

# Relationship Between Nutritional Status and Maximum Inspiratory and Expiratory Pressures in Cystic Fibrosis

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**BACKGROUND:** Malnutrition might be expected to result in reduced maximum respiratory pressure and pulmonary function in cystic fibrosis (CF). **OBJECTIVE:** To assess the relationship between nutritional status and maximum respiratory pressures in patients with CF. **METHODS:** We performed a prospective cross-sectional study of patients  $\geq 16$  y old attending the Adult CF Program at Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil. Maximum inspiratory and expiratory pressures (MIP and MEP) were measured as indexes of respiratory muscle strength. Nutritional status was assessed via body mass index (BMI), triceps-skin-fold thickness and mid-upper-arm-muscle circumference. The patients were classified into 2 groups according to BMI: normal and nutritional depletion. Spirometry was performed by all subjects. **RESULTS:** The study included 39 patients (23 female/16 male) with a mean age of  $23.7 \pm 6.4$  y. The mean  $\pm$  SD percent-of-predicted MIP was  $88.0 \pm 28.5\%$  in the normal group and  $83.2 \pm 27.3\%$  in the nutritional-depletion group ( $p = 0.605$ ). The mean  $\pm$  SD percent-of-predicted MEP was  $84.7 \pm 24.2\%$  in the normal group and  $86.1 \pm 26.3\%$  in the nutritional-depletion group ( $p = 0.874$ ). The mean  $\pm$  SD percent-of-predicted forced expiratory volume in the first second ( $FEV_1$ ) was  $55.2 \pm 27.5\%$  in the normal group and  $50.0 \pm 25.6\%$  in the nutritional-depletion group ( $p = 0.568$ ). MEP and MIP had no significant correlation to BMI or  $FEV_1$ . **CONCLUSION:** MEP and MIP had no significant relationship to nutritional status, clinical score, chest radiograph score, and pulmonary function. *Key words:* cystic fibrosis, nutrition, pulmonary function, respiratory. [Respir Care 2008;53(4):442–449. © 2008 Daedalus Enterprises]

## Introduction

Cystic fibrosis (CF) is a progressive disease associated with malnutrition, chronic air-flow limitation, pulmonary

hyperinflation, and increased respiratory muscle work.<sup>1,2</sup> Malnutrition might be expected to reduce respiratory muscle strength and to decrease pulmonary function,<sup>3</sup> but studies of respiratory muscle strength in patients with CF have had conflicting results, showing either decreased,<sup>4–8</sup> normal,<sup>9–13</sup> or supranormal values.<sup>14–16</sup> These contradictory results might be explained by the heterogeneity of the clinical profiles of the patients studied (eg, differences in age, degree of respiratory compromise, or nutritional status) or by the different methods used to assess respiratory muscle strength.<sup>17</sup>

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Maximum inspiratory pressure (MIP) (measured at the mouth) and maximum expiratory pressure (MEP) are simple ways to gauge inspiratory and expiratory muscle strength. Although MEP and MIP are volitional tests and require full cooperation, they are easy to perform and are well tolerated by patients. The recent development of hand-held spirometers means that MEP and MIP may be easily measured at the bedside. MEP and MIP are widely used specific tests of respiratory muscle strength.<sup>18</sup>

A previous report found that percent of ideal body weight is an independent predictor of mortality in CF.<sup>19</sup> However, nutritional depletion does not involve the respiratory muscles to a similar extent in all patients. Assessing nutritional status and respiratory muscle strength may help identify patients at risk of ventilatory failure. Therapeutic interventions aimed at increasing respiratory muscularity and strength might be particularly relevant in these patients.<sup>17</sup>

The main purpose of this study was to assess the relationship between nutritional status and MEP and MIP in patients in the Adult CF Program at Hospital de Clínicas de Porto Alegre, and to correlate nutritional status and MEP and MIP with chest radiograph score, clinical score, and pulmonary function in these patients.

