Long-term follow-up in adults after tetralogy of Fallot repair

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Abstract

Background: Tetralogy of Fallot (ToF) is the most common cyanotic congenital heart disease and the population of ToF repair survivors is growing rapidly. Adults with repaired ToF develop late complications. The aim of this study was to describe and analyze long-term follow-up of patients with repaired ToF.

Methods: This is a retrospective cohort study. Consecutive 83 patients with repaired ToF who did not undergo pulmonary valve replacement were included. Mean age of all patients was 30.5 ± 10.7. There were 49 (59%) male. Patients were divided into two groups according to the time since the repair (< 25 years and ≥ 25 years). The electrocardiographic (ECG), cardiopulmonary exercise testing (CPET), echocardiographic and cardiac magnetic resonance (CMR) data were reviewed retrospectively.

Results: In CPET values were not significantly different in the two groups. In CMR volumes of left and right ventricles were not significantly different in the two groups. There were no differences between the groups in ventricular ejection fraction, mass of ventricles, or pulmonary regurgitation fraction. Among all the patients, ejection fraction and left and right ventricle mass, indexed pulmonary regurgitation volume measured by CMR did not correlate with the time since repair. In ECG among all the patients, ejection fraction of the RV, measured in CMR, negatively correlated with QRS duration ($r = -0.43; p < 0.001$). There was a positive correlation between QRS duration and end diastolic volume of the RV ($r = 0.30; p < 0.02$), indexed end diastolic volume of the RV ($r = 0.29; p = 0.04$), RV mass ($r = 0.36; p < 0.001$) and left ventricle mass ($r = 0.26; p = 0.04$).

Conclusion: Long-term survival and clinical condition after surgical correction of ToF in infancy is generally good and the late functional status in ToF – operated patients could be excellent up to 25 years after the repair. QRS duration could be an utility and easy factor to assessment of right ventricular function.

Trial registration: The study protocol was approved by the local Ethics Committee. Each participant provided informed consent to participate in the study (license number 122.6120.88.2016 from 28.04.2016).

Keywords: Tetralogy of Fallot, Long term follow up, Cardiac magnetic resonance, Echocardiography cardiopulmonary exercise test

Background

Tetralogy of Fallot (ToF) is the most common cyanotic congenital heart disease [1, 2]. Surgical correction of ToF has become the treatment of choice over four decades ago [3] and is well established [4]. As a result, survival has improved significantly and the population of ToF repair survivors is growing rapidly [1], with a 20–30-year survival rate at near 90% [1, 2, 5]. Nevertheless, survival at 30 years is lower than in the normal population [2], and the risk of death in the third postoperative decade is more than triple [5]. Adults with repaired ToF develop late complications, such as progressive exercise intolerance, arrhythmias, and heart failure [4, 6]. These complications are mainly due to pulmonary regurgitation, which leads to right ventricle dysfunction [7]. Previous studies have focused on outcomes of pulmonary valve replacement [8, 9] and risk factors assessment for adverse events [2, 10], but few have
reported a long-term symptomatic status of patients after ToF repair.

The primary aim of this study was to describe and analyze long-term follow-up of patients with repaired ToF. The secondary aim was to assess the patients’ exercise capacity and type and frequency of complications.

Methods

Patient population
This is a retrospective cohort study. Consecutive patients with repaired ToF were included from the outpatients registry if they were > 18 years of age. Patients were referred for clinical assessment as part of routine clinical follow-up at the Department of Cardiac and Vascular Diseases, Institute of Cardiology Jagiellonian University College of Medicine, in the John Paul II Hospital, in Krakow. A main diagnosis was determined for every patient from hospital records, and patients were included in the study if they had only ToF as the primary diagnosis (ToF variants were excluded). To the further analysis 83 patients who did not undergo PVR were included. Patients were divided into two groups according to the time since the repair (< 25 years and ≥ 25 years). In patients population who did undergo PVR the data were obtained after PVR.

Study protocol
All clinical and demographic variables were extracted from the patients’ medical records. Body mass index (BMI) was computed as weight/height² expressed in kg/m² [11]. Information on cardiac malformations, type of previous cardiac operations, age at surgical repair, reoperations, and current medications were recorded. The electrocardiographic (ECG), cardiopulmonary exercise testing (CPET), echocardiographic and cardiac magnetic resonance (CMR) data for the patients who did not undergo pulmonary valve replacement were reviewed retrospectively.

