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The influence of body composition on respiratory muscle, lung function and diaphragm thickness in adults with cystic fibrosis ☆

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Abstract

Background: Weight loss and loss of fat-free mass (FFM) are associated with peripheral muscle wasting in cystic fibrosis (CF) although whether this co-exists with loss of diaphragm mass remains unclear.
Methods: FFM was determined by dual-energy X-ray absorptiometry and bioelectrical impedance in 40 adults with CF and 30 age-matched healthy subjects (HS). Diaphragm thickness at functional residual capacity (FRC) [TDIrel] and total lung capacity (TLC) [TDIcont] and thickening ratio (TR) were assessed by ultrasonography. Inspiratory muscle strength and work capacity were determined by maximal inspiratory pressure (PImax), and sustained PImax (SPImax); pulmonary function (RV, VC and TLC) and physical activity status (PAS) were also determined.
Results: When the CF patients were assessed as a group (low and normal FFM) they had similar age, weight, height and PAS compared to the HS, although patients had lower FFM ($p<0.05$), VC and TLC than the HS ($p<0.01$). In addition, although PImax, TDIrel, TDIcont and TR were similar between the patients and the HS, SPImax was lower in the patients ($p<0.01$). When analyses were made between patients with low versus normal FFM and between patients with low FFM and HS no significant differences were found between overall weight although TDIrel, TDIcont, TR and PAS were all reduced in patients with low FFM ($p<0.01$).
Conclusions: PImax is relatively well preserved in adults with CF although there is a relationship between the loss of inspiratory muscle work capacity, FFM, PAS and pulmonary function. Furthermore loss of FFM is associated with loss of diaphragm muscle mass.

Keywords: Body composition; Diaphragm thickness; Cystic fibrosis

Abbreviations: BMI, body mass index (kg/m^2); CF, cystic fibrosis; CRP, C-reactive protein (μg/ml); DXA, dual-energy X-ray absorptiometry; FEV_1, forced expiratory volume in 1 s (% predicted); FFM, fat-free mass (kg); FRC, functional residual capacity (litres); HS, healthy subjects; PAS, physical activity status (MET's); PImax, maximal inspiratory pressure (cm H_2O); RV, residual volume (litres); SPImax, sustained maximal inspiratory pressure (pressure/time units); TDIcont, diaphragm thickness measured by ultrasound at total lung capacity (mm); TDIrel, diaphragm thickness measured by ultrasound at functional residual capacity (mm); TR, thickening ratio (%); TLC, total lung capacity (litres); VC, vital capacity (litres).

☆ This work was performed at Llandough Hospital NHS Trust, Cardiff.

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1. Introduction

Growth retardation and undernutrition are often seen in patients with cystic fibrosis (CF) as a result of several factors including malabsorption [1,2], reduced energy intake [3], increased energy expenditure [4,5] and the inflammatory state secondary to chronic pulmonary infection [6]. Such events lead to loss of fat mass and fat-free mass (FFM). The loss of FFM leads to a reduction in skeletal muscle mass that may co-exist with inspiratory muscle wasting and loss of inspiratory muscle function [7,8]. Furthermore patients with low FFM have been shown to have low levels of physical activity [9] and the loss of body mass has been shown to be a significant predictor of survival, a factor independent of pulmonary function and gas exchange [10].

Although evidence exists that the inspiratory muscles may be affected by the general loss of muscle mass and despite the diaphragm being the largest and most important muscle of inspiration, the effect of loss of FFM on diaphragm thickness remains unclear. Indeed it has been suggested that diaphragm bulk is maintained in CF [11], even in the face of peripheral muscle atrophy [12]. The most widely held hypothesis for this phenomenon is the presence of a training effect on the respiratory muscles [11,13] due to the loads imposed by chronic hyperinflation and increased work of breathing as indices of inspiratory muscle strength, measured by non invasive methods, appear to be well preserved in CF patients. However, the assessment of volitional techniques to measure muscle strength is especially sensitive to the level of effort exerted [14] and may therefore be strongly influenced by the subject's ability and motivation. Also, the large intra subject variability of diaphragm thickness observed in some studies [11,12] indicates that the beneficial response to an increased workload on the inspiratory muscles does not occur in all CF patients. In addition, the different clinical profiles of the patients in terms of respiratory impairment and nutritional status make it difficult to interpret studies which have assessed diaphragm bulk [11,12].

