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# Letters

## Pulmonary Valve Replacement After Repair of Pulmonary Stenosis Compared With Tetralogy of Fallot

Similar to patients with tetralogy of Fallot (TOF), patients born with congenital pulmonary stenosis (PS) may initially require intervention to relieve right ventricular (RV) outflow tract obstruction. As a consequence, patients with both conditions may develop deleterious RV volume overload due to residual pulmonary regurgitation (PR) (1,2). In patients with repaired TOF, the timing of pulmonary valve replacement (PVR) to treat RV overload is usually guided by RV volume thresholds, above which optimal RV remodeling is unlikely (2,3). However, it is unknown whether these thresholds can also be applied in patients with residual PR after congenital PS repair (PS-PR). Our objective was to determine RV remodeling after PVR in PS-PR patients, and compare remodeling with matched TOF patients with residual PR (TOF-PR).

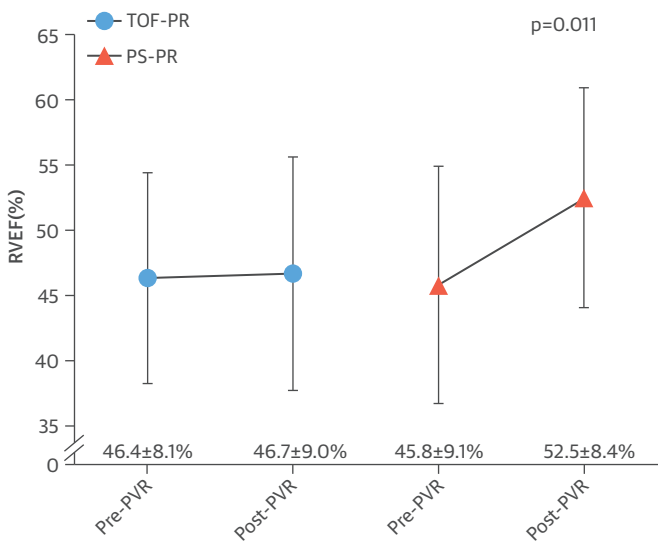
In this retrospective, multicenter, cohort study, PS-PR patients who had undergone PVR and in whom both preoperative and postoperative cardiovascular magnetic resonance (CMR) imaging was performed (previously reported protocol) (2) were matched in a 1:2 ratio with TOF-PR patients on preoperative RV end-diastolic volume (EDV) (within 20 ml/m$^2$).

Out of a total of 50 PS-PR and 157 TOF-PR patients, in 25 PS-PR patients and 105 TOF-PR patients, preoperative CMR was available. In independent samples Student *t* test, unmatched PS-PR patients had higher preoperative RV ejection fraction (EF) (48 ± 9% vs. 43 ± 8%; p = 0.012) and smaller RVEDV (142 ± 33 vs. 169 ± 40 ml/m$^2$; p = 0.003).

The final study population consisted of 19 PS-PR patients (age, 30 ± 10 years; 53% male; QRS duration 112 ± 27 ms; homograft in 74%; 42% New York Heart Association [NYHA] functional class ≥ II) and 38 matched TOF-PR patients (age, 32 ± 9 years; 50% male; QRS duration 142 ± 25 ms; homograft in 97%; 66% NYHA functional class ≥ II). In TOF-PR patients, previous shunt procedures (39% vs. none) and transannular patch repair (63% vs. 21%) were performed more frequently. The PS-PR patients were surgically repaired at a median age of 1.2 years (vs. 4.7 in TOF-PR). During PVR, TOF-PR patients more frequently required concomitant RV aneurysm resection (37% vs. none) and pulmonary artery angioplasty (25% vs. none). Concomitant tricuspid valve angioplasty was performed in 37% of PS-PR patients compared with 25% of TOF-PR patients.

