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Quality of life in adults with repaired tetralogy of Fallot

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Abstract

Introduction: Observations of patients after repair of tetralogy of Fallot (ToF) indicate good correction results and long-term survival. Few papers have been published in which the quality of life (QoL) of this population has been assessed.
Aim: To evaluate QoL in adults with repaired ToF.
Material and methods: We included 39 patients with repaired ToF and 40 age- and sex-matched healthy volunteers. Information recorded included echocardiography, cardiac magnetic resonance, cardiopulmonary exercise test, and self-reported health-related QoL questionnaire (SF-36).
Results: The perceived physical and mental domains of health were signi cantly poorer in ToF patients than in controls. A positive correlation between VO_2 peak and physical domains was observed: (VO_2 peak vs. physical domains (r = 0.6, $p \leq 0.001$), general health (r = 0.36, p = 0.03), and physical complex status (r = 0.51, p = 0.001). VO_2 peak % correlated with physical functioning (r = 0.43, p = 0.007), general health (r = 0.39, p = 0.015) and physical complex status (r = 0.49, p = 0.002). Right ventricle ejection fraction, determined with cardiac magnetic resonance, positively correlated with role physical (r = 0.38, p = 0.04). In echocardiography, pressure half time was posi- tively correlated with physical functioning (r = 0.48, p = 0.004) and role physical (r = 0.4, p = 0.02).
Conclusions: The QoL in adults after repair of ToF and healthy control subjects was compared directly. The self-perceived physical and mental domains of health were significantly poorer in ToF patients than in controls. Strong associations were found between objective exercise capacity and physical aspects of quality of life. Complex assessment and quality of life instruments should be used together to obtain an accurate view of health status of patients with repaired ToF.

Key words: tetralogy of Fallot, exercise tolerance, quality of life, SF-36.

Streszczenie

Wstęp: Obserwacje chorych poddanych operacji korekcji tetralogii Fallota (ToF) wskazują na dobre wyniki korekcji oraz długoletnią przeżywalność pacjentów. Dotychczas opublikowano niewiele prac, w których oceniano jakość życia (QoL) tej populacji chorych.
Cel: Ocena QoL dorosłych pacjentów po korekcji ToF.
Materiał i metody: Do badania włączono 39 pacjentów po korekcji ToF oraz 40-osobową grupę kontrolną, równoważną pod względem wieku i płci. Ocenę kliniczną przeprowadzono na podstawie badania echokardiograficznego, rezonansu magnetycznego, testu spiroergometrycznego oraz kwestionariusza oceny jakości życia SF-36.
Wyniki: Samoocena poszczególnych domen zdrowia fizycznego oraz psychicznego znacząco różniła się w grupie badanej i kontrolnej. Obserwowano pozytywną korelację między szczytowym VO_2 i domenami zdrowia fizycznego [VO_2 *peak vs* funkcjonowanie fizyczne (r = 0,6, $p \leq 0,001$), ogólne postrzeganie zdrowia (r = 0,36, p = 0,03), skala fizyczna (r = 0,51, p = 0,001)]. Procentowe szczytowe zużycie tlenu VO_2 *peak* % pozytywnie korelowało z funkcjonowaniem fizycznym (r = 0,43, p = 0,007), ogólnym postrzeganiem zdrowia (r = 0,39, p = 0,015), skalą zdrowia fizycznego (r = 0,49, p = 0,002). Frakcja wyrzutowa prawej komory mierzona w rezonansie magnetycznym pozytywnie korelowała z wpływem funkcjonowania fizycznego na życie codzienne (r = 0,38, p = 0,04). W echokardiografii czas połowicznego zmniejszenia gradientu ciśnień pozytywnie korelował z funkcjonowaniem fizycznym (r = 0,48, p = 0,004) oraz z wpływem funkcjonowania fizycznego na życie codzienne (r = 0,4, p = 0,02).
Wnioski: Porównywano bezpośrednio jakość życia u dorosłych po korekcji ToF i zdrowych osób z grupy kontrolnej. Fizyczne i psychiczne obszary zdrowia były znacznie gorsze u pacjentów z ToF niż w grupie kontrolnej. Stwierdzono silny związek między obiektywną oceną wydolności fizycznej a fizycznymi aspektami QoL. Kompleksowa ocena QoL i obiektywnych narzędzi wydolności fizycznej powinna być używana jednocześnie w celu oceny statusu chorych po korekcji ToF.

