Cystic fibrosis (CF) is a multisystem autosomal recessive disorder caused by the mutation of a single gene that encodes for the CF transmembrane regulator protein. Clinically, CF is characterized by chronic pulmonary infection, pancreatic insufficiency, and excessive losses of sweat electrolytes. Along with lung function, nutritional status appears one of the most important prognostic indicators in CF patients. In this study we examined the relationship between nutritional status and pulmonary function in adult CF patients. A group of 39 CF patients (mean age 23.9 ±3.7 years) was studied. The mean value of body mass index (BMI) was 19.5 ±2.9 kg/m² (12.8-24.9 kg/m²). The patients were grouped according to the presence or absence of malnutrition. Malnutrition was established in 11 patients (28.2%), 5 patients suffered from severe malnutrition. 28 patients (71.8%) had a normal nutritional status, but according to ESPEN guidelines, 9 of those patients were at risk of malnutrition. Statistical analysis revealed a significant difference between malnourished and not malnourished patients with respect to FEV₁% and FVC%. Moreover, the patients with malnutrition were significantly more frequently colonized by *P. aeruginosa* and fungi and less so by MSSA.

**Key words:** cystic fibrosis, lung function, malnutrition

**INTRODUCTION**

Cystic fibrosis (CF) is a multisystem autosomal recessive disorder caused by the mutation of a single gene that encodes for the CF transmembrane regulator protein. This protein regulates the passage of chloride through the apical membrane of secretory epithelia. Dysfunction of this protein results in altered composition of epithelial secretions. Clinically, CF is characterized by chronic pulmonary infection...
superimposed with periods of acute respiratory exacerbations, pancreatic insufficiency, and excessive losses of electrolytes in sweat (1). The mutated gene was identified in 1989 (2, 3). Since then more than 1560 CF transmembrane regulator protein mutations have been reported (4). This wide range of mutations is responsible for the variety of clinical manifestations of the disease (5).

Progressively more effective treatment of respiratory infections and more intensive nutritional support over the past 15-20 years have resulted in an impressive and continuing improvement in both physical condition and survival of many individuals with CF. Individuals born with CF today may expect to live into their 40s, double a similar prediction 20 years ago (6).

Along with lung function, nutritional status appears one important prognostic indicator in CF patients. Different studies use different indices of nutrition, but in majority of studies, poor nutritional status seems independently associated with poor prognosis (7). There is a direct association between the degree of undernutrition and the severity of pulmonary disease. Prevention of malnutrition from the time of diagnosis is associated with better lung function and improved survival (8).

MATERIAL AND METHODS

This study was conducted in the Department of Pulmonary Diseases, University of Medical Sciences in Poznan, Poland. Study protocol was approved by an institutional Ethics Committee. A group of 39 CF patients (21 females and 18 males) was enrolled into the study. The mean age was 23.9 ±3.7 years (range 18-33 years) (Table 1). The diagnosis of CF was based on positive sweat tests with typical clinical findings, with or without genotype confirmation.

Patients were grouped according to presence or absence of malnutrition. Body mass index (BMI) was used to single out the groups: normal weight (n=28) with BMI ≥18.5kg/m²; malnourished patients (n=11) with BMI <18.5kg/m² (9). The severity of lung disease was determined by spirometry. Pulmonary function was considered abnormal if forced vital capacity (FVC) or forced expiratory volume in 1 second (FEV₁) was below 80% of predicted value (10). According to the consensus report, FEV₁, expressed as the percent predicted of a healthy nonsmoking reference population, was accepted as the single objective measure of pulmonary status (11). The classification of severity of the lung disease was done on the basis of the ATS/ERS criteria (12).

The results were presented as means ±SD value (X ±SD), max-min value, and 95% of confidence interval (95%CI). Data analysis was performed according to the theoretical basis of Zar's (13), using a commercial SPSS package. The difference between two populations was assessed by a non-parametric Mann-Whitney U test. Correlations between BMI and pulmonary function parameters were assessed by Spearman's rank correlation test. A value of P<0.005 was considered to be significant.

RESULTS

The mean value of BMI was 19.5 ±2.9 kg/m² (range 12.8-24.9 kg/m²) for all CF patients (Table 1). Malnutrition was established in 11 patients (28.2%), 5 patients suffered from severe malnutrition. Twenty eight patients (71.8%) had
normal nutritional status. In the latter group (according to the ESPEN guidelines) 9 patients (23.1%) was a risk of malnutrition (18.5-19.9 kg/m$^2$) (Fig. 1).