After matching, preoperative RVEF, LVEF, RVEDV, LVEDV, and PR fraction (42 ± 12% in PS-PR vs. 45 ± 12% in TOF-PR) were comparable (all p > 0.10). Significant residual preoperative PS (>36 mm Hg on echocardiography) was present in 1 PS-PR patient (5%) compared with 8 TOF-PR patients (21%). CMR was performed 0.9 ± 1.3 years preoperatively and 3.0 ± 2.3 years postoperatively in PS-PR patients compared with 0.6 ± 0.4 years preoperatively and 1.6 ± 1.6 years postoperatively in TOF-PR patients.

**FIGURE 1 RVEF Before and After PVR in Both Groups**




Course of RVEF from preoperative to postoperative cardiovascular magnetic resonance assessment in 19 PS-PR patients and 38 matched TOF-PR patients. Average preoperative and postoperative values are indicated with standard deviation. The p value of difference in change of RVEF between groups is noted. EF = ejection fraction; PR = pulmonary regurgitation; PS = pulmonary stenosis; PVR = pulmonary valve replacement; RV = right ventricle; TOF = tetralogy of Fallot.

The PS-PR patients had a greater postoperative decrease in RVEDV (-47 ± 17 ml/m$^2$ vs. -38 ± 25 ml/m$^2$; p = 0.17) and RV end-systolic volume (-32 ± 17 ml/m$^2$ vs. -20 ± 18 ml/m$^2$; p = 0.023). The RVEF generally increased in patients with PS-PR (46 ± 8% to 53 ± 8%) and remained stable in TOF-PR patients (46 ± 9% to 47 ± 9%; p = 0.011 between groups) (**Figure 1**). Overall, the RVEF increased substantially (>5%) in 63% of PS-PR patients compared with only 24% of TOF-PR patients (chi-square: p = 0.004). Finally, multiple linear regression analysis to adjust for concomitant procedures and preoperative PS was performed. PS-PR remained associated with improved RVEF (adjusted β, 5.9; p = 0.048), whereas concomitant procedures were not (all p > 0.10).

To our knowledge, this is the first study to report CMR-derived hemodynamic effects of PVR in PS-PR patients. The RVEF improved substantially in about two-thirds of PS-PR patients, whereas it generally remained stable in matched TOF-PR patients. Preoperatively, PS-PR patients had higher RVEF and smaller RVEDV when compared with nonmatched TOF-PR patients, similar to a recent report (1). The improvement of RVEF after PVR in PS-PR patients compared with matched TOF-PR patients may be explained by factors such as a less extensive surgical history, absence of previous cyanosis, fewer RV outflow tract aneurysms, and less interventricular dyssynchrony (1,4).

Our retrospective cohort study was limited by a small sample size and missing preoperative or postoperative CMR in a subgroup.

In conclusion, PS-PR patients had superior RV remodeling after PVR when compared with matched TOF-PR patients. Waiting with PVR until symptoms or progressive RV dilation may be considered in PS-PR patients, because a more robust improvement of RV hemodynamic parameters can be expected.

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# Blunted Cortisol Stress Response and Depression-Induced Hypocortisolism Is Related to Inflammation in Patients With CAD

Both depression and psychosocial stress are associated with coronary artery disease (CAD) (1). However, the precise underlying mechanisms have not been elucidated fully. Cortisol is involved in the pathophysiological process of inflammation and atherosclerosis (2), but evidence directly linking depression and social stress with cortisol in CAD patients is limited. Bhattacharyya et al. (3) revealed a flatter diurnal cortisol slope in depressed (+CAD) compared with nondepressed (-CAD) patients, but found no relationship between the diurnal cortisol slope and depression in people without CAD (3). Our study aimed to elucidate the social stress-induced cortisol response in (+CAD) and (-CAD) patients in relation to depressive symptoms and high-sensitivity C-reactive protein (hsCRP). We hypothesized that depressed (+CAD) patients would show a blunted cortisol stress response with a close relation to systemic inflammation.

We investigated 91 subjects, 46 of whom experienced CAD with (21 [+D+CAD]) or without depressive symptoms (25 [-D+CAD]) and were compared with 22 depressed patients without CAD (+D-CAD) and 21 healthy subjects (-D-CAD). The German version of the depression subscale of the Hospital Anxiety and Depression scale (HADS) was used to rate symptom