Respiratory Medicine 142 (2018) 60–65

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Nutritional status and pulmonary outcome in children and young people with cystic fibrosis

Niovi Papalexopoulou[a,b], Theodore G. Dassios[b,c], Alan Lunt[a,b], Fiona Bartlett[d], Felicity Perrin[e], Cara J. Bossley[f], Hilary A. Wyatt[g], Anne Greenough[a,b,h,*]

[a] MRC & Asthma UK Centre in Allergic Mechanisms of Asthma, King's College London, London, United Kingdom
[b] Department of Women and Children's Health, School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London, United Kingdom
[c] Neonatal Intensive Care Centre, King's College Hospital NHS Foundation Trust, London, United Kingdom
[d] Paediatric Dietetic Department, King's College Hospital NHS Foundation Trust, London, United Kingdom
[e] Respiratory Medicine and Adult Cystic Fibrosis Service, King's College Hospital NHS Foundation Trust, London, United Kingdom
[f] Paediatric Respiratory Medicine, Kings College Hospital NHS Foundation Trust, London, United Kingdom
[g] Paediatric Cystic Fibrosis, King's College Hospital NHS Foundation Trust, London, United Kingdom
[h] NIHR Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London, United Kingdom

ARTICLE INFO

Keywords:
Respiratory muscle function
Body composition
Bioelectrical impedance analysis
Body mass index
Exercise tolerance

ABSTRACT

Background: Nutrition is closely related to mortality and pulmonary and respiratory muscle function in cystic fibrosis (CF) patients. We initially validated results from a bioelectrical impedance device against dual energy x-ray absorptiometry (DEXA). We then determined whether fat free mass assessed by a portable impedance device rather than body mass index (BMI) better correlated with pulmonary function, respiratory muscle strength and exercise capacity in CF patients.

Methods: Eighteen young people and adults (median age 19, range 12–39 years) with CF had dual energy X-ray absorptiometry and direct segmental multi-frequency impedance analysis. Body composition, pulmonary function, respiratory muscle function and exercise tolerance using the impedance device were measured in 29 young people with CF with median age 15 (range 12–19) years.

Main findings: There was a significant correlation between impedance and absorptiometry results ($r^2 = 0.947$). Fat free mass correlated with the forced vital capacity z-score ($r = 0.442$, $p = 0.016$), maximal inspiratory pressure ($r = 0.451$, $p = 0.014$) and exercise tolerance ($r = 0.707$, $p < 0.001$). BMI z-scores did not significantly correlate with pulmonary or respiratory muscle function. Subjects with a fat free mass z-score of ≤ 2 had a lower forced expiratory volume in 1 s z-score ($p = 0.007$), lower forced vital capacity z-score ($p = 0.001$), higher residual volume z-score ($p = 0.042$), lower maximal inspiratory pressure ($p = 0.039$), more days of intravenous antibiotics per year ($p = 0.016$) and a higher rate of chronic infections ($p = 0.006$).

Principal conclusions: Fat-free mass measured by impedance correlated better with pulmonary and respiratory muscle function and exercise capacity than BMI.

1. Introduction

The current median predicted survival in UK patients with cystic fibrosis (CF) is 47 years [1] and respiratory failure remains the leading cause of mortality. The most rapid decline in pulmonary function is seen during adolescence with the forced expiratory volume in 1 s (FEV_1). Nutrition is closely related to mortality in CF patients; those with a higher compared to a lower body weight have higher cumulative survival at five years [2]. Nutrition is also related to pulmonary and respiratory muscle function. Adults with CF and a body mass index (BMI) below 20 had a markedly lower FEV_1 than those with a BMI between 20 and 25 [3].

BMI is used in the clinical setting to quantify the nutritional status of CF patients. Current guidelines recommend a BMI above the fiftieth percentile in children and adolescents to support optimal pulmonary function [4]. Measurements of the proportion of lean muscle, such as fat

* Corresponding author. Neonatal Intensive Care Unit, 4th Floor Golden Jubilee Wing, King's College Hospital, Denmark Hill, London, SE5 9RS, United Kingdom.
E-mail addresses: niovi.papalexopoulou@gmail.com (N. Papalexopoulou), theodore.dassios@kcl.ac.uk (T.G. Dassios), alan.lunt@nhs.net (A. Lunt), Fiona.bartlett@nhs.net (F. Bartlett), felicity.perrin@nhs.net (F. Perrin), cara.bossley@nhs.net (C.J. Bossley), hilarycarroll@live.co.uk (H.A. Wyatt), anne.greenough@kcl.ac.uk (A. Greenough).

https://doi.org/10.1016/j.rmed.2018.07.016
Received 21 May 2018; Received in revised form 18 July 2018; Accepted 23 July 2018
Available online 26 July 2018

