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Original Article

Inspiratory muscle strength relative to disease severity in adults with stable cystic fibrosis

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Abstract

Background: Due to heterogeneity in pulmonary disease, current literature may misrepresent inspiratory muscle involvement in cystic fibrosis (CF). This study investigated inspiratory muscle strength (IMS) relative to disease severity in adults with CF.
Methods: Maximal inspiratory pressure (MIP) was assessed in 58 adults with stable CF grouped by disease severity (20 mild, 20 moderate, 18 severe) and compared to 20 controls. Relationships between MIP, lung function, dyspnea and anthropometrics were evaluated using multivariable linear models.
Results: MIP in cmH_2O and %-predicted was decreased in advanced CF lung disease as compared to mild disease and healthy controls ($p < 0.05$). Disease severity accounted for 24% of the variance in IMS after controlling for confounding variables ($p < 0.001$).
Conclusions: IMS is decreased in some adults with stable CF with moderate and severe pulmonary disease, and is related to dyspnea. Future studies should determine if decreased IMS contributes inefficient breathing patterns, respiratory pump dysfunction, and/or exercise intolerance in advanced CF.

Keywords: Cystic fibrosis; Inspiratory muscle strength; Maximal inspiratory pressure; Respiratory muscle; Adult

1. Introduction

Impaired exercise capacity is well-documented in cystic fibrosis (CF) and linked to quality of life and mortality [1,2]. Causes of exercise intolerance include dyspnea and impaired gas exchange associated with excess work of breathing (WOB) particularly in the presence of severe CF lung disease [3,4]. The inspiratory muscles must possess sufficient capacity relative to the imposed inspiratory load for normal breathing to occur in the presence of this excess WOB [5]. CF-related inspiratory muscle impairments may contribute to respiratory pump dysfunction, dyspnea, altered breathing patterns, inspiratory fatigue, and ultimately exercise intolerance [4–8].

Resistive inspiratory loads rarely exceed levels of consequence in the presence of normal inspiratory muscle strength

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(IMS) and pulmonary physiology. Studies on IMS suggest normal or above normal values in adults with CF secondary to training effects induced from a chronically elevated WOB [9,10]. Others suggest that IMS is decreased secondary to factors associated with progressive disease including hyperinflation, malnutrition, chronic infection, inflammation, and systemic corticosteroid use [11–15]. Overall, the current literature favors the preservation of IMS in adults with CF negating its clinical significance [10]; however, interpretations were based on mean values from groups with a wide range of airway obstruction. Impaired IMS may be masked in such heterogeneous samples that typically underrepresent severe disease where factors associated with decreased IMS are most prevalent.

If present, impaired IMS may have significant clinical consequences given the elevated WOB and may contribute to dyspnea, ventilatory inefficiency, and exercise intolerance associated with progressive CF-related lung disease. The extent to which CF affects the inspiratory muscles is unclear and the potential influence of disease severity on IMS has not been fully evaluated. The involvement of the inspiratory muscles in adults with CF should be further investigated as impairments in these muscles may result in hypoventilation and respiratory pump dysfunction warranting targeted interventions [5,16]. Therefore, the aim of this study was to investigate IMS relative to pulmonary disease severity in adults with stable CF.

2. Methods

A cross-sectional sample of adults (age ≥ 18 yrs) with CF, stable lung function, and no medical changes in the prior 4 weeks was recruited from a hospital-based outpatient CF clinic (Hospital of the University of Pennsylvania (HUP), Philadelphia, PA, USA) using a sample of convenience. Exclusion criteria were signs or symptoms of a pulmonary exacerbation, active smoking, secondary pulmonary diagnoses other than asthma, thoracoabdominal conditions interfering with testing, neuromuscular disease, pregnancy, unresolved pneumothorax, colonization with *Burkholderia cepacia*, lung transplant, and the presence of a cardiac pacemaker. Healthy subjects (age ≥ 18) without CF were recruited from HUP and a local University (Rutgers, the State University of New Jersey, Stratford, NJ, USA) as controls. Healthy subjects were excluded in the presence of active smoking, pregnancy, pre-existing pulmonary disease, diabetes, heart failure, respiratory infection, allergy flare, or any condition that could affect testing performance. All procedures received Institutional Review Board approvals prior to initiating study-related activities. Eligible volunteers completed the informed consent process prior to enrollment and were offered a $20 gift card upon study completion.

2.1. Demographics

Basic demographics including age, ethnicity, sex (female = 0, male = 1), and genotype were recorded. Genotype was categorized as ΔF508/ΔF508, ΔF508/other, or other/other. The presence of pancreatic insufficiency, CF-related diabetes (CFRD), concurrent systemic corticosteroid use, and sputum colonization with *Pseudomonas aeruginosa* was documented. Subjects rated their dyspnea using the Modified Medical Research Council (MMRC) dyspnea scale [17]. The MMRC dyspnea scale is a categorical scale with five levels ranging from 0 (not troubled by breathlessness) to 4 (too breathless to leave the house or breathless when dressing). Frequency counts were recorded for each level of the MMRC dyspnea scale.

2.2. Pulmonary function

Pulmonary function measurements including forced expiratory volume in one-second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, residual volume (RV), total lung capacity (TLC) and RV/TLC ratio were extracted from the medical records of subjects with CF. These measurements were performed as part of routine care by a licensed respiratory therapist according to standard guidelines [18,19]. Simple spirometry was assessed in the controls to ensure normal lung function using the Micro Plus (CareFusion Ltd., San Diego, CA, USA) handheld spirometer according to standard guidelines [18]. The best of three trials was recorded and routine calibration checks were performed.

Spirometry was completed the same day as IMS testing and expressed in liters and percent of predicted in all subjects [20]. Lung volumes were recorded in the CF subjects only and extrapolated from body plethysmography tests performed within 12 months of IMS testing provided the FEV_1 percent predicted (%FEV_1) was within 10% of current values. Updated tests were obtained if this criterion was not met. Hyperinflation was quantified by the RV/TLC ratio. Disease severity was categorized as mild (%FEV_1 ≥ 70%), moderate severity (%FEV_1 40–69%), and severe (%FEV_1 < 40%) [21].

2.3. Anthropometrics

Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared and percent of ideal body weight (%IBW) was documented [21,22]. Lean body mass (LBM) was derived from body composition measurements using the Tanita BC-418 bioelectrical impedance analyzer (Tanita Corporation of America, Arlington Heights, IL, USA) in a temperature controlled environment. Subjects refrained from caffeine and alcohol for at least 2 h and voided their bladder within 30 min before testing.

2.4. Inspiratory muscle strength

Maximal inspiratory pressure (MIP) was measured with a handheld mouth pressure meter (MicroRPM® (RPM01), CareFusion Ltd., San Diego, CA, USA) interfaced with a computer and associated software (Puma® (PU1000)). Standard guidelines were followed [23]. Subjects were seated wearing nose clips. A rubber flanged mouthpiece was used with an in-line bacterial filter. The inspiratory circuit contained a small leak to prevent the influence of the buccal muscles. Subjects refrained from using bronchodilators for at least 2 h prior to testing. A maximal static inspiratory maneuver from RV