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Commentary: Diastolic dysfunction and timing of pulmonary valve replacement in Tetralogy of Fallot

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**Central message:** Defining the role of diastolic dysfunction and pulmonary valve replacement in tetralogy of Fallot is complex.

**Central picture legend:** Dilated right ventricle in tetralogy of Fallot patient with severe pulmonary valve insufficiency.

**Figure 1 legend:** MRI of a dilated right ventricle in tetralogy of Fallot patient with severe pulmonary valve insufficiency. (LV: left ventricle, RV: right ventricle)

Traditionally, long-term outcomes in tetralogy of Fallot (TOF) have focused on the size and function of the right ventricle (RV) and left ventricle (LV) (Figure 1). RV diastolic and systolic volumes obtained with cardiac magnetic resonance imaging (MRI) are used to decide timing of pulmonary valve replacement (PVR) in these patients. [1] The risk of mortality is higher in patients with decreased right ventricular ejection fraction (RVEF) less than 40%, RV mass to volume ratio of 0.45 g/ml and age at PVR of > 28 years [2]. Recently published guidelines in the management of repaired TOF patients support the use of serial cardiac MRI to aid in the timing of PVR [3]. PVR is recommended in patients with symptoms (dyspnea, chest pain, exercise intolerance) and moderate or severe pulmonary insufficiency. In asymptomatic patients, PVR is reasonable with two of the following: mild or moderate RV/LV systolic dysfunction, RV dilation (RVEDVI ≥160 mL/m2 or RVESVI ≥80 mL/m2 or RVEDV ≥2x LVEDV), RV systolic pressure ≥2/3 systemic pressure, progressive reduction in exercise tolerance. Notably, diastolic dysfunction is absent in the decision process.
In this issue of *JTCVS*, Tominaga and colleagues [4] analyzed risk factors for cardiovascular adverse events after PVR in 63 patients (2003-2019) with repaired TOF or pulmonary atresia with ventricular septal defect. All patients underwent evaluation by cardiac catheterization, echocardiography, cardiac MRI and computed tomography (CT) before PVR. The cardiac MRI or CT were used to measure the ventricle volume, ejection fraction (EF), and the right atrial volume index (RAVI) at the end-diastolic phase. Late end-diastolic forward flow (EDFF) in the main pulmonary artery (PA) with atrial contraction was evaluated by the echocardiography. PVR was performed at the age of 38 years with no mortality observed. In 23 patients (37%) with atrial arrhythmia before PVR, either a full or right-sided maze procedure was performed. Primary outcome was post-PVR cardiac adverse events, including atrial tachyarrhythmia, sinus node dysfunction, atrioventricular block, ventricular tachycardia, and hospitalization due to heart failure. During a mean follow-up period of 6.5 years, cardiac adverse events were observed in 22 patients. The risk factors for the cardiac adverse events were three traditional parameters of diastolic dysfunction: the presence of EDFF with atrial contraction, elevated RAVI, and elevated right atrial pressure (RAP). Ventricle volume and EF (either right or left), age at initial repair or at PVR, past history of atrial arrhythmia, tricuspid regurgitation, QRS duration were not the risk factors on multivariable analysis. The authors conclude that pre-PVR EDFF, RAVI, and RAP, all of which could be diastolic dysfunction markers, were risk factors for cardiovascular adverse events after PVR. Overall, the authors should be congratulated for their excellent
clinical results as well as attempting to clarify the role of diastolic dysfunction in timing of PVR.

A few things should be highlighted prior to drawing any strong conclusions regarding diastolic dysfunction. Almost two-thirds of patients had a concomitant tricuspid valve repair at the time of PVR. The number of patients who underwent tricuspid valve repair is much higher than reported in other series with PVR [5]. We speculate that the presence of tricuspid regurgitation would cause elevated RAP and elevated RAI which, in turn, would result in atrial dilatation which provides a substrate for arrhythmias [6]. Next, one third of patients had shunt palliation prior to TOF repair. One would have to consider that interim palliation with a shunt followed by late TOF repair would result in persistent RV hypertrophy which likely alters long term diastolic function. Newer studies using echocardiography and MRI assessing atrial function with strain have shown abnormal atrial reservoir, contractile and booster function in patient with repaired TOF and these indices of atrial function are associated with abnormal systolic and diastolic function [7]. With regard to EDFF, it is determined by a combined effect of RV compliance, RV size, residual pulmonary valve function, degree of PR, and pulmonary vascular resistance, all of which interact with each other and may not always indicate RV diastolic dysfunction [8]. Finally, 37% of the patients had a concomitant maze operation which could obviously influence the presence of postoperative arrhythmias. All these coexisting issues make it difficult to focus the diastolic dysfunction only on the presence of PR, and therefore, add to the challenge of making meaningful recommendations for PVR timing.
In conclusion, the current report serves to remind us of the complex nature of PVR timing in repaired TOF patients with PR. Although this study has obvious confounders, it raises several important questions and the need for further studies to elucidate what additional variables are needed to help us decide about timing of PVR. Should diastolic markers (RA strain, RAP and EDFF) be used in these patients to help decide about timing of surgery? Should diffuse myocardial fibrosis as assessed by newer MRI modalities like T1 mapping be used as an additional marker to help guide the timing of PVR? Should there be a focus on timing of initial surgery in TOF to help with long term outcomes by avoiding cyanosis and limiting the degree of RV hypertrophy? The answer to all of these questions is likely yes and should be the subject of future large, multicenter studies.
References


