

# What can pulmonary regurgitation indices reflect in patients after tetralogy of Fallot repair?

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## Abstract

**Background:** Residual haemodynamic complications remaining after surgical correction of tetralogy of Fallot (ToF) require regular follow-up.

**Aim:** To establish the utility of pulmonary regurgitation (PR) indices in the routine clinical management of adults with repaired ToF.

**Methods:** 83 consecutive patients with repaired ToF underwent transthoracic echocardiography (TTE), cardiopulmonary exercise test (CPET), cardiac magnetic resonance (CMR), and laboratory test evaluation. They were divided into two subgroups [PR (+) vs. PR (–)] according to the degree of PR fraction (PRF > 20% vs. ≤ 20%) assessed by CMR.

**Results:** Analysis showed that PR vena contracta (PR VC) ≤ 5 mm in TTE study was 83% sensitive and 68% specific in identifying patients with PRF ≤ 20%. Furthermore, PR index (PRi) ≥ 0.73 was 85% sensitive and 43% specific in identifying patients with non-significant PR. In this group of patients, there were significant correlations of TTE parameters describing the degree of PR and right ventricle (RV) size with reference modality CMR. There was no certain influence of PR severity on RV function, physical performance, and renal or hepatic failure indices.

**Conclusions:** PRi and PR VC are helpful parameters in distinguishing between mild and significant PR and may limit the indication for CMR investigation in a group with non-significant PR. The severity of PR in our study did not seem to have an impact on RV function, physical performance, liver or kidney function indices.

**Key words:** cardiac magnetic resonance, cardiopulmonary exercise test, echocardiography, pulmonary regurgitation, tetralogy of Fallot

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## INTRODUCTION

Tetralogy of Fallot (ToF) is the most common type of cyanotic heart disease, with an estimated incidence of 5–6% of all patients with a congenital heart defect [1]. For most patients, surgical management is available with favourable outcomes [2], although life expectancy is still less than in the general population [3]. Surgical management of ToF leaves anatomical and functional abnormalities such as pulmonary regurgitation (PR), residual or recurrent pulmonary stenosis, right ventricular outflow tract (RVOT) aneurysm or residual ventricular septal defect (VSD). These complications require regular follow-up in all patients after initial correction of ToF. Transthoracic two-dimensional echocardiography (TTE) provides information on right ventricular (RV) dilatation, hypertro-

phy, systolic and diastolic dysfunction. Doppler methodology can detect tricuspid or pulmonary valvular regurgitation, residual shunts and is used to measure flow velocities. Because of well-known limitations, TTE often fails to provide reliable anatomic and haemodynamic information. Today, cardiac magnetic resonance (CMR) has become the 'gold standard' of noninvasive imaging for patients with repaired ToF [4, 5]. CMR allows quantification of the size of both ventricles, their function, and blood flow. Adult patients after surgical correction of ToF usually have satisfactory exercise capacity, though they can never tolerate a similar amount of load as healthy volunteers [6]. It is recommended to measure oxygen uptake in a cardiopulmonary exercise test (CPET) so as to make their real exercise capacity estimation objective. In addition, renal

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or hepatic failure may not facilitate a decision as to invasive procedures or pharmacological treatment.

The aim of this study was to analyse the importance of PR indices in the routine management of patients after ToF repair.