BMI was significantly lower in CF female than in male patients; 20.3 ±3.2 (12.8-24.4) kg/m$^2$ vs. 18.9 ±2.2 (15.0-22.5) kg/m$^2$ (P=0.03). The majority of the CF patients with malnutrition were females; 63.6% vs. 50% in a group with normal nutritional status. The mean age of patients with malnutrition was significantly lower than that of patients with normal nutritional status (P=0.006) (Table 2). The increase of BMI correlated with increasing CF patients' age (Fig. 2).

The mean FEV$_1$% and FVC% in CF patients were 57.0 ±31.5 (17.3-127.0) and 63.2 ±29.0 (20.2-131.0), respectively. 25.6% of patients had FEV$_1$% in the normal range, the others had lung function impairment: mild (12.8%), moderate

Table 1. Demographic and spirometric data.

<table>
<thead>
<tr>
<th></th>
<th>n=39</th>
<th>Mean ± SD</th>
<th>Mediana</th>
<th>Min-max</th>
<th>95% CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>23.9 ±3.7</td>
<td>23</td>
<td>18-33</td>
<td>22.7-25.1</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (yr)</td>
<td>7.3 ±8.0</td>
<td>5.2</td>
<td>0.1-27.0</td>
<td>4.7-9.9</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>19.5 ±2.8</td>
<td>20.0</td>
<td>12.8-24.9</td>
<td>18.6-20.4</td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ (% predicted)</td>
<td>57.0 ±31.5</td>
<td>46.7</td>
<td>17.3-127.0</td>
<td>46.8-67.2</td>
<td></td>
</tr>
<tr>
<td>FVC (% of predicted)</td>
<td>63.2 ±29.0</td>
<td>58.3</td>
<td>20.2-131.0</td>
<td>53.7-72.6</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Sex, age, and BMI in cystic fibrosis patients with malnutrition and normal nutritional status.

<table>
<thead>
<tr>
<th></th>
<th>Females n=21</th>
<th>Males n=18</th>
<th>Age (yr)</th>
<th>BMI (kg/m$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malnutrition</td>
<td>7 (63.6%)</td>
<td>4 (36.4%)</td>
<td>21.6 ±2.3</td>
<td>15.9 ±1.4</td>
</tr>
<tr>
<td>Normal nutritional status</td>
<td>14 (50%)</td>
<td>14 (50%)</td>
<td>24.9 ±3.8</td>
<td>20.9 ±1.7</td>
</tr>
<tr>
<td>P=0.007</td>
<td>P&lt;0.0001</td>
<td>P=0.006</td>
<td>P&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Differences in spirometric parameters in patients with malnutrition and normal nutritional status. Data show means ±SD and range.

<table>
<thead>
<tr>
<th></th>
<th>FEV₁%</th>
<th>FVC%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malnutrition (n=11)</td>
<td>34.3 ±10.1</td>
<td>40.6 ±10.4</td>
</tr>
<tr>
<td></td>
<td>18.6-53.0</td>
<td>20.2-53.0</td>
</tr>
<tr>
<td>Normal nutritional status (n=28)</td>
<td>65.9 ±32.6</td>
<td>72.0 ±29.3</td>
</tr>
<tr>
<td></td>
<td>17.3-127.0</td>
<td>22.8-131.0</td>
</tr>
<tr>
<td></td>
<td>P=0.009</td>
<td>P=0.002</td>
</tr>
</tbody>
</table>

(5.1%), moderately severe (2.6%), severe (23.1%), and very severe (30.8%) (Fig. 3). There were no significant correlations between FEV₁% or FVC% and the patients' age. BMI correlated with the FEV₁% and FVC% (r=0.34, P≤0.03 for both). Statistical analysis revealed significant differences between malnourished and not malnourished patients concerning FEV₁% and FVC% (Table 3).

DISCUSSION

Negative impact of malnutrition on the long-term outcome of patients with CF has long been recognized (8). Early reports of nutrition in CF suggested that with
increasing age, the prevalence and severity of malnutrition progressively increased (14). This view is reflected in the statement from the consensus report on nutrition in CF that "there is no reason to accept nutritional failure and or impaired growth in any individual with CF" (15).

