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Nutrition Status Parameters and Hydration Status by Bioelectrical Impedance Vector Analysis Were Associated With Lung Function Impairment in Children and Adolescents With Cystic Fibrosis

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Abstract

Background: (1) To compare nutrition and hydration status between a group of children/adolescents with cystic fibrosis (CFG; n = 46; median age, 8.5 years) and a control group without cystic fibrosis (CG). (2) To examine the association of nutrition and hydration status with lung function in the CFG. *Material and Methods:* A cross-sectional study. Nutrition screening, anthropometric parameters, and bioelectrical impedance analysis (BIA) were assessed. The *z* scores for body mass index for age, height for age, mid upper arm circumference, triceps and subscapular skinfold thickness, mid upper arm muscle area, resistance/height, and reactance/height were calculated. Bioelectrical impedance vector analysis was conducted. Forced expiratory volume in 1 second <80% was considered lung function impairment. An adjusted logistic regression was applied ($P < .05$). *Results:* In the CFG, lung function impairment was observed in 51.1%. All anthropometric parameters were lower, and the mean *z*-resistance/height and *z*-reactance/height were higher in the CFG ($P < .05$) compared with the CG. In the CFG, 43% were severely/mildly dehydrated, while none were in the CG ($P = .007$). In the CFG, there was an association between high nutrition risk—via nutrition screening (odds ratio [OR], 22.28; $P < .05$), lower values of anthropometric parameters, higher z-resistance/height (OR, 2.23; $P < .05$) and *z*-reactance/height (OR, 1.81; $P < .05$), and dehydration (OR, 4.94; $P < .05$)—and lung function impairment. *Conclusions:* The CFG exhibited a compromised nutrition status assessed by anthropometric and BIA parameters. Nutrition screening, anthropometric and BIA parameters, and hydration status were associated with lung function. (*Nutr Clin Pract*. XXXX;xx:xx-xx)

Keywords

cystic fibrosis; electrical impedance; nutrition status; pediatrics; forced expiratory volume; nutrition assessment

Cystic fibrosis (CF) is characterized by an abnormal transport of chloride, which causes the dehydration of secretions and the production of hyperviscous mucus. As a consequence, airway obstruction, pancreatic insufficiency, and intestinal malabsorption[1] occur. The major cause of morbidity and mortality in this population is pulmonary disease caused by multiple infections, particularly *Pseudomonas aeruginosa* and chronic inflammation.[2] In addition, most patients present gastrointestinal impairment. Pulmonary and pancreatic alterations cause loss of nutrients, increased energy expenditure, inadequate calorie intake, and a compromised nutrition status.

Malnutrition is a common complication in patients with CF, and it directly affects the prognosis of the disease. The resulting decrease in fat-free mass (FFM) may result in impairment of the diaphragm and other respiratory muscles, leading to the deterioration of lung function.[3,4] In children and adolescents with CF, nutrition status is routinely assessed through height, weight, and body mass index (BMI). However, these methods do not provide a clear indication of the nature of body composition. Thus, body composition should be evaluated to identify children at risk of malnutrition. There are simple prediction techniques based on anthropometric parameters, such as skinfold thickness and circumferences, as well as bioelectrical impedance analysis (BIA).[5]

BIA is extensively used to estimate body composition in diverse clinical situations and pediatrics.[6] The estimation of

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body composition by BIA relies on the use of predictive equations, which must be validated for each population and clinical condition. In addition, estimation of body composition is based on the assumption of a constant tissue hydration, which may be an unlikely condition in many clinical situations and in the pediatric population.[7,8]

Therefore, the use of bioelectrical vectors, such as resistance and reactance, could be used as an alternative.[7,9] There is growing evidence that BIA parameters can be used as a prognostic marker and to monitor the severity of CF in pediatric patients.[6] The primary advantage of using the vector from BIA is that it does not require equations or models for the analysis of body composition.[8]

In adults with chronic kidney disease, changes in BIA parameters have detected earlier changes in body composition when compared with serum albumin, BMI, and protein intake.[10] The use of this instrument in pediatric populations, especially in children and adolescents with CF, is a subject that has not been deeply explored. Another tool for assessing nutrition status and body fluid composition derived from by BIA vectors is bioelectrical impedance vector analysis (BIVA).[11] Based on height-standardized resistance and reactance, BIVA evaluates hydration status and body cell mass, thus allowing a qualitative assessment of body composition.[11,12] BIVA can be a useful tool for detecting malnutrition by bringing vectors to within the impedance target (50% tolerance ellipse), particularly in clinical conditions where altered body hydration is indicated.[13]

Although malnutrition is well established as a poor prognostic marker for children with CF, the majority of related studies use only weight, height, and BMI. To identify malnutrition and begin treatment as early as possible, multiple anthropometric measurements of the patient are recommended.[14,15] Considering the importance of identifying nutrition parameters that are more closely associated with lung function, this study aimed (1) to compare the nutrition and hydration status between a group of children and adolescents with CF (CFG) and a control group (CG) by using a variety of nutrition tools and (2) to verify the association of nutrition and hydration status with lung function in the CFG.