## METHODS

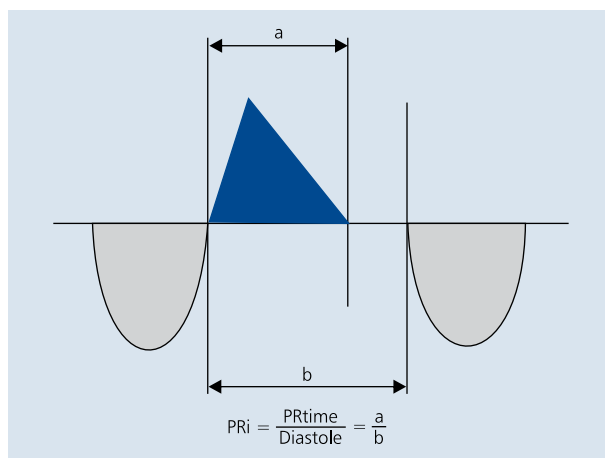
After approval by the institute's research ethics committee, 83 adult patients with repaired ToF were included in the study, regardless of residual haemodynamic complications (PR/RVOT stenosis/combination). Informed consent was obtained from each patient and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The study consisted of consecutive patients aged 18–56 (mean  $31.5 \pm 11.6$  years, who had been operated on 7–38 years earlier ( $21.64 \pm 6.88$  years) at the age of 1–46 (mean  $11.9 \pm 12.2$  years). A palliative Blalock-Taussig shunt was performed in early childhood in all patients. Afterwards, total correction was made with the use of right ventriculotomy; using the transannular patch technique (33 patients; 39.76%), or monocusp homograft (14 patients; 16.87%), or aortic homograft (11 patients; 13.25%). In the cases of 25 (30.12%) patients, we were not able to obtain information about the applied surgery technique because the procedure had taken place abroad or more than 20 years ago and the medical history had been lost. On the basis of the patients' medical history, we established that in 13 (15.66%) patients, reoperation had been necessary (3–26 years before) because of residual VSD (three patients), RVOT stenosis or PR (five patients) or a combination of both (five patients).

All patients were clinically stable, in sinus rhythm, without intracardiac devices or any important cardiac or noncardiac disorders. They were admitted to the Department for one-day hospitalisation and evaluation between November 2009 and December 2011. The routine care for patients after ToF repair at our centre includes echocardiography, electrocardiography (ECG), blood test, CMR (in cases where it was not performed before or clinically needed) and a cardiopulmonary stress test. Most of the patients have regular control visits to our department, and a follow-up study is proceeding.

### Echocardiography

All patients were examined at rest, during normal quiet respiration, in the left lateral and supine positions, according to the guidelines of the European Society of Echocardiography [7]. The study was performed with a 3 to 4.5 MHz transducer (Vivid 7, GE Medical Systems). An ECG was recorded simultaneously. Digital stores were used for all echocardiographic images.

The RV dimensions were evaluated in RVOT and RV inflow tract standard views. RV areas were manually traced in end-diastole and end-systole and were employed for the calculation of fractional area change (FAC). Tricuspid annulus plane systolic excursion (TAPSE) was measured in an apical



**Figure 1.** Method of calculating pulmonary regurgitation index (PRi). Pulmonary regurgitation duration was measured from its onset in early to the end of the regurgitant Doppler signal (a). The diastolic time was measured from the end of the forward pulmonary flow to the beginning of the next forward pulmonary flow (b). The PRi is the ratio between pulmonary regurgitation duration and total diastole

four-chamber view. Pulmonary artery and tricuspid flow velocities were recorded using pulsed or continuous (above Nyquist limit) wave Doppler echocardiography. The Bernoulli equation was applied to measure peak pulmonary pressure gradient. In order to measure the degree of PR, the most frequent parameters used in our institute were employed: the PR index (PRi, Fig. 1) — the ratio between the duration of PR and total diastole, the regurgitation jet width PR vena contracta (PR VC), and pressure half time (PHT).

### Cardiac magnetic resonance

All scans were performed with a 1.5 T scanner (Avanto, Siemens, Erlangen, Germany). For cine imaging, a segmented steady state free precession (SSPF) sequence in breath hold technique and retrospective ECG triggering were used. Ventricular volumes were calculated by summation of ventricular cavity areas, assessed by manual tracing on a stack of multi-section gradient-echo images of a specific time frame, and multiplied by section thickness. Ejection fraction was calculated from the end-diastolic and end-systolic volumes in the usual way. Velocity-mapping CMR, performed in a double-oblique plane perpendicular to the main pulmonary artery was used to quantify PR volume (PRV) and to calculate PR fraction (PRF) [8].

