

Lung function and Cardiopulmonary Exercise Capacity in Patients with Corrected Tetralogy of Fallot

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Abstract

Background: Since surgical repair of tetralogy of Fallot was introduced, follow-up studies have shown that the majority of patients lead active lives and have no subjective exercise limitation.

Objectives: To examine lung function, cardiopulmonary functional capacity and echo-Doppler assessment of pulmonary pressure in adult patients 20 years after repair of TOF.

Methods: Unselected consecutive patients performed full lung function testing, progressive cardiopulmonary exercise, and echo-Doppler assessments of pulmonary pressure.

Results: Fifty consecutive patients (33 men, 17 women) aged 29 ± 11 years who underwent surgical repair of TOF at age 10.1 ± 10.9 years were enrolled. Patients after TOF showed no restriction (forced expiratory vital capacity 80%, total lung capacity 91%) and had normal oxygen saturation (97%) and 6 minute walking distance (600 meters). Echocardiography showed normal pulmonary pressure and left ventricular ejection function (62%). Cardiopulmonary exercise testing showed mild limitation of exercise capacity with oxygen uptake at maximal effort of 75–78% predicted.

Conclusions: After corrections of TOF the study patients had normal lung function and pulmonary arterial pressure but mild limitation in their exercise capacity.

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It was Fallot's publication in 1888 [1] that attached his name to the tetrad of right ventricular outflow tract obstruction, dextroposition and overriding of the aorta, ventricular septal defect, and right ventricular hypertrophy. As a single entity, tetralogy of Fallot is the most common malformation of children born with cyanotic heart diseases, with an incidence of approximately 10% of congenital heart diseases. Infants with classic TOF undergo either a complete intracardiac repair or palliative surgery with creation of systemic to pulmonary artery shunt (Blalock-Taussig shunt). The surgical option chosen depends on the patient's symptoms and age and the size of the pulmonary arteries. To achieve complete relief from the right ventricular outflow tract obstruction after repair of TOF, a pulmonary valvotomy, insertion of an outflow tract patch, or a transannular patch is usually required [2]. Most patients surviving total correction of TOF have an excellent late clinical and hemodynamic outcome without

functional disability, significant residual intracardiac defects, or need for cardiac medications [3]. Nevertheless, complications do occur, the most common being pulmonary regurgitation. After total repair of TOF with transannular patching, severe pulmonary regurgitation is reported to develop in up to 30% of patients at follow-up of 20 years, and 10–15% or more need pulmonary valve replacement usually carried out with a homograft [4]. Other late complications include residual right ventricular outflow tract obstruction, residual ventricular septal defect, pulmonary arterial stenosis, ventricular arrhythmias, and late development of conduction disturbances.

Among patients with surgically repaired tetralogy of Fallot, a long-term survival (30 years) of 86% has been reported. This is significantly lower than the 96% survival of the control population [2,3]. In most previous studies that performed pulmonary function tests and examined exercise capacity after surgical repair of TOF the mean follow-up was 10 years. Those studies reported a very mild restrictive pulmonary function [5,6] and mildly diminished cardiopulmonary exercise capacity as compared with healthy controls [7-9]. The purpose of the present study was to examine the long-term follow-up, 20 years after repair of TOF, by assessing lung function, cardiopulmonary functional capacity and echo-Doppler measurements of pulmonary pressure.

Patients and Methods

Fifty unselected consecutive patients with documented TOF were enrolled. All had undergone intracardiac repair of TOF at Rabin Medical Center, without additional invasive procedures such as stenting or percutaneous transluminal angioplasty. Nine patients underwent systemic to pulmonary shunt operations prior to "corrective" surgery. A comprehensive medical history was taken and a complete physical examination was performed, including electrocardiogram, echo-Doppler assessment, pulmonary function test, chest X-ray and cardiopulmonary exercise test. The institutional ethics committee and review board approved the protocol. Written informed consent was obtained from all patients.

Echo-Doppler

Echo-Doppler assessment was performed with a Hewlett-Packard system (Sonos 5500, USA) equipped with 2.5 MHz

TOF = tetralogy of Fallot

transducer. Results were recorded on a super-VHS videocassette and analyzed independently by two experienced cardiologists (R.H., L.B.). Pulsed-wave Doppler ultrasound was used to detect valvular stenosis and valvular regurgitation. Right ventricular outflow velocity was recorded with a 3 MHz non-imaging continuous-wave transducer. The maximal instantaneous and mean systolic right ventricular outflow pressure gradients were calculated by the modified Bernoulli equation. Pulmonary artery pressure was estimated from the regurgitant flow across the tricuspid valve.

