

# Inspiratory Muscle Strength and Endurance in Children and Adolescents with Cystic Fibrosis

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**BACKGROUND:** Pulmonary changes that occur in cystic fibrosis may influence inspiratory muscle strength and endurance. We evaluated inspiratory muscle strength and endurance in children and adolescents with cystic fibrosis in comparison with healthy subjects. **METHODS:** This is a cross-sectional observational study with subjects with cystic fibrosis and paired healthy individuals, age 6–18 y. Spirometry, impulse oscillometry, plethysmography, manovacuometry, and a protocol of inspiratory muscle endurance were performed. **RESULTS:** Subjects with cystic fibrosis ( $n = 34$ ) had higher maximum percent-of-predicted inspiratory pressure ( $P_{I_{max}}$ ) than healthy ( $n = 68$ ) subjects ( $118.5 \pm 25.8\%$  vs  $105.8 \pm 18.0\%$ ) and no significant difference in endurance ( $60.9 \pm 13.3\%$  vs  $65.3 \pm 12.3\%$ ). When restricting the analysis to subjects without *Pseudomonas aeruginosa* colonization and with  $FEV_1 > 80\%$ ,  $P_{I_{max}}$  values were significantly higher, and inspiratory muscle endurance was lower, in comparison with the control group.  $P_{I_{max}}$  correlated significantly with FVC ( $r = 0.44$ ,  $P = .02$ ) and  $FEV_1$  ( $r = 0.41$ ,  $P = .02$ ), whereas endurance correlated better with total airway resistance ( $r = 0.35$ ,  $P = .045$ ) and with central airway resistance ( $r = 0.48$ ,  $P = .004$ ). **CONCLUSIONS:** Children and adolescents with cystic fibrosis with no colonization by *P. aeruginosa* and normal lung function present increased inspiratory muscle strength and decreased endurance compared with healthy individuals, indicating that changes in the respiratory muscle function seem to be distinctly associated with pulmonary involvement. Strength was related to pulmonary function parameters, whereas endurance was associated with airway resistance. *Key words:* cystic fibrosis; child; adolescent; respiratory muscles. [Respir Care 2016;61(2):184–191. © 2016 Daedalus Enterprises]

## Introduction

Cystic fibrosis is a disease characterized by progressive loss of pulmonary function, with obstruction of the airways caused by abnormal production of mucus and by the

presence of chronic inflammation and recurring infections.<sup>1</sup> Respiratory muscle strength has been much evaluated in these subjects, but studies are still contradictory.<sup>2</sup> Some authors report that strength may be within normality or even increased, suggesting a muscle training effect in response to airway obstruction and chronic coughing.<sup>3,4</sup> On the other hand, authors who demonstrate a diminished strength associate muscle weakness with hyperinflation and malnutrition,<sup>5</sup> suggesting that these subjects are not

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able to maintain muscle strength at advanced stages of the disease.<sup>6</sup>

Although measuring maximum static pressures supplies information about strength, it does not quantify inspiratory muscle endurance.<sup>7</sup> Evidence shows that the evaluation of muscle endurance may be more relevant than strength in subjects with chronic obstructive pulmonary disease,<sup>8,9</sup> since endurance is the capacity of a muscle or a muscle group to sustain a given task over time and is directly related to muscle fatigue.<sup>10</sup> However, few studies have evaluated inspiratory muscle endurance in subjects with cystic fibrosis, and these have shown contradictory results, just as for muscle strength. One previous study showed an apparent increase of endurance due to the adaptation of the muscles to the chronic stress of ventilating against a load generated by airway obstruction.<sup>11</sup> On the other hand, there is evidence that endurance may be diminished independent of nutritional status, the presence of airway obstruction, pulmonary hyperinflation, respiratory muscle strength, or maximum exercise capacity<sup>3,12</sup> and may be a major parameter to evaluate dyspnea in subjects with cystic fibrosis.<sup>12</sup> The individuals with cystic fibrosis who have a reduced capacity to contract the respiratory muscles become more susceptible to muscle fatigue with a limitation in the ability to carry out prolonged activities or tasks. However, the degree of inspiratory muscle endurance impairment and how that impairment is associated with important lung function parameters in children and adolescents with cystic fibrosis remain poorly understood.