The study protocol was approved by the local Ethics Committee (license number 122.6120.88.2016). Each participant provided informed consent to participate in the study. All procedures were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards. The study was funded by Jagiellonian University Collegium Medicum (CMUJ K/ZDS/007189; CMUJ K/ZDS/007820).

ECG and Holter monitoring
Standard (25 mm/s speed and 1 mV/cm) 12-lead surface ECGs were analysed for rhythm, PQ interval and QRS duration (defined as the maximal QRS length in any lead from the first inflection to the final sharp vector crossing the isoelectric line). ECGs in patients with a pacemaker were excluded from this comparison. Twenty-four-hour Holter monitoring, performed with a Pathfinder SL version 1.7.1.4557, was analysed for rhythm and conduction abnormalities.

Cardiopulmonary exercise testing
CPET was performed on a treadmill with a modified Bruce protocol (Reynolds Medical System, ZAN-600) as previously described [12]. To avoid pharmacologic influence, beta blockers were discontinued before CPET. Oxygen saturation and 12-lead ECG were continually monitored during the test, and blood pressure was measured manually every two minutes. Oxygen consumption (VO₂) and carbon dioxide production (VCO₂) were measured with computerized breath-by-breath analyzer. Peak oxygen uptake (VO₂ peak) was defined as the highest value at peak workload, expressed in ml/kg/min and as % of predicted value.

Echocardiography
During echocardiographic examination, ejection fraction of the left and right ventricle, according to the European Society of Cardiology guidelines, was measured [13]. Valves regurgitations and stenoses were evaluated with continuous wave Doppler and pulsed-wave Doppler. To estimate the severity of pulmonary stenosis, pulmonary gradient with continuous wave Doppler was measured. The severity of pulmonary and tricuspid regurgitation was estimated with the color Doppler. A quantitative assessment of the severity of pulmonary regurgitation was based on the deceleration velocity of the regurgitant flow, known as pressure half time (PHT). The PHT was measured with continuous wave Doppler. Function of the right heart was assessed by tricuspid annular-plane systolic excursion (TAPSE). Values of TAPSE lower than 18 mm were indicative of right ventricular longitudinal dysfunction [14]. Tissue Doppler imaging technique was applied at the tricuspid annulus to measure its systolic velocity (S’). The presence or absence of atrial and ventricular septal defect was checked. Images were obtained with Vivid 7 GE Medical System, USA.

Cardiac magnetic resonance: imaging protocol
Breath-hold, ECG-gated imaging was performed by use of cardiac phased-array coil on 1.5 T whole-body scanner (Magnetom Sonata Maestro Class, Siemens, Erlangen, Germany) in left and right ventricle short-axis and axial views. After scout imaging was performed, cinebiventricular imaging, using breath-hold steady-state free precision gradient echo technique, and flow-sensitive imaging at the pulmonary valve level, using free-breathing phase-contrast technique, were acquired. The imaging plane for a flow sequence was oriented perpendicularly to
the main pulmonary artery at the pulmonary valve level. The velocity encoding was set at 100–550 cm/sec to avoid an aliasing artefact.

**Cardiac magnetic resonance: image analysis**

Cine and flow images were assessed off-line with dedicated software package (MASS Medis, Leiden, the Netherlands). Left ventricular and right ventricular end-diastolic volume, end-systolic volume, ejection fraction, and myocardial mass were computed. End-diastolic volume, end-systolic volume and pulmonary regurgitation fraction were indexed to body surface area.

**Flow images**

The forward flow and backward flow were calculated. Backward flow was considered to represent the volume of pulmonary regurgitation. Based on the forward and backward flow volumes, the fraction of pulmonary regurgitation (PRF) was calculated.

