Anthropometric and dietary intake indicators as predictors of pulmonary function in cystic fibrosis patients*

Indicadores antropométricos e de ingestão alimentar como preditores da função pulmonar em pacientes com fibrose cística

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Abstract

Objective: To evaluate whether anthropometric and dietary intake indicators are predictors of pulmonary function in cystic fibrosis (CF) patients. **Methods:** This was a cross-sectional study involving 69 patients (age range, 5.4-16.5 years) diagnosed with CF under follow-up at the *Hospital de Clínicas de Porto Alegre*, located in the city of Porto Alegre, Brazil. Anthropometric assessment was based on body mass index (BMI), mid-arm muscle circumference (MAMC), and triceps skinfold thickness (TST). Dietary intake was assessed by using recall data, which were compared with the recommended dietary allowances. Pulmonary function was assessed by ventilatory capacity, expressed as FEV_1. Prevalence ratios for the outcome studied ($FEV_1 < 80\%$ of predicted) were calculated by indicator. **Results:** In patients with MAMC and TST below the 25th percentile, the prevalence of $FEV_1 < 80\%$ of predicted was significantly higher than in those with higher MAMC and TST ($p < 0.001$ and $p = 0.011$, respectively). In comparison with other patients, those with a BMI below the 50th percentile showed a 4.43 times higher prevalence of $FEV_1 < 80\%$ of predicted (95% CI: 1.58-12.41), and that prevalence was 2.54 times higher in those colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) than in those not so colonized (95% CI: 1.43-4.53). The association between dietary intake and the prevalence of $FEV_1 < 80\%$ of predicted was of only borderline significance (95% CI: 0.95-3.45). **Conclusions:** Not being colonized with MRSA and having a BMI above the 50th percentile appear to preserve pulmonary function in CF patients.

Keywords: Cystic fibrosis; Respiratory function tests; Nutrition assessment; Energy intake.

Resumo

Objetivo: Avaliar se indicadores antropométricos e de ingestão alimentar são preditores da função pulmonar em pacientes com fibrose cística (FC). **Métodos:** Estudo transversal com 69 pacientes (variação, 5,4-16,5 anos de idade) diagnosticados com FC e em acompanhamento no Hospital de Clínicas de Porto Alegre, em Porto Alegre (RS). A avaliação antropométrica consistiu nas medidas do índice de massa corpórea (IMC), da circunferência muscular do braço (CMB) e da dobra cutânea tricipital (DCT). A ingestão alimentar foi avaliada pelo recordatório de ingestão habitual e comparada com *recommended dietary allowances*. A avaliação da função pulmonar foi realizada através da capacidade ventilatória, representada pelo VEF_1. Razões de prevalência foram calculadas entre os preditores e o desfecho estudado ($VEF_1 < 80\%$ do previsto). **Resultados:** Os pacientes com CMB e DCT abaixo do percentil 25 apresentaram significativamente maior prevalência de $VEF_1 < 80\%$ do previsto ($p < 0,001$ e $p = 0,011$, respectivamente). Os pacientes com IMC menor que o percentil 50 apresentaram 4,43 vezes (IC95%: 1,58 - 12,41) a prevalência de $VEF_1 < 80\%$ do previsto. Os pacientes colonizados por *Staphylococcus aureus* resistente a meticilina apresentaram 2,54 vezes (IC95%: 1,43-4,53) a prevalência do desfecho do que os não colonizados. A associação entre consumo calórico e o desfecho estudado apresentou significância limítrofe (IC95%: 0,95-3,45). **Conclusões:** O IMC superior ao percentil 50 e a ausência de colonização por *S. aureus* resistente a meticilina apresentaram uma associação direta com função pulmonar preservada em pacientes com FC.

Descritores: Fibrose cística; Testes de função respiratória; Avaliação nutricional; Ingestão de energia.

Introduction

Cystic fibrosis (CF) is an autosomal recessive genetic disease that affects various organs and systems, especially the respiratory and digestive tracts.[1] Lung disease is the major factor responsible for morbidity and mortality in CF patients.[2]

The chronic malnutrition and the impaired growth observed in CF patients result from an energy deficit, which is due to increased losses, and from the energy expenditure, which exceeds the dietary intake.[3] Anorexia due to respiratory and gastrointestinal complications contributes to the worsening of this profile, leading to reduced energy intake.[4]

Adequate dietary intake is essential to maintaining good nutritional status in CF patients, especially when they have pancreatic insufficiency. To that end, it is recommended that there be an intake of 120-150% of the energy requirements of healthy individuals of the same gender and age.[5,6]

The nutritional status of the patient has an important relationship with the progression of lung disease, affecting quality of life and survival.[7] Maintaining adequate nutritional status is essential for the integrity of the respiratory system in CF patients.[8,9] Stallings et al.[10] found a direct association between pulmonary function and nutritional status, demonstrating that having a body mass index (BMI) above the 50th percentile is directly associated with having an $FEV_1 > 80\%$.

