evidence that PVR reduces mortality or lessens ventricular arrhythmias in rTOF patients. Age at PVR is an important determinant of long-term outcomes.

WHAT ARE THE ADVANTAGES AND DISADVANTAGES OF A TRANSCATHETER PULMONARY VALVE REPLACEMENT COMPARED WITH A SURGICAL PULMONARY VALVE REPLACEMENT?

Transcatheter pulmonary valve replacement (TPVR) was introduced in 2000 as an alternative to surgical pulmonary valve replacement (SPVR), and its use has expanded dramatically over the last 2 decades. In the modern era, commercially available TPVR is an option for implantation into surgically placed RV to pulmonary artery conduits or dysfunctional bioprosthetic pulmonary valves. In some patients with favorable anatomy, approved devices can be placed in a native RVOT. There are ongoing clinical trials of devices designed to fit in aneurysmal outflow tracts typical for patients with rTOF. TPVR can be used to treat both RVOT obstruction and regurgitation. A comprehensive review of the use of transcatheter valves in congenital heart disease is published elsewhere in this issue (see article by Aboulhosn in this issue).

At experienced centers, both SPVR and TPVR can be performed with very low mortality and few complications.[51,52] Because there has been no randomized trial comparing TPVR and SPVR, it is not possible to draw definitive conclusions on the relative safety of either approach. Observed differences may be related to patient selection because there are differences in the patients referred for TPVR compared with those referred for SPVR.

One advantage to TPVR is reduced length of stay and reduced patient discomfort. One study by Steinberg and colleagues[53] performed a risk-adjusted propensity score to compare TPVR with SPVR. After adjusting for baseline differences, mortality and major morbidity were the same between the 2 groups. However, as would be expected, patients treated with TPVR had shorter hospitalization. There is a paucity of data comparing patient-related quality of life in the immediate or long term after TPVR or SPVR. Comparative data on the durability of TPVR versus SPVR are lacking, but publications suggest good valve durability of TPVR placed inside a conduit or bioprosthetic valve.[54]

Clinical experience and recent publications suggest that the Melody valve is susceptible to endocarditis.[55] It is not known whether this risk extends to other models of TPVR. A prospective registry of more than 300 Melody valve implantations performed in clinical trials showed an annualized endocarditis incidence rate of 3.1% per patient-year; 5-year freedom from endocarditis was 89% in patients treated with a Melody valve. Patients with a postimplant peak gradient $\geq$15 mm Hg were at higher risk for endocarditis.[56]

There should be a high suspicion for TPVR-related endocarditis for patients presenting with infectious or constitutional symptoms. As always, if endocarditis is suspected, multiple sets of blood cultures should be obtained before initiation of antibiotics. It is very difficult, and often impossible, to visualize a vegetation on a TPVR using TTE or transesophageal echocardiogram. However, these modalities are important to exclude vegetations the other valves, and to evaluate for new TPVR dysfunction. Intracardiac echocardiography is the most reliable way to assess for TPVR endocarditis. Approximately half of patients can be treated medically without needing valve explantation.[56]

Answer: TPVR is a reasonable alternative to SPVR in those with previously surgically implanted valves or conduits, or favorable native RVOT anatomy. Transcatheter valves result in shorter hospital stays but a higher late risk of endocarditis. There are insufficient data to suggest either type of valve has advantages in terms of operative safety or valve durability.

WHICH PATIENTS WITH TETRALOGY OF FALLOT REQUIRE A PRIMARY PREVENTION DEFIBRILLATOR?

Patients with rTOF are at risk for ventricular arrhythmias. Sudden cardiac death remains a leading cause of cardiac death for adults with rTOF, second only to heart failure.[5] Up to 10% of patients with rTOF have clinical sustained VT, and the likelihood of lethal ventricular arrhythmias ranges between 1.6% and 6% per year and increases with age.[10,57]

