Both generic and disease specific health-related quality of life are deteriorated in patients with underweight COPD

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Summary This study evaluated the effects of body weight on both generic and disease-specific health-related quality of life (HRQoL) of patients with COPD. A total of 83 patients with stable COPD were enrolled (mean age: 74.6 yr, mean FEV\textsubscript{1}: 1.29 L). Patients were divided into two groups according to body mass index (BMI) (UW group: BMI \textless 20, NW group: 20 \textless BMI \textless 26). The degree of dyspnea and both disease-specific and generic HRQoL were compared between the two groups. An oxygen cost diagram (OCD) was used to assess the degree of dyspnea and St. George’s Respiratory Questionnaire (SGRQ) and Medical Outcomes Study Short Form 36-item Questionnaire (SF-36) were used for HRQoL evaluation. The OCD was significantly lower in the UW group. Compared with the NW group, the UW group showed significant deterioration in the total score and three subscales of SGRQ. SF-36 also showed significantly worse scores for the parameters of physical functioning, role emotional, bodily pain, and general health. The results of stepwise multiple regression analysis showed that OCD, FEV\textsubscript{1}, %pred. BMI were independent variables in the total score on SGRQ. The results of stepwise multiple regression analysis also showed that OCD was an independent variable for four of eight components of SF-36, while BMI was three of eight components of SF-36. In conclusion, low body weight in patients with COPD is related to a worsening of dyspnea and deterioration of both
Introduction

Patients with advanced COPD frequently lose weight and become malnourished. Nutritional depletion becomes a significant problem in patients with COPD. This malnourished status in patients with COPD causes deterioration of exercise performance, respiratory muscle function, and increases mortality. Health-related quality of life (HRQoL) is an important domain of measuring the impact of chronic diseases. Both generic and disease-specific instruments have been used for measuring HRQoL and both disease-specific and generic HRQoL are known to be deteriorated in patients with COPD. Although the effects of nutritional status on the mortality of patients with COPD is well established, little is known about its effects on HRQoL. A study by Shoup and coworkers showed that body weight and lean body mass abnormalities influence disease-specific HRQoL in patients with COPD. However, whether a malnourished status itself affects generic HRQoL is not known.

The present study assessed deterioration of both generic and disease-specific HRQoL in groups of normal weight and underweight patients with stable COPD and investigated whether body weight is a determinant of HRQoL in COPD patients.

Methods

Subjects

Consecutive stable COPD patients, who received monthly regular follow-up in the outpatient clinic of the Pulmonary Division of Tokyo Metropolitan Geriatric Medical Center (a main teaching hospital and major referral center in the Tokyo area) between January 2000 and December 2000, who met the following criteria were studied: (1) stable COPD, (2) an FEV1/FVC ratio less than 70%, and (3) body mass index (BMI) of less than 26 kg/m². COPD was diagnosed according to the definition by the American Thoracic Society. Clinical stability was defined as being without acute exacerbation and without changes in treatment regimen during the preceding 4 weeks. Patients with comorbidities affecting nutritional status and body weight such as malignancies, malabsorption, endocrine disorders, chronic renal failure, cardiac diseases, and neuromuscular diseases were excluded. Cognitive disorder was assessed by Mini Mental State Examination (MMSE) and patients with an MMSE less than 24 were excluded. Based on body mass index (BMI), subjects were divided into two groups: normal weight (NW group: BMI < 26 kg/m²) and underweight (UW group: BMI ≤ 20 kg/m²). The hospital ethics committee approved the study, and informed consent was obtained from all subjects.

Measurements

Body height was measured to the nearest 0.5 cm by a stadiometer with the patient stood barefoot, feet together, at the head level. Body weight was measured on a balance beam platform scale while the patients wore light clothing without shows. BMI was calculated as body weight divided by body height squared (kg/m²). Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) were measured using a pulmonary function instrument with computer processing (CHESTAC; CHEST Co, Tokyo, Japan), which fulfills the American Thoracic Society recommendation for diagnostic spirometry. The largest FEV1 and FVC values from three maneuvers were then analyzed. The predicted value of FEV1 (FEV1, %pred.) was calculated according to the Japanese Respiratory Society proposal. To assess dyspnea, Oxygen Cost Diagram (OCD) was used. The score ranges from 0 to 100; a score of 0 indicates maximal dyspnea. To assess exercise capacity, the six-minutes walking distance test (6MWD) was applied using the standard protocol. HRQoL was assessed by the Japanese version of the St. George’s Respiratory Questionnaire (SGRQ) and SF-36 (Medical Outcomes Study Short Form 36-item Questionnaire). The SGRQ includes 76 items that are weighted to produce three component scores (symptoms, activity and impact) and a total score. Each of these scores ranges 0–100; a score of 100 indicates maximal disability. The SF-36 incorporates 36 items and yields eight separate subscales including physical functioning, role physical, bodily
pain, general health, vitality, social functioning, role emotional, and mental health. Each subscale score ranges from 0 to 100, with 100 representing the most desirable score.\textsuperscript{20,21}

