

Association between nutritional status measurements and pulmonary function in children and adolescents with cystic fibrosis*

Associação entre medidas do estado nutricional e a função pulmonar de crianças e adolescentes com fibrose cística

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Abstract

Objective: To evaluate the association between nutritional status measurements and pulmonary function in children and adolescents with cystic fibrosis. **Methods:** We evaluated the nutritional status of 48 children and adolescents (aged 6-18 years) with cystic fibrosis based on body mass index (BMI) and body composition measurements—mid-arm muscle circumference (MAMC) and triceps skinfold thickness (TST)—at a referral center in the city of Rio de Janeiro, Brazil. Pulmonary function was assessed by means of spirometry, using FEV₁ to classify the severity of airway obstruction. We used Student's t-tests for comparisons between proportions and linear regression analysis for associations between continuous variables. The level of significance was set at $p < 0.05$. **Results:** The evaluation of nutritional status based on BMI identified a smaller number of malnourished patients than did that based on MAMC (14 vs. 25 patients, respectively). Most of the patients presented mild pulmonary disease. Mean FEV₁ was 82.5% of predicted. Pulmonary function was found to correlate significantly with BMI, MAMC and TST ($p = 0.001$, $p = 0.001$ and $p = 0.03$, respectively). All subjects with moderate or severe pulmonary involvement were considered malnourished based on BMI and body composition parameters. Of the 25 patients considered malnourished based on body composition (MAMC), 19 were considered well-nourished based on their BMI. **Conclusions:** In the present study, all nutritional status measurements correlated directly with the pulmonary function of children and adolescents with cystic fibrosis. However, body composition measurements allowed earlier detection of nutritional deficiencies.

Keywords: Cystic fibrosis; Body composition; Spirometry; Nutrition assessment.

Resumo

Objetivo: Avaliar a associação de medidas do estado nutricional com a função pulmonar de crianças e adolescentes com fibrose cística. **Métodos:** Foi avaliado o estado nutricional pelo índice de massa corpórea (IMC) e por medidas de composição corporal—circunferência muscular do braço (CMB) e medida da dobra cutânea tricipital (DCT)—de 48 crianças e adolescentes (6-18 anos) com fibrose cística em um centro de referência na cidade do Rio de Janeiro. A função pulmonar foi analisada por espirometria, e o parâmetro adotado para a classificação da obstrução das vias aéreas foi VEF₁. Utilizou-se o teste t de Student para a comparação entre proporções e a regressão linear para associação entre variáveis contínuas. O nível de significância adotado foi $p < 0,05$. **Resultados:** A avaliação do estado nutricional através do IMC encontrou menos pacientes desnutridos do que a realizada através da CMB (14 vs. 25, respectivamente). A maioria dos pacientes apresentou doença pulmonar leve. A média do VEF₁ foi de 82,5% do previsto. Houve associação do IMC, da CMB e da DCT com a função pulmonar ($p = 0,001$, $p = 0,001$ e $p = 0,03$, respectivamente). Todos os pacientes com comprometimento moderado e grave pulmonar eram desnutridos pela composição corporal (CMB). Entre os 25 pacientes considerados desnutridos através da composição corporal (CMB), 19 apresentavam peso adequado quando avaliados pelo IMC. **Conclusões:** Todas as medidas do estado nutricional apresentaram associação direta com a função pulmonar das crianças e adolescentes com fibrose cística no estudo. Entretanto, as medidas de composição corporal revelaram, de forma mais precoce, possíveis deficiências nutricionais.

Descritores: Fibrose cística; Composição corporal; Espirometria; Avaliação nutricional.

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Introduction

Cystic fibrosis (CF) is an autosomal recessive genetic disease characterized by a wide variety of clinical manifestations, chief among which are progressive suppurative COPD, pancreatic insufficiency, secondary malnutrition, increased sodium and chloride concentrations in sweat and male infertility in adulthood.⁽¹⁾

Chronic bacterial infection of the respiratory tract causes destruction and loss of pulmonary function, and respiratory disease is one of the leading causes of decreased longevity and of the increased frequency of hospital admissions among such patients.⁽²⁾

Maintaining adequate nutritional status is essential for the integrity of the respiratory system in CF.^(3,4) One of the leading causes of nutritional depletion is increased energy expenditure due to pulmonary inflammation and infection,⁽³⁾ characterizing the direct relationship between nutritional status and pulmonary function.