The objective of the present study was to evaluate whether anthropometric and dietary intake indicators are predictors of pulmonary function in CF patients under follow-up at a referral hospital.

Methods

This was a cross-sectional study involving 69 children and adolescents diagnosed with CF in accordance with the Cystic Fibrosis Foundation diagnostic criteria.[11] The inclusion criteria were as follows: being ≤ 18 years of age; having a confirmed diagnosis of CF (by genetic testing, sweat testing, or both); having undergone pulmonary function tests; and being under follow-up at the Pediatric Pulmonology Outpatient Clinic of the *Hospital de Clínicas de Porto Alegre* (HCPA, Porto Alegre *Hospital de Clínicas*), located in the city of Porto Alegre, Brazil. We excluded patients with pulmonary

exacerbation. This paper is part of a study that is aimed at validating a nutritional screening tool for CF patients (approved by the Graduate Research Group of the HCPA; Protocol nº. 09637).

Data were collected after written informed consent was obtained during a nutritional consultation, between March and October of 2010. Anthropometric measurements included weight, height, triceps skinfold thickness (TST), and mid-arm muscle circumference (MAMC). The details of the method employed for taking the anthropometric measurements and the assessment of dietary intake (recall data) are described in Pereira et al.[12] We calculated BMI and height-for-age percentiles, in accordance with the WHO criteria,[13] as well as MAMC and TST percentiles, in accordance with the criteria established by Frisancho.[14] Data on mutation type, bacterial colonization, albumin levels, and pulmonary function—the last two items being related to the last annual checkup—were obtained from online medical records.

Pulmonary function was assessed by spirometric measurements of ventilatory capacity, expressed as FEV_1, in the Pulmonology Department of the HCPA. The spirometric technique used followed the Brazilian Thoracic Association Guidelines for Pulmonary Function Testing.[15] Overall disease severity was assessed by the Shwachman-Kulczycki score, obtained by summing the scores for each of four items (general activity, physical examination, nutritional status, and radiological findings), as assessed by the attending physician and the staff nutritionist. After the scoring, the status of the patient was classified from excellent (score, 86-100) to severe (score, ≤ 40).[16]

Serum albumin was measured by the bromocresol green method during the annual checkup of the patients, and the results were collected from the medical records. Regarding bacterial colonization, the data extracted from the clinical records and related to sputum samples collected over the preceding 12 months revealed the presence of the following strains: *Staphylococcus aureus*; methicillin-resistant *S. aureus* (MRSA); *Pseudomonas aeruginosa*; mucoid *P. aeruginosa*; and *Burkholderia cepacia*.

The outcome analyzed in this study was FEV_1 < 80% of predicted, because values above this cut-off point represent preserved pulmonary function. Anthropometric and body composition variables, as well as serum albumin levels, dietary

intake, and bacterial colonization, were evaluated as possible predictors of this outcome.

Data were analyzed with the Statistical Package for the Social Sciences, version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables are expressed as absolute and relative frequencies. Sample characteristics represented by categorical variables were tested for associations by Pearson's chi-square test. Continuous variables are expressed as mean and standard deviation. In order to compare means, we used the Student's t-test for independent samples. In order to build the adjusted model, we used Poisson regression with robust variance, progressively including variables showing a value of $p < 0.2$ in the univariate analysis. Variables with a value of $p < 0.05$ remained in the final model. The level of significance was set at 5% ($p < 0.05$).

Results

We studied 69 patients (age range, 5.4-16.5 years), 35 (50.7%) of whom were female. Age at diagnosis ranged from 0 years (infants in the neonatal period) to 12 years, the median age being 6 months. Genetic testing was performed in 63 patients (91.3%), of whom 15 (21.7%) were homozygous for the ΔF508 mutation and 32 (46.4%) were heterozygous for the ΔF508 mutation.

Pancreatic insufficiency was present in 63 patients (91.3%), and CF-related diabetes mellitus was present in 2 (2.9%). Only 3 patients (4.3%) in the sample were using enteral nutritional therapy (gastrostomy). Mean Shwachman-Kulczycki scores were satisfactory (> 71.0%) in 55 patients (79.7%). Table 1 shows the characteristics of the sample by nutritional and clinical parameters, as well as by pulmonary function and bacterial colonization data.