**Statistical analysis**

Data were analyzed by use of statistical software package StatSoft STATISTICA 12.5. A \( p \) value of < 0.05 was considered statistically significant. Continuous variables are presented as mean ± SD or median with range. Student’s unpaired t-test and Mann-Whitney U test were used for comparison of continuous variables. All categorical variables were compared by use of the \( \chi^2 \) test. The age difference between the groups according to the time after the surgery was compensated for in statistical analysis. To assess the effects of the time-dependent covariates, repeated multivariate analyses of variance were performed. In case of significant results of these analyses, post-hoc testing was applied. Correlations between nominal variables were tested with Spearman’s rank correlation coefficient test or Pearson’s rank correlation coefficient test, depending on the distribution of interval variables.

**Results**

**Population characteristics**

The total cohort of ToF patients was 109. The median age of all patients was 28 years (interquartile range 19–64). There were 64 (59%) male; 57 (52.3%) of patients were in I NYHA class, 38 (34.9%) in II NYHA class and 14 (12.8%) in III NYHA class. The corrective surgery was performed between 1964 and 2012; the median patients age of intracardiac repair was 3.0 years (interquartile range 0.0–31.0 years). The mean time from repair to study was 26.1 ± 8.3 years. Twenty (18%) patients had received a palliative shunt (Blalock-Taussig repair) prior to complete repair. The most common surgical procedure was transannular patch, performed in 54 (49%) patients. Twenty-six patients were qualified for reoperation according to European Society of Cardiology guidelines [15] and underwent pulmonary valve replacement. The median age at PVR was 30.5 (interquartile range 19–53). To the further analysis 83 patients (76%), of median age of 26 years (interquartile range 19–64), who did not undergo PVR were included. None of the patients of this population had the criteria for reintervention at the time of the study. Patients were divided into two groups according to the time since the repair (< 25 years and ≥ 25 years). Table 1 illustrates the demographics and surgical characteristics of patients who did not undergo PVR after ToF repair.

**Cardiopulmonary exercise testing**

The results of cardiopulmonary exercise test are presented in Table 2. Patients who were ≥ 25 years since the repair had significantly lower peak heart rate. Other values were not significantly different in the two groups.

**Echocardiography**

Echocardiography was completed in all patients. The results of echocardiography are presented in Table 3. Moderate or severe pulmonary regurgitation was present in 69 subjects (83%), and severe tricuspid regurgitation was present in 4 (5%). Hemodynamically insignificant residual ventricular septal defect, was present in 16 patients (19%).

The patients with less than 25 years since the repair had significantly smaller right and left atria than did the patients operated before that time.

**Cardiac magnetic resonance**

The results of cardiac magnetic resonance are presented in Table 4. Volumes of left and right ventricles were not significantly different in the two groups. Also, there were no differences between the groups in ventricular ejection fraction, mass of ventricles, or pulmonary regurgitation fraction.

Among all the patients, ejection fraction and left and right ventricle mass, indexed pulmonary regurgitation volume measured by CMR did not correlate with the time since repair.

**ECG and Holter monitoring**

Patients’ ECG and Holter monitor findings are illustrated in the figure below (Fig. 1). Among all the patients, 77 (93%) had sinus rhythm, 6 (7%) had persistent atrial fibrillation, which was the most common arrhythmia. Most of the patients (69, 83%) had right bundle branch block; 13 (17%) had episodes of ventricular tachycardia, 9 (11%) atrioventricular block; and 40 (48%) were treated with beta blocker.

Ventricular tachycardia and the need to use beta blocker medications were significantly less frequent in
patients who were < 25 years since the repair as compared to operated later (13 vs 70; \( p = 0.002 \) and 40 vs 43; \( p = 0.003 \), respectively). There were no statistically significant differences between these groups in PQ interval duration (176 ms vs 191 ms; \( p = 0.3 \)) or QRS interval duration (138 ms vs 132 ms; \( p = 0.5 \)).

Among all the patients, ejection fraction of the right ventricle, measured in CMR, negatively correlated with QRS duration (\( r = -0.43; p < 0.001 \)). There was a positive correlation between QRS duration and end diastolic volume of the right ventricle (\( r = 0.30; p < 0.02 \)), indexed end diastolic volume of the right ventricle (\( r = 0.29; p = 0.04 \)), right ventricle mass (\( r = 0.36; p < 0.001 \)) and left ventricle mass (\( r = 0.26; p = 0.04 \)).