Słowa kluczowe: tetralogia Fallota, tolerancja wysiłku fizycznego, jakość życia, SF-36.

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Introduction

The proportion of persons with congenital heart defects who survive into adulthood has increased to more than 90% in recent decades because of advances in surgical and medical treatment [1–4]. The most common congenital cyanotic cardiac defect is tetralogy of Fallot (ToF), and the population of adult patients who have undergone repair of ToF is increasing [2]. However, the prolongation of life is not always accompanied by improved quality of life and health [1], which is defined by the World Health Organization as a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity [5]. Late complications of repair of ToF are pulmonary regurgitation, pulmonary stenosis, residual ventricular septal defect, arrhythmias, and cardiac failure. These complications may affect patients' quality of life and perception of their health status, which can influence treatment outcomes [2]. Limitations in the numbers of patient diagnostic groups and lack of a standardized assessment have restricted investigations of the late functional health of adults with repaired ToF.

Aim

Thus, the present study aimed to evaluate the quality of life of adults with repaired ToF, using the self-reporting Short Form-36 Health Survey (SF-36). The second goal of the study was to assess the relationship between the quality of life and exercise capacity, measured by echocardiography, cardiac magnetic resonance (CMR), and cardiopulmonary exercise test (CPET).

Material and methods

Study participants

Between May 2016 and July 2017, 39 patients who agreed to complete the SF-36 survey, older than 18 years with repaired ToF (who were clinically stable before enrolment) were included in the study. Patients were referred for echocardiography, CMR, exercise testing and ECG Holter monitoring 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. Forty healthy volunteers, matched with patients by gender and age, were recruited via an advertisement as controls. The control subjects were healthy at clinical examination, and had no medical history, medication or current symptoms suggesting cardiovascular disease.

Study protocol

Information on the following was recorded for each study participant: weight; height; history of cardiac operations; age at surgical repair; echocardiography; CMR; CPET; ECG Holter monitoring and SF-36. 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).

Echocardiography

During echocardiographic examination, ejection fraction of the left and right ventricle was measured according to European Society of Cardiology guidelines [6]. Valve regurgitation and stenosis were evaluated with continuous-wave Doppler and pulsed-wave Doppler. To estimate the severity of pulmonic stenosis, pulmonary gradient with continuous-wave Doppler was performed. The severity of pulmonary and tricuspid regurgitation was estimated with colour 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 pressure half time was measured with continuous-wave Doppler, and values under 100/ms were considered an index of severe pulmonary regurgitation [7]. Function of the right heart was also assessed with echocardiography. Tricuspid annular plane systolic excursion (TAPSE) measured the systolic excursion of the right ventricular annular plane toward the apex. Values of TAPSE lower than 18 mm were indicative of right ventricular longitudinal dysfunction. Tissue Doppler imaging, applied at the tricuspid annulus, was used for the assessment of right ventricular function. Isovolumic acceleration time was used to assess right ventricular contractility. The presence or absence of atrial and ventricular septal defect also was checked. Images were obtained with Vivid 7 GE Medical System, USA.

Cardiac magnetic resonance: imaging protocol

Breath-hold, electrocardiographic-gated imaging was performed using a cardiac-phased array coil on a 1.5T whole-body scanner (Magnetom Sonata Maestro Class, Siemens, Erlangen, Germany) in left ventricle and right ventricle short-axis and axial views. After scout imaging was performed, cine biventricular 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 performed. 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/s 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). Myocardial mass, left ventricular and right ventricular end-diastolic volume, end-systolic volume, and ejection fraction were computed.

Flow images

The forward flow and backward flow through the pulmonic valve were calculated, and the backward flow was considered to represent the volume of pulmonary regur-

gitation. Like Myerson [8], we considered ≥ 40% regurgitation fraction severe. According to recommendations for cardiovascular magnetic resonance in adults with congenital heart disease from the respective working groups of ESC, preoperative indexed RV end diastolic volume above 160 ml/m^2 was considered significant.