Mineral, electrolyte and energy disturbances at the muscle level are responsible for the dysfunction of and decrease in accessory respiratory muscle and diaphragm contractility. Malnutrition can affect the parenchyma, the pulmonary immune response and the respiratory drive.⁽⁵⁾ This profile results in decreased respiratory performance on exertion and increased susceptibility to pulmonary infections, as well as in respiratory failure.⁽⁶⁾

A study on protein turnover in adults suggested that individuals with CF are in a chronic state of catabolic stress or malnutrition, or both, related to recurrent pulmonary exacerbations that adversely affect energy balance and protein metabolism.⁽⁷⁾

In recent years, the importance of nutrition in the evolution of CF has been cited, in many studies, as being essential for determining the prognosis of the disease.^(4,5,7,8)

Including the use of anthropometric criteria, in order to quantify and qualify nutritional status more precisely, is essential for timely diagnosis and early appropriate intervention in changes or alterations in nutritional status.

The objective of the present study was to evaluate the association between nutritional status, determined based on anthropometric and body composition indices, and pulmonary function in children and adolescents with CF treated at a referral center in the city of Rio de Janeiro.

Methods

This was a cross-sectional descriptive study involving 48 children and adolescents with CF, according to the diagnostic criteria established in the Cystic Fibrosis Foundation consensus.⁽⁹⁾ The study inclusion criteria were as follows: being between 6 and 18 years of age; and being under treatment at the Nutrition Outpatient Clinic of the Oswaldo Cruz Foundation *Instituto Fernandes Figueira* (IFF, Fernandes Figueira Institute). Patients with diabetes or liver disease were excluded. The research project was approved by the IFF Research Ethics Committee. The legal guardians of all participating patients gave written informed consent.

Anthropometric and respiratory function data were collected between January of 2006 and January of 2008.

Weight (in kg) was measured using an anthropometric platform scale (Filizola S.A., São Paulo, Brazil), and height (in cm) was measured using a stadiometer attached to the scale. Patients were wearing no shoes and little clothing, and their heads were positioned with the Frankfurt plane parallel to the floor. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m²). Arm circumference (AC) was measured at the midpoint between the scapula acromion and the ulna olecranon of the right arm, which was relaxed. Triceps skinfold thickness (TST; in mm) was measured at the midpoint of the posterior face of the right arm using a Lange® skinfold caliper (Cambridge Scientific Industries, Cambridge, MD, USA). The measurements were performed in triplicate, and the mean value of the three measurements was used for analysis.

Mid-arm muscle circumference (MAMC) was calculated by subtracting the value obtained by

Table 1 - Characteristics of the patients with cystic fibrosis studied (n = 48).

Variable	Mean	SD	Range
Age, years	10.8	3.3	6-18
H/A, percentile	27.2	26.5	3-85
BMI, kg/m ²	17.3	3.0	13.1-24.0
TST, mm	12.5	5.1	5-27
MAMC, cm	16.6	3.8	11.2-27.7
FEV ₁ , % of predicted	82.5	22.5	33.5-118.7

H/A: height for age; BMI: body mass index; TST: triceps skinfold thickness; and MAMC: mid-arm muscle circumference.

Table 2 - Means and SD of age and anthropometric variables by pulmonary function test result (FEV₁) in the patients with cystic fibrosis studied (n = 48).

Variable	Pulmonary function test		p
	FEV ₁ ≤ 69 (n = 10)	FEV ₁ ≥ 70 (n = 38)	
	Mean ± SD	Mean ± SD	
Age, years	11.2 ± 2.8	10.8 ± 3.3	0.81
H/A, percentile	17.5 ± 22.9	31.2 ± 28.1	0.10
BMI, kg/m ²	15.2 ± 1.8	16 ± 6	< 0.01
TST, mm	9.9 ± 4.0	13.4 ± 5.0	0.03
MAMC, cm	15.0 ± 1.3	16.9 ± 3.4	0.06

H/A: height for age; BMI: body mass index; TST: triceps skinfold thickness; and MAMC: mid-arm muscle circumference.

multiplying TST (converted to cm) by ω from AC (cm), according to the following equation⁽¹⁰⁾:

$$MAMC_{(cm)} = AC_{(cm)} - (TST_{(cm)} \times \omega)$$

The population reference for nutritional assessment was the graph developed by the National Center for Health Statistics in 2000.⁽¹¹⁾ Nutritional assessment data were analyzed in percentiles, in accordance with the Consensus Report on Nutrition for Pediatric Patients with Cystic Fibrosis.⁽⁷⁾ Patients presenting BMI for age (BMI/A) below the 10th percentile were considered malnourished, those presenting BMI/A between the 10th and 25th percentiles were considered to be at nutritional risk, and those presenting BMI/A above the 25th percentile were considered well-nourished. Low height was defined as height-for-age below the 5th percentile.⁽⁷⁾

