A 32-year-old woman with a history of tetralogy of Fallot (TOF) was referred for cardiac evaluation. She was diagnosed with TOF as an infant and at 8 months of age underwent complete repair, including ventricular septal defect closure, resection of right ventricular (RV) outflow tract (RVOT) muscle bundles, and pulmonary valvotomy. She was evaluated by a cardiologist at 17 years of age and was subsequently lost to follow-up because she thought she was “cured.” Overall, she feels well and denies cardiac symptoms. She runs 1 to 2 miles daily, although more slowly than her friends. She is considering having children.

On physical examination, her vital signs were normal. She had a well-healed midline sternotomy scar. Her lungs were clear to auscultation. The heart rhythm was regular with a normal S1 and a single S2. There was a low-pitched, delayed diastolic murmur in the pulmonary area. Her ECG demonstrated normal sinus rhythm, a right bundle-branch block, and a QRS duration of 170 milliseconds.

A transthoracic echocardiogram showed a dilated and hypokinetic RV, with severe pulmonary regurgitation (PR) and mild tricuspid regurgitation. There was no RVOT obstruction or residual ventricular septal defect. The left ventricle was normal in size and function, with mild mitral regurgitation. Because RV size and function were not well quantified with echocardiography, cardiac magnetic resonance imaging was performed. The RV end-diastolic and end-systolic volumes were 179 and 109 mL/m², respectively, and the RV ejection fraction was 39%. A Holter study did not reveal significant ectopy or arrhythmia. A cardiopulmonary exercise test demonstrated a moderately depressed peak V̇o₂. Given her severe PR associated with a dilated and hypokinetic RV and moderately reduced exercise tolerance, she was referred for surgical pulmonary valve replacement (PVR).

**Adult Congenital Heart Disease**

This woman is 1 of ≈1 million adults with congenital heart disease (CHD) in the United States. Of those, about half have complex CHD, many of whom had surgical intervention as children. In most patients with complex CHD, surgery is palliative. Accordingly, patients and their physicians should be aware that there are lifelong risks of cardiac and noncardiac complications and reinterventions. Unfortunately, many patients with CHD are lost to follow-up, and <30% of adults with CHD are evaluated by a CHD specialist, which has treatment implications. When patients return to specialized care, many have newly diagnosed lesions requiring intervention.

**Evaluation and Outcomes in Adults With Repaired TOF**

Life expectancy in patients with repaired TOF is shorter than in the population at large, even accounting for perioperative mortality. The most common causes of late mortality are sudden death and heart failure. Operative mortality has steadily declined, and although long-term survival has improved as a result, there has not been a concomitant reduction in the risks of reoperation, arrhythmia, or late death.

Among the clinically important complications that can affect adults with repaired TOF, PR is the most common. Without intervention, PR results in RV dilation and may lead to a cascade of other complications, including biventricular dysfunction.
tachyarrhythmias, exercise intolerance, heart failure, and death. Understanding the anatomic features and details of the original repair can be helpful in anticipating late complications.7

Patients with PR can remain asymptomatic for many years. When symptoms develop, they do not always correspond to the degree of PR or RV dysfunction. Because patients may have noncardiac morbidities that affect exercise, it is not always clear whether symptoms are related to PR or its effects on the RV. In addition, many patients cannot accurately assess their functional capacity, and others do not volunteer symptoms. Cardiopulmonary exercise testing provides an objective measurement of exercise function, and changes in serial testing may indicate difficulties not otherwise apparent. Exercise performance is inversely related to PR severity, and patients with significant PR and a peak $\dot{V}O_2 <20 \text{mL-kg}^{-1}\cdot\text{m}^{-2}$ have a higher surgical risk, suggesting an important role for testing in determining the optimal timing of PVR.8

Because echocardiography is often inadequate for evaluating the abnormal RV, magnetic resonance imaging has become an integral tool in determining the need for intervention and risk stratification.6 Cardiac magnetic resonance imaging allows quantitative evaluation of RV volumes and mass, systolic function, regional abnormalities, and the extent of fibrosis and scar.

**PVR in Patients With Repaired TOF**

Approximately 50% of patients who survived TOF repair undergo reoperation within 30 years; PVR is the most common reoperation.4 Although numerous studies have demonstrated the benefits of PVR, criteria for PVR in patients with repaired TOF are still in evolution. Guidelines for PVR in adults with CHD have been published by the American, Canadian, and European cardiac societies (Table).5,9,10 and various investigators have suggested even more detailed criteria.6,11 In patients with severe PR and overt symptoms of failure of the right side of the heart, guidelines agree that PVR is indicated.5,9,10 In asymptomatic patients, the benefit of PVR is less certain.