### Cardiopulmonary exercise test

The test was performed on a running track (ZAN Ergo 600, Delmar Reynolds). Two protocols of CPET examination were used for the best evaluation of physical activity. Patients with good exercise tolerance were tested by classic Bruce protocol. For subjects with deterioration of physical activity, the modified Bruce protocol was used. Ventilation, oxygen uptake

**Table 1.** Clinical data

	Mean ± SD	Number (n)	Range	Per cent
Age [years]	31.51 ± 11.6		18–56	
Men (n)		57		68.67
Women (n)		26		31.33
Body mass index [kg/m <sup>2</sup> ]	24.26 ± 4.12		17.3–34.4	
Systolic blood pressure [mm Hg]	120 ± 15.1		87–164	
Diastolic blood pressure [mm Hg]	74.16 ± 10.1		43–103	
Heart rate [bpm]	72.87 ± 19.3		50–98	
NYHA functional class (value)		I — 66 (79.5%); II — 17 (20.5%); III–IV — 0		
Saturation [%]	96 ± 1.7		89–100	
QRS duration [ms]	150.41 ± 25.8		80–194	
Right bundle branch block		71		85.54
RVH in ECG		24		28.92

ECG — electrocardiography; NYHA — New York Heart Association; RVH — right ventricular hypertrophy; SD — standard deviation

(peak VO<sub>2</sub>), and carbon dioxide production were measured continuously. Heart rate was assessed by continuous ECG. Blood pressure was recorded manually by cuff sphygmomanometry every 2 min. The tests were finished when planned performance (appropriate maximal heart rate) was achieved, or when the patient declared exhaustion. The system was calibrated with a standard gas mixture of predetermined concentration before each test. The investigators evaluated the results of the CPET unaware of the results of the other tests.

**Blood samples**

In the cases of all patients, the blood samples were drawn from an antecubital vein prior to all tests and after a 15 min rest in the supine position. Blood was analysed with regard to cardiac (NT-proBNP — N-terminal prohormone of B-type natriuretic peptide) as well as renal (creatinine, GFR — glomerular filtration rate) and hepatic function (Alat — alanine aminotransferase, Aspat — aspartate aminotransferase). Patients with known diseases of these systems were excluded from the study.

**Statistical analysis**

All parameters were checked for normal distribution (based on standardised skewness and standardised kurtosis) and were log transformed, when values departed significantly from normality. Pearson product moment correlations were used for the evaluation of the relationship between pairs of variables. P values ≥ 0.05 were considered statistically insignificant. One-way analysis of variance (ANOVA) was applied to discriminate among the means of the parameters (Tukey HSD test at p ≤ 0.05 level) obtained in the different groups of patients. The homogeneity of the variance was investigated by Levene’s test. The model of multivariable correlation was obtained from automatic statistical software and was used to test the impact of different independent variables on PRV.

The points for the assumed critical values were calculated on the basis of regression equation. Regression with the strongest definition of tested parameters was selected (the highest coefficient of determination). A Statgraphics Centurion version XV program was employed for the statistical evaluation.

**RESULTS**

**Patient characteristics**

Demographic and clinical data of 83 adults with repaired ToF included in our research are presented in Table 1.

**Pulmonary valve**

The patients were divided into two subgroups according to the severity of PR assessed by CMR: PRF > 20% [PRF (+), n = 52], and PRF ≤ 20% [PR (-), n = 31]. The PRF > 20% is considered significant because it is associated with the same magnitude of RV enlargement as regurgitant fraction exceeding 40%, which is rarely seen [9, 10].

PR had variable degrees of severity in the whole group and there were significant and expected differences in PHT, PR VC, PRi, PRV and PRF between the two subgroups. The differences between the two subgroups and the mean values of selected parameters of TTE, CMR, CPET and laboratory tests are shown in Table 2.