Analysis of the sample for the outcome studied revealed that patients with an $FEV_1 < 80\%$ had concomitant lower nutritional parameters (Table 2). Patients with preserved pulmonary function ($FEV_1 > 80\%$) were, on average, 2.8 years younger than were those with an $FEV_1 < 80\%$. Patients with more severe pulmonary impairment had lower mean serum albumin levels, although their serum albumin levels were within the normal range. With regard to dietary intake, we found that, on average, patients with an $FEV_1 < 80\%$ did not meet the CF dietary recommendation of

> 120% of the recommended dietary allowance (RDA).

Analysis of body composition as a predictor of FEV_1 demonstrated that, in patients with MAMC and TST below the 25th percentile, the prevalence of $FEV_1 < 80\%$ was significantly higher than in those with higher MAMC and TST ($p < 0.001$ and $p = 0.011$, respectively). Analysis of bacterial colonization revealed no statistically significant differences among colonized patients in terms of $FEV_1 < 80\%$, except for those colonized with MRSA, in whom the prevalence of $FEV_1 < 80\%$ was higher ($p = 0.017$).

Patients with a BMI below the 50th percentile showed a 4.43 times higher prevalence of $FEV_1 < 80\%$ than did those with a BMI above the 50th percentile, the model being adjusted for age, %RDA < 120%, albumin, height-for-age percentile, MAMC < the 25th percentile, TST < the 25th percentile, and colonization with MRSA (Table 3). Colonization with MRSA was significantly associated with the outcome studied. The prevalence of $FEV_1 < 80\%$ was 2.54 times higher in those colonized with MRSA than in those not so colonized, the model being adjusted for the other predictor variables. The association between dietary intake and pulmonary function was of only borderline significance.

Discussion

The results of the present study support the recommendations in the literature, i.e., anthropometric measurements above the 50th percentile as a protective factor against pulmonary impairment in CF patients.[10] In addition, colonization with MRSA, which is a cause for concern among CF patients in Brazil, was found to be likewise associated with pulmonary impairment.

Our sample was found to be in good nutritional and clinical status, the values for these parameters being similar to those found in CF referral centers in developed countries.[17] The mean BMI percentile found in the present study was similar to that reported by the Cystic Fibrosis Foundation, i.e., 48.7.[17] The mean FEV_1 found in our sample was equivalent to that used for classifying lung disease as mild, being similar to the mean FEV_1 in the USA (76.3%); the median diagnosis was also similar.[17]

Analysis of the nutritional parameters, compared with the outcome studied ($FEV_1 < 80\%$

Table 1 – Clinical, nutritional, and laboratory data for the cystic fibrosis patients included in the study.

Nutritional indicators	Results[a]
BMI, percentile	45.41 ± 29.36
Weight-for-age, percentile[b]	51.37 ± 28.01
Height-for-age, percentile	47.47 ± 27.49
MAMC < p5	4 (5.8)
MAMC > p25	17 (24.6)
TST < p5	3 (4.3)
TST > p25	23 (33.3)
Serum albumin, g/dL[c]	4.34 ± 0.39
Dietary intake indicators	
RDA, %	126.45 ± 28.88
Carbohydrates, %	50.55 ± 7.19
Proteins, %	16.17 ± 3.25
Lipids, %	32.55 ± 6.10
Pulmonary function	
FEV_1, % of predicted	88.23 ± 21.52
Pulmonary colonization	
Staphylococcus aureus	32 (46.4)
Methicillin-resistant *Staphylococcus aureus*	5 (7.2)
Pseudomonas aeruginosa	15 (21.7)
Mucoid *Pseudomonas aeruginosa*	9 (13.0)
Burkholderia cepacia	11 (15.9)
Shwachman-Kulczycki score[c]	82.60 ± 11.47

BMI: body mass index; MAMC: mid-arm muscle circumference; p5: 5th percentile; p25: 25th percentile; TST: triceps skinfold thickness. RDA: recommended dietary allowance. [a]Values expressed as mean ± SD or as n (%). [b]n = 25. [c]n = 68.

Table 2 – Nutritional and pulmonary function parameters for the cystic fibrosis patients included in the study.[a]

Parameter	Groups		p
	FEV_1 < 80% of predicted	FEV_1 ≥ 80% of predicted	
Age, years	12.26 ± 3.04	9.42 ± 4.20	0.005
BMI, percentile	26.50 ± 18.02	54.29 ± 28.96	< 0.001
Height-for-age, percentile	36.14 ± 26.74	51.84 ± 27.01	0.055
Serum albumin, g/dL	4.11 ± 0.46	4.41 ± 0.35	0.003
RDA, %	115.52 ± 22.18	138.64 ± 38.48	0.01

BMI: body mass index; and RDA: recommended dietary allowance. [a]Data expressed as mean ± SD.