Despite the high rate of VT in patients with rTOF, it is challenging to decide which patients with repaired TOF benefit from a primary prevention implantable cardioverter-defibrillator (ICD). It would be inappropriate to implant a primary prevention ICD in all adults with rTOF because the costs-benefit ratio would not support that approach: compared with patients with dilated cardiomyopathy, patients with rTOF have more device-related complications and are less likely to receive appropriate therapy from ICDs. Patients with rTOF have high rates of oversensing,

inappropriate antitachycardia pacing, and inappropriate shocks. In addition, rTOF patients have a higher incidence of lead failure and device-related infection.[58–60] The rate of inappropriate shocks in patients with rTOF ranges between 6% and 10% per year, a rate that is much higher than that seen in dilated cardiomyopathy. Inappropriate shocks are associated with reduced quality of life. The increased device-related complication rates may be related to the fact that rTOF patients are younger and have a high incidence of atrial arrhythmias, both of which are risk factors for device-related complications. In addition to higher complication rates, patients with rTOF are less likely to receive appropriate shocks than those with other forms of heart disease.[58,59,61] Because adults with rTOF have a high rate of VT but indiscriminate implantation of ICDs would be associated with high rates of complications, it is important to identify high-risk patients who would benefit from ICDs.

Risk Factors for Ventricular Tachycardia in Tetralogy of Fallot

Numerous investigators have described clinical features that are associated with an increased risk of ventricular arrhythmias. Some of the more strongly validated are listed as follows:

1. QRS duration greater than 180 milliseconds[10,62,63]
2. Fragmentation of the QRS complex[64–66] (**Fig. 3**)
3. Left ventricular or RV systolic or diastolic dysfunction[8,61,63,67–69]
4. RV hypertrophy or extensive scar seen on CMR[5,28,48,49,70]
5. History of VT[48,61,69]
6. Inducible sustained VT or high-risk substrate seen at electrophysiology (EP) study[59,69,71,72]

Overall, ventricular function (both systolic and diastolic) and electrocardiogram abnormalities are more predictive of VT than is the degree of PR or RV dilation.

Predicting Risk in Patients Undergoing Pulmonary Valve Replacement

There remains no consensus as to which combination of risk factors warrants implantation of an ICD. Patients with none of the risk factors listed above are unlikely to benefit from a primary prevention ICD, and ICD is not recommended in this context.[73] For patients with at least one or 2 risk factors, ICD can be considered. Invasive EP study with programmed ventricular stimulation has the ability to reclassify intermediate-risk patients for whom ICD is being considered.[74]

Answer: Patients with multiple risk factors for VT, or risk factors plus a positive ventricular stimulation study, should be offered a defibrillator.

WHAT IS THE IMPACT OF ABLATION IN PREVENTING VENTRICULAR TACHYCARDIA IN PATIENTS WITH REPAIRED TETRALOGY OF FALLOT?

Most VT in rTOF is related to macro-reentry circuits and depends on slow conduction through a limited number of discrete anatomic isthmuses

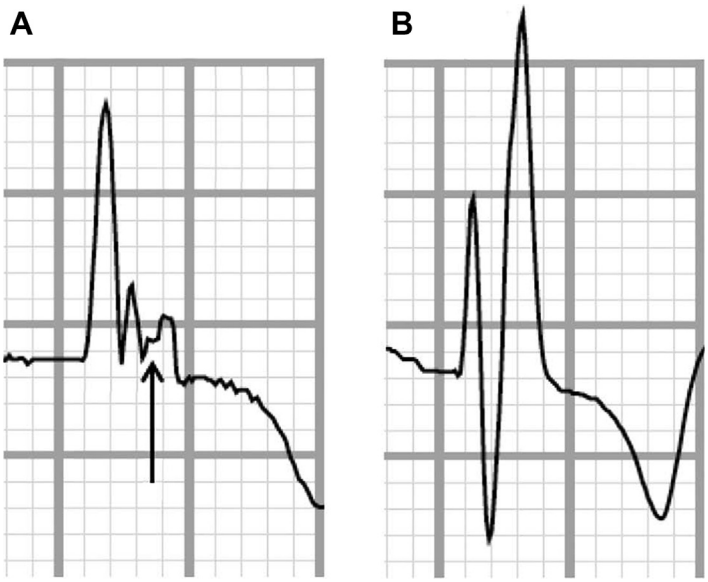

Fig. 3. Right bundle branch block (RBBB) with and without QRS fragmentation. Lead V2 of an ECG in a patient with TOF (*A*) with RBBB and evident fragmentation (*arrows*) of the prolonged QRS complexes compared with a patient with TOF (*B*) with a wide RBBB without fragmentation of prolonged QRS complexes. (*From* Bokma JP, Winter MM, Vehmeijer JT, et al. QRS fragmentation is superior to QRS duration in predicting mortality in adults with tetralogy of Fallot. Heart. 2017;103(9):666-671; with permission.)