In all patients, there was a highly significant correlation between echocardiographic and CMR parameters of PR (PR VC, PRi, PRV, PRF) — see Table 3. In the subgroup without significant PR, a moderate correlation between the above parameters of PR was found. In the PR (+) subgroup, there was no correlation between TTE and CMR parameters of PR except for a weak relationship between PR VC and PRV. Further analysis revealed that PR VC ≤ 5 mm was 83% sensitive and 68% specific in identifying patients with PRF ≤ 20% (PPV 0.80, NPV 0.72 and accuracy 0.77). Furthermore, PRi ≥ 0.73 was

**Table 2.** Selected echocardiographic, cardiac magnetic resonance and cardiopulmonary exercise testing measurements — mean value (SD)

	All patients (n = 83)	PR (+) (n = 52)	PR (-) (n = 31)	P: PR (+) vs. PR (-)
Main pulmonary artery [mm]	24.43 (4.17)	24.82 (4.43)	23.77 (3.67)	NS
Peak pulmonary gradient [mm Hg]	21.97 (13.87)	20.75 (11.56)	24.00 (17.07)	NS
Mean pulmonary gradient [mm Hg]	11.10 (7.6)	10.44 (6.37)	12.20 (9.23)	NS
Pressure half time [ms]	83.48 (45.99)	90.50 (25.43)	111.15 (49.17)	0.0223
PR VC [mm]	6.53 (3.76)	8.39 (2.61)	3.42 (3.34)	< 0.00001
RVED area [cm <sup>2</sup> ]	29.76 (7.91)	31.84 (7.47)	26.28 (7.48)	0.0015
RVES area [cm <sup>2</sup> ]	19.53 (6.14)	20.48 (6.19)	17.93 (5.83)	NS
RVED volume [mL]	268.19 (80.36)	293.19 (78.97)	226.25 (64.40)	0.0001
RVES volume [mL]	146.46 (53.98)	161.67 (51.11)	121.45 (49.74)	0.0008
PR volume [mL]	32.54 (26.28)	48.27 (20.58)	7.69 (9.93)	< 0.00001
PR fraction [%]	24.6 (17.06)	36.36 (9.17)	6.03 (7.08)	< 0.00001
Metabolic equivalents	8.05 (2.03)	7.90 (2.10)	8.32 (1.92)	NS
VO <sub>2</sub> max [mL/kg/min]	20.29 (5.52)	19.65 (5.34)	21.37 (5.73)	NS
Creatinine [mmol/L]	72.36 (15.71)	73.12 (16.25)	71.08 (14.91)	NS
Alanine aminotransferase [U/L]	29.84 (17.26)	28.50 (15.50)	43.32 (66.82)	NS
Aspartate aminotransferase [U/L]	27.73 (13.44)	26.65 (10.47)	29.55 (17.37)	NS
NT-proBNP [ng/L]	260.72 (402.87)	275.97 (432.71)	235.13 (352.50)	NS

NS — statistically non significant; NT-proBNP - N-terminal prohormone of B-type natriuretic peptide; PR — pulmonary regurgitation; RVED — right ventricular end-diastolic; RVES — right ventricular end-systolic; SD — standard deviation; VC — vena contracta; VO<sub>2</sub> max — maximal oxygen uptake

**Table 3.** Correlation coefficients between echocardiographic and cardiac magnetic resonance parameters characterising pulmonary regurgitation (PR)

		PR volume		PR fraction	
		r	p	r	p
All patients	PHT		NS		NS
	PR VC	0.75	< 0.00001	0.69	< 0.00001
	PRi	0.68	< 0.00001	0.67	< 0.00001
PR (+)	PHT		NS		NS
	PR VC	0.34	0.0170		NS
	PRi		NS		NS
PR (-)	PHT		NS		NS
	PR VC	0.60	0.0003	0.50	0.004
	PRi	0.55	0.0015	0.52	0.0032

PHT — pressure half time; PRi — pulmonary regurgitation index; VC — vena contracta

85% sensitive and 43% specific in identifying patients with non-significant PR (PPV 0.69, NPV 0.62 and accuracy 0.81).