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing was performed on a treadmill, using a modified Bruce protocol (Reynolds Medical System, ZAN-600) as described [9]. Oxygen saturation and 12-lead ECG were continually monitored during the test, and blood pressure was measured manually every 2 min. Oxygen consumption (VO_2), carbon dioxide production (VCO_2) and minute ventilation (V_e) were measured with a computerized breath-by-breath analyser. Peak oxygen uptake (VO_2 peak) was defined as the highest value at peak workload and expressed in ml/kg/min and % of predicted value. Oxygen pulse (pulse O_2) was defined as the amount of oxygen consumed per heartbeat.

ECG Holter monitoring

Twenty-four-hour Holter monitoring, performed with a Pathfinder SL version 1.7.1.4557, was analysed for supraventricular arrhythmias and ventricular pauses. Twenty-four-hour Holter monitoring, performed with a Pathfinder SL version 1.7.1.4557, was analysed for supraventricular or ventricular arrhythmias and ventricular pauses. We defined significant arrhythmias as ventricular tachycardia ≥ 3 consecutive ventricular complexes at a rate > 100 bpm, atrial fibrillation – complete absence of P waves, supraventricular tachycardia (SVT) ≥ 3 consecutive supraventricular complexes at a rate > 100 bpm, ≥ 3 s pause, second degree Mobitz II or third degree AV block, or symptomatic bradycardia. Serious arrhythmias were defined as: ventricular tachycardia > 120 for 30 s, complete or third degree heart block, symptomatic second degree heart block, type II, pause > 6 s and symptomatic bradycardia < 40 beats per minute for > 30 s.

Quality of life assessment

Patients' quality of life was assessed with the SF-36 questionnaire (license number: QM037376). A Polish language version of the SF-36 questionnaire, prepared by the Institute of Cardiology, was used. The SF-36 is a generic measure that uses a multiple-item scale to assess each of the following eight domains: physical functioning, role functioning-physical, bodily pain, general health, vitality, social functioning, role limitations caused by emotional problems, and mental health [5]. Functional health assessment, using the SF-36, was completed in all 39 patients and 40 controls. Scores were analysed according to published guidelines described previously [10]. A score between 0 and 100 was calculated for each domain. The physical complex status and mental complex status also were calculated as the weighted combinations of the 8 scales of the SF-36.

Statistical analysis

All statistical analyses were performed using the statistical software package StatSoft Statistica 12.5. All data are expressed as mean with 95% confidence interval or median with interquartile range. A *p*-value of less than 0.05 was considered statistically significant. Categorical variables were expressed as frequency and percentage; continuous variables were expressed as mean and standard deviation. Continuous variables were tested for normal distribution using the Shapiro-Wilk test and compared using the two-tailed Student's *t*-test and Mann-Whitney *U* test where appropriate. Correlations between nominal variables were tested with Spearman's rank correlation coefficient test or Pearson's rank correlation coefficient test, depending on normal distribution of interval variables. Correlations between ordinal variables data were analysed by Kendall's tau test. All ordinal and interval data were tested by the Spearman test.

Results

Population characteristics

The study population consisted of 39 patients (20 male) who had ToF surgery and 40 controls (22 male). The mean age of patients at ToF repair was 4.9 ±5.3 years and at evaluation was 31.6 ±11.3 years; the control group had a mean age of 27.7 ±5.2 years at the time of evaluation.

Complete repair was performed using a transannular patch in 37 (94.9%) patients. In 4 (10.3%) patients, a palliative procedure with Blalock-Taussig shunt was performed; the mean age at Blalock-Taussig anastomosis was 3.3 ±2.4 years. Thirteen (35%) patients had reoperation due to significant pulmonary regurgitation (mean indexed RV end diastolic volume was 137.99 ±30.12 ml/m^2 and mean pulmonary regurgitation fraction was 43.7 ±10.5%); the mean age of reoperation was 27.4 ±8.6.