Methods

Design Study and Population

A cross-sectional study was conducted from July 2013 to April 2014 at a CF treatment center in the state of Santa Catarina in southern Brazil. The project was approved by the Ethics Committee for Human Research at the Federal University of Santa Catarina (No. 297.17). All parents and guardians signed the informed consent form before the study began.

The study included 2 groups of children and adolescents: the CFG and the CG (Figure 1). For the CFG, the criteria for inclusion were as follows: outpatient children and adolescents between 6–15 years of age with a CF diagnosis according to the quantitative pilocarpine iontophoresis sweat test (sweat chloride >60 mmol/L).[1] The exclusion criteria were the presence of pulmonary exacerbation, according to Bilton et al.[16] The CG comprised apparently healthy children and adolescents without CF, paired by sex and age, who had adequate *z* scores for BMI for age (*z* scores from –2 to 2).[17]

The anthropometric parameters and BIVA were assessed in both the CFG and the CG. Demographic data, clinical assessment, pancreatic insufficiency, and genetic mutation for ΔF508 were drawn exclusively from the CFG medical records. The presence of *Staphylococcus aureus, P aeruginosa*, and *Burkholderia cepacia* in oropharyngeal secretions were collected and processed according to the method of Gilligan.[18] To assess disease severity, the Shwachman and Kulczycki score was used,[19] in which items related to general activities, clinical examinations, nutrition status, and x-rays were scored. For children and adolescents without clinical signs of exacerbation, x-rays were not requested, and items were scored as excellent. For general classification, the sum of the scores for each category was considered as follows: ≥86 scores, excellent; 71–85, good; 56–70, average; 41–55, poor; and ≤40, severe.

Nutrition Status

Weight was measured with a BK 50 F digital scale (Balmak; Santa Barbara d'Oeste, São Paulo, Brazil) with a maximum capacity of 150 kg and a precision of 0.1 kg. Height was measured with an anthropometer (Alturaexata; Belo Horizonte, Minas Gerais, Brazil) with a precision of 0.1 cm.[20] The *z* scores for BMI for age and height for age were calculated according to World Health Organization standards.[17]

Triceps skinfold thickness (TSF) and subscapular skinfold thickness (SsSF) were collected with a Lange skinfold caliper (Beta Technology, Santa Cruz, CA) with an accuracy of 0.5 mm and the mid upper arm circumference (MUAC) with an inelastic tape measure (TBW/ACT Medical, Sao Paulo, Brazil). The mid upper arm muscle area (MUAMA)[21] and the *z* scores for TSF, SsSF, and MUAC were calculated according to Frisancho[22] because the World Health Organization does not provide reference parameters for these anthropometric measurements for children >5 years old.

BIA was performed with a tetrapolar Biodynamics analyzer model 310 (Biodynamics Corp, Seattle, WA), which applies an electric current of 800 μA at a single frequency of 50 kHz. Based on the resistance and reactance, the resistance index was calculated from the relationship between the square of the height in centimeters and the resistance in ohms. In addition, the ratio of resistance and reactance by height in meters was calculated and expressed in a *z* score according to the reference for children and adolescents as proposed by De Palo et al.[23] Phase angle was calculated from reactance and resistance, according to the following formula: phase angle = arc tangent (reactance/resistance) × 180°/π.[24] BIVA was conducted by charting tolerance ellipses of 50%, 75%, and 95%.[11] BIVA 2002 software was employed (Piccoli A, Pastori G, Department of Medical and Surgical Sciences, University of Padova, Padova, Italy; available at email: apiccoli@unipd.it), according to the study by De Palo et al[23] as a