The multivariable correlation was used to reveal the parameters influencing the PR size estimated by CMR (PRV). We took into consideration the following variables: patients' clinical stage (age, age at the time of total ToF correction, time from total correction, body mass index), technique of total ToF management (transannular patch, monocusp

homograft, aortic homograft, unknown technique, need for reintervention) and selected TTE and CMR parameters (degree of pulmonary stenosis, degree of tricuspid regurgitation, RV systolic function, systolic pressure in RV, diastolic time of RV). Eventually we obtained a formula: **PRV = 46.8752 - 0.899892 × A - 25.6065 × R**, where A is age at total correction of ToF and R is reintervention.

Therefore, we conclude that PRV depends in 29.3% (r<sup>2</sup> of formula) on the age at surgical correction and need of reoperation. The reason for repeat intervention was non-contributory. A p value < 0.00001 means a highly statistically significant relationship between the obtained variables using 95% confidence intervals.

### Right ventricle dimension and function

Echocardiographic and CMR RV dimensions were mildly increased in patients included in the research compared to normal values [11]. The RV volume indices acquired by CMR (RVEDV, RVESV, RVEDV BSA, RVESV BSA) and RV end-diastolic area were substantially higher in patients with significant PR (Table 2). There were only moderate direct correlations between CMR indices defining PR (PRV, PRF) and TTE and CMR parameters of RV dimension (Table 4). The influence of PR severity on end-diastolic area or volume was stronger than on end-systolic measurements. We found a similar relationship in the subgroup with significant PR, but such a correlation was not proven in the PR (-) subgroup.

**Table 4.** Correlation coefficients between pulmonary regurgitation (PR) and right ventricular size parameters

		CMR-PR volume		CMR-PR fraction	
		r	p	r	p
All patients	TTE-RVED area	0.45	< 0.00001	0.4528	< 0.00001
	TTE-RVES area	0.29	0.0082	0.2936	0.0082
	CMR-RVED volume	0.42	0.0001	0.3815	0.0005
	CMR-RVES volume	0.38	0.0005	0.3434	0.0019
PR (+)	TTE-RVED area	0.42	0.0023		NS
	TTE-RVES area	0.32	0.0257		NS
	CMR-RVED volume	0.53	0.0001		NS
	CMR-RVES volume	0.44	0.0020		NS
PR (-)	TTE-RVED area	0.43	0.0169	0.4258	0.0169
	TTE-RVES area		NS		NS
	CMR-RVED volume		NS		NS
	CMR-RVES volume		NS		NS

CMR — cardiac magnetic resonance; RVED — right ventricular end-diastolic; RVES — right ventricular end-systolic; TTE — transthoracic echocardiography

**Table 5.** Correlation coefficients between echocardiographic and cardiac magnetic resonance (CMR) parameters characterising right ventricle size

		CMR-RVED volume [mL]		CMR-RVES volume [mL]	
		r	p	r	p
All patients	TTE-RVED area [cm <sup>2</sup> ]	0.76	< 0.00001	–	–
	TTE-RVES area [cm <sup>2</sup> ]		–	0.75	< 0.00001
PR (+)	TTE-RVED area [cm <sup>2</sup> ]	0.66	< 0.00001	–	–
	TTE-RVES area [cm <sup>2</sup> ]		–	0.75	< 0.00001
PR (-)	TTE-RVED area [cm <sup>2</sup> ]	0.82	< 0.00001	–	–
	TTE-RVES area [cm <sup>2</sup> ]		–	0.72	< 0.00001

PR — pulmonary regurgitation; RVED — right ventricular end-diastolic; RVES — right ventricular end-systolic; TTE — transthoracic echocardiography

We found a strong correlation between TTE and CMR parameters characterising RV size (RVED area/RVEDV, RVES area/RVESV) — see Table 5. In the PR (+) group, this correlation was slightly weaker considering end-diastolic parameters. In the group without significant PR, the correlation between end-diastolic dimensions was a little bit stronger.

