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A single bout of maximal exercise improves lung function in patients with cystic fibrosis☆

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Abstract

Background: Responses to a single bout of exercise may provide critical information for maximizing improvements in pulmonary function following exercise training in cystic fibrosis (CF). We sought to determine if acute maximal exercise improves pulmonary function in patients with CF.
Methods: Thirty-three patients with CF completed a comprehensive assessment of pulmonary function to determine forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and lung clearance index (LCI) prior to and immediately following maximal aerobic exercise on a cycle ergometer.
Results: Following exercise, FVC (Δ 0.08 ± 0.14 L) and FEV_1 (Δ 0.06 ± 0.15 L/min) increased, while LCI decreased (Δ-0.71 ± 0.93) (all $p < 0.05$). Changes in FEV_1 (%predicted) were associated with peak work ($r = 0.40$, $p = 0.02$) and peak pulmonary ventilation ($r = 0.45$, $p = 0.01$).
Conclusions: A single bout of maximal exercise acutely improves pulmonary function in patients with CF and improvements may be related to peak work and peak pulmonary ventilation.

Keywords: Spirometry; Impulse oscillometry; Exercise capacity; Multi-breath washout

1. Introduction

Cystic fibrosis (CF) is associated with a number of systemic disorders but is primarily characterized by a progressive decline in pulmonary function [1,2] and reduced exercise capacity [3]. While the main cause of morbidity and mortality is pulmonary infection and impaired lung function [4], reduced exercise capacity has been shown to predict mortality and an increased risk for hospitalization, independent of lung function [5–7]. Thus, preserving both exercise capacity and pulmonary function have significant implications for overall health and well-being in patients with CF.

Maximal exercise capacity is reduced in patients with CF [8,9] and among others, may be a consequence of multiple physiological mechanisms including impaired oxygen uptake kinetics [10], abnormal pulmonary function [8,9], and oxidative stress [11]. Exercise training can lead to a number of positive outcomes in patients with CF, including improved exercise capacity, preservation of pulmonary function over time, and

Abbreviations: CPET, maximal cardio-pulmonary exercise test; CRP, C-reactive protein; DXA, dual-energy X-ray absorptiometry; FeNO, fractional exhaled nitric oxide; RPE, rating of perceived exertion; RER, respiratory exchange ratio; VE, ventilatory equivalent; VO_2, volume of oxygen uptake

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improved health-related quality of life [3,12–14]. The pulmonary function response to chronic exercise training, however, is considerably variable [12–16] and may be attributable to various combinations of the type of training modality used, duration of training, or the exercise intensity of individual training sessions. Given that chronic exercise training consists of repeated acute bouts of physical exertion, the advantage of utilizing an acute exercise paradigm to examine the effects on pulmonary function in patients with CF could more efficiently 1) provide insight into how chronic exercise training elicits positive pulmonary function outcomes (e.g., acute changes in airway inflammation and/or mechanical function), and 2) elucidate information regarding an optimal exercise dose-response relationship.

Therefore, the purpose of this study was to investigate the effect of a single bout of maximal aerobic exercise on pulmonary function in patients with CF. Further, we examined potential relationships between pre- to post-exercise changes in pulmonary function and cardiopulmonary variables collected during the maximal exercise test. We hypothesized that an acute bout of maximal exercise would improve pulmonary function in patients with CF.