of predicted), demonstrated that BMI, height, and %RDA values were low in our study sample. Patients with an FEV_1 > 80% had concomitant mean BMI and height percentiles above the 50th percentile, whereas patients with an FEV_1 < 80% had mean BMI percentiles close to the cut-off point for nutritional risk for CF patients (BMI < the 25th percentile). Chaves et al. found a statistically significant association of BMI and TST with the degree of pulmonary impairment (FEV_1 < 70%).[18]

Patients with an FEV_1 < 80% had a dietary intake that was lower than that recommended for CF patients, unlike patients with better pulmonary function values, who met the nutritional recommendations for CF patients. Simon et al.[19] demonstrated that 51.7% of CF patients met the recommendations of 120% of the RDA and that those patients had a median BMI percentile of 56, whereas the patients whose intake was below the recommendations had a median BMI percentile of 34.9. In another study, which assessed dietary intake in a group of CF patients in the 6-9 year age bracket, the median dietary intake was 115% of the RDA, and only 39% met the dietary recommendations.[20]

In the present study, patients with a lower mean age had preserved pulmonary function (FEV_1 > 80%); this finding is in agreement with

Table 3 – Final Poisson regression model of the association of nutritional and clinical predictors with the outcome studied.[a]

Predictor	PR	95% CI
BMI < the 50th percentile	4.43	1.58-12.41
RDA < 120%	1.81	0.95-3.45
Colonization with MRSA	2.54	1.43-4.53

PR: prevalence ratio; BMI: body mass index; RDA: recommended dietary allowance; and MRSA: methicillin-resistant *Staphylococcus aureus.* [a]Model adjusted for age, albumin, height-for-age percentile, mid-arm muscle circumference < the 25th percentile, and triceps skinfold thickness < the 25th percentile.

the literature, which indicates that FEV_1 decreases with age, especially from adolescence onward.[10,17] Döring et al.[21] reported a progressive reduction in pulmonary function in CF patients, at an estimated rate of 1-2% per year; however, it is clear that this rate can vary according to the frequency and severity of pulmonary exacerbations.

Despite being within the normal range, albumin levels were significantly different in the group of patients with an FEV_1 < 80%. Albumin is a potent antioxidant that can be essential for maintaining pulmonary glutathione levels[22,23] and has been related to lung disease severity, the prognosis for CF patients being consequently poorer.[24,25]

Analysis of body composition in this group revealed that patients with worse pulmonary function values had a concomitant higher prevalence of muscle mass and fat mass below the 25th percentile. Pedreira et al.[26] found a positive association between lean body mass and FEV_1 in CF patients in the 7-17 year age bracket.

The indicator of nutritional status used in the final model, i.e., a BMI < the 50th percentile, was found to be a strong predictor of pulmonary function in CF patients, meaning that these patients showed a nearly five times higher prevalence of FEV_1 < 80% in comparison with those with a BMI > the 50th percentile. Stallings et al.[10] showed that having an FEV_1 close to or higher than 80% was directly associated with having a BMI ≥ the 50th percentile.

The outcome analyzed in this study, however, cannot be explained solely by impaired nutritional status. Dietary intake and bacterial colonization are other factors that affect the outcome studied. Poisson regression analysis with robust variance, adjusted for age, BMI percentile, albumin levels,

height-for-age percentile, MAMC < the 25th percentile, TST < the 25th percentile, and colonization with MRSA, revealed that a dietary intake of less than 120% of the RDA was of borderline significance in predicting deterioration of pulmonary function. This was due to low sample power. However, colonization with MRSA was found to be strongly associated with the outcome studied. Dasenbrook et al.[27] observed an association between colonization with MRSA and poorer survival in CF patients. Among patients colonized with MRSA, the mortality rate was 27.7 deaths per 1,000 patient-years, whereas, among those not so colonized, the mortality rate was 18.3 deaths per 1,000 patient-years. The attributable risk percentage of death associated with MRSA was 34%.

The limitations of the present study are related to its cross-sectional design, which does not allow us to establish a causal relationship, meaning that the association between the factors studied and the prevalence of FEV_1 < 80% of predicted might be subject to reverse causality. The association between adequacy of dietary intake and the outcome studied was not significant, because of a lack of study power. In this case, we would need a minimum of 100 patients per category of dietary adequacy (RDA) in order to detect an association with the outcome studied. The present study sample has a power of only 28% to measure this association. However, the present study is relevant because findings in CF patients in Brazil corroborated those in CF patients worldwide and because it underscores the importance of effective nutritional care and prevention of MRSA colonization.

The present study allows us to conclude that having a BMI above the 50th percentile and not being colonized with MRSA appear to preserve pulmonary function in CF patients.

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