However, over years this disease was said to be more impressive due to its severe lung involvement, which is still one of the leading causes of death in both children and adults (16). Despite the fact that malnutrition becomes clinically visible in almost all patients over time, it is seems that, for a significant number of health professionals who deal with theses patients, nutrition is a second line problem. This is also substantiated by the number of presentations at the European Cystic Fibrosis meetings, e.g, in 2003 only 4.6% of total papers and presentations dealt with nutrition (17).

The present study demonstrates that malnutrition, or risk of malnutrition, remains a frequent complication of CF in adult patients. In almost 1/3 of the study group (28.2%) malnutrition was revealed, including 5 patients (12.8%) with severe malnutrition. Patients with malnutrition, and with risk of it, make up more than half the of study group (51.3%). These results are similar to those based on national registers from other European countries and the Cystic Fibrosis Foundation (CFF). According to the German 1997 and CFF 1998 reports, malnutrition is diagnosed in 21.6% and 38.0% CF patients, respectively (18, 19).

One inconvenience in a discussion on the nutritional status is that various authors use different parameters to assess it. Furthermore, the definition of malnutrition varies in the literature, e.g., according to the American consensus,
malnutrition is defined as BMI below 19.0 kg/m$^2$ (20), whereas others define it as BMI 16-20.0 kg/m$^2$. It seems that comparison of the mean BMI value may give a more objective interpretation. The mean BMI in our study group was 19.5 kg/m$^2$. An identical mean value of MBI was revealed in a group of 1009 adult CF patients in France (21) and somewhat larger one, 19.8 kg/m$^2$, in 150 adults with CF in Wales (22). This data suggest that the nutritional status of Polish adult CF patients is akin to that in other counties.

The assessment of lung function revealed that 29 patients (74.4%) had spirometric parameters out of normal range. The mean values of FEV$_1$ and FVC - 57.0 and 63.2% predicted, respectively - are comparable with the data from other CF centers. For example, the US Registry found that FEV$_1$ was less than 70% predicted in 68% of adult patients (19), and in Germany it is 54.5% (18). Accordingly, we can conclude that both the lung involvement and nutritional status are similar in CF adult patients across various nationalities. That is also confirmed by a study White et al (23) in which the only difference is the number of patients forming the study groups (82 vs. 39), concerning the mean age, BMI, FEV$_1$, or FVC% the results are similar.

Several reviews on nutrition tackled the relationship between the severity of pulmonary involvement and nutrition in CF patients, but supportive evidence has been limited and the studies usually involved mixed, pediatric and adults populations (24). The current study, similarly to those of Bell et al (22) and Nir et al (25), demonstrated a strong correlation between BMI and FEV$_1$%, and BMI and FVC. Despite the presence of a statistical correlation, FEV$_1$% for a given BMI is large, e.g., for a BMI of 19 kg/m$^2$, the FEV$_1$% in the current population ranged from 20.2 to more than 100% of predicted.

As nutritional supplementation with a high fat, high energy diet has been advised for over 10 years in Poland, improved nutrition might be expected in younger patients. Since the severity of lung involvement and nutrition are related, malnutrition may be expected to increase with advancing age. Yet, BMI positively correlated with age in the present study. The mechanism of the relationship is unclear, but, possibly, age and the preservation of a better nutritional status are related to a milder disease phenotype.

A study of Kerem et al (26) indicates that the best predictor of mortality is lung function, especially FEV$_1$%, which is closely related to survival. In contrast, the authors have found that the nutritional status is neither a good predictor nor closely related to survival. Another recent article has shown that the yearly rate of decline of the percentage of predicted FEV$_1$% is the most important variable to predict mortality, and that nutrition, presence of diabetes, or other variables serve as cofactors, having no appreciable on mortality of its own (27). The question of whether low weight is the cause or effect of declining pulmonary function has been repeatedly asked and remains to be determined.

In summary, this study demonstrates that malnutrition remains a common complication of adults with CF, despite the provision of high fat, high energy
dietary advice in the majority of patients. Poor clinical outcome is associated with significant loss of body weight. An aggressive approach to maintain body weight is likely to be of benefit in patients with CF.

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**REFERENCES**


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