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Original article

Number of thoracotomies predicts impairment in lung function and exercise capacity in patients with congenital heart disease

Jan Müller (PhD)[a,b,*], Peter Ewert (MD)[a], Alfred Hager (MD)[a]

[a] Department of Pediatric Cardiology and Congenital Heart Disease, Deutsches Herzzentrum München, Technische Universität München, München, Germany
[b] Institute of Preventive Pediatrics, Technische Universität München, München, Germany

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ABSTRACT

Objective: Many patients with congenital heart disease (CHD) require surgery to ensure survival into adulthood. But history of previous thoracotomies is associated with respiratory muscle weakness, impairments in chest wall compliance, and moderately to severely impaired lung function. This study evaluated the impact of thoracotomies on functional outcome in patients with CHD.
Patients and methods: In total 1372 adolescents and adults with CHD (32.4 ± 11.5 years, 624 female), who underwent spirometry and cardiopulmonary exercise testing in our institution from January 2010 to August 2015, were analyzed.
Results: After adjusting for confounding variables, with every thoracotomy the prevalence for a restrictive ventilatory pattern increased by 1.8-fold (CI: 1.606–2.050; $p < 0.001$). The number of thoracotomies had no direct influence on an impaired exercise capacity in a multivariate model, but with every percentage point increase in forced vital capacity probability of impaired exercise capacity diminished (OR: 0.944, CI: 0.933–0.955, $p < 0.001$). There was a moderate correlation of forced vital capacity and peak oxygen uptake ($r = 0.464$, $p < 0.001$). After a follow-up of 2.1 ± 1.6 years 21 patients had died. Survival was only related to age ($p < 0.001$) and peak oxygen uptake ($p < 0.001$) after considering together with thoracotomies, oxygen saturation at rest and forced vital capacity in a multivariate model.
Conclusions: Independent of CHD complexity and other risk factors, multiple thoracotomies lead to restrictive lung pattern. It could be suggested that those limitations in forced vital capacity contribute to impairments in exercise capacity, which turned out to be the strongest predictor for survival.

Introduction

Patients with critical congenital heart disease (CHD) often undergo surgery in the first days of life to assure survival. Later, further surgery is often necessary to avoid further deterioration in functional status and impairments in quality of life. That results in a high number of patients with CHD that had received one or even more thoracotomies before adolescence [1,2]. Consequences of the thoracotomies, which are primarily performed through the sternum, are chest deformities and chest wall incompliances, accumulation of fibrotic tissue from surgical scars, weakened inspiratory muscles, and diaphragmatic palsy [3]. All of them together contribute to impairments in functional outcome such as restrictive lung function [1,2,4,5], limitations in exercise capacity [1–4], and impairment in motor competence and other basic sport characteristics such as flexibility [6,7].

Since other reports only focused on restrictive lung disease or restrictive lung pattern [1,4,8–10], this study investigated the number of thoracotomies, whether they were performed in infancy, and their association with the functional outcome. Currently, on the one hand surgery is performed earlier to avoid long-lasting cyanosis, on the other hand minimal invasive procedures performed in the catheter laboratory have increased to avoid thoracotomies.

The hypothesis was that the number of thoracotomies affects lung function, exercise capacity, and/or survival.

Patients and methods

Study subjects

We analyzed our database including all patients with CHD referred for cardiopulmonary exercise testing (CPET) and

* Corresponding author at: Department of Pediatric Cardiology and Congenital Heart Disease, Deutsches Herzzentrum München, Technische Universität München, Lazarettstr. 36, D-80636 München, Germany.
E-mail address: j.mueller@tum.de (J. Müller).

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accompanied spirometry in our institution from January 2010 to September 2015. In total 1372 adolescents ≥14 years and adults with various types of CHD (624 female, 746 male; 32.4 ± 11.5 years, range 14–79 years) were included in the statistical analysis (Table 1).

Complexity of the defects were graded into simple, moderate, and severe [11]. The study was in accordance with the declaration of Helsinki (revision 2013). Patients agreed to the anonymous publication of their data. Ethical approval was waived because of the pure retrospective character of the data and the written consent of the patients to publish their data anonymized.

Spirometry

Spirometry was conducted according to the recommendations of the American Thoracic Society and European Respiratory Society [12]. Forced expiratory volume in first second (FEV_1) and forced vital capacity (FVC) were assessed using the best of three cycles. Reference values were calculated according to Morris [13] for adults and according to Quanjer et al. [14] for adolescents.

A restrictive ventilatory pattern was defined by impaired FVC < 80% but preserved FEV_1/FVC > 70%. Patients with an obstructive ventilatory pattern defined as FEV_1 < 80% and FEV_1/FVC < 70% were excluded from the study.

Cardiopulmonary exercise test

After spirometry all patients underwent a symptom limited cardiopulmonary exercise test (CPET) on a bicycle in upright position as previously reported [15,16]. After a 3-min rest to define baseline, patients had a 3-min warm up without load, followed by a ramp wise increase of load with 5, 10, 15, 20, or 30 W/min depending on the expected individual physical capacity estimated by the investigator. The aim was to reach a cycling time of about 8–12 min after warm up. The end of the CPET was marked by symptom limitation and was followed by a 5-min recovery period, with the first 2–3 min cycling with minimal load.