2. Materials and methods

2.1. Patients

Thirty-three patients with CF were recruited to participate in this study. Patients reported to the Laboratory of Integrative Vascular and Exercise Physiology at Augusta University for testing. Patients were excluded if they (1) had a forced expiratory volume in one second (FEV_1) < 30%predicted; (2) had a resting oxygen saturation (SpO_2) < 85%; (3) self-reported to be a smoker; (4) were diagnosed with pulmonary hypertension; (5) were diagnosed with sleep apnea or sleep disorders; (6) had a clinical diagnosis of cardiovascular disease or hypertension, or (7) were prescribed any vasoactive medications (i.e., nitrates, b-blockers, etc.). During a preliminary screening visit, body mass and height were assessed using a standard scale and stadiometer, respectively, and used for subsequent calculations of body mass index (BMI). Body fat percentage was determined via dual-energy X-ray absorptiometry (DXA; QDR-4500W, Hologic, Inc., Marlborough, MA) and a small blood sample was taken to evaluate C-reactive protein (CRP), an index of systemic inflammation. All study related procedures were approved by the Institutional Review Board at Augusta University, and patients and/or parents, when appropriate, provided written informed consent/assent prior to participation.

2.2. Comprehensive assessment of pulmonary function

A comprehensive assessment of pulmonary function, including spirometry, impulse oscillometry, exhaled nitric oxide, diffusion capacity, and lung clearance index was performed before and starting 10 min following a maximal exercise test. All testing took place in the morning, with patients performing their regular airway clearance techniques ~1–2 h prior to reporting to the laboratory. Consequently, the last treatment was approximately 3 and 4 h prior to pre- and post-exercise pulmonary function testing, respectively, and thus, likely had little to no effect on outcome variables. The time-course of post-exercise testing was chosen based on the recommended timing of assessing pulmonary function following a bronchodilator challenge [17]. The order of pulmonary function testing was the same pre- and post-exercise and took approximately 30 min to complete. All pulmonary function tests were performed by a qualified respiratory therapist according to standards set by the American Thoracic Society [18].

2.2.1. Impulse oscillometry

Impulse oscillometry (IOS) was performed three times (Jaeger MasterScreen IOS, Würzburg, Germany) for ~30 s while participants wore a nose clip and placed their hands against their cheeks to decrease upper airway shunt. Oscillometric pressure impulses occurred at a pulse sequence of 5 per second across a frequency spectrum of 5–20 Hz. The oscillations provide a measure of total airway impedance which can be further divided into resistive (resistance, R) and capacitive/inertive (reactance, X) properties of the airways. Resistance at 5 Hz (R5) represents total airway resistance and resistance at 20 Hz (R20) represents resistance of the proximal airways. Thus, the change in resistance across these frequencies (i.e., R5–R20) serves as an indicator of peripheral properties of the respiratory tract [19]. The area of reactance (AX) represents the total reactance (area under the curve) at all frequencies between 5 Hz and the resonant frequency (where all reactance is null) and provides an additional index of peripheral airway obstruction [19].

2.2.2. Spirometry

Spirometric assessments were performed using the EasyOne Pro® LAB system (ndd Medical Technologies, Andover, MA) to evaluate FEV_1, forced vital capacity (FVC), FEV_1/FVC ratio, and forced expiratory flow at 25–75% ($FEF_{25–75}$). Patients performed spirometry according to the American Thoracic Society Standards [18]. Maximal voluntary ventilation (MVV) was calculated as 27.7(FEV_1) + 8.8(predicted FEV_1) [20] for patients aged ≤18 years or FEV_1 × 40 for patients aged >18 years [21]. The European Respiratory Society Global Lung Function Initiative spirometric reference standards [22] were used to determine the percentage predicted data set.

2.2.3. Exhaled nitric oxide, diffusion capacity, and lung clearance index

Fractional exhaled nitric oxide (FeNO) was measured using a NIOX MINO® analyzer (Solna, Sweden). Single breath diffusion capacity (DL_{CO}^{SB}) was performed in duplicate with patients exhaling fully before performing a maximal inhalation of gas containing 0.3% CO and holding their breath for 10 s before exhaling normally (EasyOne Pro® LAB). Lung clearance index (LCI) was assessed in duplicate via multiple-breath washout of N_2 (EasyOne Pro® LAB) and was equal to cumulative expired volume divided by functional residual capacity (FRC) at 1/40th of the initial tracer concentration (2% N_2).

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