Journal of Cystic Fibrosis 15 (2016) 825 – 833

www.elsevier.com/locate/jcf

Original Article

Bioelectrical impedance in young patients with cystic fibrosis: Validation of a specific equation and clinical relevance

A.M. Charatsi [a,1], P. Dusser [a,1], R. Freund [b], G. Maruani [c], H. Rossin [d], A. Boulier [c], M. Le Bourgeois [a], F. Chedevergne [a], J. de Blic [a], A. Letourneur [d], G. Casimir [e], J.P. Jais [b], I. Sermet-Gaudelus [a,*]

[a] *Pediatric Pulmonology Department, Hôpital Universitaire Necker Enfants Malades, Paris, France*
[b] *Bio-statistics Department, Hôpital Universitaire Necker Enfants Malades, Paris, France*
[c] *Physiology Department, Hôpital Universitaire Necker Enfants Malades, Paris, France*
[d] *Aminogram, La Ciotat, France*
[e] *Pediatric Pulmonology Department, Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Brussels, Belgium*

Received 13 December 2015; revised 28 April 2016; accepted 7 May 2016
Available online 9 June 2016

Abstract

Background: Body composition (BC) analysis based on bioelectrical impedance analysis (BIA) provides conflicting results. The purpose of the study was to validate an equation specific for young patients with cystic fibrosis (CF), describe their BC and investigate its association with lung function.
Methods: Fifty-four young CF patients were evaluated by BIA and dual X-ray absorptiometry (DXA). An empirically derived CF-specific equation for fat-free mass (FFM) estimation by BIA was elaborated after stepwise multivariate regression and the agreement between BIA and DXA was assessed by Bland–Altman plots. The association between BC and lung function was investigated by regression analysis.
Results: The mean difference between the BIA and DXA assessment was close to zero. A total of 22.5% of patients ($n = 9$) presented a FFM z-score ≤ -2. They had a worse pulmonary function and diaphragmatic impairment. Among these 9 patients, 7 had a normal BMI z-score > -1.
Conclusions: BIA, based on a CF-specific equation, is a reliable method for BC assessment and allows the identification of patients at risk of nutritional degradation and bad respiratory prognosis.

Keywords: Cystic fibrosis; Body composition; Bioelectrical impedance analysis; Fat-free mass; Lung function; Diaphragm

1. Introduction

The crucial role of nutritional status in the survival of cystic fibrosis (CF) patients has been identified from first identifications of the disease [1]. This was further demonstrated by Corey et al. with the comparison between patients followed in Boston and in Toronto [1]. The latter were administered pancreatic enzyme replacement therapy with unrestricted fat diet in contrast to a low-fat diet in Boston and had a consequently better nutritional status with a significantly

Abbreviations: CF, cystic fibrosis; BMI, body mass index; FM, fat mass; FFM, fat-free mass; BC, body composition; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; BIA, bioelectrical impedance analysis; DXA, dual x-ray absorptiometry; PFT(s), pulmonary function test(s); Cl, chloride; NIV, non-invasive ventilation; TS, Tanner stage; Z, impedance; PA, phase angle; RE, resistance; X, reactance; IGF-1, insulin growth factor-1; FRC-He, forced residual capacity by helium dilution; RV, residual volume; TLC, total lung capacity; PI max, maximal inspiratory pressure; PE max, maximal expiratory pressure; IQR, interquartile range; BI, bias; LOA, limits of agreement.

* Corresponding author at: 149 rue de Sèvres, Paris 75015, France.
E-mail address: isabelle.sermet@nck.aphp.fr (I. Sermet-Gaudelus).

[1] Charatsi AM and Dusser P are equal first authors.

http://dx.doi.org/10.1016/j.jcf.2016.05.004
1569-1993/

better survival rate. The independent correlation between nutritional status and prognosis on the one hand and lung disease on the other hand was further confirmed by other studies [2–5].

Nutritional status can be assessed by anthropometric methods, such as weight and height, expressed to normal values for age, and weight-for-stature assessments, such as body mass index (BMI) [6]. BMI represents a widely used indicator of nutritional status and has proved to be independently correlated to lung function in CF [7,8]. However, not all BMI is equal, given that individuals with the same BMI may have different distributions of fat (FM) and fat-free mass (FFM) and patients with normal BMI may lack FFM [9,10]. Indeed, BMI is imprecise, and can overestimate adiposity in people who are very muscular and underestimate adiposity in those who are very unfit (normal weight obesity). On the other hand, body composition (BC) has proved to be correlated to CF respiratory disease, mainly in adult cohorts [10–13]. In children, different studies have shown positive correlations between FFM and percent predicted forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC) and Shwachman score [12,14–16]. Thus, BMI is an imprecise measure for the assessment of nutritional status in CF and direct measurement of BC needs to be included in the routine follow-up of patients.