The RV function assessed by TTE (RV TAPSE, RV FAC) and CMR (RV ejection fraction) was normal. There was only a weak correlation between RV FAC and RV ejection fraction in the whole group and in the group with significant PR;  $r = 0.29$ ,  $p = 0.008$ ;  $r = 0.42$ ,  $p = 0.002$ , respectively. In all patient groups, we did not observe any correlation between severity of PR and RV systolic function assessed by echocardiography or CMR.

**The influence of pulmonary valve dysfunction on other parameters**

There was no correlation between severity of PR and physical capacity (METS and peak VO<sub>2</sub> measured in CPET or degree in

New York Heart Association class) in the group of all patients and in the subgroup without significant PR. In the PR (+) group, we found a moderate correlation between PRV (CMR) and METS;  $r = 0.39$ ,  $p = 0.005$ .

Neither did we observe a relationship between TTE and CMR parameters of PR and biochemical indices of renal (creatinine, GFR) or hepatic failure (Aspat, Alat) or NT-proBNP in the group of all patients and in the PR (-) subgroup. In the group with significant PR, there was a weak negative correlation between PHT and Alat or PRi and Alat ( $r = -0.34$ ,  $p = 0.01$ ;  $r = -0.29$ ,  $p = 0.04$ , respectively).

**Echocardiographic reproducibility**

Inter-observer variability was based on 23 randomly selected patients. Intraclass correlation coefficient (ICC) was used to assess the reproducibility of heart chamber size and conventional Doppler variables. ICC for right and left ventricle dimensions was 0.64–0.84, for pulmonary flow measurements was 0.51–0.65, TAPSE — 0.39, and RV systolic pressure — 0.48.



### **Follow-up data**

During a follow-up lasting 35–62 months (mean 52 months), two patients died because of complications after pulmonary valve surgery, and ten patients underwent successful pulmonary valve replacement, in two of them with simultaneous correction of tricuspid valve regurgitation. In six patients, there was a percutaneous pulmonary valve implantation, (Melody valve [Medtronic] in one, and Edwards Sapien in five [Edwards Lifesciences]). One patient out of these six required a tricuspid valve replacement (Hancock II; Medtronic) and the closure of residual VSD in further observation. One patient had DDDR pacemaker implantation because of tachycardia-bradycardia syndrome and one patient underwent percutaneous pulmonary valvuloplasty due to severe stenosis. Nine patients were lost to follow-up.

### **DISCUSSION**

In ToF patients, PR is a risk factor for RV dysfunction, exercise intolerance, and life-threatening arrhythmias [12, 13]. For the last 30 years, the echo study has been a standard non-invasive imaging modality for diagnostics and follow-up of patients from these groups [14]. Nowadays, CMR is considered an accurate and reproducible technique for assessing RV size and severity of PR [4]. However, each of the techniques has its limitations and disadvantages. The aim of our study was to analyse the importance of PR in routine clinical evaluation and to establish a proper selection to CMR in patients with repaired ToF. In this work, we focused on relatively easy echocardiographic parameters, and that is why we did not show results based on advanced techniques such as strain echocardiography or three-dimensional echocardiography.

### **Pulmonary valve**

In all the patients, there was a highly significant correlation between echocardiographic and CMR parameters of PR. The useful echocardiographic parameters were PR VC, PRi, and PR duration. We did not prove the value of PHT as a single indicator for PR assessment. Reliable estimation of PR by TTE could be applicable in a group of patients with insignificant PR, i.e. PRF  $\leq$  20%. We calculated the TTE values corresponding to PRF  $\leq$  20%, which were PR VC  $\leq$  5 mm and PRi  $\geq$  0.73. We also found that PRV depended in 29.3% on the age at surgical correction and on the need for reoperation. The reason for repeat intervention was non-contributory.