PVR improves symptoms and functional status, but the sickest patients may receive the least benefit and incur the highest risk. Waiting too long to implant a valve increases the risks, highlighting the importance of considering PVR before overt symptoms and significant RV dilation and dysfunction occur.13 Guidelines suggest performing PVR when normalization of the RV volume is probable.9–11 Despite reduction in RV volume with PVR, normalization does not always occur, and there is often no concurrent improvement in RV function.12 Several magnetic resonance imaging–based studies have found that RV volumes return to normal after PVR if the preoperative RV end-diastolic volume is <150 to 170 mL/m² or the RV end-systolic volume is <82 to 90 mL/m².14,15 RV volume normalization is also associated with a preoperative QRS duration ≤140 milliseconds, whereas a QRS duration ≥160 milliseconds and an RV ejection fraction ≤45% are associated with persistent RV dilation and dysfunction.16 Coexisting problems such as RVOT aneurysm or obstruction, residual shunts, and aortic regurgitation or dilation requiring surgical intervention should also be considered.11 Insofar as biventricular dysfunction and RV hypertrophy, but not RV volume, are associated with poor outcome in patients with repaired TOF,17 earlier intervention should be considered to decrease RV pressure and before ventricular dysfunction and adverse ventricular interaction occur. Despite current recommendations, there are no data showing that the proposed thresholds are sensitive or specific or that following them reduces the risk of adverse outcomes.

Guidelines advise PVR in patients with severe PR and new-onset arrhythmias.5,9,10 Nevertheless, it is unclear whether performing PVR when RV normalization is possible decreases the risk of VT or death. In matched cohort studies of patients who underwent PVR compared with those who did not, there was no significant difference in these outcomes, but the studies were limited by intrinsic selection bias.13,18 In patients with risk factors for VT and sudden death,10 preoperative electrophysiology study and implantation of a cardioverter-defibrillator should be considered.

Another important consideration for the timing of PVR is pregnancy. PR is usually tolerated well during pregnancy, but surgical intervention should be considered in women with severe PR before pregnancy because the hemodynamic changes of pregnancy may precipitate failure of the right side of the heart, arrhythmia, and adverse long-term effects.9 Even if PVR is not performed, thorough evaluation is advisable before pregnancy.

In addition to the recommended indications for PVR, the risks and benefits should be weighed in each patient. Early mortality after PVR surgery is ≈1% to 2%,8 and freedom from RVOT reintervention after PVR is 66% to 96% at 10 years.8,10,19 Younger patients have more consistent improvements in RV function with PVR20 but also shorter freedom from valve failure.21,22 Replacing the pulmonary valve too early may yield less benefit with similar risk but can effectively increase the lifetime number of procedures, which is important because the risk of intervention increases with each sternotomy.11 Patients should be counseled to expect reintervention on the implanted valve.

Various valves and conduits can be used for PVR.19,21,22 The preferred option is a bioprosthetic valve or a valved homograft. Data on the relative performance of different valves are mixed, and long-term data are limited. In addition, transcatheter PVR has become an important tool in the management of patients with complex TOF, including those with bioprosthetic valve dysfunction after surgical PVR,23 but it is not yet a viable option in most patients with a dilated RVOT and PR after TOF repair.
Summary

The above case history is not uncommon among young adults with repaired TOF, who report no symptoms but have significant abnormalities on anatomic, functional, and electrophysiological evaluation that are indications for PVR. This patient is doing well after PVR, with noticeable improvement in her objective exercise capacity. Determining the optimal criteria for and timing of PVR for patients with repaired TOF is difficult. There is agreement that PVR is indicated in patients with significant PR and symptoms, heart failure, or new arrhythmias.

In the absence of these findings, there is agreement that PVR is indicated in patients with significant PR and symptoms, heart failure, or new arrhythmias.

Table. Indications and Levels of Evidence for PVR in Adults With CHD as Recommended by Guidelines of the American College of Cardiology/American Heart Association, Canadian Cardiovascular Society, and European Society of Cardiology

<table>
<thead>
<tr>
<th>Society</th>
<th>Indications for PVR</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC/AHA, 2008</td>
<td>Severe PR and symptoms or decreased exercise tolerance</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>CCS, 2009</td>
<td>Free PR with Preoperative or moderate to severe RV enlargement (RV EDV &gt;170 mL/m²)</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>ESC, 2010</td>
<td>Symptomatic patients with severe PR or stenosis</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Asymptomatic patients with severe PR or PS and Decrease in objective exercise capacity</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Progressive RV dilatation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Progressive RV systolic dysfunction</td>
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<tr>
<td></td>
<td>Progressive TR (at least moderate)</td>
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<td></td>
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<tr>
<td></td>
<td>RVOTO with RV systolic pressure &gt;80 mmHg</td>
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<td></td>
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<tr>
<td></td>
<td>Sustained atrial/ventricular arrhythmias</td>
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</tbody>
</table>

ACC indicates American College of Cardiology; AHA, American Heart Association; CCS, Canadian Cardiovascular Society; CHD, congenital heart disease; EDV, end-diastolic volume; ESC, European Society of Cardiology; PR, pulmonary regurgitation; PS, pulmonary stenosis; PVR, pulmonary valve replacement; RV, right ventricle; RVOTO, right ventricular outflow tract obstruction; and TR, tricuspid regurgitation.

Disclosures

Dr McElhinney serves as a proctor and consultant for Medtronic, Inc. Dr Weinberg reports no conflicts.

References


Pulmonary Valve Replacement in Tetralogy of Fallot
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