The observation that adults with repaired tetralogy of Fallot (TOF) outnumber children is a testament to the exponential improvements in the medical and surgical management of the disease (1). The first Black-Taussig shunt placement in 1945 (2,3), improved life expectancy from a few months to years. Lillehei et al. (4) followed with the first open heart repair in 1954. The current early survival of TOF is excellent, approximating 90% through the first 2 decades of life. In the third decade, however, mortality rate increases (5,6) with residual sequelae truncating long-term life expectancy and affecting quality of life (7). Risk factors that predict adverse outcome are: (1) older age of repair; (2) evidence of sustained ventricular tachycardia or longer QRS duration; (3) and hemodynamic compromise due to long-term pulmonary regurgitation with right ventricular (RV) dilation and dysfunction of both right and left ventricles (1, 8–11).

Whereas earlier age of repair, pulmonary valve preservation, and limited ventriculotomy are likely to improve long-term ventricular function and reduce incidence of arrhythmia, the pulmonary valve is not always easily preserved, necessitating a long-term strategy for mitigating the impact of pulmonary regurgitation on the RV.

As with the left ventricle, the RV dilates and hypertrophies in response to volume overload. Early after repair, the RV stiffness and decreased capacitance of the pulmonary arteries reduces the impact of pulmonary regurgitation. With time, the RV becomes more compliant and dilates, and the increased capacitance of the pulmonary bed exacerbates regurgitation. After years of chronic pulmonary regurgitation, compensatory mechanisms eventually break down (12) leading to RV failure, deterioration in left ventricular function, and increased incidence of arrhythmias (8,10,12–16). To ameliorate the impact of pulmonary regurgitation, pulmonary valve replacement (PVR) has emerged as an effective option; however, there appears to be a limit to improvements as valve replacement in patients with severe RV dilation does not lead to improved ventricular function and functional capacity in all cases (17).

Cardiovascular magnetic resonance imaging (CMR) has evolved as an valuable tool to evaluate RV hemodynamics (18). Whereas other modalities for measurement of RV function are available, CMR can provide detailed and reproducible data regarding right and left ventricular volume, function and severity of regurgitation, and anatomic abnormalities without radiation exposure. CMR markers such as severe RV dilation and biventricular dysfunction have been described as independent predictors of death, sustained ventricular tachycardia, and heart failure (10). In this issue of Journal, Lee et al. (19) provide a retrospective CMR analysis of 170 patients with TOF who underwent PVR. Optimal outcome measures were defined as normalization of RV volume and function by CMR. After PVR, this cohort demonstrated overall improvement in RV volumes, biventricular function, tricuspid regurgitation, pulmonary regurgitation, and functional American Heart Association heart classification. No change was demonstrated in history of arrhythmia or oxygen consumption by cardiopulmonary stress testing. There were 2 deaths related to the PVR with actuarial survival at 10 years of 97.5 ± 1.6%. Freedom from redo PVR at 10 years was 74.5% and freedom from valve failure at 10 years was 50.3 ± 10%. Subgroup analysis on 67 patients with pre- and post-CMR images generated cutoff values for optimal outcome as defined by normalization of CMR parameters: normal RV end-diastolic volume index (RVEDVI) <108 ml/m²; end-systolic volume index (RVESVI) <47 ml/m²; and ejection fraction (RVEF) >49%. Receiver-operating characteristic curves suggest that a pre-operative RVEDVI of 168 ml/m² (sensitivity: 74%, specificity: 74%) and pre-operative RVESVI ≤80 ml/m² (sensitivity: 68%, specificity: 68%) are predictors for optimal outcome. A receiver-operating characteristic curve for right ventricle ejection fraction (RVEF) was not determined.