The MAMC and TST values were determined using the parameters established by Frischno,⁽¹⁰⁾ values below or at the 5th percentile being considered low. Pubertal stage was assigned using Tanner staging.⁽¹²⁾

Pulmonary function was assessed at the IFF Pulmonary Function Laboratory. To ensure the validity of the results, the minimum age for participants was set at 6 years, since spirometry requires patient cooperation. We used FEV₁ to classify pulmonary impairment in terms of obstruction. The technique used to perform the tests, as well as the reference values, were in accordance with the recommendations of the American Thoracic Society, which classifies predicted percentage values as follows: mild obstruction, ≥ 70%; moderate obstruction, 60-69%; moderately severe obstruction, 50-59%; severe obstruction, 35-49%; extremely severe obstruction, < 35%.⁽¹³⁾ Overweight patients were excluded.

Data were analyzed using the program Statistical Package for the Social Sciences, version 8.0 for Windows (SPSS Inc., Chicago, IL, USA). We used Student's t-tests for comparisons between proportions and linear regression analysis for associations between continuous variables. The level of significance was set at p < 0.05.

Results

Of the 48 patients studied, 29 were female and 19 were male. The mean age was 10.8 ± 3.3 years (Table 1). Most of the individ-

Table 3 - Nutritional status measurements by degree of airway obstruction (FEV₁) in the patients with cystic fibrosis studied (n = 48).

Measurement	Pulmonary function test					Total n
	FEV ₁ (≥ 70%)	FEV ₁ (60-69%)	FEV ₁ (50-59%)	FEV ₁ (35-49%)	FEV ₁ (< 35%)	
BMI						
≤ 10th P	10		1	2	1	14
10th P < BMI ≤ 25th P	4		1	2		7
> 25th P	24	2				26
H/A						
≤ 5th P	5	2		2	1	10
> 5th P	31	3	1	2	1	38
MAMC						
≤ 5th P	15	1	2	5	2	25
> 5th P	22	1				23

BMI: body mass index; P: percentile; H/A: height for age; and MAMC: mid-arm muscle circumference.

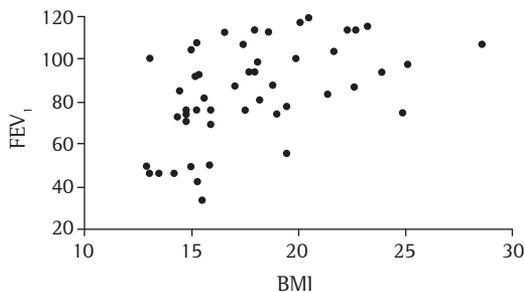


Figure 1 - Dispersion of FEV_1 (% of predicted for gender and age) vs. body mass index (BMI in percentile; $r = 0.48$, $p < 0.0001$).

uals (79%) presented mild pulmonary function impairment (Table 2).

None of the patients presented decreased fat deposition based on TST. The prevalence of low height in the group was 19.6%, and none of the patients presented delayed puberty.

Nutritional assessment based on MAMC revealed a higher percentage of malnutrition (52%) than did that based on BMI/A, which revealed that 31.2% of the participants were malnourished and 14.5% were at nutritional risk (Table 3). Of the patients considered malnourished based on MAMC, 24% were classified as being at nutritional risk and 39% were classified as well-nourished based on BMI/A.

All patients with moderate or severe airway obstruction were considered malnourished based on MAMC (Table 3).

Although the degree of pulmonary impairment presented a statistically significant association with BMI and with TST ($p = 0.001$ and $p = 0.03$, respectively), it presented only a tendency toward an association with MAMC ($p = 0.06$; Table 2). Linear regression revealed a moderate relationship between BMI and FEV_1 ($r = 0.46$;

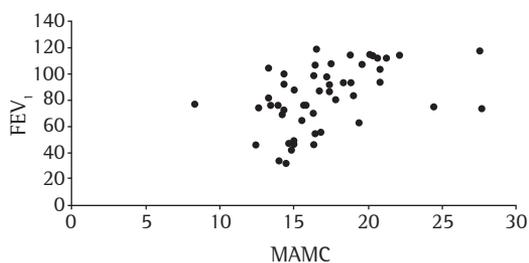


Figure 2 - Dispersion of FEV_1 (% of predicted for gender and age) vs. mid-arm muscle circumference (MAMC in percentile; $r = 0.48$; $p < 0.001$).

$p = 0.00001$) and between FEV_1 and MAMC ($r = 0.46$; $p = 0.0001$; Figures 1 and 2).