Reoperation is not planned for the rest of the group (26 patients) due to pulmonary insufficiency or because they do not comply with the European Society of Cardiology guidelines for pulmonary valve replacement (PVR). In this group mean indexed RV end diastolic volume was 114.14 ±28.23 ml/m^2, and mean PRF was 32.3 ±11.2%.

Quality of life

The perceived physical and mental domains of health of the ToF patients and controls are tabulated in Table I. The scores for physical functioning, role physical, general health, social functioning and role emotional were significantly lower for ToF patients than for control subjects. Mental complex status and physical complex status also were poorer for patients than for controls. There was no relationship of patients' quality of life with age, gender, weight, or height at first repair. Physical functioning, vitality, mental health, and mental complex status were negatively correlated with patients' age. Physical functioning and role physical negatively correlated with time since repair and presence of reoperation. We did not find a significant association with arrhythmias or quality of life.

Table I. Results for SF-36 questionnaire in patients after ToF repair and controls

Parameter	Patients after ToF repair	Controls	*P*-value
Age [years]	30.6 ±11.3	27.7 ±5.2	0.14
Male, *n* (%)	20 (52)	22 (55)	0.74
Physical functioning	75.06 ±22.89	97.25 ±4.5	< 0.001
Role physical	58.55 ±35.96	93.75 ±16.5	< 0.001
Bodily pain	72.44 ±25.09	81.5 ±22.34	0.09
General health	51.19 ±22.16	77.43 ±16.64	< 0.001
Vitality	57.14 ±15.39	63.25 ±15.3	0.08
Social functioning	73.4 ±20.11	86.43 ±19.21	0.004
Role emotional	72.6 ±40.37	91.67 ±23.57	0.012
Mental health	67.6 ±14.7	72.9 ±16.09	0.13
Mental complex status	46.43 ±9.22	78.56 ±14.56	< 0.001
Physical complex status	46.37 ±8.89	87.48 ±11.89	< 0.001

Correlation of quality of life scores with cardiopulmonary exercise test results

We investigated the correlation between domains of health and echocardiography, CMR, and CPET, as described below.

VO_2 peak, physical functioning ($r = 0.6$, $p \leq 0.001$), general health ($r = 0.36$, $p = 0.03$), and physical complex status ($r = 0.51$, $p = 0.001$) were positively correlated. Also, the percentage peak oxygen uptake per kg was positively correlated with physical functioning ($r = 0.43$, $p = 0.007$), general health ($r = 0.39$, $p = 0.015$) and physical complex status ($r = 0.49$, $p = 0.002$).

Right ventricle ejection fraction measured with CMR positively correlated with role physical ($r = 0.38$, $p = 0.04$). End-diastolic and end systolic volumes of both ventricles and pulmonary regurgitation parameters did not correlate with quality of life domains.

In echocardiography, pressure half-time was positively related to physical functioning ($r = 0.48$, $p = 0.004$), role physical ($r = 0.4$, $p = 0.02$), and physical complex status ($r = 0.46$, $p = 0.006$). Other parameters such as TAPSE and S' did not correlate with quality of life domains.

Table II shows SF-36 results in ToF patients with significant PHT (< 100/ms) compared with those with non-significant PHT (≥ 100/ms). Physical functioning and role physical were significantly lower in those who had significant PHT.

In Table III SF-36 results in ToF patients who did not undergo PVR compared with those who had PVR are shown. Only the scores for role physical and physical complex status were significantly different.

We also found that the presence of tricuspid valve regurgitation negatively correlated with role physical ($r = –0.34$, $p = 0.03$) and vitality ($r = –0.35$, $p = 0.03$).

Discussion

In the present study, using an objective questionnaire, we compared the quality of life of persons who had ToF repair with that of a healthy control group. Our investigation confirmed that adults with repaired ToF had significantly abnormal functional health in almost all physical functioning domains and in 2 domains of the mental component related to social function and role emotional. These findings are consistent with the reported results in all patients with congenital heart disease compared with those of similarly aged people in the general population [5]. In contrast to previous studies [1, 2, 4, 11], which did not find significant differences from the healthy population, except for physical functioning, we found impairments in the mental scale of the ToF patients. This finding illustrated that patients with repaired ToF do not adapt their psychosocial status, except for mental health and vitality, and indicate that they cope well with life and try to normalize functioning.