This study is now one of several with recommendations for optimal timing of PVR-based on pre-operative CMR parameters. Reported RVEDVI for optimal outcome has fallen from an initial report by Therien et al. (20) of ≤170 ml/m² to ≤160 ml/m² by Oosterhov et al. (21), and finally Beuchel et al. (22) to ≤150 ml/m². Previously reported indexed pre-operative systolic volume for optimal outcome was ≤85 ml/m² by Therien et al. (20) and <90 ml/m² by Geva et al. (23). As surgical remodeling may considerably alter RV diastolic dimension, indexed systolic volume may

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be a more sensitive CMR parameter of success after PVR. However, sensitivity and specificity of 68% for RVESVI (74% for RVEDVI) in the current paper by Lee et al. (19) suggest that a moderate percentage of patients below and above the cutoff values will not demonstrate optimal outcome based on CMR parameters. In addition, there is overlap of QRS duration and RVEF in both the optimal and suboptimal groups. In a prospective study of patients referred for PVR with or without surgical remodeling therapy by Geva et al. (23), pre-operative RVESVI <90 ml/m² and QRS duration of <140 ms were predictors of optimal post-operative result (CMR normalization of RV volumes and function). In contrast, a RVEF <45% and QRS duration of ≥160 ms demonstrated evidence of persistent RV dilation and dysfunction (23). Therefore, additional measures such as QRS duration, history of arrhythmia, and symptoms continue to be important in the evaluation of the pre-operative decision making.

Despite the lack of CMR evidence of ventricular improvement in some cases, short-term clinical benefit with PVR is well documented (20–22,24–28). Unfortunately, the long-term clinical impacts of PVR are mixed. In a matched retrospective cohort study by Gengsakul et al. (29), 84 patients’ status after PVR were compared with the status of patients in a non-PVR group. Even though there was improvement in New York Heart Association functional class and symptoms in the PVR group versus the non-PVR group, results were tempered by no documented differences in prevalence of sudden cardiac death, ventricular tachycardia, or oxygen consumption. In a similarly designed study of 77 patients with TOF and PVR, Harrild et al. (30) demonstrated that PVR did not result in improved long-term survival. However, the findings of the Herrild et al. (30) study are tempered by baseline differences RV size of the control group compared to the PVR group (RVEDVI = 132 ml/m² vs. 196 ml/m²). In an earlier study, Therien et al. (31) suggested that there is a threshold where PVR may not have benefit. Conversely, electing not to replace a pulmonary valve in patients with severe RV dilation likely leads to further deterioration of functional clinical status. Knauth et al. (10) demonstrated by CMR that a RVEDVI z-score ≥7 and LVEF <55% or RVEF <45% as independent risk factors for death, sustained ventricular tachycardia, and increase in New York Heart Association functional class. At present, PVR replacement demonstrates evidence of functional improvement (in most cases) balanced by no clear alteration in life expectancy.

Pulmonary valve replacement is not without risks. Whereas mortality for PVR is considered acceptable (0% to 2%) (32), major complications and prolonged hospital stay are prevalent. A trend in earlier PVR will increase the number of pulmonary valve interventions. Lee et al. (19) note that 50% of their cohort demonstrated evidence of pulmonary valve failure or dysfunction at 10 years. In addition, a previous review of their cohort estimated 80% requiring reoperation at 10 years (33). Consequently, if the pulmonary valve is replaced at a mean age of 16 to 20 years (26), most patients will undergo a second valve replacement by age 30 to 35 years. Determining factors that influence longevity of valve function are under intense examination (34). Therefore, the decision for pulmonary valve replacement should be individualized for each patient and thought to the future regarding the potential for percutaneous valve replacement should be considered for each case (35). Discussions of the balance between RV preservation versus the number of potential pulmonary valve interventions continue to evolve.

Based on pre-operative CMR findings, Lee et al. (19) support PVR on the basis of RVEDVI >163 ml/m² or RVESVI of >80 ml/m². However, given the failure rate of pulmonary valves and mixed data regarding long-term reduction in sudden death, an individual approach to PVR is mandatory. A large longitudinal multicenter dataset to further refine best parameters for surgical or percutaneous PVR as well as provide better evidence for counseling of expected post-PVR outcomes is clearly needed to assist in management in patients with TOF.

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