BC can be evaluated by anthropometric methods such as the measurement of 4 skinfold thickness and arm circumference [17] or more sophisticated methods including total body potassium [18], total body water by isotope dilution, total body electrical conductivity, bioelectrical impedance analysis (BIA) [19] and dual energy X-ray absorptiometry (DXA) [20]. DXA, initially developed in the 1980s for the measurement of mineral bone mass, has been established as the method of reference for the BC study [21]. However, its limited availability, the radiation production and the long duration of the examination (10–20 min) preclude its use routinely for longitudinal follow-up of patients.

BIA is a bedside, non-irradiating method of BC evaluation, which is simpler and less expensive than DXA. This measure allows the quantification of FFM with a validated equation that is appropriate with regard to physiopathology, age and race [22]. In CF, the use of a specific equation is important, because the altered sodium content in the sweat of patients may modify the impedance [19]. Previous studies [23–30] led to conflicting results. Very recently, Alicandro et al. [31] observed poor intra-individual agreement between body composition data provided by DXA and FFM estimated from BIA and concluded that this latter technique could not be part of the standard nutritional assessment of CF patients. In order to further assess the agreement between the two methods, we hypothesized that they would provide the same results of FFM and FM on the condition that the BIA equation is adapted to the CF population. We present here the results of a 2-step study aiming to implement an equation specific for young CF patients. This allowed us to describe the BC in this population and to investigate the association between BC, lung function and diaphragmatic force.

2. Materials and methods

2.1. Population

We conducted a two-step prospective study, as shown in Fig. A, Supplemental material. During the first phase, CF patients (CF1, $n = 54$) were assessed by DXA and BIA in order to validate a specific FFM_{BIA} equation, using DXA as a reference method. Thirty-one patients (CFA) of the first phase who did not have reliable pulmonary function tests (PFTs) were excluded in the second phase. The remaining patients of the first phase with reliable PFTs (CFB, $n = 23$) in addition to seventeen other patients (CFC, $n = 17$) were assessed by BIA, PFTs and blood sampling.

CF patients were all followed in the CF clinic of "Necker-Enfants Malades" Hospital in Paris, France. The diagnosis of CF was confirmed by positive sweat test (Cl > 60 mmol/L) and the presence of two CF-causing mutations for all patients. They were all in a stable condition without respiratory exacerbation (defined by Fuchs criteria [32]) within the last 2 weeks and without signs of oedema or dehydration. The overall CF respiratory disease was assessed by collecting history of chronic oxygen supplementation, non-invasive ventilation (NIV), the number of days under antibiotic treatment during the previous year (with the exclusion of inhaled antibiotics, anti-viral and anti-mycotic agents) and sputum microbiology. Chronic infection by *Staphylococcus aureus* or *Pseudomonas aeruginosa* was defined by at least 3 positive cultures in 6 months. History of pancreatic insufficiency, CF liver disease, CF diabetes and enteral nutrition were also collected.

Height was measured to the nearest 0.1 cm using a calibrated stadiometer and weight was measured to the nearest 0.1 kg using an electronic scale (Seca, Hamburg). Weight and height *z*-scores were calculated according to the CDC growth charts [33]. BMI was calculated and expressed in kg/m^2 and *z*-score, according to Cole's reference data [34]. Pubertal status was assessed using Tanner stages (TS); patients were considered pre-pubertal when Tanner stage was 1 (TS 1), pubertal when TS was equal or above 2 (TS 2–5). All participants were informed about the purpose of the study and consented to participate, according to the Helsinki rules.

2.2. DXA

The DXA scanning technique measures the differential attenuation of two different energy level x-rays as they pass through the body and allows the determination of soft tissue mass on a pixel-per-pixel basis [20]. Participants underwent whole-body DXA scans performed by Hologic QDR-4500 W (Hologic Inc., Waltham, MA, USA), using the Hologic software version 21.6.1:5. The manufacturer's precision of measures is reported to be 1%. After DXA scans and within an interval of maximum 2 h, patients were evaluated by BIA. They were not allowed to eat, drink or urinate between the two tests in order to avoid modification of hydration.