The exercise test featured a breath by breath gas exchange analysis using a metabolic chart (Encore, Carefusion, San Diego, CA, USA). Peak oxygen uptake was defined as the highest mean uptake of any 30-s interval during exercise. Reference values for age, body mass, body height, and gender, expressed in "% predicted" were calculated as previously described [17]. Reference values for peak heart rate were calculated 208 − 0.7 × age according to Tanaka and colleagues [18].

Impaired exercise capacity was defined by a peak oxygen uptake <70% of predicted reference value.

CPETs were excluded if signs of insufficient compliance were present. Criteria for insufficient compliance were the combination of a respiratory exchange ratio (RER) ≤1.05 and a peak heart rate ≤85% [15,19,20]. However, cyanotic patients defined as having oxygen saturation <90% at rest or at peak exercise were included in the study independent of their RER or peak heart rate, because those patients are rarely able to reach the above mentioned thresholds.

Data analyses

All descriptive data are expressed as mean ± standard deviation and categorical variables are presented in absolute numbers or as percentages if appropriate.

Comparison of patients with normal and restrictive ventilatory pattern, of patients with normal and limited exercise capacity, and of survivors and none-survivors, was performed using unpaired Student's *t*-test and chi^2 test if appropriate.

Multiple logistic regression analysis was performed to find predictors for a restrictive ventilator pattern and an impaired exercise capacity. Independent variables included in the model were age, body mass index, sex, number of thoracotomies, cyanosis defined as oxygen saturation at rest <90%, complexity (simple, moderate, severe), beta-blocker medication, angiotensin-converting enzyme inhibitor medication, and age at first thoracotomy.

Predictors for survival were tested with multiple logistic regression analysis. Only age, thoracotomies, peak oxygen uptake, FVC, and oxygen saturation at rest were included in the model because of the limited amount of fatal events.

For all analyses, a probability value of $p < 0.05$ was considered to be statistically significant. All analyses were performed using SPSS 23.0 software (IBM Inc, Armonk, NY, USA).

Results

Results from spirometry and CPET are shown in Table 1. Not included in all tables are the 65 (4.2%) patients with an obstructive ventilatory pattern that were excluded from the study.

Restrictive ventilatory pattern

There were 563 (41.0%) patients with a restrictive ventilatory pattern. Independent of other risk factors, for every thoracotomy the odds ratio for a restrictive ventilatory pattern increased by 81.5% (OR: 1.815, CI: 1.606–2.050, $p < 0.001$) (Fig. 1). In addition,

Table 1
Patient characteristics.

	All patients (n = 1372)	Non-survivors (n = 21)	*p*-value[a]
Sex (female)	615 (45.4%)	9 (42.8%)	.830
Age (years)	32.4 ± 11.5	42.2 ± 13.7	**<.001**
Body mass index (kg/m^2)	24.1 ± 4.1	23.8 ± 4.4	.629
Thoracotomies (*n*)	1.49 ± 1.26	2.1 ± 1.27	**.016**
Age at first thoracotomy (years)	6.4 ± 10.3	14.4 ± 15.1	**.001**
Peak oxygen uptake (%predicted)	82.3 ± 22.2	54.2 ± 17.9	**<.001**
Respiratory exchange ratio	1.17 ± 0.9	1.14 ± 1.1	.883
Forced vital capacity (%predicted)	82.6 ± 16.5	67.0 ± 17.8	**<.001**
FEV1 (%predicted)	88.2 ± 17.7	72.7 ± 20.0	**<.001**
Oxygen saturation at rest (%)	96.6 ± 5.1	93.4 ± 6.0	**.004**
Beta-blocker	174 (12.7%)	10 (47.6%)	**<.001**
ACE-inhibitor	53 (3.9%)	1 (4.8%)	.565
Pacer	63 (4.6%)	3 (14.3%)	.068

FEV1, forced expiratory volume in the first second; ACE, angiotensin-converting enzyme.
[a] Comparing survivors and non-survivors by a Student's *t*-test or chi^2 if appropriate.

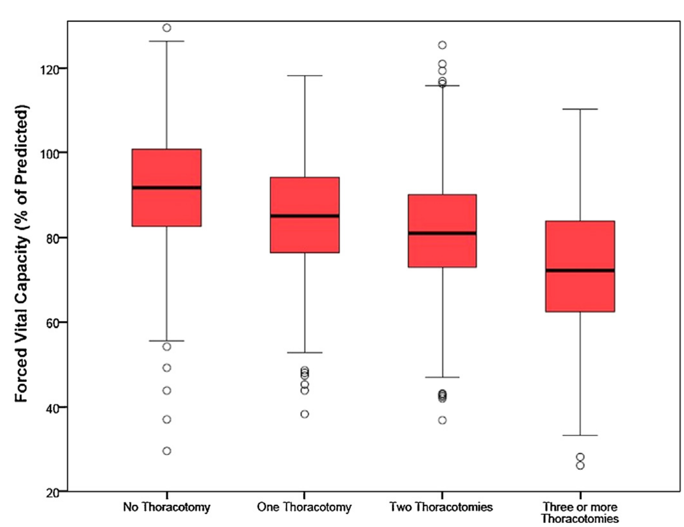

Fig. 1. Forced vital capacity according to thoracotomies.

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