Abbreviations

BMI	body mass index
CF	cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator
DEXA	dual energy X-ray absorptiometry
FEV_1	forced expiratory volume in 1 s
FFM	fat free mass
FFM_{BIA}	fat free mass by bioelectrical impedance analysis
FFM_C	fat free mass corrected
FFM_{C2}	fat free mass corrected based on Charatsi et al.
FFMDEXA	fat free mass by dual energy X-ray absorptiometry
FFMI	fat free mass index
FMI	fat mass index
FRC	functional residual capacity
FVC	forced vital capacity
LM	lean mass
LMT	lean mass trunk
LMT_C	LMT corrected
LMT_{BIA}	LMT by bioelectrical impedance analysis
LMUL	lean mass upper limbs
$LMUL_{BIA}$	lean mass upper limbs by bioelectrical impedance analysis
$LMUL_C$	LMUL corrected
$LMUL_{DEXA}$	lean mass upper limbs by dual energy X-ray absorptiometry
MEP	maximal expiratory pressure
MIP	maximal inspiratory pressure
$MMEF_{25-75}$	maximal mid-expiratory flow between 25 and 75% of vital capacity
NIV	non-invasive ventilation
PFT	pulmonary function test
RMFT	respiratory monitoring function test
Rrs5	respiratory system resistance at 5 Hz
Rrs20	respiratory system resistance at 20 Hz
RV	residual volume
TLC	total lung capacity

free mass and lean body mass, however, may better describe the nutritional status in CF. Engelen et al. retrospectively analysed pulmonary function tests, BMI and body composition assessed by dual energy X-ray absorptiometry (DEXA). They identified a subgroup of CF patients who had a normal BMI, but low fat free mass and a lower FEV_1 than those with normal fat free mass [5]. Peripheral muscle weakness has been described in children and adolescents with CF and knee extensor muscle strength has been shown to moderately correlate with BMI [6]. Segmental lean body mass has not been assessed in CF children and young people in relation to pulmonary and respiratory muscle function tests.

DEXA scanning is used to estimate body composition, but involves ionizing radiation rendering it unsuitable for serial use. Alternatively, bioelectrical impedance analysis could be used. This method has been shown to give conflicting results when compared to DEXA in CF, potentially due to the affected electrical potentials from the underlying defect in chloride permeability and abnormal sodium transport [7,8]. Validation of impedance analysis in relation to DEXA with a creation of a disease-specific equation has been suggested as a way of overcoming this [9]. An aim of this study was to validate a portable, segmental, multi-frequency impedance device to calculate body composition against DEXA results and to create CF specific equations.

The main aim of this study was to determine whether fat free mass rather than BMI using a portable bioelectrical impedance analysis would better predict both pulmonary and respiratory muscle function. Furthermore, we examined whether pulmonary and respiratory function results correlated with exercise tolerance and assessed whether a specific distribution of lean body mass depletion related to pulmonary and respiratory muscle function or exercise tolerance.

2. Materials and methods

2.1. Study design

Two studies were conducted between June 2016 and May 2017 at a tertiary CF centre at King's College Hospital NHS Foundation Trust, London, UK. The first compared DEXA scan with impedance analysis performed on the same day in patients with CF aged 10 years and older. Patients were studied who were undergoing routine DEXA scans and gave informed written consent to also undergo impedance monitoring. The second study investigated clinically stable children and young people with CF who were aged between 12 and 19 years. Consecutive children and young people who fulfilled these inclusion criteria had none of the exclusion criteria and parents/patients gave informed written consent. Exclusion criteria were pulmonary exacerbation in the past two-weeks and acute illness or hospitalisation. Age, gender and genotype were recorded. Genotype was classified into: ΔF508 homozygotes, ΔF508 heterozygotes, and other mutations. Information on the presence of chronic infection (three or more positive microbiology sputum cultures in the preceding 12 months) [10], CF-related diabetes, CF-related liver disease (abnormal liver enzymes and/or ultrasonography), pancreatic insufficiency, presence of percutaneous endoscopic gastrostomy tube and days of intravenous antibiotics administered in the past year was collected.

Participants underwent body composition evaluation via bioelectrical impedance analysis, pulmonary, respiratory muscle and exercise tolerance tests. Ethical approval was granted by the London - Camberwell St Giles Research Ethics Committee for the first study and the East Midlands - Nottingham 2 Research Ethics Committee for the second study. Participants aged 16 years and older gave written consent whilst participants younger than 16 years gave written assent and consent was provided by their parents/guardians.

2.2. Methods – study one

Body composition was measured firstly with DEXA Lunar Prodigy (GE, Healthcare, Belgium) followed by bioelectrical impedance analysis with the Inbody S10 Body Composition Analyser (Inbody Ltd, Cerritos, California, USA). Body composition was estimated by impedance using the four compartment model representing the body in terms of water, protein, fat and mineral components. Inbody S10 measures impedance separately in the four limbs and trunk. Body mass index (BMI), fat free mass, fat mass and segmental lean mass (LM)-upper limbs, LM-trunk, LM-lower limbs were recorded. Measurements were taken using the tetra-polar 8-Point Tactile Electrode system in the sitting position, following 2-h of fasting and micturition within 30 min prior to testing.

3. Methods – study two

3.1. Anthropometric measurements & body composition

Height, weight and body composition using Inbody S10 were measured and BMI-z scores and percentiles were calculated [11]. Fat free mass and fat mass were adjusted using the correction equation generated in the first study.

3.2. Pulmonary function testing

Height was measured to the nearest 0.1 cm by stadiometer and weight to the nearest kilogram by digital scales. Spirometry, impulse oscillometry and body plethysmography were performed on the same