### Discussion

The main finding of the study is to show that the late functional status in ToF – operated patients could be excellent up to 25 years after the repair. However, after more than 25 years since the repair, significant changes can occur, manifesting itself as progressive RV dilation and dysfunction or clinical arrhythmia.

Good functional status up to 25 years after the operation corresponds with other reports of excellent long-term outcomes [17–19]. Most prior studies focused on risk factors for pulmonary valve regurgitation and preoperative or postoperative testing. In contrast with some studies [16], we did not evaluate patients who had undergone reoperation; thus, our data are unique in this regard.

### Table 1 Baseline demographics and surgical characteristics of patients who did not undergo PVR

| All patients \((n = 83)\) | Group 1 < 25 years since repair \((n = 51)\) | Group 2 ≥ 25 years since repair \((n = 32)\) | \(P\) values |
|-------------------------|---------------------------------|---------------------------------|----------|
| Median age with interquartile range (yr) | 26 (19–64) | 25 (19–49) | 37 (21–64) | < 0.001 |
| Male/female | 49/34 | 32/19 | 17/15 | 0.39 |
| Height | 168.3 ± 10.8 | 169.9 ± 12.2 | 165.8 ± 7.7 | 0.11 |
| Weight | 64.7 ± 14.8 | 63.5 ± 15.4 | 66.6 ± 14.0 | 0.40 |
| BMI | 22.8 ± 4.4 | 21.9 ± 4.5 | 24.1 ± 4.0 | 0.04 |
| BSA | 1.7 ± 0.2 | 1.7 ± 0.2 | 1.7 ± 0.2 | 0.94 |
| Median age with interquartile range at ToF repair (yr) | 3 (0–30) | 3 (0–30) | 3 (0–30) | 0.66 |
| Time since ToF repair (yr) | 23 (6–53) | 21 (6–24) | 31 (25–53) | < 0.001 |
| Number with prior Blalock – Taussig shunt | 17 | 6 | 11 | 0.02 |
| Number with transannular patch | 39 | 29 | 10 | 0.02 |
| NYHA functional class | NYHA I – 56 | NYHA I – 38 | NYHA I – 18 | 0.23 |
| NYHA II – 23 | NYHA II – 13 | NYHA II – 10 | NYHA I – 0.08 |
| NYHA III – 4 | NYHA III – 0 | NYHA III – 4 | NYHA II – 0.38 |
| NYHA IV – 0 | NYHA IV – 0 | NYHA IV – 0 | NYHA III – 0.98 |

*BMI* Body mass index, *BSA* Body surface area, *NYHA* New York Heart Association

### Table 2 Results of patients’ cardiopulmonary exercise testing of patients who did not undergo PVR

| Variable | All patients \((n = 83)\) | Group 1 < 25 years since repair \((n = 43)\) | Group 2 ≥ 25 years since repair \((n = 40)\) | \(P\) value |
|----------|--------------------------|---------------------------------|---------------------------------|----------|
| T [min] | 16.3 ± 3.3 | 16.9 ± 3.6 | 15.5 ± 2.8 | 0.08 |
| HR peak [beat/min] | 157 ± 29 | 164 ± 29 | 146 ± 26 | < 0.001 |
| HR peak [%N] | 70 ± 33 | 71 ± 29 | 69 ± 35 | 0.27 |
| SBP peak [mmHg] | 141 ± 23 | 141 ± 18 | 141 ± 30 | 0.96 |
| DBP peak [mmHg] | 73 ± 12 | 71 ± 12 | 75 ± 12 | 0.23 |
| VO2 peak [ml/min*kg] | 1.8 ± 0.7 | 1.9 ± 0.7 | 1.7 ± 0.6 | 0.42 |
| VO2 peak [%N] | 69.1 ± 23.0 | 67.1 ± 23.5 | 72.0 ± 22.3 | 0.39 |
| VO2Ag peak [ml/min*kg] | 27.6 ± 8.2 | 28.6 ± 8.6 | 25.9 ± 7.5 | 0.18 |
| VO2max/kg [%N] | 76.3 ± 22.1 | 73.4 ± 22.3 | 80.5 ± 21.5 | 0.19 |
| VCO2 peak [ml/min] | 2.0 ± 0.8 | 2.0 ± 0.9 | 1.9 ± 0.7 | 0.34 |
| VCO2 peak [%N] | 57.5 ± 18.3 | 56.8 ± 19.5 | 58.4 ± 16.8 | 0.72 |
| RER peak | 1.1 ± 0.2 | 1.1 ± 0.2 | 1.1 ± 0.1 | 0.84 |

