Right Ventricular Remodeling After Pulmonary Valve Replacement: Early Gains, Late Losses

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Background. **Although early results of pulmonary valve replacement (PVR) after tetralogy of Fallot repair have been described, information about late postoperative ventricular size and function is lacking. This study was designed to characterize right ventricular (RV) remodeling up to 10 years after PVR.**

Methods. **Retrospective analysis was conducted of cardiovascular magnetic resonance (CMR) data from 2002 to 2011 in 101 patients (244 studies) who underwent PVR and had one or more post-PVR CMR studies at five post-PVR time intervals up to 10 years.**

Results. **Compared with pre-PVR values, in the 0- to 1-year post-PVR group, pulmonary regurgitation (PR) fraction decreased from 49 ± 11% to 3 ± 2% ($p < 0.001$), RV end-diastolic volume index (EDVi) decreased by 39% ($p < 0.001$), RV end-systolic volume index (ESVi) decreased by 33% ($p < 0.001$), and RV ejection fraction (EF) decreased from 48 ± 8% to 44 ± 8% ($p = 0.01$). These values remained unchanged through the sixth post-PVR year. However, by 7 to 10 years after PVR (n = 15), RVEDVi and RVESVi were significantly increased and had returned to 84% and 104% of pre-PVR volumes, respectively, and RV EF had declined further. Increasing RV EDVi correlated with increasing grades of PR ($r_s = 0.36$, $p < 0.001$), tricuspid regurgitation ($r_s = 0.33$, $p < 0.001$), and RV pressure ($r_s = 0.32$, $p = 0.03$).**

Conclusions. **In this cohort, early reduction in RV size showed a gradual return toward preoperative values by 7 to 10 years after PVR. The late adverse RV remodeling was associated with increased RV volume and pressure loads. These findings highlight the palliative nature of PVR and the importance of continued surveillance.**

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Surgical reconstruction of the right ventricular outflow tract (RVOT) in patients with tetralogy of Fallot (TOF) and other conotruncal anomalies often leads to pulmonary valve dysfunction with varying degrees of right ventricular (RV) volume and pressure overload [1, 2]. Coupled with other surgical sequelae, such as patch material and scar tissue in the RVOT, tricuspid regurgitation (TR), and conduction delay, the abnormal hemodynamic load results in RV dilatation and dysfunction. Studies in these patients have shown that RV dilatation, dysfunction, and hypertrophy, as well as left ventricular (LV) dysfunction, are associated with increased risks of tachyarrhythmias and death [3–7]. Pulmonary valve replacement (PVR) has been increasingly used to reduce the hemodynamic load on the RV with the goals of reversing the adverse chamber remodeling and improving long-term clinical outcomes. Although the goal of improving long-term outcomes has not yet been demonstrated, several reports have documented the early results of the PVR procedure [3, 6, 8–10]. These studies have consistently shown that after PVR, RV systolic and diastolic volumes decrease by 30% to 40%, RV ejection fraction (EF) remains mostly unchanged, LV volume increases slightly, and LV EF is stable. Although symptomatic improvement is consistently reported early after PVR [6, 8–10], data regarding exercise values and arrhythmia burden are conflicting [6, 8–12].

The literature on ventricular remodeling after PVR is limited to short-term results, with little information beyond the first 2 to 3 years after valve implantation. Therefore, we undertook this study to characterize changes in RV and LV volumes, mass, and function up to 10 years after PVR and to explore preoperative and postoperative factors associated with these changes.

Patients and Methods

Patients

The database of the Boston Children's Heart Center (Boston, Massachusetts) was searched for patients fulfilling the following inclusion criteria: (1) diagnosis of repaired TOF or similar physiology; (2) a history of surgical PVR between 2002 and 2011; (3) a cardiovascular magnetic resonance (CMR) study before PVR, with a pulmonary regurgitation (PR) fraction of 25% or greater and an RV end-diastolic volume index (EDVi) Z-score of 3

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Abbreviations and Acronyms

CMR	= cardiovascular magnetic resonance
EDVi	= end-diastolic volume index
EF	= ejection fraction
ESVi	= end-systolic volume index
LV	= left ventricle or left ventricular
PR	= pulmonary regurgitation
PVR	= pulmonary valve replacement
RV	= right ventricle or right ventricular
RVOT	= right ventricular outflow tract
TOF	= tetralogy of Fallot
TR	= tricuspid regurgitation

or greater; and (4) at least 1 CMR study after PVR. Exclusion criteria included (1) age at PVR less than 4 years; (2) prior surgical or transcatheter PVR; and (3) acute dysfunction of the bioprosthetic pulmonary valve, defined as moderate or severe stenosis (peak Doppler gradient ≥60 mm Hg) or moderate or severe regurgitation within 1 month of the surgical procedure.