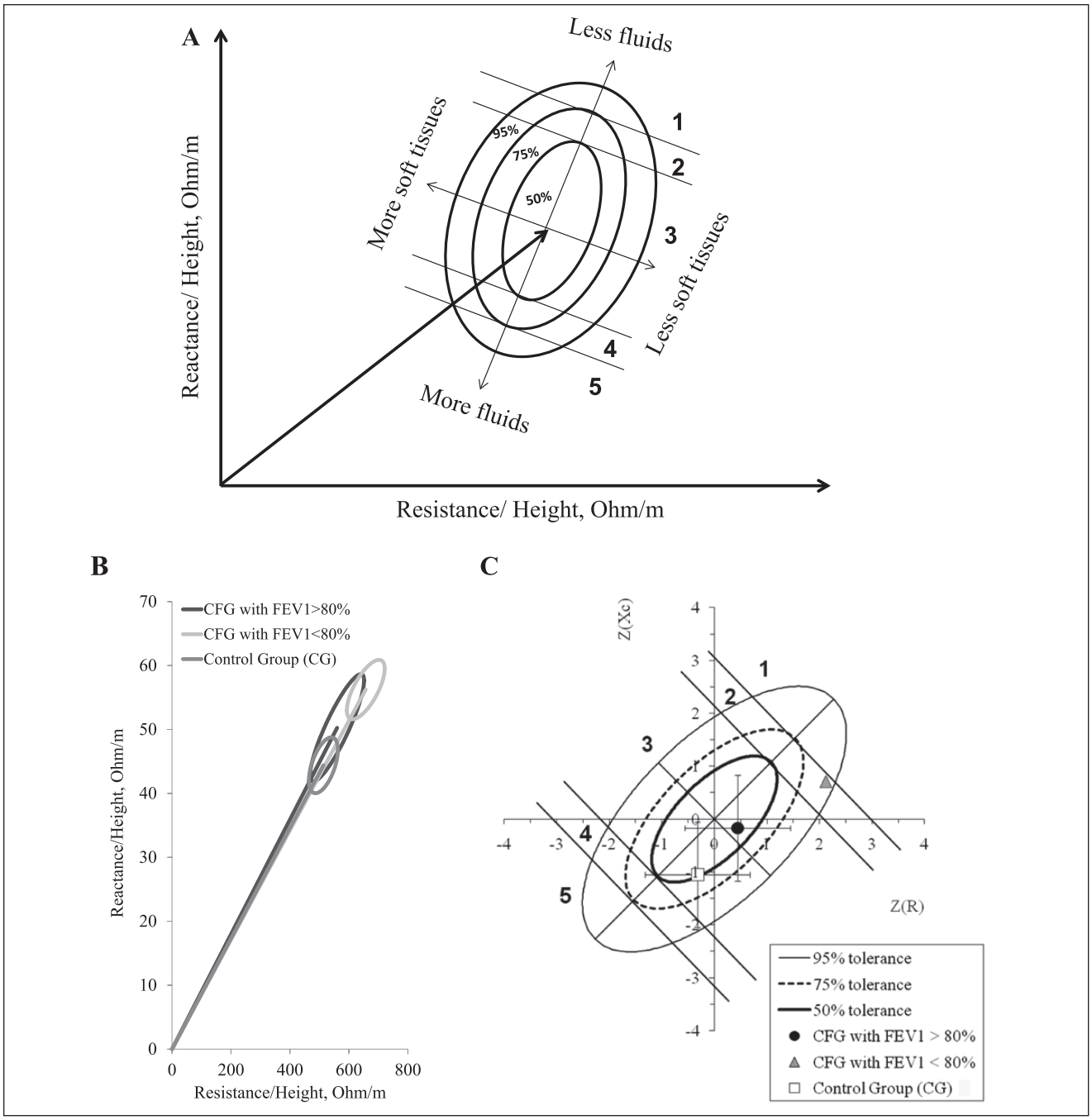

Figure 1. Graphic vector analysis of bioelectrical impedance. (A) Graphic regions of elliptical probabilities (50%, 75%, and 95% tolerance ellipse) and the vector trajectory indicating combined changes in hydration and tissue mass and the 5 points of the hydration scale, with 1 = being severely dehydrated and 5 = being severely hyperhydrated (adapted from Rösler et al[25]). (B) Mean vectors of 95% confidence limits in the CFG with lung function impairment (light gray circle), the CFG without lung function impairment (black line circle), and the CG (dark gray circle); $P < .001$ between CG and CFG with lung function impairment. (C) Position of the mean vectors and respective standard deviations of CG (white square), CFG with lung function impairment (gray triangle), and CFG without lung function impairment (black circle). CFG, cystic fibrosis group; FEV_1, forced expiratory volume in 1 second; R, resistance; Xc, reactance.

reference population (Figure 1A). Hydration status was classified into 5 sections per a biovector-normogram: 1, severely dehydrated; 2, mildly dehydrated; 3, normally hydrated; 4, mildly hyperhydrated; 5, severely hyperhydrated[25] (Figure 1A).

A nutrition screening tool developed specifically for CF by McDonald[26] was applied to the CFG. This tool included 3 data categories: weight gain, growth rate, and current BMI. Children and adolescents were classified as at low, moderate, or high nutrition risk for malnutrition. For children >10 years of age, a self-administered instrument was used to assess the stage of sexual maturation according to Tanner scale.[27]