## Methods

### Patient Population

The study included 39 patients (23 female, 16 male)  $\geq 16$  years old, recruited from the Adult CF Program at Hospital de Clínicas de Porto Alegre. The diagnosis of CF required abnormal sweat test and clinical features, according to the consensus statement of the Cystic Fibrosis Foundation Consensus Panel.<sup>20</sup> At the time of the study, all the patients were in stable condition and had no recent changes in pulmonary function, radiographic appearance, or increase in cough, sputum amount, or fever. No change was made in the patients' routine therapy in the month before inclusion in the study. None of the patients were receiving oral steroids or supplemental feeding through a gastrostomy tube. Patients were excluded if they were pregnant or had a condition that we thought could impair our ability to perform the maximum static expiratory and inspiratory pressure maneuvers.

### Study Design

This was a single-center, prospective, cross-sectional study. All patients attending the Adult CF Program at Hospital de Clínicas de Porto Alegre who volunteered for the study were included. Each patient had a comprehensive evaluation in the out-patient clinic. The senior member of the research team (PTRD) performed the assessment of clinical stability. In the same week an evaluation

of nutritional status, a pulmonary function test, a chest radiograph, and the MEP and MIP maneuvers were performed with each patient. The protocol was approved by the Hospital de Clínicas de Porto Alegre ethics committee, and informed consent was obtained from each patient.

### Maximum Static Inspiratory and Expiratory Pressures

MEP and MIP were used as indices of respiratory muscle strength. MEP and MIP measurements were made with the subject in the seated position, with a digital manometer (MVD [-500/+500], version 1.0, Microhard, Porto Alegre, Brazil). All subjects wore nose clips and pressed their lips tightly against the mouthpiece to prevent air leaks.

MIP was measured starting at residual volume. MEP was measured starting at total lung capacity. The pressure measured was maintained for at least 1 s. Five repeated measurements were made, with a suitable rest pause between the measurements, until a plateau value was reached and no further learning effect was seen.<sup>21</sup> Once the operator was satisfied, the MEP and MIP of 2 maneuvers that differed by  $< 10\%$  were recorded. All MEP and MIP measurements were performed by the same member of the research team (BZ), in the out-patient setting.

The predicted MIP and MEP values were from Neder et al.<sup>22</sup>

### Clinical and Radiograph Scores

All the clinical scores were determined by the same senior member of the CF team (PTRD), in the out-patient setting, with the Shwachman-Kulczycki scoring system for CF severity.<sup>23</sup> The chest radiographs were scored with the Brasfield scoring system<sup>24</sup> by another senior member of Serviço de Pneumologia, Hospital de Clínicas de Porto Alegre, who was blinded to the clinical severity status of the patients.

### Pulmonary Function Tests

Pulmonary function tests were measured with a computerized spirometer (Jaeger, version 4.31a, Würzburg, Germany). The forced expiratory volume in the first second (FEV<sub>1</sub>), forced vital capacity (FVC), and FEV<sub>1</sub>/FVC were measured 3 times, and the best trial was reported, per the guidelines of the American Thoracic Society and European Respiratory Society.<sup>25</sup> The pulmonary function variables are expressed in absolute values and percent-of-predicted values for age, stature, and sex.<sup>26</sup>

### Anthropometric Variables

Nutritional status was assessed via body mass index (BMI), BMI percentile,<sup>27</sup> triceps-skin-fold thickness, mid-

upper-arm circumference, and mid-upper-arm-muscle circumference.<sup>28</sup> Triceps-skin-fold thickness was measured with a skin-fold caliper (Lange, Beta Technology, Santa Cruz, California) at the mid-point of the left arm, between the acromion process and the tip of the olecranon. The mean of 3 readings was recorded. Mid-upper-arm circumference was determined with a flexible tape, at the mid-point of the left arm, between the acromion process and the tip of the olecranon. Mid-upper-arm-muscle circumference was calculated as follows: mid-upper-arm circumference - (0.314 × triceps-skin-fold thickness). All anthropometric measurements were made by the same researcher (CLO). Triceps-skin-fold thickness, mid-upper-arm circumference, and mid-upper-arm-muscle circumference are expressed as percent-of-predicted at the 50th percentile for a specific age.<sup>29</sup>