Discussion

The present study found that the prevalence of malnutrition based on MAMC was higher than that based on BMI/A, although the latter presented a higher malnutrition cut-off point for patients with CF (10th percentile) than for the general population (5th percentile). Of the patients considered malnourished based on MAMC, 39% were considered normal based on BMI/A. These data reveal the relevance of analyzing body composition to assess nutritional status more accurately.

The moderate relationship found between nutritional status and FEV_1 (Figures 1 and 2) in the patients in our sample is probably due to the fact that decreased pulmonary function cannot be explained solely by increased impairment of nutritional status. Noncompliance with treatment and noncompliance with regular respiratory therapy are examples of other factors that destabilize pulmonary function.

The mild impairment of pulmonary function presented by most of the patients in our sample might have played a role in the tendency ($p < 0.06$) toward an association between pulmonary function and nutritional status assessment based on MAMC. In cases of mild pulmonary impairment, nutritional depletion occurs due to other factors, such as the type of genetic mutation, pancreatic insufficiency, loss of bile salts and acids, gastroesophageal reflux, intestinal resection and the emotional status of patients. Therefore, the pathophysiology of malnutrition found in the present study is similar to that of primary malnutrition, which retains muscle mass at the expense of fat mass.

Adiposity presented a statistically significant association with pulmonary function ($p = 0.03$), although the TST measurements of all patients were within the range of normality (Table 2). It is possible that the TST cut-off point (5th percentile) should be higher for patients with CF. One group of authors also found a positive association between adiposity and pulmonary function after having studied the body composition of 50 pediatric patients with CF by means of dual-energy X-ray absorptiometry.⁽⁶⁾

All patients with moderate or severe airway obstruction were considered malnourished based

on MAMC (Table 3). This result was expected, since there is a consensus in the literature that pulmonary inflammation and infection increase energy expenditure and are some of the leading causes of nutritional depletion, especially of muscle mass, even in patients whose food intake is adequate or above that recommended.^(2,5,14,15)

The low height found in the present study could be attributed to genetics. However, the lack of a data record for the determination of the genetic target precludes such an assumption. Studies involving Brazilian and American children found similar results and showed that low height in patients with CF does not depend on the level of development of the country or on the genetic load but is related to factors inherent to the pathophysiology of the disease.^(16,17)

The age-related decline in pulmonary function is universal in CF.⁽¹⁸⁾ However, in the present study, the mean age of the patients was similar in the two groups divided based on the degree of pulmonary impairment.

In our study, 10 patients (19.6%) presented low height, and, of those, 60% presented moderate or severe pulmonary function impairment. This result is in accordance with data from a report by the Cystic Fibrosis Foundation,⁽¹⁹⁾ in which height-for-age indices were found to be below the 5th percentile in 20% of children with CF. It has long been recognized that nutritional deficiency can significantly affect pulmonary function, as well as that chronic pulmonary disease can lead to growth deficit and delayed development, creating a vicious cycle between malnutrition and respiratory disorders.^(14,20)

Various studies have demonstrated that BMI is a more sensitive parameter than is weight for height.^(4,17,21,22) In the present study, BMI presented a statistically significant association with pulmonary function. However, BMI should not be used in isolation to assess the nutritional status of patients with CF, since it does not determine body composition.

In CF, the imbalance between protein synthesis and protein degradation to meet the energy requirements of the body can lead to a disproportionate loss of lean body mass, with muscle atrophy, including respiratory muscle atrophy.⁽¹⁸⁾ Therefore, a change in body composition can lead to malnutrition and decreased pulmonary function.^(6,7,23)

Since body weight is composed primarily of fat mass and fat-free mass, observing these two body compartments separately can provide more accurate information about nutritional status, which is directly related to pulmonary disease—the leading cause of morbidity and mortality in CF.

The results of the present study show that the change in body composition occurs prior to the decrease in weight and height in children and adolescents with CF. Since the assessment of nutritional status, including the measurement of fat and muscle reserves based on TST and AC, is an inexpensive and easily performed method, health professionals should be encouraged to use it during routine visits, identifying patients at risk of malnutrition earlier, so that the nutritional intervention can be immediately recommended, and possibly delaying the progression of the pulmonary disease.

In the present study, nutritional status measurements correlated with pulmonary function in children and adolescents with CF. However, body composition measurements allowed earlier detection of nutritional deficiencies. Therefore, the combination of anthropometric measurements (BMI) and body composition measurements increases accuracy in the nutritional diagnosis and detects early changes in nutritional status, informing decisions regarding nutritional interventions and delaying the decline in pulmonary function in such patients.

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