*Pseudomonas aeruginosa* is the most common pathogen in cystic fibrosis lung disease and is associated with gradual decline of pulmonary status in children and young adults.<sup>13</sup> Once infection is established, there is an accelerated decline in lung function, quality of life, and survival.<sup>14,15</sup> Furthermore, chronic *P. aeruginosa* infection has been related to decreased maximum inspiratory pressure ( $P_{I_{max}}$ ) and is probably an independent predictor of respiratory muscle compromise in cystic fibrosis,<sup>16</sup> although its relation to muscle endurance remains unclear.

The aim of our study was to evaluate muscle strength and inspiratory muscle endurance in children and adolescents with cystic fibrosis and to compare them with age-matched healthy controls. The role of *P. aeruginosa* and lung function compromise was assessed, and we further examined possible associations of strength and endurance with other pulmonary function parameters, such as FEV<sub>1</sub>, total lung capacity, residual volume (RV), and airway resistance. A better understanding of inspiratory muscle strength and endurance could contribute to the development of earlier preventive measures and help in the therapeutic intervention processes in cystic fibrosis.

## QUICK LOOK

### Current knowledge

Cystic fibrosis is a disease characterized by progressive loss of pulmonary function, with obstruction of the airways caused by abnormal production of mucus and by the presence of chronic inflammation and recurring infections. These pulmonary derangements can negatively impact inspiratory muscle strength and endurance.

### What this paper contributes to our knowledge

Children and adolescents with cystic fibrosis, but without *Pseudomonas aeruginosa* colonization and FEV<sub>1</sub> > 80%, had increased inspiratory muscle strength and decreased endurance compared with healthy individuals. Strength was related to pulmonary function parameters, whereas endurance was associated with airway resistance. These findings suggest that changes in respiratory muscle function were associated with pulmonary involvement.

## Methods

A cross-sectional observational study was performed in children and adolescents with cystic fibrosis, age 6–18 y, who were regularly followed at the cystic fibrosis outpatient clinics of São Lucas Hospital at Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, Brazil. Healthy children, age 6–18 y, from 1 private and 2 public schools in Porto Alegre also participated in the study. Healthy individuals were paired with children and adolescents with cystic fibrosis using the variables sex, age, height, and weight, at a proportion of 2 healthy controls for each subject with cystic fibrosis. Subjects who presented signs indicating pulmonary exacerbation, such as a temperature, increased coughing, and sputum production, were excluded. Likewise, children and adolescents who were unable to understand how the pulmonary function tests were performed or could not do them correctly were also excluded from the study. Data were collected from November 2012 to November 2013.

Sample size was estimated based on inspiratory muscle endurance (in percent of maximum inspiratory pressure [ $P_{I_{max}}$ ]) data from the study by De Jong et al<sup>3</sup> with a mean of 48.0% and an SD of 12.0%. Adopting a significance level of 0.05, a power of 90%, and a minimum difference of 10.0, the estimated sample size was approximately 34 individuals with cystic fibrosis and 68 healthy controls. The study was approved by the Ethics in Research Committee of the Pontifical Catholic University of Rio Grande do Sul under number 04850312.9.0000.5336. Parents or legal guardians signed the free and informed consent form before inclusion in the study.

Eligible subjects selected were invited to participate in the study at the time they came to the cystic fibrosis out-patient clinics at São Lucas Hospital-PUCRS. They were then referred to the Institute of Biomedical Research at PUCRS to undergo the procedures in the following order: anthropometric evaluation, impulse oscillometry, plethysmography, spirometry, manovacuometry, and respiratory muscle endurance protocol.

Likewise, healthy children and adolescents underwent the following procedures at their schools: anthropometric assessment, manovacuometry, and respiratory muscle endurance protocol. Only individuals who did not have respiratory illnesses evaluated by a pediatric pulmonologist (PJCM) using a respiratory health questionnaire based on the questionnaire recommended by the American Thoracic Society, Division of Lung Diseases (ATS-DLD-78-C), previously adapted and validated for use in Brazil,<sup>17</sup> were included.