Our study showed an association between age and physical function and vitality, which supports suggestions that deterioration in ToF patients is progressive.

The relation between physical health status and adult reoperations is known and abnormal lower general functional health status scores were associated with time of repair and higher incidence of reoperation [4]. We found that role physical and physical complex status were lower in the group of patients who underwent PVR. This association also might be related to decreasing functional health with age.

Cardiopulmonary exercise testing and quality of life have been described in adults with congenital heart disease [4, 5, 12], and peak oxygen uptake is considered the best objective measure of exercise capacity [3]. Our report confirmed that exercise capacity, measured by peak oxygen uptake in CPET, correlates with physical functioning and general health. These results are concordant with those of others [3, 12, 13], who found a correlation of the physical function domain and exercise function. In contrast, Frigiola

Table II. Results for SF-36 questionnaire in patients after ToF repair who had significant pressure half time (PHT) (< 100/ms) or non-significant PHT (≥ 100/ms)

Quality of life domain	PHT < 100/ms (n = 23)	PHT ≥ 100/ms (n = 16)	P-value
Physical functioning	69.45 ±24.21	86.36 ±19.07	0.04
Role physical	52.17 ±35.29	79.55 ±35.03	0.04
Bodily pain	70.00 ±25.92	78.73 ±24.64	0.36
General health	50.07 ±21.58	52.63 ±26.68	0.76
Vitality	55.14 ±15.56	64.55 ±15.72	0.11
Social functioning	71.20 ±20.10	76.14 ±20.50	0.51
Role emotional	75.36 ±37.89	75.76 ±42.40	0.98
Mental health	66.18 ±15.00	73.45 ±13.89	0.19
Physical complex status	44.18 ±9.05	50.67 ±8.03	0.05
Mental complex status	46.63 ±9.58	47.87 ±9.03	0.72

et al. [11] reported that patients with repaired ToF may not have good objectively measured exercise capacity and good subjectively estimated quality of life in the physical domain score. However, those authors used a subjective health-related quality of life questionnaire that was different from ours.

Moreover, physical functioning is assessed by abilities and limitations in daily-life activities and sports [2]. For that reason, we closely examined other parameters that affect exercise performance, including predicted percentage peak oxygen uptake, maximal time of exercise, and maximal heart rate during CPET, which highlight relationships between physical component summary and exercise capacity.

This study also found not correlation of peak oxygen uptake with any of the psychosocial scales of the SF-36. This finding is similar to that of Gratz *et al.* [3, 13], who analysed adolescents and adults with various congenital heart diseases, not only ToF. Significant limitations in exercise capacity without associated mental component summary contrast with data of patients with acquired heart disease [14], and may be explained by the years-long adaptations of patients with congenital defects, both with physical and mental aspects of their illness.

In the present study, we also found impairments in physical scores to be associated with echocardiographic and CMR abnormalities.

Pulmonary regurgitation is often a late consequence of right ventricular outflow tract reconstruction in patients with ToF due to transannular patching [15, 16]. Previous investigations demonstrated that pulmonary regurgitation is directly linked with right ventricular function [17, 18] and can lead to volume overload, dilatation of the right ventricle and tricuspid regurgitation [4, 18]. Pulmonary and tricuspid regurgitation, measured in echocardiography, ap-

Table III. Results for SF-36 questionnaire in patients after ToF repair who did not undergo PVR and patients after ToF repair who did undergo PVR