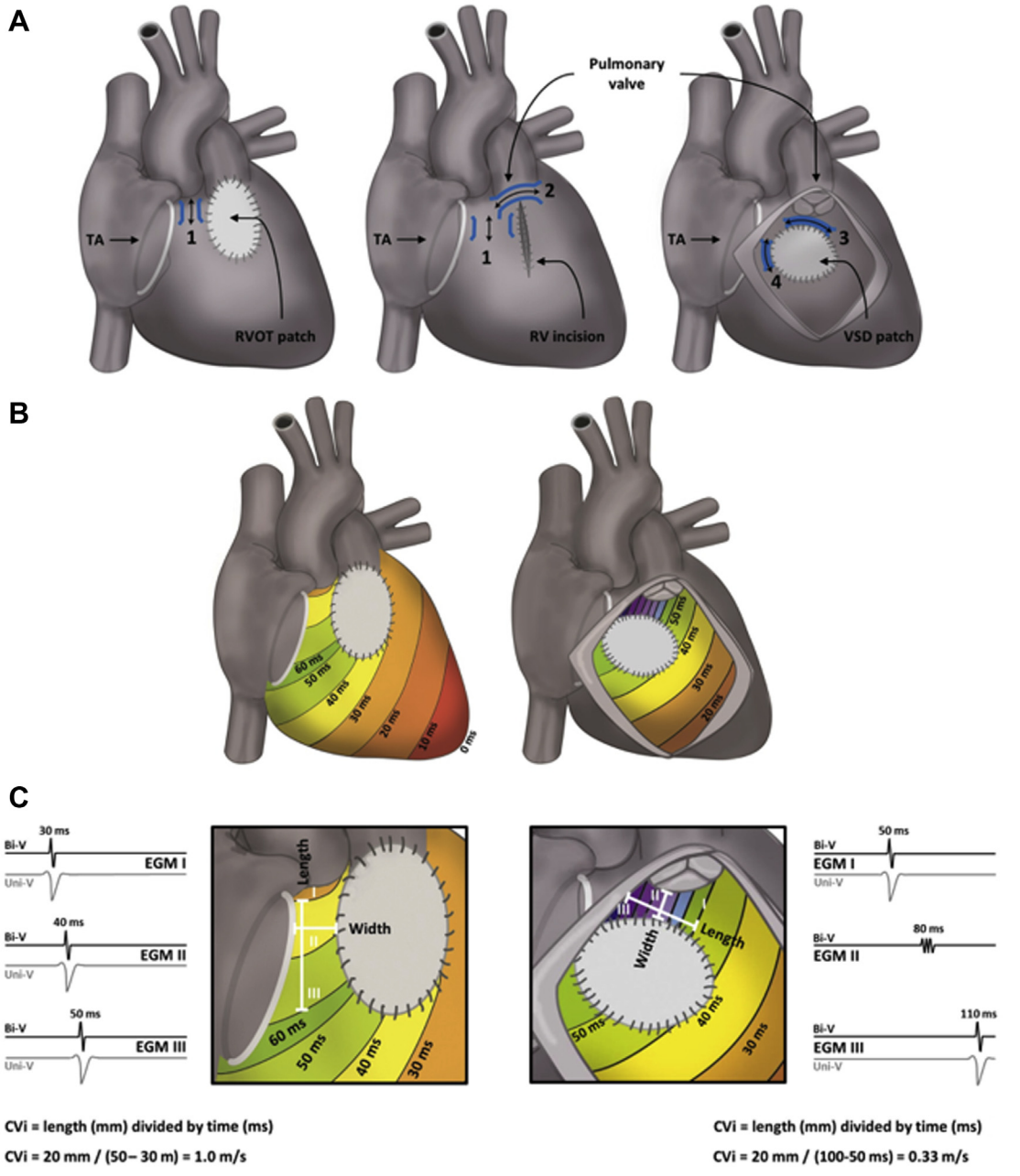

Fig. 4. (*A*) The 4 potential anatomic isthmuses (*blue brackets*): isthmus 1 bordered by tricuspid annulus and RV outflow tract patch/RV incision; isthmus 2 bordered by RV incision and pulmonary valve; isthmus 3 bordered by pulmonary valve and ventricular septal defect patch; isthmus 4 bordered by ventricular septal defect patch and tricuspid annulus. (*B*) Schematic activation of the right ventricle during SR displayed as color-coded isochronal (10 milliseconds) map from red (early activation) to purple (latest activation). (*C*) Enlarged views of anatomic isthmus 1 (*left*) and 3 (*right*) with corresponding electrograms recorded from sites I–II–III, as indicated. Isthmus width, distance between unexcitable anatomic boundaries; isthmus length, distance between normal electrograms (I and III) recorded at entrance and exit site of the anatomic isthmus. Conduction time through the anatomic isthmus, difference in local activation time between the entrance and exit of the anatomic isthmus. Conduction velocity index calculated as indicated. Bi-V, biventricular; CVi, conduction velocity index; EGM, electrogram. (*From* Kapel GF, Sacher F, Dekkers OM, 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(4):268-276; with permission.)