Anthropometric evaluation was performed by measuring weight and height in triplicate or until 2 identical values were obtained using a digital scale (G-Tech, Glass 1 FW, Rio de Janeiro, Brazil) previously calibrated to a 100 g precision and a portable stadiometer (AlturaExata, TBW, São Paulo, Brazil) with a 1 mm precision,<sup>18</sup> respectively. Body mass index (BMI) Z score was calculated using the program WHO Anthroplus.<sup>19</sup>

Evaluation of airway resistance was performed using impulse oscillometry (Erich Jaeger, Friedberg, Germany). Tests were performed with the subject in the seated position, using a nose clip, and cheeks were supported by the examiner. Subjects were told to breathe through a mouthpiece, spontaneously, at tidal volume rate. At least 3 acceptable and reproducible measures were required for validity. Impulse oscillometry data were considered acceptable when correlation between oscillatory pressure and flows used to calculate resistance and reactance was  $>0.8$ . Parameters used for analysis were total resistance of the airways (R5), central resistance of the airways (R20), resistance of the airway at a frequency of 10 Hz (R10), and resonance frequency ( $f_{res}$ ). Data were expressed in absolute values and in percentages of the predicted reference values for oscillometry.<sup>20</sup>

Pulmonary volumes, including total lung capacity, functional residual capacity, and RV, were measured by whole body plethysmography. The equipment used was the Vmax 22 (Viasys Healthcare, Hörsching, Germany) plethysmograph. Tests were performed, and criteria of acceptability and reproducibility were applied in accordance with American Thoracic Society/European Respiratory Society guidelines.<sup>21</sup> Briefly, tests were performed with the subject seated, inside the closed booth, in a comfortable position. A series of 3–5 technically satisfactory maneuvers were performed. Tests would be considered valid when at least 3 acceptable and reproducible maneuvers were obtained, with a variation of  $<5\%$ . Data were expressed in absolute

values and in percentage of the predicted, using the equations of Koopman et al.<sup>22</sup>

Lung function was performed using a flux-based spirometer (KoKo, Louisville, Colorado). Spirometric parameters evaluated included FEV<sub>1</sub>, FVC, and forced expiratory flow between 25 and 75% of vital capacity. Spirometry was performed in the standing position without using a nose clip,<sup>23</sup> followed by quick maximum inspiration sustained for at least 3 s. Three acceptable curves and 2 reproducible curves were obtained.<sup>24</sup> The international equation GLI 2012<sup>25</sup> was used to normalize the spirometric data.

The strength of the inspiratory muscles was evaluated using a digital manuvacuometer (MVD 500, Globalmed, Scottsdale, Arizona) by measuring P<sub>I<sub>max</sub></sub>, with the subject in the sitting position. A connector was used between the mouthpiece and the apparatus with an orifice to reduce the pressure generated in the oral cavity. Subjects with cystic fibrosis and healthy controls were told to perform maximum inspiration against the occluded valve, using a nose clip, based on the residual volume. Five maneuvers were performed, at 40-s intervals between one maneuver and the other, and the highest value recorded in cm H<sub>2</sub>O, was used for the study. Data were expressed in absolute values and percentage of predicted.<sup>26,27</sup>

After P<sub>I<sub>max</sub></sub> evaluation, a protocol of inspiratory muscle endurance was performed through a linear load device (Threshold-IMT, Philips Respironics, Murrysville, Pennsylvania) during an incremental loading test to measure inspiratory muscle endurance. The spring and structure of the apparatus were modified to obtain pressures of  $>41$  cm H<sub>2</sub>O. With the help of the Biomedical Engineering Department of PUCRS, based on a commercial spring from the Threshold-IMT, a new stainless steel spring was made with an elastic constant of 0.035 newtons/mm, thus allowing us to obtain pressures up to 145 cm H<sub>2</sub>O. Subjects began the protocol inspiring against a fixed load of 30% of P<sub>I<sub>max</sub></sub> during 2 min. To begin the inspiratory flow, it was necessary to generate a sufficient inspiratory pressure to open the valve. Every 2 min, the load was increased by 10% of P<sub>I<sub>max</sub></sub>. The maximum load was defined as the highest percentage of P<sub>I<sub>max</sub></sub> achieved and maintained for at least 1 min.<sup>3</sup> The breathing pattern was controlled and maintained at 20 respiratory incursions/min. The interruption criteria of the protocol were intense fatigue or failure to open the valve at least 3 consecutive times. At the beginning of the protocol and in the last 10 s of each level of loading, subjects were asked to classify the subjective degree of dyspnea using the modified Borg scale.