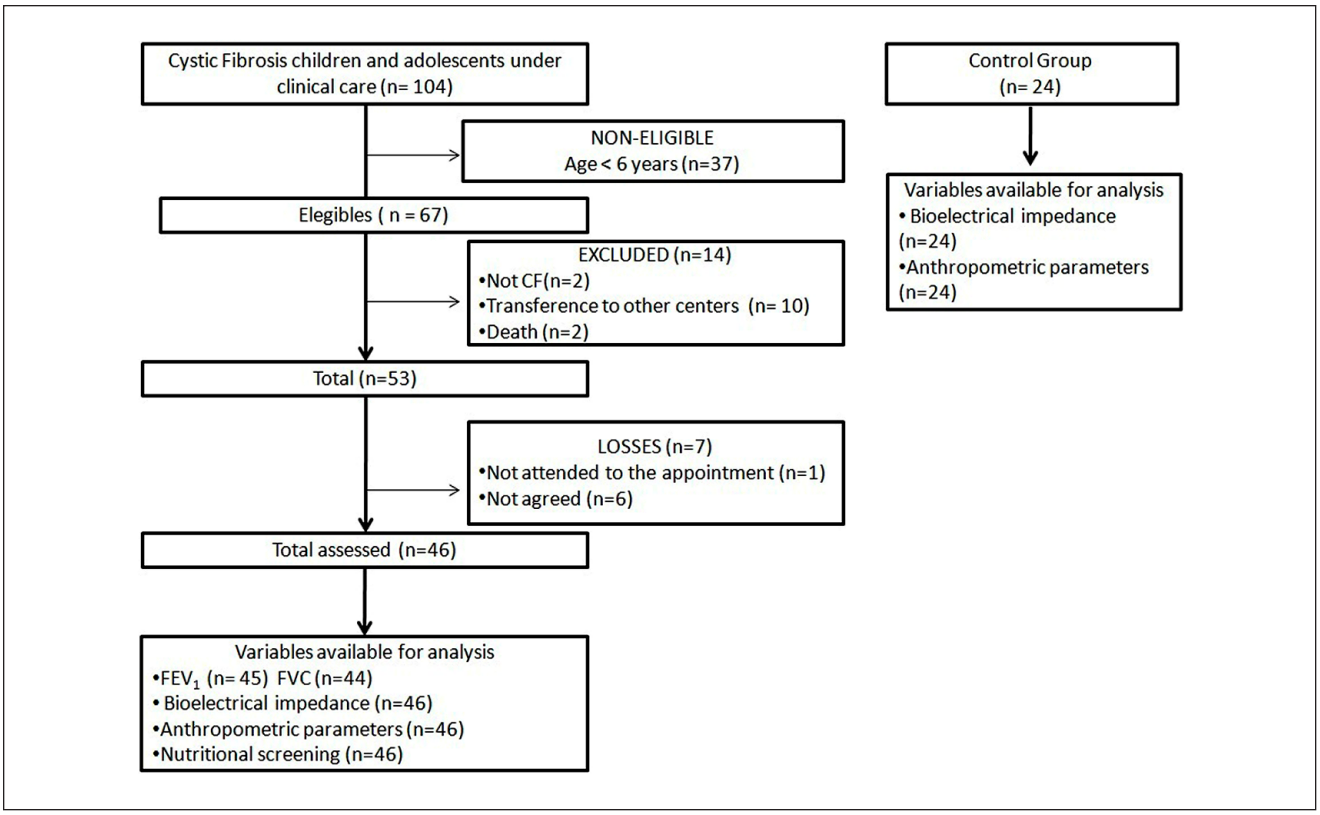

Figure 2. Flowchart of the selection of children and adolescents with cystic fibrosis. FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Lung Function

To assess the lung function in the CFG, spirometry was performed with a Spirolab II spirometer (Medical International, Research, Rome, Italy) following the protocol proposed by Miller et al.[28] Forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) parameters, as a percentage of estimated values, were also determined. Children and adolescents with parameters <80% for FEV_1 and FVC were classified as having impaired lung function.[29]

Statistical Analysis

Data were organized into a database with Microsoft Office Excel 2007 software. The statistical analysis was performed by STATA 11.0 (Stata Corp, College Station, TX). The data distribution was evaluated to verify its normality. Quantitative variables were described and presented as mean values and standard deviation or median and interquartile range (IQR). Nominal variables were described in percentages with 95% confidence intervals (95% CIs). To check for differences between the CFG and the CG, either the *t* test or Mann-Whitney test was used, depending on the distribution of variables, and the chi-square test. In the case of missing values, 1 blank per space was added manually. BIVA mean vectors were analyzed by 2-sample Hotelling's T^2 test. To evaluate the association of nutrition parameters with pulmonary function, a logistic regression was applied, and the results were expressed as an odds ratio and the respective 95% CI. In addition, an adjusted analysis for sex and age variables was performed. For all tests, $P < .05$ was considered significant.

Results

Characteristics of the Sample Population

According to the last national report in 2012, there were 134 patients with CF being treated in Santa Catarina.[30] Of these, 104 children and adolescents were treated at the outpatient clinic, and among these, 67 were eligible. Of these, 53 met the inclusion criteria. One did not attend the appointment during the collection period, and 6 did not agree to participate, resulting in a sample size of 46 children and adolescents with CF. In the CG, 24 children and adolescents were assessed (Figure 2).

The median age in the CF group was 8.5 years (IQR, 7.55–10.78) and 8.8 years (IQR, 7.12–11.42) in the CG ($P = .719$). There were 24 boys in the CFG (52%) and 14 (58%) in the CG ($P = .623$).