**Statistical analysis**

Unpaired Student’s \(t\)-tests and confidence intervals (CI) were used for comparisons between the NW group and the UW group. Pearson’s correlation coefficient was used to determine the relationship between HRQoL measures and clinical variables. Stepwise multiple regression analysis was performed to determine independent variables of HRQoL measures. Data are expressed as means ± se, and \(P\)-values less than 0.05 are considered significant.

**Results**

**Patient characteristics**

Patient characteristics are shown in Table 1. Eighty-three consecutive COPD patients (male: 73, female: 10) were studied. Mean age was 74.6 ± 0.7 years, and mean FEV\(_1\) was 1.29 ± 0.05 L. In 49 (59%) patients, BMI was within the normal range (normal weight group: NW group) and in 34 (41%), BMI was low (underweight group: UW group). Comparison of patient characteristics between two groups are shown in Table 1. As shown in Table 1, age, height, and degree of airflow obstruction were similar in two groups. However, when compared with the NW group, UW group significantly showed low body weight (\(P<0.0001\)), low BMI (\(P<0.0001\)), and deterioration of exercise capacity assessed by 6MWD (\(P<0.05\)).

**Comparison of the degree of dyspnea**

Comparison of the degree of dyspnea assessed by OCD between the NW group and UW group are shown in Table 1. The severity of dyspnea by OCD was significantly lower (i.e., more dyspneic) in the UW group compared with the NW group (difference of the mean: \(-15.24, 95\% CI: -22.97\) to \(-7.51, P<0.001\)).

**Comparison of the HRQoL measures**

Comparison of the SGRQ total score and three subscores between the NW group and UW group are shown in Fig. 1. The UW group showed significantly higher (i.e., greater impairment) in activity

![Figure 1](image-url)

**Figure 1** Comparison of the SGRQ between UW and NW groups: The UW group showed significantly higher (i.e., greater impairment) in activity (\(P<0.05\)), symptoms (\(P<0.05\)), impact (\(P<0.05\)), and total score (\(P<0.05\)) than the NW group.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics in the study group.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total ((n = 83))</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>74.6 ± 0.7</td>
</tr>
<tr>
<td>Male/Female</td>
<td>73/10</td>
</tr>
<tr>
<td>FEV(_1) (L)</td>
<td>1.29 ± 0.05</td>
</tr>
<tr>
<td>FEV(_1), %pred</td>
<td>53.9 ± 22.2</td>
</tr>
<tr>
<td>6MWD (m)</td>
<td>376.6 ± 9.0</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>55.2 ± 1.0</td>
</tr>
<tr>
<td>Body height (m)</td>
<td>1.60 ± 0.01</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>20.8 ± 0.3</td>
</tr>
<tr>
<td>OCD</td>
<td>71.4 ± 2.1</td>
</tr>
</tbody>
</table>

\textsuperscript{1}\(P<0.05\) compared with NW group.
\textsuperscript{2}\(P<0.0001\) compared with NW group.
\textsuperscript{3}\(P<0.001\) compared with NW group.
Correlation between the HRQoL measures and clinical variables

Relationship between body weight category and OCD, FEV1, %pred., and 6MWD were examined. Both OCD and 6MWD significantly correlated with BMI (BMI vs. OCD; \( r = -0.35, P < 0.01 \), BMI vs. 6MWD; \( r = 0.34, P < 0.01 \)). However, FEV1, %pred. did not correlate with BMI (\( r = -0.10 \)).

Relationship between HRQoL measures and various clinical variables are examined. Relationship between the HRQoL measures by the SGRQ and clinical variables are shown in Table 2. Dyspnea assessed by OCD significantly correlated with total score and three components of the SGRQ. BMI, 6MWD, and FEV1, %pred. significantly correlated with total score and activity and impact of SGRQ, however, these variables did not correlate with symptoms score of the SGRQ.