### Statistical Analysis

Distribution of variables was evaluated using the Kolmogorov-Smirnov test, and, since they presented a normal

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Table 1. Characterization of the Study Population

	Healthy (n = 68)	Cystic Fibrosis (n = 34)	P
Age, y	13.9 ± 2.6	14.0 ± 2.7	.80
Male sex	58.8%	58.8%	
Weight, kg	48.6 ± 12.7	46.2 ± 14.3	.39
Height, cm	155.7 ± 12.9	154.7 ± 14.9	.71
BMI			
Absolute, kg/m <sup>2</sup>	19.7 ± 3.1	18.8 ± 3.3	.21
Z score	0.06 ± 0.99	-0.37 ± 1.17	.055
P <sub>I<sub>max</sub></sub>			
Absolute, cm H <sub>2</sub> O	110.9 ± 23.7	119.03 ± 20.7	.09
% predicted	105.8 ± 18.0	118.5 ± 25.8	.005
Endurance			
Absolute, cm H <sub>2</sub> O	72.8 ± 21.5	73.2 ± 22.3	.92
Percentage	65.3 ± 12.3	60.9 ± 13.3	.10

Values are expressed as mean ± SD, except for male sex (%).  
 BMI = body mass index  
 P<sub>I<sub>max</sub></sub> = maximum inspiratory pressure

distribution, the continuous variables were presented as mean and SD. Categorical variables were presented in absolute and percentage frequencies. Correlations were evaluated using Pearson's linear correlation test. Differences between subjects with cystic fibrosis and healthy individuals were evaluated using the Student *t* test for independent samples. All of the analyses and data processing were performed using SPSS 18.0 (SPSS, Chicago, Illinois). The level of significance was accepted whenever *P* was ≤.05.

## Results

Thirty-four children and adolescents with cystic fibrosis, age 6–18 y, mean age 14.0 ± 2.7 y, were included; 20 of the subjects (58.8%) were male. Six subjects who did not manage to perform plethysmography correctly were excluded from the study, so that lung volume results are presented with a final number of 28 individuals. Subjects with cystic fibrosis presented a mean percent-of-predicted P<sub>I<sub>max</sub></sub> of 118.5 ± 25.8% and a mean endurance (percent of P<sub>I<sub>max</sub></sub>) of 60.9 ± 13.3%. Sixty-eight healthy children and adolescents were also included, paired by sex, age, weight, and height, with a mean percent-of-predicted P<sub>I<sub>max</sub></sub> of 105.8 ± 18.0% and endurance of 65.3 ± 12.3%. There was no significant difference between subjects with cystic fibrosis and healthy individuals when age, weight, height, and BMI were compared. As to P<sub>I<sub>max</sub></sub>, subjects with cystic fibrosis presented significantly greater strength than healthy children. On the other hand, no significant difference was found in endurance between subjects with cystic fibrosis and healthy individuals. Table 1 presents the data that characterize the study population.

Table 2. Pulmonary Function Values of the Cystic Fibrosis Subjects

Variables	Absolute	% Predicted
Spirometry (n = 34)		
FVC, L	2.94 ± 0.99	88.9 ± 23.8
FEV <sub>1</sub> , L	2.31 ± 0.90	80.1 ± 27.7
FEV <sub>1</sub> /FVC	0.77 ± 0.12	
FEF <sub>25-75%</sub> , L/s	2.22 ± 1.22	65.0 ± 34.3
Impulse oscillometry (n = 34)		
R5, kPa/L/s	0.58 ± 0.21	125.8 ± 38.7
R20, kPa/L/s	0.40 ± 0.10	116.3 ± 22.7
R5 – R20 (%)	23.30 ± 15.71	
f <sub>res</sub> , Hz	17.61 ± 5.49	
Plethysmography (n = 28)		
TLC, L	4.29 ± 0.86	97.7 ± 11.8
FRC, L	2.11 ± 0.60	71.9 ± 14.9
RV, L	1.31 ± 0.52	137.0 ± 53.9
RV/TLC	0.31 ± 0.12	

Values are expressed as mean ± SD.  
 FEF<sub>25-75%</sub> = forced expiratory flow between 25 and 75% of vital capacity  
 R5 = total resistance of airways  
 R20 = central resistance of airways  
 f<sub>res</sub> = resonance frequency  
 TLC = total lung capacity  
 FRC = functional residual capacity  
 RV = residual volume