The patients' nutritional status was classified as either normal (BMI ≥ 20 kg/m<sup>2</sup> in patients ≥ 18 years old, BMI percentile > 25 in patients < 18 years old) or nutritional depletion (BMI < 20 kg/m<sup>2</sup> in patients ≥ 18 years old, BMI percentile < 25 in patients < 18 years old).<sup>2,27,28</sup>

### Statistical Analysis

The data are expressed as number of cases, mean ± SD, or median with interquartile range. Student's *t* test or Mann-Whitney U test was used to compare continuous variables. Categorical comparisons were via chi-square test, Fisher's exact test, and Yates's corrected chi-square when indicated. Correlations of MIP and MEP with FEV<sub>1</sub>, FVC, and BMI were via Pearson linear correlation. Correlations of MIP and MEP with mid-upper-arm circumference, triceps-skin-fold thickness, Shwachman-Kulczycki score, and Brasfield score were via Spearman's rank correlation. Data analysis was carried out with statistics software (SPSS 13.0, SPSS, Chicago, Illinois). Differences were considered statistically significant when *p* < 0.05. All probabilities reported were 2-tailed. We calculated the sample size with correlation for MIP/MEP and BMI. We determined an adequate sample size to be at least 37 subjects at  $\alpha = 0.05$ ,  $1 - \beta = 80\%$ , and the expected correlation coefficient (effect size) was 0.4.<sup>30</sup>

### Results

Thirty-nine of 41 patients who attended the Adult CF Program at Hospital de Clínicas de Porto Alegre during the study period were included. One patient refused to participate. Another patient did not attend the out-patient clinic during the study period. The subjects' mean ± SD age was 23.7 ± 6.4 y (range 16–47 y). There were 16 male and 23 female subjects. All the subjects were white.

Table 1 shows the data relative to the subjects' nutritional status. There were 24 subjects in the normal-nutri-

tion group and 15 in the nutritional-depletion group. The mean ± SD BMI was 21.5 ± 1.7 kg/m<sup>2</sup> in the normal-nutrition group and 18.3 ± 1.1 kg/m<sup>2</sup> in the nutritional-depletion group. The 2 groups did not differ significantly in age, age at diagnosis, sex, Schwachman-Kulczycki score, Brasfield score, percent-of-predicted FEV<sub>1</sub>, percent-of-predicted FVC, MIP, percent-of-predicted MIP, MEP, or percent-of-predicted MEP. In 17 subjects (43.6%), MIP was below the lower limit of normal (10 in the normal-nutrition group and 7 in the nutritional-depletion group, *p* > 0.05). In 19 subjects (48.7%), MEP was below the lower limit of normal (12 in the normal-nutrition group and 7 in the nutritional-depletion group, *p* > 0.05). The median values of triceps-skin-fold thickness and mid-upper-arm-muscle circumference were significantly lower in the nutritional-depletion group (100.0% and 90.9% of predicted, respectively) than in the normal-nutrition group (80.0% and 84.0% of predicted, respectively, *p* < 0.05).

In the normal-nutrition group, 10 subjects (25.6%) had mid-upper-arm-muscle circumference below 80% of predicted, 6 subjects (15.4%) had triceps-skin-fold thickness below 80% of predicted, and 3 subjects (7.7%) had both mid-upper-arm-muscle circumference and triceps-skin-fold thickness below 80% of predicted.

