# Optimal timing for pulmonary valve replacement in asymptomatic patients after tetralogy of Fallot repair using cardiac magnetic resonance imaging

Peter Olejník<sup>1, 2</sup>, Vladimír Neuschl<sup>3</sup>, Zuzana Bérecová<sup>3</sup>, Andrea Glézlová<sup>3</sup>, Jana Šimková<sup>3</sup>

<sup>1</sup>Department of Paediatric Cardiology, Faculty of Medicine, Comenius University, Bratislava, Slovakia <sup>2</sup>Paediatric Cardiology, National Institute of Cardiovascular Diseases, Children's Cardiac Centre, Bratislava, Slovakia <sup>3</sup>Institute of Diagnostic Imaging, MRI s.r.o., Trnava, Slovakia

## **INTRODUCTION**

Severe pulmonary regurgitation (PR) is the most common late complication in patients with tetralogy of Fallot (TOF) after surgery including transannular patch. Long-term severe PR results in significant right ventricular (RV) dilatation and, ultimately, dysfunction [1]. Although RV volume load can be tolerated for many years during childhood and adolescence, the incidence of arrhythmias, exercise intolerance, heart failure, and sudden cardiac death nearly triple during the third postoperative decade and afterwards [1–3].

Pulmonary valve replacement (PVR) is the only available treatment of severe PR associated with significant reduction of PR and improvement of RV metric parameters [4]. Cardiovascular magnetic resonance (CMR) has become a gold standard imaging tool in this patient population, providing unique RV volumetric and functional data [1]. For many years progressive exercise intolerance, heart failure symptoms, syncope, or ventricular tachycardia have been indications for PVR in patients with severe PR [1]. As Geva et al. [5] clearly demonstrated, severely symptomatic patients referred for PVR had already had markedly increased RV volumes and RV dysfunction, and their postoperative RV volumes could not reach normal values. Therefore, a tremendous effort to analyse the optimal timing of PVR by identifying preoperative RV volume threshold values associated with RV size normalisation has been made over the past two decades [6-8].

#### METHODS

Between 2009 and 2015, 26 asymptomatic TOF patients after complete surgical correction including transannular patch, treated at our institution, were recruited for the study. All of them underwent surgical PVR due to severe PR. CMR was performed < three years prior to PVR and after PVR in each patient. Each CMR study evaluated RV volumetric parameters and RV ejection fraction (RVEF). The objective of the study was to compare the improvement and normalisation of post-PVR volumetric and functional ventricular parameters between patients with preoperative RV end-diastolic volume index (RVEDVi) > 170 mL/m<sup>2</sup> (group A) and preoperative RVEDVi < 170 mL/m<sup>2</sup> (group B), as well as between patients with preoperative RV end-systolic volume index (RVESVi) > 85 mL/m<sup>2</sup> (group C) and preoperative RVESVi < 85 mL/m<sup>2</sup> (group D).

#### Statistical analysis

Data were analysed using the JMP 5.0.1 (Statistical Analysis, Cary, NC, USA) statistical software. T test was used for continuous data comparison. The continuous data are presented as mean  $\pm$  standard deviation. Comparison of nominal parameters was evaluated by Fisher exact test. A p-value < 0.05 was considered significant. The standard CMR values for children and adults summarised in the study by Kawel-Boehm et al. [9] were considered as normal RV volumetric and functional values.

# **RESULTS AND DISCUSSION**

Data on RVEDVi and RVESVi decrease, and RVEF improvement in individual groups, as well as a comparison of the improvement and normalisation of each parameter between groups A and B and groups C and D are summarised in Table 1. A higher rate of postoperative RVEDVi (p < 0.015) and RVESVi (p < 0.001) normalisation was observed in patients with preoperative RVEDVi < 170 mL/m<sup>2</sup>. Similarly, a higher rate of post-PVR RVESVi (p < 0.001) and RVEF (p < 0.001)

Address for correspondence:

Dr. Peter Olejník, Paediatric Cardiology, National Institute of Cardiovascular Diseases, Children's Cardiac Centre, Bratislava, Limbová 1, 83101, Slovakia, tel: +42 1907152641, e-mail: petoolejnik@gmail.com