Stepwise multiple regression analysis was used to identify those variables that may predict total score on the SGRQ. Variables such as OCD, FEV1, %pred., and BMI were adopted as independent variables in analyzing the total score on the SGRQ (OCD; \( r^2 = 0.25 \), FEV1, %pred. \( r^2 = 0.06 \), BMI; \( r^2 = 0.04 \)).

Correlations for the components for the SF-36 and clinical variables are shown in Table 3. OCD was significantly correlated with six components of the
SF-36 including physical functioning (P<0.0001), social functioning (P<0.05), role physical (P<0.001), role emotional (P<0.05), bodily pain (P<0.05), and general health (P<0.001). However, BMI was significantly correlated with only four components: physical functioning (P<0.05), role emotional (P<0.01), bodily pain (P<0.01), and general health (P<0.01).

Stepwise multiple regression analysis was used to identify those variables that may predict each component of the SF-36. Multiple regression analysis showed that the OCD was a significant independent variable for four of eight components of the SF-36 including physical functioning \(r^2=0.23\), social functioning \(r^2=0.16\), role physical \(r^2=0.16\), and general health \(r^2=0.13\). BMI was also an independent variable for three of eight components of the SF-36 including role emotional \(r^2=0.09\), bodily pain \(r^2=0.10\), and general health \(r^2=0.10\). Both FEV1, %pred. and 6MWD were not predicted variable of any components of the SF-36.

### Discussion

In the present study, we demonstrated that low body weight was associated with increased dyspnea and poor HRQoL assessed by both SGRQ and SF-36. This is the first report to clearly show that malnutritional status has a significant impact on both generic and disease specific HRQoL in patients with COPD.

Although a malnourished status is a common problem in COPD patients,1-3 there are few studies evaluating the effects of nutritional status on HRQoL in patients with COPD. Shoup and coworkers evaluated body weight and composition in patients with obstructive lung disease and compared these to HRQoL assessed by SGRQ.11 They showed that underweight and overweight patients and patients with reduced lean mass had significantly reduced disease specific HRQoL compared with normal weight patients and patients with normal lean mass. A similar relationship between tissue depletion and deterioration of disease-specific HRQoL was reported by Mostert et al.23 Our study added the information that low body weight was a significant contributor for not only disease-specific but also generic HRQoL in patients with COPD.

The present study showed that the UW group showed significantly more dyspneic compared with NW group (Table 1). Traditionally, COPD patients are divided into two clinical subtypes namely "pink puffers" and "blue bloaters."24 Pink puffers are described as a thin, cachexic, and dyspneic patients with emphysema. Our results confirm that patients with COPD who are distinguished as "pink puffers" and who are characterized as malnourished are more dyspneic than COPD patients with normal weight. These finding support the results by Sahebjami et al.25 who showed that under weight COPD patients demonstrated significantly higher Medical Research Council dyspnea scale than normal weight COPD patients.

According to the correlation data between clinical variables and disease-specific HRQoL assessed by SGRQ (Table 2), the most significant factor related to disease-specific HRQoL was dyspnea. The multiple regression data showed that dyspnea assessed by OCD was the greatest contributing factor to the total score on the SGRQ and that this variable explained 25% of total score on the SGRQ. This finding is in agreement with a study by Shoup et al.11 that dyspnea is the most

### Table 3  Correlation between SF-36 and clinical variables.

<table>
<thead>
<tr>
<th>SF-36 components</th>
<th>OCD</th>
<th>BMI</th>
<th>FEV1, % pred</th>
<th>6MWD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>0.48*</td>
<td>0.24(^i)</td>
<td>0.24(^i)</td>
<td>0.42*</td>
</tr>
<tr>
<td>Social functioning</td>
<td>0.24(^i)</td>
<td>0.05</td>
<td>0.22(^i)</td>
<td>0.21</td>
</tr>
<tr>
<td>Role physical</td>
<td>0.40*</td>
<td>0.21</td>
<td>0.19</td>
<td>0.22(^i)</td>
</tr>
<tr>
<td>Role emotional</td>
<td>0.26(^i)</td>
<td>0.29(^i)</td>
<td>0.11</td>
<td>0.12</td>
</tr>
<tr>
<td>Mental health</td>
<td>0.07</td>
<td>0.18</td>
<td>0.17</td>
<td>0.13</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>0.27(^i)</td>
<td>0.32(^i)</td>
<td>0.06</td>
<td>0.25(^i)</td>
</tr>
<tr>
<td>Vitality</td>
<td>0.17</td>
<td>0.18</td>
<td>0.21</td>
<td>0.13</td>
</tr>
<tr>
<td>General health</td>
<td>0.36*</td>
<td>0.29(^i)</td>
<td>0.32(^i)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