Variable	Patients after ToF repair who did not undergo PVR	Patients after ToF repair who did undergo PVR	P-value
Physical functioning	81.4 ±18.17	68.46 ±20.65	0.05
Role physical	68.00 ±31.89	40.38 ±37.56	0.02
Bodily pain	68.35 ±29.77	69.38 ±24.05	0.91
General health	52.19 ±20.74	50.23 ±23.28	0.79
Vitality	58.33 ±15.48	52.69 ±14.23	0.28
Social functioning	74.92 ±21.19	70.15 ±18.09	0.49
Role emotional	74.32 ±39.25	69.23 ±44.02	0.72
Mental health	67.68 ±15.49	67.38 ±13.65	0.95
Mental complex status	46.85 ±8.83	47.32 ±9.2	0.88
Physical complex status	47.36 ±7.9	40.95 ±8.8	0.03

pear to be related to impaired physical function. Moreover, not only presence of pulmonary and tricuspid regurgitation influence the physical component. In our study, we proved that the degree of pulmonary regurgitation plays an important role in physical functioning. Similar findings on the echocardiogram have been described by Hickey *et al.* [4], who found that not solely tricuspid regurgitation, but also left ventricular dysfunction, residual septal defects, and high right ventricular systolic pressures are associated with abnormal physical performance. However, the assumption that quality of life will follow left ventricular performance was refuted in analyses for all patients with congenital heart diseases [19]. Moreover, right ventricular ejection fraction correlates with decreased role physical function. Lu *et al.* [20] described a correlation only between right ventricle ejection fraction when above ≥ 45% and physical component summary scores. According to Lu *et al.* [21], right ventricular end diastolic volume and pulmonary regurgitation did not influence the quality of life, an observation that suggests that cardiac dysfunction is not directly responsible for impaired quality of life.

Our study has three limitations: 1) the small patient population is a limitation, even though the patients were extensively studied, with echocardiography, CMR, CPET, and the SF-36 questionnaire, thus giving rich data for comparison of patients with healthy control subjects. 2) Apart from being selected on the grounds of the definition of the study population – patients with tetralogy of Fallot who underwent repair – patients in this study were not purposely selected. We were not informed about the reasons why patients who did not participate in the study refused. However, all patients were approached uniformly, and there were no significant differences in any of the baseline characteristics between patients who participated in the study. 3) The quality of life was assessed by only a single standardized questionnaire, the SF-36. Although different tests have been used in other studies, we chose the SF-36 because it is one of the most widely used. However, CMR is not readily available in all institutions and is not as readily accomplished in all patients as compared to echocardiography, which therefore remains the mainstay for routine assessment of the post-surgical TOF patient. As Mercer-Rosa *et al.* [22] reported, echocardiography was 97% sensitive to identify cases with regurgitation fraction > 20% (107 of 110 patients; 95% CI: 92–99%) qualitatively, and also to a pressure half time < 100 ms has good sensitivity and specificity for severe pulmonary regurgitation.

Conclusions

This study directly compared the quality of life in adults after repair of ToF with that of healthy control subjects. The self-perceived physical and mental domains of health were significantly poorer in ToF patients than in controls. Strong associations were found between objective exercise capacity and physical aspects of quality of life. Also, right ventricular function and severity of the pulmonary regurgitation were associated with patients' quality of life. Complex assessment and quality of life instruments should be used together to obtain an accurate view of health status of patients with repaired ToF.

Disclosure

Authors report no conflict of interest.