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Parameter	Group A (n = 14); preoperative RVEDVi > 170 mL/m <sup>2</sup>	Group B (n = 12); preoperative RVEDVi < 170 mL/m <sup>2</sup>	Group C (n = 16); preoperative RVESVi > 85 mL/m <sup>2</sup>	Group D (n = 10); preoperative RVESVi < 85 mL/m <sup>2</sup>
Male/female sex [n]	8/6	6/6	9/7	5/5
Age at the time of PVR [years]	17.1 ± 5.7	19.3 ± 4.7	19.0 ± 5.1	17.2 ± 5.6
Time interval of CMR before PVR [months]	10.2 ± 7.6	8.4 ± 6.9	10.2 ± 7.6	$8.4 \pm 6.9$
Time interval of CMR after PVR [months]	16.6 ± 14.3	19.0 ± 16.1	16.6 ± 14.3	19.0 ± 16.1
Pre-PVR RVEDVi [mL/m²]	189.8 ± 18.9	154.6 ± 14.7	183.1 ± 22.9	158.3 ± 19.3
Post-PVR RVEDVi [mL/m <sup>2</sup> ]	$120.8 \pm 27.4$	99.3 ± 13.5	$120.2 \pm 24.0$	$95.9 \pm 16.5$
Rate of RVEDVi normalisation [%]	42.9	91.7	50	80
Comparison of RVEDVi normalisation	p < 0.015		p = 0.22	
Pre-PVR RVESVi [mL/m²]	$107.1 \pm 25.5$	83.7 ± 17.9	$111.8 \pm 17.6$	$71.6 \pm 10.0$
Post-PVR RVESVi [mL/m²]	$65.9\pm24.2$	$27.8\pm7.4$	$67.7 \pm 21.0$	38.6 ± 11
Rate of RVESVi normalisation [%]	21.4	100	6.3	89
Comparison of RVESVi normalisation	p < 0.001		p < 0.001	
Pre-PVR RVEF [%]	$44.1 \pm 9.8$	$46.1\pm8.8$	$39.1 \pm 5.1$	$54.5~\pm~7.5$
Post-PVR RVEF [%]	$46.8\pm8.2$	$52.3\pm8.8$	$44.7\pm6.0$	$56.8\pm7.0$
Rate of RVEF normalisation [%]	33	50	0.0	70
Comparison of RVEF normalisation	p = 0.66		p < 0.001	

Table 1. Evaluation of cardiac magnetic resonance parameters in patient groups A, B, C, and D

Data are shown as mean ± standard deviation, number, or percentage. CMR — cardiac magnetic resonance; PVR — pulmonary valve replacement; RVEDVi — right ventricular end-diastolic volume index; RVEF — right ventricular ejection fraction; RVESVi — right ventricular end-systolic volume index

normalisation was found in patients with preoperative RVESVi  $< 85 \text{ mL/m}^2$ .

The timing of PVR in asymptomatic patients after TOF repair with severe residual PR is still controversial. The risk versus benefit of procedure-associated risks and "overmature" volume-overloaded RV associated with irreversible dysfunction must be taken into account [1].

In comparison to the study by Buechel at al. [7], in which RV size returned to normal in all patients whose preoperative RVEDVi was  $< 150 \text{ mL/m}^2$ , we observed postoperative RVEDVi normalisation in 91.7% of patients with preoperative RVEDVi  $< 170 \text{ mL/m}^2$ .

We found postoperative RVESVi normalisation in 88.9% of patients with preoperative RVESVi < 85 mL/m<sup>2</sup>. This finding is comparable with the results of the study by Oosterhof et al. [8], in which a cut-off value 82 mL/m<sup>2</sup> was established as the threshold to achieve RV normalisation.

In our study RVEDVi did not normalise in 6/10 (60%) patients, RVESVi in 10/10 (100%) patients, and RVEF in 10/10 (100%) patients with preoperative RVEDVi > 170 mL/m<sup>2</sup> along with preoperative RVESVi > 85 mL/m<sup>2</sup>, which supports the results of the study by Therrien et al. [6] reporting 0% RV size normalisation in patients with pre-PVR RVEDVi > 170 mL/m<sup>2</sup>.

Taking into account the patients with preoperative RVEDVi < 170 mL/m<sup>2</sup> along with preoperative RVESVi < 85 mL/m<sup>2</sup>, RVEDVi normalised in 6/6 patients (100%), RVESVi in 6/6 patients (100%), and RVEF in 4/6 patients (66.7%) in our study. This finding correlates with the results of the study by Oosterhof et al. [8] identifying pre-PVR RVEDVi < 160 mL/m<sup>2</sup> and RVESVi < 82 mL/m<sup>2</sup> as predictors of a normal postoperative RV size.

The limitations of the study comprise a relatively small number of patients and short post-PVR follow-up.

In conclusion, we found that RV volumetric and functional parameters in asymptomatic patients after TOF repair normalised if PVR was performed not later than when preoperative RVEDVi reached 170 mL/m<sup>2</sup> or preoperative RVESVi reached 85 mL/m<sup>2</sup>. Based on this finding and the results of analogous studies, patients after TOF repair should be referred for PVR after reaching the RVEDVi range of 160–170 mL/m<sup>2</sup> or RVESVi range of 80–85 mL/m<sup>2</sup>.

## Conflict of interest: none declared

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