Figure 1 shows the correlations between MEP and MIP and clinical and chest radiograph score. Figure 2 shows the correlations between MEP and MIP and body mass index and FEV<sub>1</sub>. There was no correlation between percent-of-predicted MIP and Shwachman-Kulczycki clinical score (*r* = -0.12, *p* = 0.468) (see Fig. 1), Brasfield score (*r* = -0.25, *p* = 0.134) (see Fig. 1), percent-of-predicted FEV<sub>1</sub> (*r* = -0.08, *p* = 0.640) (see Fig. 2), percent-of-predicted FVC (*r* = -0.13, *p* = 0.450), BMI (*r* = 0.12, *p* = 0.480) (see Fig. 2), percent-of-predicted triceps-skin-fold thickness (*r* = 0.04, *p* = 0.831), or percent-of-predicted mid-upper-arm-muscle circumference (*r* = 0.13, *p* = 0.441). There was no correlation between percent-of-predicted MEP and Shwachman-Kulczycki clinical score (*r* = -0.24, *p* = 0.130) (see Fig. 1), Brasfield score (*r* = -0.02, *p* = 0.929) (see Fig. 1), percent-of-predicted FEV<sub>1</sub> (*r* = -0.27, *p* = 0.111) (see Fig. 2), percent-of-predicted FVC (*r* = 0.13, *p* = 0.445), BMI (*r* = 0.02, *p* = 0.922) (see Fig. 2), percent-of-predicted triceps-skin-fold thickness (*r* = 0.05, *p* = 0.779), or percent-of-predicted mid-upper-arm circumference (*r* = -0.12, *p* = 0.487).

### Discussion

The present study found no relationship between nutrition status and MEP and MIP in patients with CF ≥ 16 years old. MIP was below the lower limit of normal in 43.6% of the subjects. MEP was below the lower limit of normal in 48.7% of the subjects. Previous studies<sup>14–16</sup> found

Table 1. Results Grouped According to Nutritional Status

Variable	Normal Subjects (n = 24)	Subjects With Nutritional Depletion (n = 15)	p
Age (mean ± SD y)	24.1 ± 7.4	23.0 ± 4.5	0.615*
Age at diagnosis (mean ± SD y)	8.0 (18.0)	10.0 (13.0)	0.259*
Male/female	10/14	6/9	0.999*
BMI (mean ± SD kg/m <sup>2</sup> )	21.5 ± 1.7	18.3 ± 1.1	< 0.001*
Triceps-skin-fold thickness (% predicted and interquartile range)	100.0 (81.5–128.0)	80.0 (53.0–92.4)	0.014†
Mid-upper-arm-muscle circumference (% predicted and interquartile range)	90.9 (83.5–97.5)	84.0 (74.5–91.0)	0.031†
Schwachman-Kulczycki score (mean ± SD)	76.3 ± 10.7	73.7 ± 14.5	0.555*
Brasfield score (mean ± SD)	15.6 ± 4.0	17.3 ± 3.2	0.184*
FEV <sub>1</sub> (mean ± SD % predicted)	55.2 ± 27.5	50.0 ± 25.6	0.568*
FVC (mean ± SD % predicted)	66.4 ± 25.0	65.6 ± 21.4	0.920*
MIP (mean ± SD cm H <sub>2</sub> O)	100.6 ± 35.1	91.8 ± 30.1	0.425*
MIP (mean ± SD % predicted)	88.0 ± 28.5	83.2 ± 27.3	0.605*
MIP below the lower limit of normal (n)	10	7	0.815‡
MEP (mean ± SD cm H <sub>2</sub> O)	102.5 ± 40.2	102.3 ± 38.5	0.988*
MEP (mean ± SD % predicted)	84.7 ± 24.2	86.1 ± 26.3	0.874*
MEP below the lower limit of normal (n)	12	7	0.419‡

\*Via Student's *t* test

†Via Mann-Whitney U test for continuous variables

‡Via chi-square test for categorical variables

BMI = body mass index

FEV<sub>1</sub> = forced expiratory volume in the first second

FVC = forced vital capacity

MIP = maximum inspiratory pressure

MEP = maximum expiratory pressure

that MEP and MIP were normal or above normal in patients with CF. The absolute MEP and MIP values in those studies were compared with MEP and MIP values from control subjects, whereas we obtained our predicted values from Neder et al.<sup>22</sup> Our findings closely compare to those reported by Mier et al,<sup>6</sup> who obtained their predicted MIP and MEP values from Wilson et al.<sup>31</sup> They reported MIP below 75% of predicted in 56%, and MEP below 75% of predicted in 64% of CF subjects.