In the CFG, approximately 42% of the individuals were heterozygous for ΔF508, and 93% had pancreatic insufficiency. The most prevalent infections were *S aureus* (60.87%), followed by *P aeruginosa* (15.22%; Table 1). The mean FEV_1 was 76.77% ± 26.77, and FVC was 79.65% ± 26.30 (Table 1). Among the 11 (23.9%) children and adolescents from the CFG

Table 1. Demographic and Clinic Characterization of Children and Adolescents With Cystic Fibrosis, Florianópolis, Brazil.

Variables	n (%)	95% CI
Sex		
Male	24 (52.17)	37.17–67.17
Female	22 (47.83)	32.82–62.82
Age, y[a]	8.5 (7.55–10.78)	—
Mutation		
Homozygous for ΔF508	12 (30.00)	15.16–44.84
Heterozygous for ΔF508	17 (42.50)	26.49–58.51
Negative for ΔF508	11 (27.50)	13.04–41.96
Pancreatic insufficiency	43 (93.48)	86.06–100.00
Shwachman-Kulczycki score[a]	90.0 (80.0–95.0)	—
Colonization		
Negative	13 (28.26)	14.74–41.78
Pseudomonas aeruginosa	7 (15.22)	4.43–26.00
Staphylococcus aureus	28 (60.87)	46.21–75.52
Burkholderia cepacia	1 (2.17)	0.00–6.55
FEV_1 <80%	23 (51.11)	35.92–66.30
FVC <80%	22 (50.00)	34.62–65.37

CI, confidence interval; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.
[a]Median (interquartile range).

whose maturation stage was assessed, 2 (18.2%) were in stage I, 3 (27.3%) in stage II, 6 (54.5%) in stage IV, and none in stage V according to the Tanner scale.

Comparison of Nutrition and Hydration Status Between the CFG and CG

The *z*-BMI for age and height for age were lower in the CFG in comparison with the CG. Similarly, the median MUAC *z* score in the CFG was lower in comparison with the CG ($P < .001$). All other anthropometric parameters (TSF, MUAMA, and SsSF) were significantly lower in the CFG, showing a reduction of muscle and fat mass. The median resistance/height *z* score of was higher in the CFG than the CG. The median value of the resistance index was lower in the CFG ($P = .036$). There was no difference in the phase angle between the CG and the CFG ($P = .877$; Table 2).

The mean vector of the CG was close to the 50% tolerance ellipse, within the right lower quadrant, and was considered as adequate nutrition status. In contrast, the mean vector of the CFG with lung function impairment was close to the 95% ellipse in the right upper quadrant ($P < .001$, Hotelling's T^2; Figure 1B and 1C). The longer vector from the CFG with lung function impairment, near the upper pole, in comparison with the CG, indicates relative dehydration. The vector from the CFG with lung function impairment toward the right side indicates less cell mass contained in the soft tissues when compared with the CG. Therefore, these vectors indicate combined changes in hydration status and soft tissue mass (Figure 1B and 1C). Considering only the CFG without lung function impairment, the mean vector was close to the 50% tolerance ellipse, which was considered adequate nutrition and hydration status.

Approximately 43% of children and adolescents in the CFG were severely or mildly dehydrated, as classified on the hydration scale (Figure 1A), while none in the CG were in this class ($P = .007$; Table 2). The mean vector from the CFG with lung function impairment was located in the region equivalent to dehydration, according to the hydration scale (Figure 1C).

Association of Nutrition Status Parameters With Lung Function in the CFG

Children and adolescents with CF classified as high risk by the nutrition screening showed an odds ratio of 22.28 (95% CI, 2.87–172.95) for lung function impairment. Lower values for the anthropometric parameters associated with lung function impairment were verified, whereas higher values of *z*-resistance/height and *z*-reactance/height were associated with lung function impairment. The presence of dehydration significantly increased the odds for FEV_1 <80% (4.94; 95% CI, 1.13–21.59; $P < .050$; Table 3).

Discussion

To our knowledge, this is the first study that describes hydration status and its association with lung function in children and adolescents with CF by means of BIVA. It found that all nutrition parameters were impaired and significantly different in the CFG versus the GC. There were more dehydrated subjects in the CFG, and the presence of dehydration was associated with lung function impairment in the CFG. Lower values of the anthropometric parameters and higher values of *z*-resistance/height and *z*-reactance/height were associated with lung function impairment.