The study was approved by the Scientific Review Committee of the Department of Cardiology and the Committee on Clinical Investigation of Boston Children's Hospital.

Study Design

We retrospectively evaluated ventricular remodeling after PVR by 2 methods (Fig 1): (1) a cross-sectional analysis of all 244 CMR studies in 101 patients, and (2) a longitudinal analysis of 184 CMR examinations in 47 patients who had 2 or more post-PVR CMR studies without an intervening cardiac procedure. In the cross-sectional analysis, post-PVR CMR studies were grouped according to the following time periods: 0 to less than 1 year (n = 48), 1 to less than 2 years (n = 33), 2 to less than 4 years (*n* = 43), 4 to less than 7 years (n = 18), and 7 to 10 years (n = 15). Patients were censored at the time of the latest post-PVR CMR that preceded any subsequent surgical or transcatheter intervention. When a patient had more than one CMR study in a given time period, the latest study was included in the analysis.

Cardiovascular Magnetic Resonance Imaging and Analysis

Studies were performed with commercially available 1.5-tesla scanners (GE Medical Systems, Waukesha, WI, and Philips Healthcare, Best, The Netherlands). The technical details of our institutional CMR imaging protocol for assessment of patients with repaired TOF have been described in detail [2].

Offline measurements were performed using a commercially available software package (Medis Medical Imaging Systems, Leiden, The Netherlands). Details of the measurement techniques used in our laboratory in patients with repaired TOF, as well as the intraobserver, interobserver, and test-retest variability, have been reported [2, 13, 14].

Echocardiography

Echocardiograms were performed using commercially available cardiac scanners (Philips Medical Systems, Andover, MA). Using the echocardiogram performed closest to the CMR study, the severity of TR was graded based on the color Doppler vena contracta width as none/trivial, mild, moderate, or severe, according to the American Society of Echocardiography guidelines [15]. RV pressure load was classified as normal, mild, moderate, or severe based on the peak Doppler gradient across the RVOT, peak TR jet velocity, and systolic septal configuration (Table 1).

Factors Associated With Right Ventricular Remodeling

To evaluate the impact of RV pressure and volume loads on remodeling, we used CMR and echocardiographic data to develop the scoring system shown in Table 1. In each category, a score of 0 or 1 was considered a low load, whereas a score of 2 or 3 was considered a high load. Patients were then classified at each time span into one of the following four loading condition categories: (1) low pressure, low volume; (2) low pressure, high volume; (3) high pressure, low volume; and (4) high pressure, high volume.

To explore pre-PVR variables associated with adverse RV remodeling early (0 to 2 years) and late (5 to 10 years) after PVR, we compared patients with optimal versus suboptimal RV EDVi and EF. Optimal post-PVR RV remodeling was defined as an EDVi of 120 mL/m^2 or less or an EF of 47% or greater. Suboptimal RV remodeling was defined as an EDVi of 170 mL/m^2 or greater or an EF of 40% or less.

Statistical Analysis

Continuous variables were summarized as median and range or mean ± standard deviation, as appropriate. Categorical data were summarized as frequency and percentage. For the cross-sectional analysis, mean values of CMR measurements of ventricular size and function were compared across six predefined time periods (pre-PVR period and five post-PVR intervals) by using linear

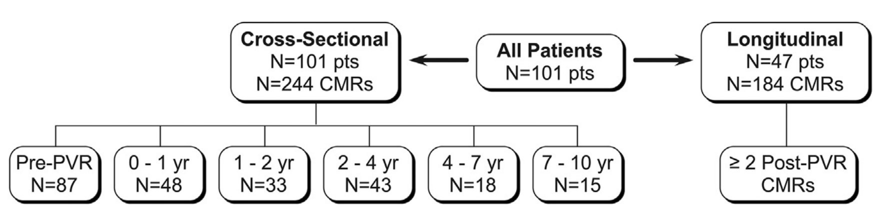

Fig 1. Diagram of study outline. All 101 patients were included in the cross-sectional analysis. Of those, 47 patients had 2 or more cardiovascular magnetic resonance examinations (CMRs) after pulmonary valve replacement (PVR) and were included in the longitudinal analysis.