References

1. Daliento L, Mapelli D, Russo G, Scarso P, Limongi F, Iannizzi P, Melendugno A, Mazzotti E, Volpe B. Health related quality of life in adults with repaired tetralogy of Fallot: psychosocial and cognitive outcomes. Heart 2005; 91: 213-218.
2. Bygstad E, Pedersen LC, Pedersen TA, Hjortdal VE. Tetralogy of Fallot in men: quality of life, family, education, and employment. Cardiol Young 2012; 22: 417-423.
3. Hager A, Hess J, Hager A. Comparison of health related quality of life with cardiopulmonary exercise testing in adolescents and adults with congenital heart disease. Heart 2005; 91: 517-520.
4. Hickey EJ, Veldtman G, Bradley TJ, Gengsakul A, Webb G, Williams WG, Manlhiot C, McCrindle BW. Functional health status in adult survivors of operative repair of tetralogy of fallot. Am J Cardiol 2012; 109: 873-880.
5. Lane DA, Lip GYH, Millane TA. Quality of life in adults with congenital heart disease. Heart 2002; 88: 71-75.
6. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein S, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015; 28: 1-39.e14.
7. Silversides CK, Veldtman GR, Crossin J, Merchant N, Webb GD, McCrindle BW, Siu SC, Therrien J. Pressure half-time predicts hemodynamically significant pulmonary regurgitation in adult patients with repaired tetralogy of Fallot. J Am Soc Echocardiogr 2003; 16: 1057-1062.
8. Myerson S. Heart valve disease: investigation by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2012; 14: 7.
9. Tomkiewicz-Pajak L, Podolec P, Kostkiewicz M, Tracz W. Lung function and exercise tolerance in patients with heart failure. Acta Cardiol 2002; 57: 80-81.
10. Smaś-Suska M, Dłużniewska N, Weryński P, Pająk J, Płazak W, Olszowska M, Podolec P, Tomkiewicz-Pająk L. What determine the quality of life of adult patients after Fontan procedure? Cardiol J 2018; 25: 72-80.
11. Frigiola A, Bull C, Wray J. Exercise capacity, quality of life, and resilience after repair of tetralogy of Fallot: a cross-sectional study of patients operated between 1964 and 2009. Cardiol Young 2014; 24: 79-86.
12. Kamphuis M, Ottenkamp J, Vliegen H, Vogels T, Zwinderman KH, Kamphuis RP, Verloove-Vanhorick SP. Health related quality of life and health status in adult survivors with previously operated complex congenital heart disease. Heart 2002; 87: 356-362.
13. Gratz A, Hess J, Hager A. Self-estimated physical functioning poorly predicts actual exercise capacity in adolescents and adults with congenital heart disease. Eur Heart J 2008; 30: 497-504.
14. Lavie C, Milani R. Adverse psychological and coronary risk profiles in young patients with coronary artery disease and benefits of formal cardiac rehabilitation. Arch Intern Med 2006; 166: 1878-1883.
15. Hickey EJ, Veldtman G, Bradley TJ, Gengsakul A, Manlhiot C, Williams WG, Webb GD, McCrindle BW. Late risk of outcomes for adults with repaired tetralogy of Fallot from an inception cohort spanning four decades. Eur J Cardiothorac Surg 2009; 35: 156-164.
16. Carvalho J, Shinebourne E, Busst C, Rigby ML, Redington AN. Exercise capacity after complete repair of tetralogy of Fallot: deleterious effects of residual pulmonary regurgitation. Br Heart J 1992; 67: 470-473.
17. Geva T, Sandweiss B, Gauvreau K, Lock JE, Powell AJ. Factors associated with impaired clinical status in long-term survivors of tetralogy of Fallot repair evaluated by magnetic resonance imaging. J Am Coll Cardiol 2004; 43: 1068-1074.
18. Lee C, Kim YM, Lee CH, Kwak JG, Park CS, Song JY, Shim WS, Choi EY, Lee SY, Baek JS. Outcomes of pulmonary valve replacement in 170 patients with

chronic pulmonary regurgitation after relief of right ventricular outflow tract obstruction. J Am Coll Cardiol 2012; 60: 1005-1014.
19. Moons P, Van Deyk K, De Geest S, Gewillig M, Budts W. Is the severity of congenital heart disease associated with the quality of life and perceived health of adult patients? Heart 2005; 91: 1193-1198.
20. Lu JC, Christensen JT, Yu S, Donohue JE, Ghadimi Mahani M, Agarwal PP, Dorfman AL. Relation of right ventricular mass and volume to functional health status in repaired tetralogy of Fallot. Am J Cardiol 2014; 114: 1896-1901.
21. Lu J, Cotts T, Agarwal P, Attili AK, Dorfman AL. Relation of right ventricular dilation, age of repair, and restrictive right ventricular physiology with patient-reported quality of life in adolescents and adults with repaired tetralogy of Fallot. Am J Cardiol 2010; 106: 1798-1802.
22. Mercer-Rosa L, Yang W, Kutty S, Rychik J, Fogel M, Goldmuntz E. Quantifying pulmonary regurgitation and right ventricular function in surgically repaired tetralogy of Fallot: a comparative analysis of echocardiography and magnetic resonance imaging. Circ Cadiovasc Imaging 2012; 5: 637-643.