*T* Time, *HR* Heart rate, *SBP* Systolic blood pressure, *DBP* Diastolic blood pressure, *VO2peak* Peak oxygen uptake, *VO2peak/kg* Peak oxygen uptake per kilogram, *VCO2peak* Peak carbon dioxide uptake, *RER* Respiratory exchange ratio
Table 3 Results of patients' echocardiography of patients who did not undergo PVR

| Echocardiography parameter | Mean value ± SD (n = 83) | Group 1 < 25 years since repair (n = 51) | Group 2 ≥ 25 years since repair (n = 32) | p value |
|---------------------------|--------------------------|------------------------------------------|------------------------------------------|---------|
| RVOT prox [mm]            | 30.5 ± 6.7               | 29.6 ± 5.8                               | 31.9 ± 7.9                               | 0.14    |
| RDVs [mm]                 | 36.1 ± 8.9               | 37.7 ± 9.3                               | 33.9 ± 7.7                               | 0.10    |
| RDVd [mm]                 | 71.6 ± 9.9               | 72.4 ± 10.6                              | 70.3 ± 8.8                               | 0.41    |
| LVD [mm]                  | 44.3 ± 5.9               | 43.9 ± 6.1                               | 44.9 ± 5.6                               | 0.45    |
| LVS [mm]                  | 28.2 ± 6.0               | 28.5 ± 4.7                               | 27.7 ± 7.6                               | 0.54    |
| RA area [cm²]             | 19.3 ± 7.2               | 17.9 ± 4.9                               | 21.5 ± 9.4                               | 0.04    |
| LA area [cm²]             | 14.9 ± 5.3               | 12.8 ± 2.3                               | 17.8 ± 6.6                               | < 0.001 |
| EF [%]                    | 58.7 ± 20.3              | 57.9 ± 20.1                              | 60.0 ± 20.8                              | 0.64    |
| PV gr.max [mmHg]          | 24.3 ± 21.2              | 22.5 ± 16.3                              | 27.2 ± 27.1                              | 0.33    |
| PV gr.mean [mmHg]         | 14.0 ± 12.9              | 12.7 ± 8.6                               | 16.0 ± 17.6                              | 0.26    |
| PV PHT                    | 104.3 ± 58.9             | 91.1 ± 42.0                              | 126.2 ± 75.2                             | 0.01    |
| Tricuspid annulus [mm]    | 36.5 ± 7.3               | 36.0 ± 7.6                               | 37.4 ± 6.8                               | 0.57    |
| TAPSE [mm]                | 21.2 ± 4.3               | 21.3 ± 4.1                               | 21.2 ± 4.5                               | 0.94    |
| S’ [cm/s]                 | 11.7 ± 2.0               | 11.8 ± 1.9                               | 11.4 ± 2.1                               | 0.43    |
| RVSP (mmHg)               | 38.8 ± 16.5              | 36.0 ± 12.3                              | 42.2 ± 20.4                              | 0.20    |

RVOT Right ventricle outflow track, RDVs Right ventricle dimension at end systole, RDVd Right ventricle dimension at end diastole, LVD Left ventricle diastolic dimension, LVS Left ventricle systolic dimension, RA Right atrium, EF Ejection fraction, PV gr max Maximal pulmonary valve gradient, PV gr min Minimal pulmonary valve gradient, PV PHT Pulmonary valve pressure half time, TAPSE Tricuspid annular plane systolic excursion, S’ Systolic velocity of tricuspid annulus, RVSP Right ventricular systolic pressure