Studies of respiratory muscle function in CF are difficult to compare because of age differences among the study subjects, the study methods, and the indices of muscle function.<sup>4</sup> MIP or MEP have been the main measurements used.<sup>6,8,15,16</sup> The tendency has been for MIP in particular to appear to be well preserved in patients with CF,<sup>4,6,8,15,16</sup> which is in keeping with our findings.

The habituation session may increase the subject's ability to perform the MEP and MIP maneuvers. The rationale for the habituation session was demonstrated by the work of Volianitis et al,<sup>21</sup> who studied 14 healthy subjects to investigate the influence of a specific respiratory warm-up on the repeated measurement of inspiratory muscle strength and to establish a procedure by which MIP can be assessed with maximum reliability in the smallest number of maneuvers. The present data suggest that a specific respira-

tory warm-up may attenuate the learning effect during the repeated MIP measurements, which is one of the main contributors to test variability. Respiratory warm-up may help obtain reliable MIP values in just 3 measurements.

MIP and MEP have wide intra-subject variability. This has been attributed to the patient's motivation and abilities, day-to-day fluctuations in performance, coordination of the respiratory muscles, learning effects, and the lung volumes from which measurements were obtained. Enright et al<sup>32</sup> recruited 20 subjects with CF (mean ± SD age 23.7 ± 3.4 y) and 20 matched healthy controls to investigate the reproducibility of MIP and respiratory muscle endurance, by measuring respiratory work capacity on 2 occasions after a period of habituation. That study suggests that this measure may be considered reliable and reproducible in both controls and patients with CF. Other researchers<sup>21,33</sup> who used a period of familiarization with the maneuver also found positive results for MEP and MIP reproducibility.

The functioning of the respiratory muscles can be compromised by various factors, including hyperinflation, skeletal abnormalities, restrictive or obstructive lung disease (increased work of breathing), neuromuscular disease, malnutrition, age, and obesity.<sup>3</sup>