Table 2 presents pulmonary function data, including FEV<sub>1</sub>, FVC, R5, R20, total lung capacity, functional residual capacity, and RV, of subjects with cystic fibrosis. In general, results were within or close to the limits of normality. When correlating P<sub>I<sub>max</sub></sub> and endurance with other variables of pulmonary function tests in subjects with cystic fibrosis, there was a significant correlation of P<sub>I<sub>max</sub></sub> with FVC (*r* = 0.44, *P* = .02) and FEV<sub>1</sub> (*r* = 0.41, *P* = .02). On the other hand, endurance presented a correlation with airway resistance in both R5 (*r* = 0.35, *P* = .045) and R20 (*r* = 0.48, *P* = .004). Fig. 1 shows the graphs of the correlations found. In addition, there was a significant correlation of BMI Z score with P<sub>I<sub>max</sub></sub> (*r* = 0.34, *P* = .048) but not with endurance (*r* = 0.05, *P* = .77).

Subjects with cystic fibrosis chronically colonized by *P. aeruginosa* presented a significantly lower FEV<sub>1</sub> (*P* = 0.046) and higher R5 (*P* = .001) and R20 (*P* = .002) than the non-colonized ones. Likewise, subjects with FEV<sub>1</sub> < 80% presented R5 (*P* = .001), functional residual capacity (*P* = .025), and RV (*P* = .001) significantly greater than subjects with FEV<sub>1</sub> > 80%. Next, strength and endurance of children's and adolescents' inspiratory muscles were compared. They were divided into groups with or without chronic *P. aeruginosa* colonization and with an FEV<sub>1</sub> greater or smaller than 80% of predicted and were compared with their healthy peers. A significantly greater P<sub>I<sub>max</sub></sub> (Fig. 2, A and C) was shown in subjects with cystic fibrosis without *P. aeruginosa* colonization (119.54 ± 27.4) compared with healthy individuals

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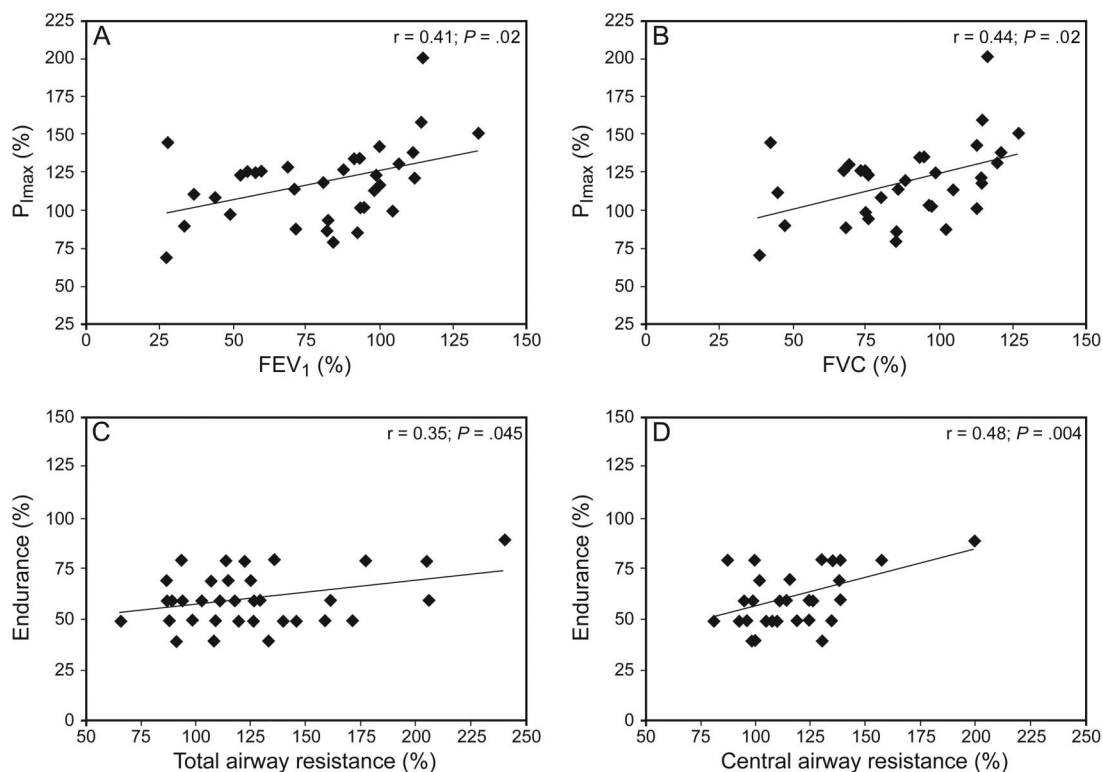


Fig. 1. Correlations between inspiratory muscle strength, endurance, spirometry, and impulse oscillometry. A: Correlation between maximal inspiratory pressure ( $P_{I_{max}}$ ) and FEV<sub>1</sub>. B: Correlation between  $P_{I_{max}}$  and FVC. C: correlation between inspiratory muscle endurance and total airway resistance (R5). D: Correlation between inspiratory muscle endurance and central airway resistance (R20).