Li et al. [15], in a study of 52 patients after ToF repair, showed that PRi  $<$  0.77 was 100% sensitive and 84.6% specific in identifying patients with PRF  $>$  24.5%. Similarly, PR VC  $>$  0.98 cm was 92% sensitive and 74% specific in identifying significant PRF. In contrast to Li et al.'s [15] research, the innovation of our work is the statistical analysis conducted separately for groups of patients with and without significant PR.

This demonstrated that only in the PR (–) group was this relation reproducible, although in all patient groups the correlation between TTE and CMR parameters was significant. The criteria for significant PR that we used were based on the latest research and therefore we suggested a different cut-off value in identifying patients with non-significant PR. On the other hand, PHT, the well-known parameter for predicting significant PR [10], appeared to be non-contributory in our research. One of the reasons may be the dependence of PHT on dynamic pressure changes, notably expressed in restrictive RV physiology. In such a situation of a rapid increase of RV, filling pressure may falsely lower PHT [16]. An interesting study was conducted by Mercer-Rosa et al. [17]: they suggested that the diastolic and systolic time-velocity integrals ratio may be a helpful quantitative tool for PR assessment. However, this method seems impractical in the concomitant pulmonary stenosis.

The multivariable analysis of PRV employed in our work is also unique. Previous studies investigating the impact of other parameters on PR were based on animal studies, experimental studies and mathematical assumptions [18, 19]. The fact that the PRV depends on the variables used in our analysis in only 29.3%, and that the model does not include the haemodynamic parameters, indicates that further investigation is required.

### **Right ventricle dimension and function**

The RV size and its relatively high correlation with CMR parameters were in line with other observation studies [20]. As in Margossian et al.'s [21] study, we reaffirmed the stronger effect of severe PR on RV end-diastolic volumes than on end-systolic volumes. Our results are also consistent with an interesting study by Greutmann et al. [22]. The authors compared different parameters describing RV size in TTE to referential modality CMR. The highest correlation coefficient was achieved for RV end-diastolic area (TTE) and RV end-diastolic volume (CMR). The correlation with CMR RV size parameters was stronger when TTE RV assessment included RVOT and RV short axis measurements. However, these two parameters were not reaffirmed in multivariable analysis.

The assessment of RV systolic function was more precarious. A moderate correlation between TAPSE and RV ejection fraction assessed in CMR was found by Kjaergaard et al. [20]. In our investigation, we did not find such a relation in any group of patients. It may correspond to Kempny et al.'s [23] study. However, we noticed a weak correlation between RV FAC (TTE) and RV ejection fraction (CMR) in the whole group and in the group with significant PR, whereas Kjaergaard et al. [20] did not observe such an agreement. RV FAC has been proven to be the best echocardiographic parameter describing CMR-derived RV function [24]. In our research, we did not observe any correlation between severity of PR and RV systolic function. This corresponds to the abovementioned

Kempny et al. [23] study. In other studies [25, 26], the RV ejection fraction did not change significantly after pulmonary valve replacement. This might be related to relatively good RV systolic function and low scatter of results in all groups of patients in our research. On the other hand, in patients with severe PR, the effective ejection fraction might be overestimated because PR can increase the end-diastolic volume. Our results contradict a previous study where reduced RV contractile function was related to more severe PR [27].

### **An influence of pulmonary valve dysfunction on other parameters**

In our study, as in other reports, the mean peak  $VO_2$  values were lower than predicted [6, 28]. We found a moderate relation between PRV and METS in the PR (+) group. This relation may result from a restrictive RV physiology. Gatzoulis et al. [29] showed that diastolic dysfunction and restrictive RV physiology shortened the PR duration and improved exercise tolerance. The presence of an above abnormal haemodynamic in most patients in the PR (+) group could explain the correlation found in our study. Another explanation could be connected with dilated RV with preserved ejection fraction in the PR (+) group. Thus, physical capacity could be improved by preserved intrinsic myocardial mechanisms. This could be supported by Meadows et al. [30]. The authors of that study confirmed that RV ejection fraction (CMR) was the only imaging predictor of a percentage of predicted peak oxygen consumption, oxygen consumption at ventilatory anaerobic threshold, and oxygen pulse.

