G Model
IHJ 1260 No. of Pages 6

ARTICLE IN PRESS

Indian Heart Journal xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Effect of ventricular function and volumes on exercise capacity in adults with repaired Tetralogy of Fallot

Natalia Dłużniewska[a,*], Piotr Podolec[a], Tomasz Miszalski-Jamka[b,c], Maciej Krupiński[b], Paweł Banyś[d], Małgorzata Urbańczyk[d], Bogdan Suder[e], Grzegorz Kopeć[a], Maria Olszowska[a], Lidia Tomkiewicz-Pająk[a]

[a] *Department of Cardiac and Vascular Disease, Jagiellonian Collegium Medicum, Jagiellonian University, John Paul II Hospital, Krakow, Poland*
[b] *Department of Radiology and Diagnostic Imaging, John Paul II Hospital, Krakow, Poland*
[c] *Jagiellonian Centre for Experimental Therapeutic (JCET), Jagiellonian University, Krakow, Poland*
[d] *Magnetic Resonance Imaging Laboratory, John Paul II Hospital, Krakow, Poland*
[e] *Department of Cardiovascular Surgery and Transplantation, Collegium Medicum, Jagiellonian University, John Paul II Hospital, Krakow, Poland*

A R T I C L E I N F O

Article history:
Received 1 February 2017
Accepted 29 July 2017
Available online xxx

Keywords:
Cardiopulmonary exercise test
Magnetic resonance
Fallot tetralogy

A B S T R A C T

Objectives: Investigate the effects of left and right ventricular function and severity of pulmonary valve regurgitation, quantified by cardiac magnetic resonance (CMR), on exercise tolerance in adult patients who underwent ToF repair at a young age.
Methods: This is a retrospective cohort study of 52 patients after ToF surgery and 33 age- and sex-matched healthy volunteers. CMR and cardiopulmonary exercise testing (CPET) were performed on all patients; CPET was performed on control subjects.
Results: The main finding of CPET was a severe decrease in oxygen uptake at peak exercise VO_{2peak} in TOF patients. The patients were characterized also by lower pulse O_{2peak} and heart rate at peak exercise. Ejection fraction of the right and left ventricles was correlated ($r = 0{,}32$; $p = 0{,}03$). Left ventricle ejection fraction was negatively correlated with right ventricular volumes ($r = -0{,}34$; $p = 0{,}01$) and right ventricular mass ($r = -046$; $p < 0{,}00$). Right ventricular mass was positively correlated with left ventricular variables (left ventricle end diastolic volume, $r = 0{,}43$; $p = 0{,}002$; left ventricle end systolic volume, $r = 0{,}54$; $p < 0{,}00$) as was $VO_{2peak:}$ LVEDV ($r = 0{,}38$; $p = 0{,}01$); LVESV ($r = 0{,}33$; $p = 0{,}03$) and LV mass ($r = 0{,}42$; $p = 0{,}006$).
Conclusion: Exercise intolerance in adults with repaired ToF is markedly depressed. The decreased exercise capacity is correlated with impaired RV function and may be associated also with LV dysfunction, which suggests right-to-left ventricular interaction.

1. Introduction

Tetralogy of Fallot (ToF) is one of the most prevalent cyanotic congenital heart diseases requiring surgery early in life.[1] The common consequence of the primary surgery is pulmonary regurgitation, which may be well tolerated for decades. However, the presence of residual lesion can lead to progressive enlargement and dysfunction of the right ventricle (RV), exercise intolerance, ventricular and atrial arrhythmias, heart failure and sudden cardiac death.[2] RV dysfunction may also affect left ventricular (LV) function.[3] Implantation of the pulmonary valve may be performed to avoid these consequences[2]. Bedside clinical criteria, ventricular volume and function are factors in determining whether pulmonary valve replacement (PVR) is feasible.[4]

Cardiac magnetic resonance (CMR) is the current gold standard for evaluating RV performance and pulmonary valve regurgitation in patients after ToF operation. Cardiopulmonary exercise testing (CPET) provides objective information about the function of the

Abbreviations: TOF, Tetralogy of Fallot; RV, right ventricle; CPET, cardiopulmonary exercise testing; CMR, cardiac magnetic resonance; PVR, pulmonary valve replacement; PR, pulmonary regurgitation; EDV, end diastolic volume; ESV, end systolic volume; LV, left ventricle; RV, right ventricle EF ejection fraction; NYHA, New York Heart Association; VO2, oxygen uptake.