( $103.67 \pm 16.82$ ) ( $P = .003$ ) and in subjects with FEV<sub>1</sub> > 80% ( $122.40 \pm 28.29$ ) compared with the controls ( $105.58 \pm 17.85$ ) ( $P = .005$ ). On the other hand, endurance was significantly lower in subjects without *P. aeruginosa* ( $58.80 \pm 12.01$ ) ( $P = .02$ ) and with FEV<sub>1</sub> > 80% ( $60.0 \pm 11.83$ ) ( $P = .050$ ) compared with their healthy peers ( $66.00 \pm 13.09$  and  $66.43 \pm 13.03$ , respectively). There was no significant difference in the strength and endurance of the subjects colonized by *P. aeruginosa* and with FEV<sub>1</sub> < 80% compared with their healthy controls (Fig. 2, B and D).

Separately correlating children and adolescents with cystic fibrosis colonized by *P. aeruginosa* and with FEV<sub>1</sub> < 80%,  $P_{I_{max}}$  did not show a significant correlation with other pulmonary function parameters. However, there was a significant correlation between inspiratory muscle endurance and the airway resistances (R10 and R20). Likewise, when separately analyzing subjects with *P. aeruginosa* colonization and with FEV<sub>1</sub> > 80%, there was a significant correlation of  $P_{I_{max}}$  with FVC, FEV<sub>1</sub>, and total lung capacity, whereas endurance was not significantly correlated with other pulmonary function parameters. These results are presented in Table 3.

## Discussion

The results of the present study show that individuals with cystic fibrosis and a milder presentation of the disease (ie, without chronic colonization by *P. aeruginosa* and with a FEV<sub>1</sub> within the normal limits) present increased inspiratory muscle strength and reduced endurance compared with healthy individuals. On the other hand, subjects with chronic colonization by *P. aeruginosa* and reduction of FEV<sub>1</sub> do not show differences compared with their healthy peers.

In general, considering the entire sample studied, our findings demonstrate that subjects with cystic fibrosis present an increase of inspiratory muscle strength. Other researchers found similar results.<sup>3,4,28,29</sup> Dunnink et al<sup>4</sup> suggest that the increased work of breathing due to airway obstruction could cause an effect of conditioning the respiratory muscles. On the contrary, some studies<sup>5,12,30,31</sup> showed a reduction of respiratory muscle strength, associating this finding with hyperinflation and malnutrition. Furthermore, Dassios et al<sup>32</sup> showed that maximum respiratory pressures were significantly diminished in subjects with no severe lung disease; however, no correlation between  $P_{I_{max}}$  and BMI was found. The results of the present study in children and adolescents demonstrate a positive