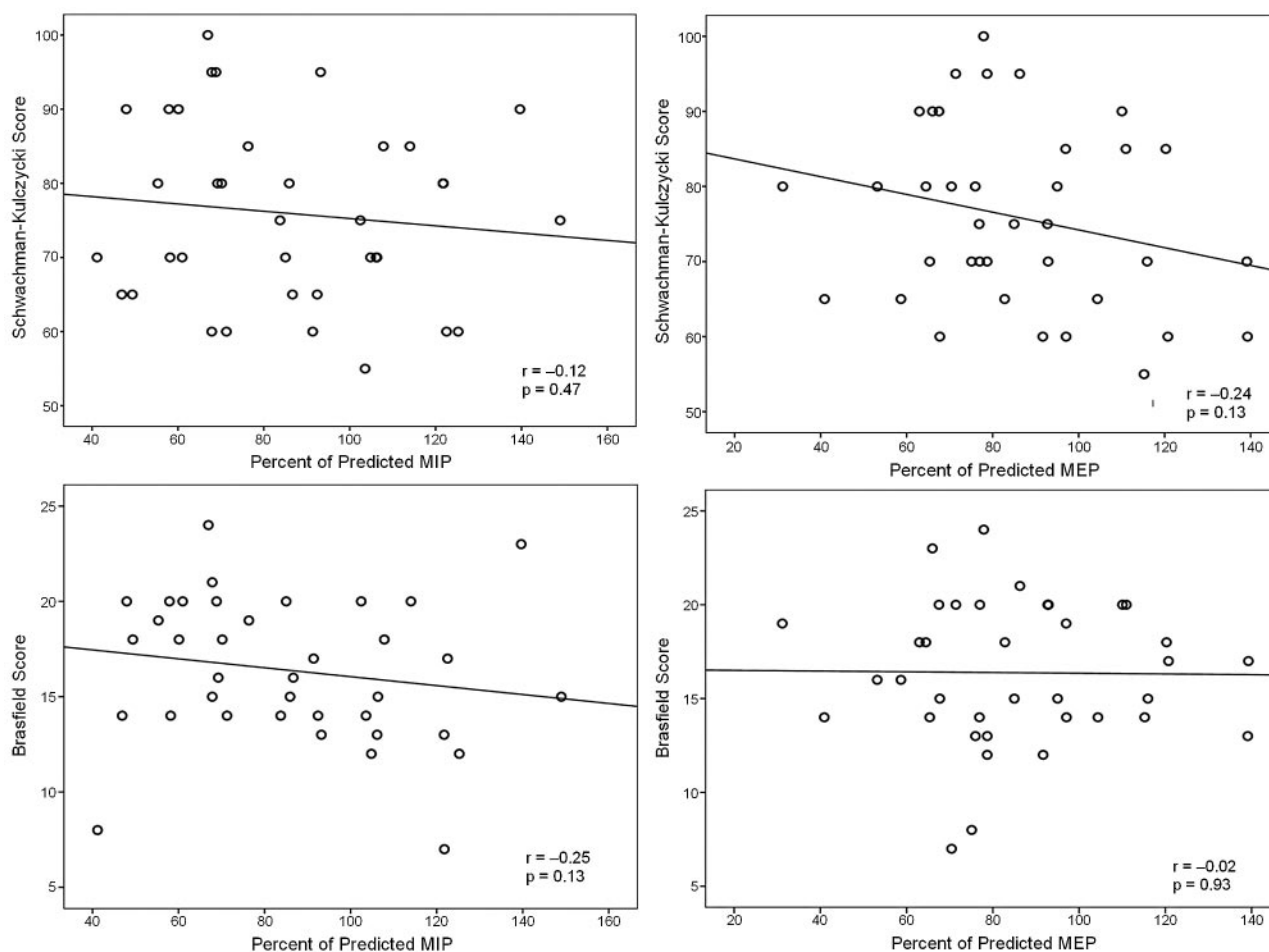


Fig. 1. Correlations between maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), Schwachman-Kulczycki score (scoring system for clinical severity of cystic fibrosis), and Brasfield score (chest radiograph scoring system).

In previous studies MIP and MEP were significantly associated with nutritional status and were related to arm-muscle circumference in patients with CF.<sup>8</sup> Ionescu et al<sup>4</sup> reported lower MIP and sustained MIP in patients with CF with low lean body mass, ideal body weight percentage compared with patients with CF with normal lean body mass, and ideal body weight percentage. When related to absolute lean body mass, the MIP and sustained MIP were not different between the low and normal groups. Our findings are consistent with those of O'Neill et al<sup>16</sup> and Marks et al,<sup>15</sup> who found that in patients with CF the MEP and MIP were not significantly related to nutritional status. Other potential factors should be considered to explain the differences between the reports. Pinet et al<sup>17</sup> studied diaphragm function and bulk in patients with CF and matched controls. They concluded that diaphragm strength is decreased in CF. Diaphragm muscle bulk was not affected by the general muscle wasting, which suggests that there may be a training effect of CF on respiratory muscles. However, the variability of diaphragm mass indicates that this

beneficial response does not occur in all patients with CF and that wasting does not involve the diaphragm to a similar extent in all patients. Others reports demonstrated that inspiratory muscle strength improved after inspiratory muscle training.<sup>14,34</sup>

Malnutrition in CF is multifactorial and might include the energy cost of the gene defect itself, poor energy intake, increase in resting energy expenditure, less efficient pulmonary mechanics, and catabolic intermediary metabolism secondary to pulmonary infection and inflammation.<sup>35,36</sup> These mechanisms are likely to lead to a negative energy balance, with consumption of host tissues as substrate. The main impact of weight loss in adults with CF is likely to fall on skeletal muscle mass because there is usually a reduced fat mass.<sup>4</sup> Clinical assessment of nutritional status is primarily via anthropometry of height, weight, mid-upper-arm-muscle circumference, and triceps-skin-fold thickness. Normative data are available for these measurements in adults.<sup>27,29</sup> For adults older than 18 years of age, the