* Corresponding author.
E-mail address: natalia.dluzniewska@gmail.com (N. Dłużniewska).

http://dx.doi.org/10.1016/j.ihj.2017.07.021
0019-4832/

heart, lungs and muscles and has been proposed as a useful tool for optimal timing of PVR.[5] Previous studies have reported on exercise intolerance in adults with repaired ToF.[2,6] Babu-Narayan SV et al.[2] showed that in ToF patients undergoing PVR, preoperative oxygen uptake was predictive of early postoperative mortality. However, the relationship between right-side cardiac abnormalities and exercise capacity in this patient group is poorly understood.[7]

The goal of the present study was to determine the effect of the left and right ventricular function and severity of pulmonary valve regurgitation, quantified by CMR, and to determine the relationship of the ventricular function to exercise tolerance in adult patients who had undergone ToF repair at an early age.

2. Methods

2.1. Patient population

This is a retrospective cohort study. The echocardiography, CMR and CPET data for all patients with repaired ToF were reviewed retrospectively. Patients were referred for exercise testing 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 ToF as primary diagnosis (ToF variants were excluded). In addition, age- and sex-matched healthy controls for comparison were voluntarily recruited via an advertisement. The control subjects were healthy at clinical examination, and had no medical history, medication or current symptoms suggesting cardiovascular disease.

2.2. Study protocol

From the patients' medical records, we extracted all clinical and demographic variables. The New York Heart Association functional class was recorded, and selected vital signs were measured, i.e. weight and height, from which we computed the body mass index (weight/height^2 expressed in kg/m^2).[8] Information on cardiac malformation, type of previous cardiac operations, age at surgical repair, and current medications were recorded. CMR and CPET were performed on every patient; CPET only was performed on controls.

2.3. CMR: imaging protocol

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

2.4. CMR: image analysis

Cine and flow images were assessed off-line by use of a dedicated software package (MASS Medis, Leiden, the Netherlands). For cine images, endocardial and epicardial borders were outlined on short-axis images as described.[9] If the basal slice contained both ventricular and atrial myocardium, contours were drawn up to their junction and joined by a straight line through the blood pool. In the basal slice, if the pulmonary valve was visible, only the volume below the pulmonary valve level was included. For calculation of RV inflow portion, blood volume was excluded from RV volume if the surrounding wall was thin and not trabeculated, as it was considered to be in right the atrium. LV and RV end-diastolic volume (LVEDV, RVEDV), end-systolic volume (LVESV, RVESV), myocardial mass and ejection fraction (LVEF, RVEF) were computed. EDV, ESV and myocardial mass were indexed to body surface area.

For flow images, vessel contours were drawn and propagated throughout the cardiac cycle. 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 and classified as mild (<20%), moderate (20% to 39%), or severe (≥40%). Based on Myerson et al.,[10] we decided to accept ≥40% regurgitation fraction as severe, and accordingly divided patients into those with severe or non-severe PR with respect to CPET and CMR imaging study variables.

2.5. Cardiopulmonary exercise testing

CPET was performed on a treadmill with a modified Bruce protocol (Reynolds Medical System, ZAN-600) as described.[11] To avoid pharmacologic influence, beta blockers were discontinued before CPET was done. Oxygen saturation and 12-lead electrocardiogram were continually monitored during the test, and blood pressure was measured manually every two minutes. Oxygen consumption (VO_2), carbon dioxide production (VCO_2), and minute ventilation (V_e) were measure with computerized breath-by-breath analyzer. Peak oxygen uptake (VO_2 peak) was defined as the highest value at peak workload and was expressed in ml/kg/min and as% of predicted value. Oxygen pulse (pulse O_2) was defined as the amount of oxygen consumed per heart beat. The ventilator equivalent for oxygen (V_e/VCO_2) was the amount of ventilation needed for the uptake of a given amount of oxygen; the ventilatory equivalent for carbon dioxide (V_e/VCO_2) was the amount of ventilation needed for the elimination of a given amount of carbon dioxide. The respiratory exchange ratio (RER) was calculated by dividing the VO_2 by VCO_2.

2.6. Statistical analysis

All statistical analyses were performed by use of the statistical software package StatSoft STATISTICA 12.5. All data are expressed as mean with 95% confidence interval or median with interquartile range. Continuous variables were tested for normal distribution by use of the Shapiro-Wilk test and compared by use of the two-tailed Student's *t*-test (in case of normal distribution) and Mann–Whitney *U* test (in case of non-normal distribution). Correlations between nominal variables were tested with Spearman's rank correlation coefficient or Pearson rank correlation coefficient test, depending on normal distribution of interval variables. Correlations between ordinal variables data were analyzed by use of Kendall's tau test. All ordinal and interval data were tested with Spearman test. A p value of <0.05 was considered statistically significant.

3. Results

3.1. Population characteristics

Table 1 shows the demographics of the 52 patients with ToF repair and 33 control subjects. There were no significant differences between the patients and controls in the variables measured.

Table 2 gives the characteristics of the patients who underwent ToF repair.

Please cite this article in press as: N. Dłużniewska, et al., Effect of ventricular function and volumes on exercise capacity in adults with repaired Tetralogy of Fallot, Indian Heart J (2017), http://dx.doi.org/10.1016/j.ihj.2017.07.021