In this study, a mean FEV_1 of 76.77% was found, which is close to that of the Brazilian national survey of 2012 in which the mean of FEV_1 in children and adolescents between 5–15 years of age was >80%.[30] Higher FEV_1 values were found in 3787 children with CF <12 years old in the United States, with a mean FEV_1 of 95.06%, and in 1011 children <12 years old in the UK where the mean FEV_1 was 87.76%. The differences found between these countries could be explained by the differences in treatment protocol, pulmonary therapies, age of diagnosis, or differences in mutation profiles.[31]

In the present study, the median BMI for age was slightly lower than the values found in a study with 63 patients at 10.6 ± 2.9 years of age in which the mean *z*-BMI for age[32] was 0.2 ± 0.7. Similarly, in a study with 211 children and adolescents with CF between 5–21 years old, the mean *z*-BMI for age was −0.33 ± 0.83 in males and −0.20 ± 0.88 in females. Additionally in this study, a difference of 0.83 in the *z* score for BMI for age in males and a difference of approximately 1.0 in the *z* score for females were observed when compared with a CG ($P < .001$).[33] Furthermore, the CFG showed lower BMI for age and height for age when compared with the CG. Also, a reduction in *z*-TSF, *z*-MUAC, *z*-SsSF, and *z*-MUAMA scores were noticed when compared with those of the CF, reflecting nutrient depletion found in subcutaneous and muscle tissues. It has

Table 2. Comparison of Nutrition Status Parameters Among Children and Adolescents With Cystic Fibrosis and a Control Group, Florianópolis, Brazil.

Variable	Cystic Fibrosis Group (n = 46)	Control Group (n = 24)	*P* Value
Anthropometric parameters			
z-BMI for age[a]	–0.58 (–1.44 to 0.10)	0.83 (0.12–1.21)	<.001[c]
z-Height for age[a]	–0.76 (–1.96 to 0.31)	0.18 (–0.47 to 1.03)	.004[c]
z-MUAC[b]	–1.40 ± 1.39	–0.25 ± 0.81	<.001[d]
z-TSF[b]	–0.63 ± 1.14	–0.05 ± 1.07	.044[d]
z-MUAMA[b]	–1.26 ± 1.23	–0.33 ± 0.74	.001[d]
z-SsSF[a]	–0.51 (–1.23 to 0.00)	–0.13 (–0.74 to 0.25)	.020[c]
Bioelectrical impedance parameters			
Phase angle[a]	4.99 (4.97–5.03)	5.00 (4.5–5.03)	.877[c]
z-resistance/height[b]	1.29 ± 1.92	–0.32 ± 0.85	.001[d]
Resistance index[a], cm^2/Ω	20.26 (17.86–26.86)	25.13 (21.53–28.27)	.036[c]
z-reactance/height[b]	0.29 ± 1.52	–1.03 ± 1.15	.001[d]
Hydration status, n (%)			
Severe dehydration	14 (30.43)	0.00	
Mild dehydration	5 (10.87)	0.00	.007[e]
Normal dehydration	21 (45.65)	17 (70.83)	
Mild hyperhydration	2 (4.35)	6 (25.00)	
Severe hyperhydration	4 (8.70)	1 (4.17)	

BMI, body mass index; MUAC, mid upper arm circumference; MUAMA, mid upper arm muscle area; SsSF, subscapular skinfolds thickness; TSF, triceps skinfolds thickness; *z, z* score.
[a]Values presented in median (interquartile range).
[b]Values presented in mean and standard deviation.
[c]Mann-Whitney test.
[d]*T* test.
[e]Chi-square test—added manually 1 each space.

Table 3. Association of Lung Function With Nutrition Status Parameters by Children and Adolescents With Cystic Fibrosis, Florianópolis, Brazil.[a]

	FEV_1 <80%, OR (95% CI)		FVC <80%, OR (95% CI)	
Variables	Crude	Adjusted	Crude	Adjusted
Nutrition screening				
Low risk	1.00	1.00	1.00	1.00
Moderate risk	4.44 (0.74–26.67)	3.84 (0.61–24.23)	5.00 (0.82–30.46)	4.66 (0.71–30.37)
High risk	21.67 (3.02–155.36)[b]	22.28 (2.87–172.95)[b]	15.00 (2.25–99.63)[b]	14.01 (2.07–94.91)[b]
Anthropometric parameters				
z-BMI for age	0.41 (0.21–0.79)[b]	0.41 (0.21–0.80)[b]	0.46 (0.25–0.86)	0.47 (0.25;0.88)
z-Height for age	0.59 (0.37–0.96)[b]	0.59 (0.36–0.98)[b]	0.56 (0.34–0.92)[b]	0.55 (0.33-0.92)[b]
z-MUAC	0.51 (0.29–0.89)[b]	0.52 (0.29–0.91)[b]	0.54 (0.32–0.93)[b]	0.55 (0.32–0.94)[b]
z-TSF	0.48 (0.25–0.92)[b]	0.46 (0.22–0.94)	0.47 (0.24–0.91)[b]	0.47 (0.24–0.93)[b]
z-MUAMA	0.41 (0.21–0.79)[b]	0.43 (0.22–0.84)[b]	0.46 (0.24–0.86)[b]	0.48 (0.25–0.89)[b]
z-SsSF	0.45 (0.22–0.92)[b]	0.41 (0.19–0.90)[b]	0.48 (0.24–0.96)[b]	0.46 (0.22–0.96)[b]
Bioelectrical impedance parameters				
z-resistance/height	1.81 (1.18–2.80)[b]	2.23 (1.30–3.82)[b]	1.78 (1.16–2.72)[b]	2.10 (1.26–3.51)[b]
Resistance index, cm^2/ohm	0.91 (0.84–0.99)[b]	0.73 (0.59–0.91)[b]	0.92 (0.85–1.00)[b]	0.74 (0.61–0.91)[b]
z-reactance/height	1.60 (1.03–2.48)[b]	1.81 (1.09–2.99)[b]	1.57 (1.01–2.42)[b]	1.76 (1.07–2.88)[b]
Hydration status				
Normal	1.00	1.00	1.00	1.00
Dehydration	4.2 (1.08–16.32)[b]	4.94 (1.13–21.59)[b]	4.8 (1.20–19.12)[b]	5.6 (1.27–24.54)[b]
Hyperhydration	0.3 (0.03–3.01)	0.20 (0.01–2.34)	0.34 (0.03–3.56)	0.23 (0.02–2.75)