Pulmonary function

Complete pulmonary function tests including spirometry, static lung volumes and diffusion capacity by single breath technique were performed. Testing was performed with the Medical Graphics Pulmonary Function System (1070-series 2; St. Paul, MN). Lung volumes were obtained by body plethysmography (model 1085, Medical Graphics). The predicted values of the parameters were obtained from the regression equations of the European Community for Coal and Steel [10].

Six minute walking test

Following the PFT assessment, each patient underwent a 6 min walking test. A 50 meter corridor in the pulmonary institute area was used for testing, and the maximum distance that could be walked (6 min walking distance) was measured, as previously described [11,12]. The test was repeated twice and the longer distance walked was used in the analysis. A 6 minute walking distance of ≥ 530 m was considered as normal [11,12].

Exercise protocol

The exercise protocol was conducted between 8:30 a.m. and 12:00 noon in the exercise physiology laboratory. Patients were encouraged to take their regular medications. Each participant underwent an incremental exercise test according to the protocol of Wasserman et al. [13] on an electrically braked cycle ergometer (Ergoline 800). After a 3 minute rest period, unloaded paddling was performed at a rate of 60 rpm for 2 minutes. The effort was then progressively increased by 10–20 watts/min until the patient could no longer maintain a cycling frequency of at least 40 rpm. Cardiopulmonary parameters: heart rate, minute ventilation (VE), oxygen uptake (VO_2), carbon dioxide production (VCO_2) and oxygen pulse (O_2P) were recorded, analyzed and stored by an exercise metabolic unit (CPX, Medical Graphics). A multiple-lead electrocardiogram system (Cardiofax, Nihon Kohden, Tokyo, Japan) and a single lead V5 ECG monitor (VC-22, Nihon Kohden) were used for continuous ECG, monitoring. Oxygen saturation (SaO_2) was monitored separately with a pulse oximeter on the finger (Nellcor, NPB-190, CA, USA). Blood pressure was measured manually with a sphygmomanometer (Tyco, USA) at rest, every 2 minutes, and at peak exercise. Results are expressed as mean \pm SD, when not otherwise specified.

PFT = pulmonary function test

Results

The study sample comprised 33 men and 17 women. The patients' age at the time of the study was 28.9 ± 11.3 years (range 15–55 years) while age at surgical repair was 10.1 ± 10.9 (range 1–43). Male to female ratio was 1.94:1. Nine patients had undergone a previous systemic artery to pulmonary artery shunt: Blalock Taussig shunt in eight and Waterston shunt in one. Ten patients underwent repeated (re-do) surgery for residual lesions at age 4.5–46 years (mean 23). Of the 50 patients, 10 were found to have a small residual shunt between the ventricles (ventricular septal defect) on echocardiography and 34 had right bundle branch block.

Echo-Doppler

Physical and echo-Doppler findings are shown in Table 1. Estimated pulmonary artery pressure was 21.5 ± 7.0 mmHg. Conduction disturbances including right bundle branch block and/or left anterior hemiblock were observed in the majority of patients ($82 \pm 37\%$); however, normal left ventricular ejection fraction was measured by echo-Doppler ($\text{LVEF } 62.6 \pm 6.1\%$) in all patients.

Table 1. Physical and echo-Doppler characteristics of the subjects (n=50)

Age (yrs)	28.9 \pm 11.3	
Age at repair (yrs)	10.1 \pm 10.9	
Male/female	33/17	
Height (cm)	174 \pm 13	
Weight (kg)	66 \pm 18	
Cardiothoracic ratio (%)	52.3 \pm 5.5	
Conduction disturbances (%)*	82 \pm 37	
Pulmonary gradient (mmHg)	21.47 \pm 7.0	
Tricuspid regurgitation (mmHg)	29.78 \pm 10.82	
LVEF (%)	62.6 \pm 6.1	

* Conduction disorders, including right bundle branch block and/or left anterior hemiblock.

Table 2. Pulmonary function test results (n=50)

FEV1 (L)*	82.86 \pm 16.46	3.31 \pm 0.55
FVC (L)*	80.28 \pm 16.21	3.78 \pm 0.61
FEV1/FVC (%)	88.03 \pm 9.99	
Dlco (ml/min/kg)*	85.93 \pm 15.47	28.47 \pm 4.41
TLC (L)*	91.37 \pm 13.89	5.97 \pm 0.83
SaO ₂ (%)	96.84 \pm 2.58	
6MWD (m)	601 \pm 92	

* Expressed as percent of predicted value (second column) and absolute value (third column)

FEV1 = forced expiratory volume in the first second, FVC = forced vital capacity, DLco = single breath diffusion lung capacity, TLC = total lung capacity, SaO₂ = oxygen saturation of arterial blood, 6MWD = 6 minute walking distance, expressed in meters

LVEF = left ventricular ejection fraction

Table 3. Cardiopulmonary exercise test results (n=50)