Table 2
Selected studies of ventricular tachycardia ablation in patients with repaired tetralogy of Fallot[8,60,77–79]

Author, Year	Number of TOF Patients Ablated	Acute Success Rate, %	Follow-Up, mo	Results
Zeppenfeld et al,[78] 2007	9	100	30.4 ± 29.3	No recurrence of VT
Kriebel et al,[79] 2007	10	80	35.4 (range 3–52)	Recurrence in 25% of acutely successful ablations
Kapel et al,[60] 2015	28	75	46 ± 28	No recurrence of VT in patients with procedural success
van Zyl et al,[77] 2016	21	57	33 ± 7	No recurrence of VT if successful block. No events in 95%
Laredo et al,[80] 2017	34	82	112 ± 62	18% VT recurrence, including sudden death in 2

(Fig. 4). These features make VT in rTOF appealing for catheter ablation because creation of a conduction block across the isthmus can eliminate the substrate for VT. Because the isthmuses usually appear in predictable locations, ablation can be possible using substrate mapping, even for hemodynamically unstable VTs, which cannot be mapped with entrainment techniques.[72,75,76]

Several investigators have reported on the outcomes of catheter-based VT ablation. Results of selected studies are shown in Table 2.[60,77–80] Overall, the data suggest that most patients who undergo an ablation have an acutely successful procedure with achievement of block. In addition, most patients who had an acutely successful ablation are free of arrhythmia over the next 3 to 5 years. Importantly, however, ablation is not 100% reliable in preventing late VT, even in those who were thought to have a successful procedure, as shown in Table 2.

It is common for patients being considered for PVR to be evaluated for VT at the time of surgical referral. Many centers perform an EP study before surgical PVR on patients who are thought to be at increased risk for VT. The rationale for this approach is to facilitate surgical cryoablation at the time of PVR. One advantage of performing ablation at the time of surgery is that it allows for complete exposure and targeted ablation of the defined anatomic isthmuses. However, performing ablation at the time of surgery does not allow for the confirmation of block or demonstration of noninducibility of VT. For this reason, postoperative EP studies are required to confirm success of the surgical ablation. Two series that studied the outcomes of patients who underwent surgical ablation at the time of PVR documented that a substantial number of patients (16%–45%) remained inducible for VT during a postoperative EP study.[81,82]

In summary, it appears that patients who are inducible for VT and have a successful catheter ablation are at low risk for future clinical VT, but the risk is eliminated. Patients who have a surgical ablation need to have successful block confirmed on a follow-up EP study.

Answer: Catheter ablation is not a replacement for a secondary prevention ICD in patients with a history of clinical VT. Ablation can be complementary to an ICD to reduce shocks in patients with clinical VT. It remains uncertain whether patients with a positive EP study and a successful ablation require a primary prevention ICD following an acutely successful catheter-based VT ablation.

SUMMARY

The authors have addressed some of the common clinical questions encountered in the management of adults with rTOF. Echocardiography remains important for the longitudinal follow-up for patients with rTOF, and CMR is a gold-standard imaging tool for quantification of RV size, function, and PR. Whereas traditionally the indication for PVR involved symptomatic patients, the recommendations now include intervention

for asymptomatic rTOF patients with significant ventricular dilation, any degree of ventricular dysfunction, and exercise limitations. PVR results in improved symptomatic status and reduced RV size, but does not reduce mortality. Age at PVR appears to be an important determinant of long-term outcomes. Choice of PVR now includes not only surgical options but also transcatheter delivery. There are insufficient data to suggest either type of valve has advantages in terms of operative safety or valve durability. Risk stratification for rTOF patients is important, and patients with multiple risk factors for VT, or risk factors plus a positive ventricular stimulation study, should be offered a defibrillator. Catheter ablation can be complementary to an ICD to reduce shocks in patients with clinical VT.

SUPPLEMENTARY DATA

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