BMI, body mass index; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; MUAC, mid upper arm circumference; MUAMA, mid upper arm muscle area; OR, odds ratio; SsSF, subscapular skinfold thickness; TSF, triceps skinfold thickness; *z, z* score.
[a]Adjustment model: sex, age.
[b]$P < .05$, logistic regression.

been shown that children and adolescents with CF present less FFM and fat mass as evaluated by skinfold thickness measurements, the doubly labeled water method,[34] and dual energy x-ray absorptiometry.[35]

Children and adolescents with lower *z*-TSF, *z*-SsSF, *z*-MUAC, and *z*-MUAMA scores had higher odds for lung function impairment. FFM reduction can result in the impairment of respiratory muscles in the diaphragm and accessory respiratory muscles, resulting in a worsening of lung function.[3] In a cross-sectional study with 69 children and adolescents with CF, lower values in TSF and mid upper arm muscle circumference were observed, which were associated with a higher prevalence of FEV_1 <80%.[36]

Based on weight gain, growth rate, and current BMI, nutrition screening is intended to identify children and adolescents at risk of malnutrition who would benefit from a more complete nutrition assessment and intervention.[26] In our study, there was a significant association between a high risk for malnutrition and lung function impairment, which confirms the need for an up-to-date longitudinal study of nutrition status in regard to these conditions. A longitudinal nutrition status follow-up would also be necessary, as observed in a cohort of 3142 children with CF in which more weight at 4 years of age was associated with better lung function, fewer complications, and better survival rates through to 18 years of age.[37] However, this nutrition screening identifies the impairment of nutrition status already established, thus demonstrating the need for tools that could identify risk of nutrition status changes more early.

In this study, the BIA parameters were evaluated as an alternate tool for assessing nutrition status in this population. The resistance and reactance were normalized per height and transformed into *z* scores to control for the different conductor lengths and to allow for the utilization of standard reference intervals for impedance vectors to assess a qualitative measure of soft tissues.[38] In this study, higher values in *z*-resistance/height were found in the CFG. Because resistance reflects the restriction of electric current flowing through the body, it is inversely related to the amount of water present in the tissues. Therefore, high resistance values indicate lower water content and less hydrated tissue and, as a consequence, a potentially higher content of fat tissue, skin, and bones.[7,9] Hence, in illness, high resistance values may be related to dehydration and wasting.[39] In adults, resistance/height was negatively correlated with muscle function, as measured by handgrip strength.[40] Additionally, resistance was higher in adults with cachexia when compared with adults without cachexia in cases of sarcopenic obesity and chronic stable heart failure.[41,42] Previous studies have shown an association between resistance index and total body water, both in healthy individuals and in those with CF.[43-45] Based on total body water, it is possible to estimate the FFM.[46,47] Therefore, low resistance index values are associated with low body FFM,[48] suggesting low FFM in the CFG and confirming the anthropometric findings of the present study.

Reactance is related to the properties of cell membrane capacitance—that is, its capacity to store electrons across tissue interfaces and cell membranes in a way that variations may occur, depending on the integrity, function, and composition of the cell membrane.[7,9] In children and adolescents with CF, higher values for *z*-reactance/height were found. This finding could be explained by the change in sodium content in the sweat of individuals with CF because the serum sodium concentrations may change the reactance generated by the BIA. Similarly, changes in the electrolyte content may influence the electric potential measured, which could lead to an invalid result for assessing body composition in CF patients. A higher electric potential due to reduced chloride absorption in the sweat glands appears to occur in patients with CF.[44,45,49-51]

BIVA allows noninvasive assessment of the tissue hydration status, and the main advantage of this method for patients with alterations in water metabolism is that it is independent of body weight and assumptions about the consistent hydration soft tissues.[52] It uses the values of resistance and reactance instead. Thus, BIVA is a useful clinical tool capable of detecting changes in hydration and children's body composition.[12] A study with 114 adolescents aged 12–14 years who had been monitored for 2 years found that during growth there was an increase in bone, muscle, and adipose tissues as well as body water. There were significant differences in the hydration status according to adiposity such that obese children presented a higher percentage of water than lean children. Therefore, it is necessary to take into consideration the hydration status for a correct evaluation of the body composition.[53] Taken together, this indicates that BIVA is a useful clinical method for detecting children at risk of pathologic changes in body composition.[12]