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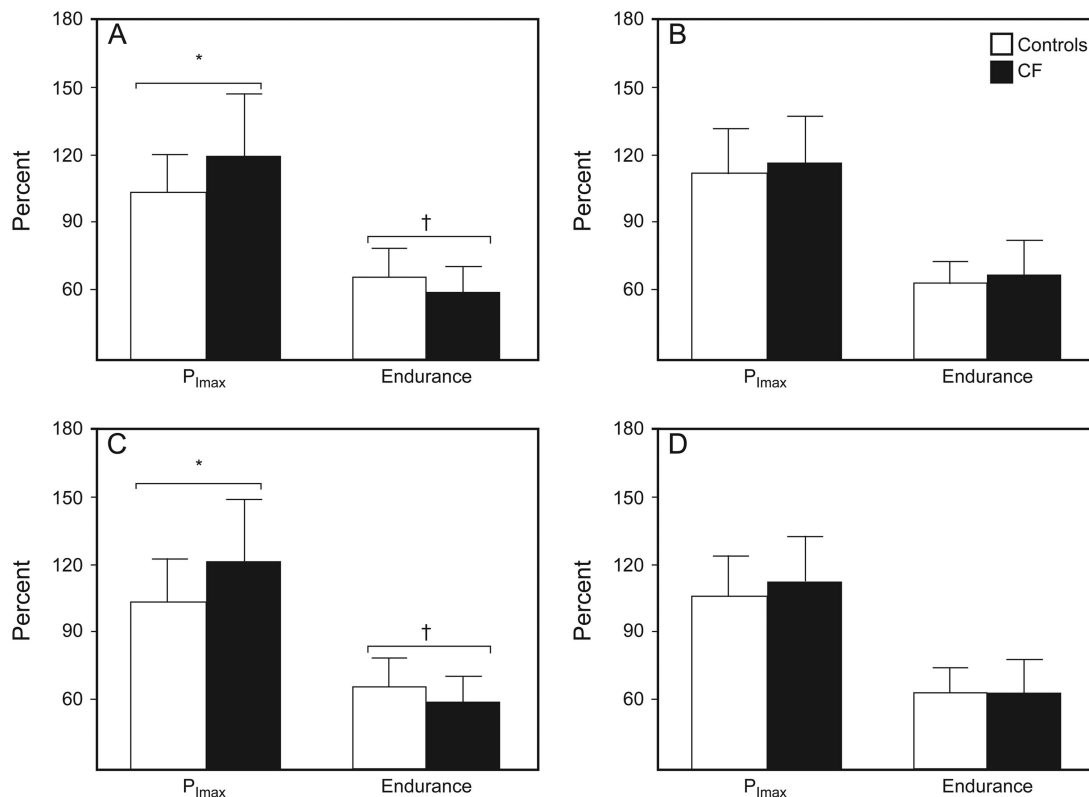


Fig. 2. Comparison of the inspiratory muscle strength ( $P_{Imax}$ ) and endurance between subjects with cystic fibrosis and healthy controls. A: Comparison between subjects with cystic fibrosis without colonization by *P. aeruginosa* and healthy subjects. B: Comparison between subjects with cystic fibrosis with colonization by *P. aeruginosa* and healthy individuals. C: Comparison between subjects with cystic fibrosis with  $FEV_1 > 80\%$  and healthy subjects. D: Comparison between subjects with cystic fibrosis with  $FEV_1 < 80\%$  and healthy subjects. A: \*,  $P = .003$ ; †,  $P = .02$ ; C: \*,  $P = .005$ ; C: †,  $P = .050$ .

Table 3. Pearson Correlation Coefficients for Airway Resistance, Spirometry, and Plethysmography in Relation to the Values of Strength and Endurance of the Inspiratory Muscles: Data Presented Separately for Subjects With and Without Colonization by *P. aeruginosa* and With  $FEV_1$  Greater or Less Than 80%

Variables	No PA (n = 25)		PA (n = 9)		$FEV_1 > 80\%$ (n = 21)		$FEV_1 < 80\%$ (n = 13)	
	$P_{Imax}$	Endurance	$P_{Imax}$	Endurance	$P_{Imax}$	Endurance	$P_{Imax}$	Endurance
R5	-0.33	-0.01	-0.21	0.64	-0.38	0.09	-0.15	0.49
R10	-0.38	0.09	0.06	0.86*	-0.49†	0.21	0.08	0.64†
R20	-0.32	0.06	0.05	0.82*	-0.36	0.20	0.01	0.65†
$FEV_1$	0.46*	-0.03	0.31	0.05	0.68*	-0.24	0.41	0.42
FVC	0.51*	0.07	0.26	0.23	0.62*	-0.06	0.31	0.68†
TLC	0.63*	-0.01	-0.06	0.10	0.51†	0.16	0.09	0.20

No PA = without chronic colonization by *P. aeruginosa*

PA = with chronic colonization by *P. aeruginosa*

$P_{Imax}$  = maximum inspiratory pressure

TLC = total lung capacity

R5 = total resistance of airways

R10 = resistance of the airway at a frequency of 10 Hz

R20 = central resistance of airways.

\*  $P < .01$ .

†  $P < .05$ .

correlation between  $P_{I_{max}}$  and BMI Z score, indicating influence of the nutritional aspect on respiratory muscle strength. However, in the study by Ziegler et al,<sup>5</sup> the reduction of strength was not related to the nutritional status in adult subjects with cystic fibrosis. It can be suggested that airway obstruction and compromised nutritional status interact in opposite directions in the different subjects, making it difficult to separately interpret the correlations obtained.