\(^iP<0.0001,\) \(^*P<0.001,\) \(^\dagger P<0.01,\) \(^\ddagger P<0.05.\)
important factor affecting disease-specific HRQoL measured by SGRQ.

On comparison of the total score and three components of the SGRQ between the UW and NW groups, the total score and three components of the SGRQ were significantly higher in the UW group. Although the contribution of BMI is weaker than the degree of dyspnea, our multiple regression analysis also demonstrated that BMI is an independent variable affecting the total score of the SGRQ. These results suggest that the importance of nutritional status on disease specific HRQoL in patients with COPD.

According to the correlation data between clinical variables and generic HRQoL assessed by SF-36, OCD correlated with six of eight subscale of SF-36, suggesting that dyspnea was a highly significant factor affecting generic HRQoL in patients with COPD. This finding is in agreement with a study by Mahler and coworkers showing that dyspnea was a highly significant factor affecting generic HRQoL measured by SF-36. However, on comparison of eight subscales of SF-36 between UW and NW groups, scores on subscales such as physical functioning, role emotional, bodily pain, general health were significantly lower in the UW group. Multiple regression analysis also showed that BMI was an independent variable affecting role emotional, bodily pain and general health and that BMI was the only variable affecting scores on role emotional and bodily pain subscales of SF-36. These findings suggest that not only the degree of dyspnea but also malnourished status are important variables determining generic HRQoL. These findings also suggest that both low body weight and dyspnea influence different aspects of generic HRQoL.

It is well known that a normal weight individual with COPD is at significant risk for having reduced fat-free or lean mass and this deficiency is also related to increased morbidity. Schols et al. reported that 10% of COPD patients had normal weight with fat-free mass depletion. The study by Mostert et al. showed that COPD patients who had normal weight with fat-free mass depletion demonstrated significant deterioration in activity, impacting scores on the SGRQ. Our study only examined the correlation between body weight categories and generic and disease-specific HRQoL. It is not clear whether COPD patients maintaining normal weight with fat-free mass depletion demonstrated deterioration in generic HRQoL. Further study is needed to evaluate correlation between generic HRQoL and tissue depletion.

Considering the contribution of low body weight to both generic and disease specific HRQoL, nutritional intervention should be included in the treatment for COPD. However, a recent meta-analysis including nine randomized controlled trial showed that the clinical effectiveness of nutritional intervention is not significant. The outcome measures assessed in these trials included body weight, arm muscle circumference, triceps skinfold thickness, the 6MWD, FEV₁, maximal inspiratory pressure, and maximal expiratory pressure. However, these trials did not include HRQoL as an outcome measure. The present results emphasize the importance of measuring HRQoL in underweight patients with COPD and the outcomes of nutritional intervention should be assessed in this regard.

Some limitations of this study should be discussed. In this study, to determine disease specific HRQoL, we used the Japanese version of the SGRQ in a Japanese population. One may concern as to whether Japanese version of the SGRQ behaves in the same manner as original English version. When HRQoL questionnaires are translated into other languages, careful translation and back translation procedures are necessary to maintain similar discriminative properties and responsiveness. The Japanese version of the SGRQ was translated into this procedure and it has been reported that the Japanese version of the SGRQ appeared to perform in a similar manner to the English originals. These facts indicated that the Japanese version of the SGRQ have similar discriminative properties and responsiveness as original English versions. However, when translating English version of HRQoL questionnaires into another languages, some cultural differences may influence the translation of HRQoL questionnaires. It is not clear whether the results shown in this study could apply in another populations such as English speakers. Generalization of these results to population of another languages should be examined.

In conclusion, our results indicated that low body weight in COPD patients is related to worsening of dyspnea and deterioration of both generic and disease-specific HRQoL. The present results also indicate that nutritional intervention may be important for improving dyspnea and HRQoL in patients with COPD. Further longitudinal study is needed to clarify these findings.

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References