Table 4 Results of patients' cardiac magnetic resonance of patients who did not undergo PVR

| CMR parameter | Mean value ± SD (n = 83) | Group 1 < 25 years since repair (n = 51) | Group 2 ≥ 25 years since repair (n = 32) | p value |
|---------------|--------------------------|------------------------------------------|------------------------------------------|---------|
| LA area [cm²] | 20.2 ± 5.1               | 19.6 ± 5.4                               | 21.1 ± 4.5                               | 0.18    |
| RA area [cm²] | 26.3 ± 8.2               | 24.9 ± 7.2                               | 28.4 ± 9.2                               | 0.04    |
| RV area [cm²] | 41.9 ± 10.3              | 43.2 ± 11.0                              | 40.3 ± 9.4                               | 0.42    |
| LVD [cm]      | 4.8 ± 0.5                | 4.7 ± 0.5                                | 4.8 ± 0.5                                | 0.47    |
| LVS [cm]      | 3.2 ± 0.5                | 3.2 ± 0.5                                | 3.2 ± 0.5                                | 0.72    |
| RV EF [%]     | 50.7 ± 9.9               | 50.2 ± 8.9                               | 51.5 ± 11.3                              | 0.57    |
| RV EDV [ml]   | 197.4 ± 61.9             | 202.6 ± 58.0                             | 189.0 ± 67.8                             | 0.33    |
| RV EDV indexed [ml/m²] | 112.9 ± 33.8       | 118.4 ± 28.4                             | 103.8 ± 40.0                             | 0.07    |
| RV ESV [ml]   | 104.0 ± 47.8             | 95.4 ± 35.8                              | 122. ± 65.5                              | 0.17    |
| RV ESV indexed [ml/m²] | 59.8 ± 27.9            | 55.9 ± 16.8                              | 66.7 ± 41.5                              | 0.39    |
| RV mass [g]   | 46.3 ± 19.5              | 47.3 ± 19.6                              | 44.9 ± 19.5                              | 0.59    |
| RV mass indexed [g/m²] | 27.5 ± 10.6             | 28.8 ± 10.6                              | 25.7 ± 10.4                              | 0.23    |
| LV EF [%]     | 57.7 ± 7.6               | 56.6 ± 7.5                               | 59.3 ± 7.4                               | 0.11    |
| LV EDV [ml]   | 129.8 ± 35.1             | 129.9 ± 36.9                             | 129.6 ± 32.5                             | 0.97    |
| LV EDV indexed [ml/m²] | 76.3 ± 17.0            | 76.3 ± 16.1                              | 76.3 ± 18.7                              | 0.99    |
| LV ESV [ml]   | 56.1 ± 17.9              | 59.5 ± 18.9                              | 49.7 ± 14.7                              | 0.19    |
| LV ESV indexed [ml/m²] | 31.6 ± 8.2              | 33.6 ± 8.7                               | 28.7 ± 6.6                               | 0.19    |
| LV mass [g]   | 100.9 ± 31.2             | 99.6 ± 33.4                              | 102.8 ± 27.9                             | 0.66    |
| LV mass indexed [g/m²] | 58.3 ± 14.8            | 58.3 ± 16.7                              | 58.3 ± 11.8                              | 0.98    |
| PRV [ml]      | 54.4 ± 30.5              | 53.7 ± 26.8                              | 55.6 ± 37.0                              | 0.84    |
| PRV indexed [ml/m²] | 30.0 ± 17.2             | 28.0 ± 13.1                              | 34.3 ± 23.7                              | 0.30    |
| PRF [%]       | 42.0 ± 10.3              | 42.6 ± 10.7                              | 40.9 ± 10.1                              | 0.67    |

CMR Cardiac magnetic resonance, LA Left atrium, RA Right atrium, RV Right ventricle, LVD Left ventricle diastolic dimension, LVS Left ventricle systolic dimension, RVEDV Right ventricle end-diastolic volume, RVESV Right ventricle end-systolic volume, RVEF Right ventricle ejection fraction, RV mass Right ventricle mass, LVEF Left ventricle ejection fraction, LVEDV Left ventricle end-diastolic volume, LVESV Left ventricle end-systolic volume, LV mass Left ventricle mass, PRV Pulmonary regurgitation volume, PRF Pulmonary regurgitation fraction
In our cohort, exercise performance in both groups did not have significant differences in regard to time since repair. O’Meagher et al. [21] found that the age at ToF repair did not explain the disparity in exercise capacity. Others [20] have reported that patients after ToF repair have markedly depressed exercise capacity but in comparison with healthy controls.