Unlike respiratory muscle strength, few studies have evaluated inspiratory muscle endurance in subjects with cystic fibrosis. In 1977, Keens et al,<sup>11</sup> despite using a different methodology, demonstrated increased endurance, supposedly due to the adaptation of the muscles to the chronic stress of ventilating against a load generated by airway obstruction. On the other hand, few studies found a reduction of this capacity, and they did not find evidence of a relationship with nutritional status, presence of airway obstruction, pulmonary hyperinflation, respiratory muscle strength, or maximum capacity for exercise.<sup>3,12</sup> Likewise, our results did not present a correlation of endurance with BMI Z score or with lung volumes. When we analyzed the entire sample studied, we did not identify differences in endurance compared with healthy controls. It is possible that this is related to the inclusion of many young subjects with little respiratory compromise in the present study and to the variability of endurance according to different levels of pulmonary involvement. In a study of subjects with COPD, diminished endurance was related to pulmonary hyperinflation.<sup>9</sup> However, our results demonstrate a significant correlation with airway resistance, indicating that increased resistance may influence the regulation of endurance.

Colonization by *P. aeruginosa* is associated with greater deterioration of lung function and is seen as a limiting factor in subjects' survival.<sup>33,34</sup> Our results show that children and adolescents with chronic *P. aeruginosa* colonization present worse FEV<sub>1</sub> values and increased total and central airway resistances, corroborating the study by Welsh et al,<sup>35</sup> who demonstrated that *P. aeruginosa* infection is a major predictor for FEV<sub>1</sub> decline. Likewise, subjects with FEV<sub>1</sub> reduction, regardless of *P. aeruginosa* colonization, present increased resistance of the airways, RV, and functional residual capacity.<sup>36</sup> Subjects with a milder presentation of the disease show greater strength and less inspiratory muscle endurance. On the contrary, subjects with diminished pulmonary function and *P. aeruginosa* colonization do not present any difference in strength and endurance compared with healthy individuals. Thus, it is possible that patients with cystic fibrosis develop decreasing muscle strength and increasing endurance, demonstrating that the decline of pulmonary status affects these 2 parameters differently, although a longitudinal study would be necessary to specifically answer this question. More-

over, a reduction of endurance has already been demonstrated in adults,<sup>12</sup> and further studies showed a reduction of 15–40% of  $P_{I_{max}}$  in subjects with moderate air flow obstruction. These findings could suggest that at advanced stages of the disease, patients are no longer able to maintain respiratory muscle strength.

Our findings also demonstrate that in individuals with cystic fibrosis, inspiratory muscle strength is more dependent on pulmonary function, since it was correlated with spirometry and plethysmography. However, endurance appears to depend more on airway resistance, especially with the central component, since we found a correlation with R20. Thus, we can suggest that the increased airway resistance over time generates increased muscle endurance, because ventilation with an increased load caused by airway obstruction can lead to endurance training. This training, on the other hand, does not appear to generate a significant effect on inspiratory muscle strength. Further, diminished pulmonary function, as a consequence of disease progression and associated with increased RV, would have the opposite effect, contributing to weakening the inspiratory muscles, since subjects with less pulmonary involvement present increased muscle strength. This may be explained by the positioning of the diaphragm dome and diminished zone of diaphragm apposition, so that the traction forces of the diaphragm fibers are placed in an almost horizontal position,<sup>37</sup> generating a mechanical disadvantage, with reduction of their capacity to distend and with consequent reduction of inspiratory muscle strength.<sup>38</sup> As far as we know, this is the first study demonstrating that strength and endurance of inspiratory muscles depend on the degree of pulmonary involvement and are associated with distinct pathophysiological mechanisms in children and adolescents with cystic fibrosis.

The main limitation of our study is the use of analyses with subsamples, since the reduced sample size in subgroups may influence the results. However, post-analysis power calculations indicate sufficient power to support the conclusions. The use of controls at a proportion of 1:2 may have helped to minimize these effects in the present study.

## Conclusions

In conclusion, children and adolescents with cystic fibrosis with no colonization by *P. aeruginosa* and normal lung function present increased inspiratory muscle strength and decreased endurance compared with healthy individuals, indicating that changes in respiratory muscle function seem to be distinctly associated with pulmonary involvement. In addition, strength appears to be more closely related to lung function parameters, whereas endurance has a greater correlation with airway resistance.

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