In the case of our patients, NT-proBNP levels did not differ in the two subgroups [PR (+) vs. PR (-)], and there was no direct correlation between PR severity and NT-proBNP. Some authors [31] have reported an increased concentration of these markers in patients with severe PR, whereas others [32] did not confirm this.

We did not find any studies addressing the impact of PR severity on renal or hepatic failure. We noticed a weak negative correlation between PHT and Al<sub>1</sub> or PR<sub>1</sub> and Al<sub>2</sub>, without other important relationships. It is necessary to investigate this subject further.

### **CONCLUSIONS**

1. PR<sub>1</sub> and PR VC seem to be the most helpful parameters for the echocardiographic assessment of PR. PR VC values  $\leq 5$  mm and PR<sub>1</sub>  $> 0.73$  can help in the identification of mild PR and in practice may limit the indication for CMR investigation. In this group of patients, there is a significant correlation of TTE parameters describing the degree of PR and RV size with reference modality CMR.
2. The model of multivariable correlation helped us to establish that the volume of the PR depends inversely on the patient's age at the time of surgical correction and the necessity for reoperation, regardless of the reason.

3. The influence of PR severity on exercise tolerance is unclear.
4. Pulmonary regurgitation, even in its more severe degree, does not seem to affect liver or kidney function.

**Conflict of interest:** none declared

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# Co odzwierciedlają parametry określające niedomykalność płucną u pacjentów po korekcji tetralogii Fallota?

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## Streszczenie

**Wstęp:** Pacjenci po korekcji tetralogia Fallota (ToF) wymagają regularnej kontroli ze względu na resztkowe powikłania hemodynamiczne.

**Cel:** Celem pracy było określenie znaczenia parametrów oceny niedomykalności płucnej (PR) w codziennej praktyce klinicznej u chorych po korekcji ToF.

**Metody:** U 83 kolejnych pacjentów po korekcji ToF wykonano przezklatkowe badanie echokardiograficzne (TTE), test ergospirometryczny (CPET), rezonans magnetyczny (CMR) i badania laboratoryjne. Całą grupę badaną podzielono na dwie podgrupy [PR (+) vs. PR (-)] wg wartości frakcji PR (PRF > 20% vs. ≤ 20%) określonej w CMR.

**Wyniki:** Na podstawie przeprowadzonej analizy stwierdzono, że PR *vena contracta* ≤ 5 mm, oceniana w TTE, z 83% czułością i 68% specyficznością identyfikuje pacjentów z PRF ≤ 20%. Ponadto, określono wartość wskaźnika PR ≥ 0.73, która z 85% czułością i 43% specyficznością charakteryzuje pacjentów z nieistotną PR. W tej grupie chorych wykazano istotną korelację między parametrami echokardiograficznej oceny wielkości fali zwrotnej płucnej i wielkości prawej komory a wartościami referencyjnym uzyskanymi za pomocą CMR. Nie znaleziono wpływu PR na czynność prawej komory, wydolność fizyczną i funkcję nerek lub wątroby.

**Wnioski:** Do parametrów pozwalających zróżnicować łagodną od istotnej hemodynamicznie PR należą: wskaźnik PR i PR *vena contracta*. Echokardiograficzna ocena za pomocą tych parametrów może ograniczyć wskazania do wykonania badania CMR. Wielkość fali zwrotnej płucnej nie wpływa na funkcję RV, wydolność fizyczną oraz czynność nerek i wątroby.

**Słowa kluczowe:** rezonans magnetyczny, test ergospirometryczny, badanie echokardiograficzne, niedomykalność płucna, tetralogia Fallota

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