In a study with 46 children aged 2–14 years with chronic kidney disease, a progressive increase of the impedance vector was observed at the most severe stage of the disease, which indicates hydric alteration in this population.[54] In the present study, a difference in the BIVA vector distribution was observed between the CG and the CFG regarding lung impairment. Although the phase angle was not different between the CG and the CFG, the longer vector displacement of the CFG regarding impaired lung function was characterized by an increase of the resistance and reactance components, whereas the mean vector of the CG was close to normal. Therefore, the mean vector of the CFG regarding impaired lung function indicated less fluid and less soft tissues as compared with the CG.

Also, children and adolescents with CF classified as dehydrated by BIVA demonstrated higher odds for presenting lung function impairment, indicating the importance of assessing both nutrition status and body fluid. One typical CF clinical manifestation is a reduced amount of liquid on the airway surface—that is, the presence of dehydrated secretions and a consequent production of hyperviscous mucus. Based on this mechanism, it has been proposed that the CFTR function causes airway surface dehydration, resulting in the stasis of mucus and impaired mucociliary clearance, inviting the onset of chronic bacterial infection with a worsened lung function and, ultimately, respiratory insufficiency, which accounts for the death of >90% of the CF population.[55] Other factors that

may contribute to a dehydrated status as revealed by BIVA are hyponatremic dehydration and gastrointestinal losses. Children and adolescents with CF are at higher risk of hyponatremic dehydration, especially in warm climates.[56] The primary function of the sweat gland is to wet the skin surface for evaporative cooling. However, due to CFTR mutation, the absorption of sodium and chloride in the epithelia is inefficient, causing a significant loss of these electrolytes through sweat and possibly leading to severe dehydration.[57] Gastrointestinal losses can also contribute to dehydration due to salt depletion and metabolic alkalosis. It is important to highlight that stool frequency was not assessed in this study.[58] In a study conducted with 26 Greek-Cypriot patients with CF, most dehydration episodes occurred within the first 4 years of life, although some episodes continued to appear until 10 years of age.[59] Because clinical evaluation of hydration status is frequently difficult in children and adolescents, BIVA could be a viable instrument for detecting early stages of dehydration. Also, BIVA can be used to assess minor fluid overload and steroid-associated weight gain following steroid treatment.[54] Considering the results found in the present study, we hypothesized that dehydration contributes to the worsening of airway surface dehydration, leading to the stasis of mucus and, consequently, the impairment of lung function.

The present study has certain limitations. Although sexual maturation was assessed as part of the nutrition screening,[26] it could be a possible confounding factor. A study with 143 premenarcheal and postmenarchal girls aged 10–15 years demonstrated that the stage of sexual maturation should be considered when bioelectrical impedance is evaluated. Difference in pubertal status has a greater impact on bioelectrical impedance parameters than age difference.[60] Even though the sample size was small, it represents almost 78% of the total patients with CF from the state of Santa Catarina and 87% of children and adolescents who met the inclusion and exclusion criteria for the CF treatment study. This study also has the limitation of being cross-sectional such that it is not possible to establish a cause-and-effect relationship. Because the age range was chosen to properly evaluate lung function, the results could be generalized only for children and adolescents between 6–14 years old. There are few studies assessing the nutrition status described by BIA vectors in children and adolescents with CF in association with lung function. More studies with a larger samples and a longitudinal design are needed to examine the applicability of BIVA in determining nutrition status parameters for the prediction of lung function impairment and its inclusion in the assessment protocol. In addition, more studies are necessary to verify the association between dehydration and clinical outcomes, including lung function.

In conclusion, children and adolescents with CF showed a compromised nutrition status assessed by BMI, height, *z*-TSF, *z*-MUAC, *z*-MUAMA, *z*-SsSF, and BIA parameters. In addition, it was found that nutrition screening tools, anthropometric parameters, and BIA vectors were associated with lung function. The presence of dehydration assessed by BIVA was also associated with the presence of lung function impairment.

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Statement of Authorship

D. B. Hauschild, E. A. M. Moreira, E. Wazlawik, and Y. M. F. Moreno contributed to conception/design of the research; E. Barbosa, N. Ludwig Neto, V. Platt, and E. Piacentini Filho contributed to acquisition, analysis, or interpretation of the data; D. B. Hauschild and Y. M. F. Moreno contributed to drafting the manuscript; E. A. M. Moreira, E. Wazlawik, E. Barbosa, N. Ludwig Neto, V. Platt, and E. Piacentini Filho critically revised the manuscript. All authors read and approved the final manuscript and agree to be fully accountable for ensuring the integrity and accuracy of the work.

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