The aim of this study was to investigate the effect of loss of fat-free mass on pulmonary function, physical activity and diaphragm thickness in patients with CF. In order to investigate these aims, patients with low versus normal fat-free mass were compared with a group of healthy age-matched controls. The relationships between fat-free mass, diaphragm thickness, physical activity status, lung function and indices of inspiratory muscle endurance were also determined.

2. Methods and materials

2.1. Subjects

Forty adult CF patients (22 males) with proven CF and 30 age-matched healthy subjects (15 males) were studied. Mean age of the patients was 22.4 (age range, 18–32 years); mean age of the healthy subjects was 21.7, (age range, 18–33 years) (Table 1). Patients were excluded from the study based on the following criteria: liver cirrhosis, cor pulmonale or an exacerbation of their respiratory symptoms (increased respiratory symptoms, weight loss, fever, or reduction in FEV_1 of >10% than the usual value) or elevated C-reactive protein (>15.5 μg/ml). None of the patients had obvious signs of malabsorption; all had pancreatic insufficiency and were taking supplementary pancreatic enzyme products with meals. All healthy subjects were non-smokers, had no evidence of pulmonary pathology (e.g. asthma) or were suffering from any known metabolic or endocrine disorder. An adequate sample size was found to be at least 10 subjects per group at $\alpha=0.05$ and $1\beta=90\%$. All subjects were informed of the nature of the study and gave full written consent prior to the study which had Research Ethics Committee approval.

Table 1
Body composition, diaphragm thickness and inspiratory muscle function in cystic fibrosis (CF) patients and in healthy subjects

Variables	CF patients ($n=40$)	Healthy subjects ($n=30$)
Age (years)	22.4 (21.2–23.6)	21.7 (20.3–23.1)
Height (cm)	166 (160.1–171.9)	168 (164.4–171.6)
Weight (kg)	60.2 (58.5–62.0)	64.4 (60.9–67.9)
BMI (kg/m^2)	22.0 (21.0–23.0)	23.0 (22.2–23.8)
FFM (kg)	44.6 (38.6–50.6)	56.8 (49.8–63.8)[a]
PAS (MET's)	37.0 (35.0–39.0)	41.5 (40.0–43.0)
FEV_1 (% pred)	46.5 (46–47)	96.2 (95.2–97.2)[a]
VC (litres)	3.6 (3.3–3.9)	4.1 (3.7–4.5)[a]
RV (litres)	1.7 (1.6–1.8)	1.5 (1.4–1.6)
FRC (litres)	2.6 (2.2–3.0)	2.9 (2.6–3.1)
TLC (litres)	4.6 (4.2–5.0)	5.8 (5.6–6.0)[a]
Diaph (TDIrel) (mm)	2.8 (2.6–3.1)	3.4 (3.0–3.8)
Diaph (TDIcont) (mm)	3.9 (3.6–4.2)	4.4 (4.2–4.6)
TR (%)	2.7 (2.4–3.0)	2.9 (2.7–3.2)
PImax (cm H_2O)	116 (109–123)	124 (119–129)
SPImax (PTU)	609 (543–675)	788 (733–843)[a]

Data are presented as mean (95% CI). FFM=fat-free mass. PAS=physical activity status (in MET's=metabolic equivalents [1 MET=3.5 ml/kg/min]), TDIrel and TDIcont=diaphragm thickness at FRC (rel) and at TLC (cont). TR=diaphragm thickening ratio (%). PImax=maximum inspiratory pressure. SPImax=sustained maximum inspiratory pressure. PTU=pressure time units.
[a] $p<0.01$.

2.2. Study design

This was an observational, cross-sectional study comparing 40 CF patients to 30 healthy subjects (controls). Following this analysis the CF patients were classified as having either severe (mean FEV_1 36.7 and FFM 36.2 kg respectively) or moderate disease (mean FEV_1 56.3 and FFM 53.0 kg respectively) and analysed separately with the controls. At the initial screening visits, in all patients and controls, body composition, pulmonary function and physical activity status were determined. In addition, all subjects had an assessment of their inspiratory muscle function and diaphragm thickness (Table 1). All measurements of these variables were obtained by persons who were blinded to the nature of the study.