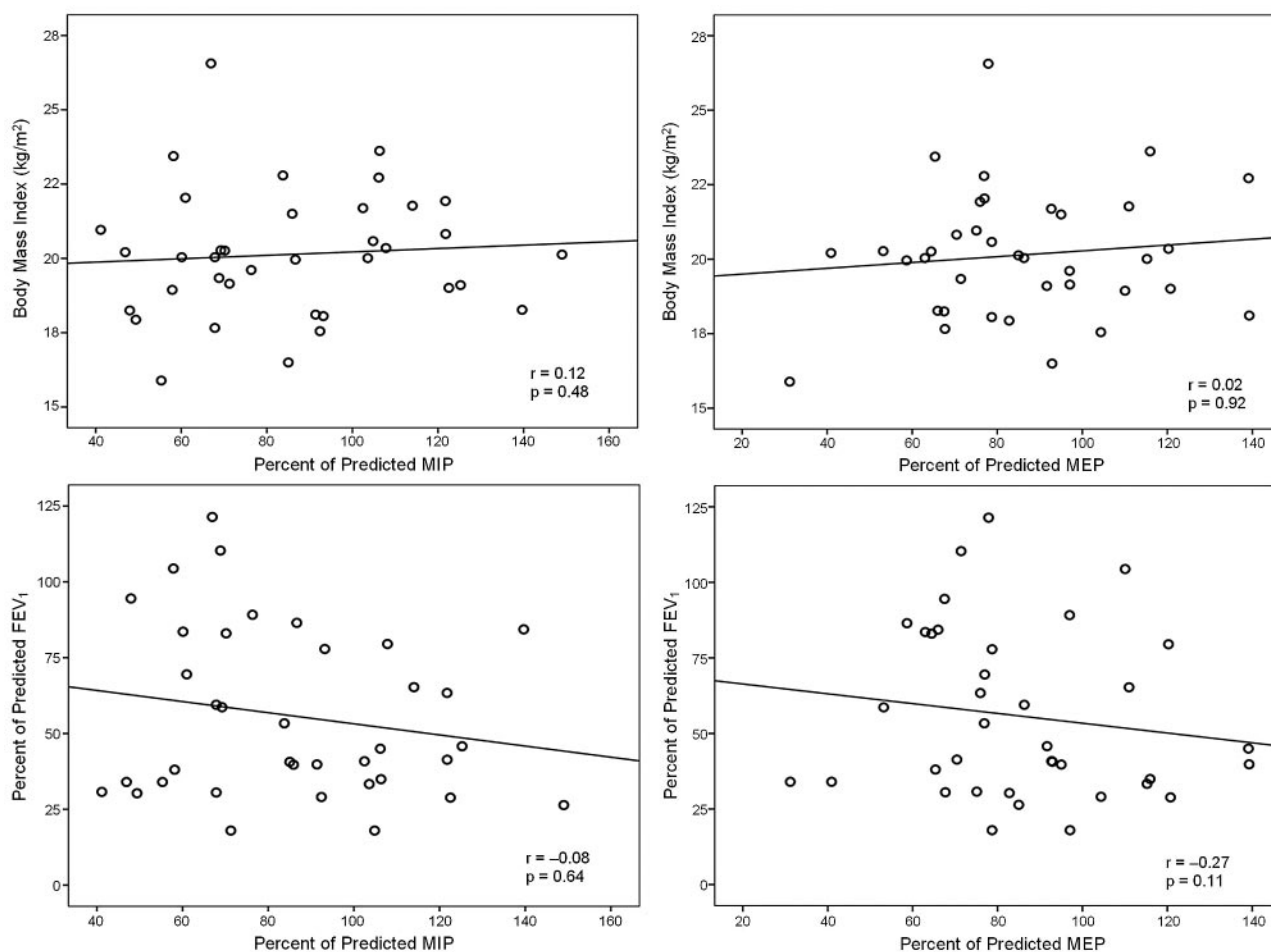


Fig. 2. Correlations between maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), body mass index, and forced expiratory volume in the first second (FEV<sub>1</sub>).