Work (watts)*	59.75 ± 20.15	122 ± 24.58
VO ₂ max (L/min)*	76.85 ± 21.46	2004 ± 430
VO ₂ @AT (L/min)**	50.6 ± 12.0	1319 ± 31.2
Heart rate (beats/min)*	78.16 ± 12.0	148 ± 18
VE (L/min)	46.68 ± 15.33	72 ± 11.04
O ₂ P*	96.73 ± 19.15	

* Expressed as percent of predicted (second column) and absolute value (third column)

** Expressed as percent of predicted VO₂ max.

VO₂ max = oxygen uptake at maximal effort, AT = anaerobic threshold, VE = minute ventilation, O₂P = oxygen pulse

Pulmonary function testing

Results are shown in Table 2. Patients showed normal PFT. There was no evidence of obstructive ventilation defect (forced expiratory volume at 1 second 82.8% of predicted) or of restriction (FVC 80.2% of predicted, TLC 91.4% of predicted). Diffusion capacity and oxygen saturation were normal. Six minute walking distance (601 ± 92 m) was also normal.

Exercise capacity

Results of the progressive exercise ergometry are shown in Table 3. Patients showed mild limitation in their exercise capacity with 76.8% maximal oxygen consumption without evidence for ventilatory limitation or cardiac limitation (maximal oxygen pulse 96.7% of predicted value). This suggests mostly poor effort or low exercise training.

Discussion

This study on the long-term follow-up of patients after correction of TOF did not demonstrate lung function mechanics or mildly reduced exercise capacity. Neither hypoxemia nor pulmonary hypertension was noted in any patient. Conduction disturbances, such as bundle branch block and/or left anterior hemiblock, were observed in 82% of the patients. In a recent study, RBBB was found in 81% of 21 patients 20 years after TOF repair [14]. To determine predictive markers for future development of arrhythmia and sudden cardiac death, Berul et al. [15] examined 101 resting ECGs in patients (age 12 ± 6 years) with postoperative TOF and RBBB, 14 of whom developed late ventricular tachycardia or sudden death. They found that a prolonged QRS duration in postoperative TOF with RBBB predicted vulnerability to ventricular arrhythmias in this population. Complete atrioventricular block was also associated with worse prognosis [16], but this complication did not appear in our patients.

Gaultier and co-workers [17] showed that children who underwent surgical repair of TOF during the first 2 years of life had normal lung function, whereas in patients in whom TOF was repaired late, vital capacity was significantly decreased. In another

study, normal lung function occurred late after repair of TOF [6]. Median FEV1 was similar to our findings (83% of predicted) but DLco (77% of predicted) was slightly decreased as compared to our results (86%). In another recent study, 21 patients with repaired TOF underwent clinical assessment, electrocardiogram, echocardiogram and measurements of plasma B-type natriuretic peptide and N-terminal pro-BNP as well as the 6 minute walking test. Patients were divided into two groups according to the time after surgical repair (more or less than 10 years). The authors found that in these patients, with similar age at operation and pulmonary regurgitation, most clinical, echocardiographic and humoral parameters were not worse in the second decade after repair of TOF as compared to the first postoperative decade [18].

The impact of complete repair of TOF on exercise performance is incompletely understood. Jonsson and co-authors [6] described a mildly reduced work capacity after repair of TOF that did not cause symptoms. Mahle et al. [19] found that intermediate-term exercise performance in patients who underwent primary complete repair of TOF in early childhood was near normal. Tricuspid and pulmonary valve incompetence as well as right ventricular enlargement and reduced function may also play a role in reduced exercise capacity [20].

In the present study we found mild limitation in exercise capacity, with 76.8% maximal oxygen consumption. There was no evidence of ventilatory or cardiac limitation, suggesting mostly poor effort or low exercise training. However, one limitation of this study was that pulsed-wave Doppler was used to detect valvular regurgitations and not color Doppler, which may possibly have led to under-diagnosis of regurgitation. According to other studies, abnormal pulmonary artery flow, enlargement of the heart, and elevated right ventricular pressure are the best predictors of post-repair outcome and exercise capacity [21,22]. Kusuvara and colleagues [23] reported an elevated heart/lung ratio (> 60%) in 42 patients with abnormal exercise capacity, with a higher frequency in symptomatic patients. In our study the cardiothoracic ratio was normal (52%). Chaturvedi et al. [24] and Singh et al. [25] claimed that abnormal function due to pulmonary insufficiency only manifests after very long-term follow-up (30–40 years), whereas our patients were tested on average 20 years after surgery.

We conclude that patients 20 years after TOF repair may have no disturbance in lung function, mild limitation of cardiopulmonary exercise indices, and normal pulmonary pressure and left ventricular ejection fraction.

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DLco = diffusion capacity by single breath technique

FVC = forced vital capacity

TLC = total lung capacity

RBBB = right bundle branch block

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