Chronic right ventricular overload due to pulmonary valve insufficiency can lead to right ventricle dilatation, dysfunction of both ventricles and arrhythmias [19, 21–23]. Although previous studies documented that pulmonary regurgitation can be well tolerated for many years [24, 25], our data extend these observations and showed, as did Bacha et al. [23], that right ventricular volume can be preserved without deterioration for more than 25 years.

QRS duration is strongly associated with right ventricular function [10], as was first recognized by Gatzoulis et al. [26], and QRS prolongation has been correlated with the presence of ventricular arrhythmias [19]. In contrast to previous findings [10], we found that QRS interval was not correlated with the length of follow-up and was not prolonged after 25 years from date of operation, even though the presence of ventricular tachycardia increased with time. This should be obviously noted that beta blockers may affect the QRS.

The relationship between QRS duration and right ventricular enlargement and mass was found primarily in studies of Book et al. [27] and Neffke et al. [28]. In our study, we confirmed a significant correlation between QRS duration and right ventricular mass and end diastolic volume in patients with ToF; also, we made the new finding of a strong negative relationship between QRS duration and right ventricular ejection fraction.

Supraventricular and ventricular tachycardia are well-documented complications of ToF repair [6, 24]. We found an increasing incidence of these arrhythmias with time from the repair. Abnormal right atrial size has been shown as a strong predictor of tachyarrhythmia [6], and we found significant increases in right atrial area with time since the repair.

Pulmonary regurgitation is a frequent late consequence of repair in ToF patients [25] is associated with right ventricle dilatation. In natural history, pulmonary regurgitation leads to ventricular dysfunction and heart failure developing over time [29]. Our study did not confirm time related impairment both ventricles ejection fractions and relationship to pulmonary regurgitation volume. This finding supports those of studies which showed that the right ventricle fails after 40 years of successful adaptation [19]. Moreover, in our study, in both groups right ventricle parameters were not adequate.
according to current guidelines to meet criteria of pulmonary valve replacement or right ventricular failure.

In conclusion, long-term survival and clinical condition after surgical correction of ToF in infancy is generally good. Our observations indicate an optimistic clinical function and exercise capacity in the patients operated more than 25 years ago. QRS duration could be an utility and easy factor to assessment of right ventricular function. Additionally longer prospective follow up is still needed and may provide a clearer understanding of this group.

**Study limitations**
The limitations of the study should be mentioned. First, the small sample of patients population and retrospective cohort study. Second, this is a cross sectional study and the parameters and the history of adverse event was collected at the time of patient enrollment.

**Abbreviations**
CMR: Cardiac magnetic resonance; CPET: Cardiopulmonary exercise testing; ECG: Electrocardiographic; PHT: Pressure half time; PVR: Pulmonary valve replacement; TAPSE: Tricuspid annular-plane systolic excursion; ToF: Tetralogy of Fallot; VO$_2$ peak: Peak oxygen uptake

**Acknowledgements**
None of the authors contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data. All authors are working for Jagiellonian University College of Medicine, John Paul II Hospital, Krakow, Poland.

**Availability of data and materials**
All data generated or analysed during this study are available from the corresponding author or reasonable request.

**Authors’ contributions**
ND acquisition of data, analysis of data and major contributor in writing the manuscript; PP involved in revising manuscript critically for important intellectual content; MS involved in revising manuscript; MSS involved in revising manuscript; JP involved in revising manuscript; MUZ involved in revising manuscript; WP involved in revising manuscript critically for important intellectual content; MO involved in revising manuscript critically for important intellectual content; LTJ made substantial contributions to conception and design, interpretation of data and involved in giving final approval of the version to be published. All authors read and approved the final manuscript.

**Authors’ information**
Not applicable.

**Ethics approval and consent to participate**
The study protocol was approved by the local Ethics Committee (license number 122.6120.88.2016). Each participant provided informed consent to participate in the study. All procedures were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards.

**Consent for publication**
Not applicable.

**Competing interests**
All authors declare that they have no competing interests.

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