BMI also is used for studies of under-nutrition.<sup>2</sup> The normal BMI range is 20–25 kg/m<sup>2</sup> and is independent of age and sex in adults. BMI does not reflect body composition, so triceps-skin-fold thickness (which reflects fat mass) and mid-upper-arm-muscle circumference (which reflects muscle mass) are useful adjuncts to height and weight measurements.<sup>27</sup> In our study, 15 of 39 subjects (39%) were classified as having nutritional depletion, with a mean BMI of  $18.3 \pm 1.1$  kg/m<sup>2</sup>. The normal-nutrition and nutritional-depletion groups did not differ significantly in Schwachman-Kulczycki score, Brasfield score, FEV<sub>1</sub>, or FVC. This finding could be explained by other variables that affect pulmonary disease but this was not evaluated in this study. Our normal-nutrition subjects had significantly larger triceps skin-folds and mid-upper-arm-muscle circumference than did our nutritional-depletion subjects, but we did not perform a secondary analysis of this. And there was no significant correlation of those variables with MIP and MEP.

### Limitations

In this study BMI was the main anthropometric variable used to assess nutritional status. The use of BMI in isolation could be considered a methodological limitation. Ionescu et al<sup>37</sup> studied 56 patients with proven CF (mean age 23.0 y) and 20 age-matched healthy subjects (mean age 23.6 y) to study the hypothesis that some adults with CF and a normal BMI have evidence of hidden fat-free mass and bone mineral density depletion. They found that a proportion of patients have a hidden depletion of fat-free mass while BMI and fat mass are maintained. Patients with CF had a lower total fat-free mass than did healthy subjects, whereas fat mass was similar. BMI has been found to be normal in 40% of nutritionally depleted patients. Instead, the BMI is used routinely to assess the nutritional status in many CF centers, as recommended by international consensus.<sup>28</sup>

We did not use correction for abnormal lung volume. In patients with abnormally high lung volume a low MIP

may partly reflect the shortened inspiratory muscle fiber length associated with increased lung volume at residual volume rather than reduced inspiratory muscle strength.<sup>18</sup> This would have caused the MIP values to be spuriously low and would have underestimated inspiratory muscle force in our study. In a previous study<sup>38</sup> we found that our patients had normal-or-lower total lung capacity, despite the increase in air-flow limitation and residual volume, so it is unlikely that MEP was affected by lung volume.

Another concern is the volitional nature of the MEP and MIP tests. One would presume that poor effort would increase variability and bias MEP and MIP to lower values. It can be difficult to ensure that the subject is making a truly maximal effort during the MIP or MEP maneuver, so it is hard to be certain whether low mouth pressure measurements represent reduced strength or merely reduced neural activation.<sup>18</sup> However, we used standardized MIP and MEP methods to reduce that risk, according to the standardized approach to test performance and measurements.<sup>18</sup> This presumably reduces the effort-dependent variability of the test.

Another important limitation was the small number and substantial heterogeneity of patients in our sample. We also lacked a control group; rather, our conclusions about MEP and MIP in this group refer to reference values from the literature.

### Conclusions

We found no significant relationship between nutritional status and MEP and MIP in these 39 patients with CF. However, MEP and MIP were reduced in these patients. We also found no significant relationship between MEP and MIP and clinical score, chest radiograph score, or pulmonary function. Though the present study suggests that in adult patients with CF there is no relationship between respiratory muscle strength and malnutrition, these results might be explained on the basis of the heterogeneity of the older CF population we studied.

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