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Nutritional status, dietary energy intake and the risk of exacerbations in patients with chronic obstructive pulmonary disease (COPD)

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Summary Loss of body weight, as a result of imbalance between increased energy demand and/or reduced dietary intake, is a common problem in patients with COPD. The aim of this investigation was to examine the relationship between nutritional intake, change in body weight and the risk of exacerbation in patients with COPD.

The study comprised 41 patients who were hospitalised because of an exacerbation of COPD. The follow-up period was 12 months. Weight, height and lung function were measured at baseline. At the 12-month follow-up, weight change and current weight were assessed by an interview and nutritional intake was recorded in a food diary for 7 days. An acute exacerbation was defined as having been admitted to hospital and/or making an emergency visit to hospital, due to COPD during the follow-up period.

At baseline, 24% of the patients were underweight (body mass index (BMI) $< 20\,kg/m^2$), 46% were of normal weight (BMI 20–25 kg/m^2) and 29% were overweight (BMI $> 25\,kg/m^2$). Energy intake was lower than the calculated energy demand for all groups. During the follow-up period, 24 of the 41 patients had an exacerbation. A low BMI at inclusion and weight loss during the follow-up period were independent risk factors for having an exacerbation ($P = 0.003$ and 0.006, respectively).

We conclude that, in patients who are hospitalised because of COPD, underweight and weight loss during the follow-up period are related to a higher risk of having new exacerbations.

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Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of disability and mortality in the world.[1,2] Patients with COPD often have exacerbations which lead to a more rapid decline in Forced expiratory volume in 1 s (FEV_1),[3] impaired quality of life[4] and higher mortality.[5] Exacerbations also lead to an increase in the need for medical care and hospitalisation, thereby causing increases in health-care costs.[2]

Loss of body weight, as a result of imbalance between increased energy demand and/or reduced dietary intake, is a common and serious problem for patients with COPD.[6–8] Moreover, weight loss is an independent predictor of morbidity[9,10] and mortality.[10–14] There is also evidence to suggest that weight gain can reverse this increased mortality risk.[12] Loss of body weight in COPD is of multifactorial origin. Eating difficulties,[15,16] higher metabolic rate and cost of ventilation,[17] together with oxidative stress causing systemic inflammation,[18,19] are important factors. Even though weight loss is of multifactorial origin, eating habits and energy intake probably is of major importance. Most studies of energy intake in COPD patients are supplementation studies and few are available in which the relationship between exacerbations, habitual energy intake and different classes of body mass index (BMI) are examined.

The aim of this investigation was to study the possible connections between nutritional status body mass index (BMI), dietary energy intake, weight change and the risk of acute exacerbations, in patients with COPD.

Method

The study population was recruited from the Swedish part of a prospective multicentre, re-admission study of consecutive patients with acute exacerbations of COPD, admitted to hospital in the five Nordic countries.[20] All the patients had COPD according to the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) criteria.[21]

Data were obtained before patients were discharged and at a follow-up 1 year after inclusion. During the first admission, height was measured to the nearest 0.5 cm, while weight was measured on a balance scale to the nearest 0.1 kg and BMI was calculated as weight (kg)/length $(m)^2$. Assessments were made in the morning and within the first 48 h of admission.

A structured interview protocol was used and the patients were asked about smoking habits and history, social situation, education and disease duration.

Spirometry was performed at discharge in most patients. The spirometry was performed with a Jaeger master scope spirometer (Jaeger, Höchberg, Germany). In the ten patients in whom spirometry was not performed, the result from the most recent previous spirometry was used. FEV_1 was expressed as a percentage of the predicted value using the references values from the European Coal and Steel Union.[22]

At the follow-up after 1 year, a telephone interview was held with all patients. The patients were then asked about their current weight, if they had been given information om COPD and nutrition and use of diet supplementation. At follow-up, patients were also asked to complete a food diary for 7 days.

Nutritional intake was assessed by a food diary.[23] After the telephone interview, the food diary was sent to the patients by mail, together with instructions on how to fill it in. Instructions were also given by phone at the interview and patients were encouraged to call the interviewer if they had any problems. Patients were asked to record everything they had to eat and drink for 7 consecutive days. From the food diary results, energy need and energy intake were calculated using with the Dietist computer program (Kost och Näringsdata AB, Bromma, Sweden) using food data from the Swedish National Food Administration. The computer program uses the Harris–Benedict equation and a basal metabolic rate (BMR) of 140 kJ for ill yet mobile persons.

The patients were divided into three groups, underweight (BMI <20), normal weight (BMI 20–25) and overweight (BMI >25). Weight change during the 12-month period was calculated as the reported weight at the follow-up minus the measured weight at baseline.

Information on COPD exacerbations was collected from patient records. An exacerbation was defined as an emergency visit to and/or admission to hospital because of COPD.

The Ethics Committee at the Medical Faculty at Uppsala University has approved of the study.

Statistics

Statistical analyses were performed using Stat View 5.0 (SAS Institute Inc, Cary, NC, USA). A chi-squared test and one way analysis of variance were used when comparing patients in the different BMI

categories. Linear and multiple linear regression analyses were used to study the relationship between changes in body mass and energy deficiency after adjustment for age, gender and baseline BMI. The Kaplan–Meier survival analysis and Cox regression analysis were used to study relationships between nutritional data and the time to the next COPD exacerbation. In the Cox regressions adjustments were made fore age, gender, FEV_1 and pack years. A *P*-value of <0.05 was considered statistically significant.

Result

Of the 87 patients with COPD that were included in the study, 13 had died within 12 months. The remaining 74 took part in a follow-up phone interview. Of these 74 patients, 42 completed a food diary for 1 week. At baseline, there were no statistically significant differences between the patients who filled in or did not fill in the food diary in terms of gender, age, pack years, FEV_1 or BMI.

In one of the 42 patients who completed the diary, body mass had not been recorded at baseline. The subsequent analyses therefore included 41 patients. In Table 1, the baseline characteristics of this patient group divided into BMI categories are presented. The underweight group had significantly fewer pack years than the normal-weight patient group and a significantly lower FEV_1 than the overweight group. Underweight patients also had significantly more exacerbations during the year before inclusion in the study.

During the follow-up period, 78% of the patients in the underweight group had been given advice about their diet compared with 50% and 17% in the normal and overweight patient groups, respectively ($P = 0.01$). The proportion of patients using diet supplementation was 60% in the underweight group compared with 5% and 0% in the normal and overweight groups, respectively ($P<0.001$). Energy intake was lower than energy demand in all groups (Table 2). The level of energy deficiency was significantly lower in the underweight group compared with the other groups ($P<0.01$).

Table 1 Characteristics of the study patients, by BMI categories (n (%) or mean ± SD).

	Underweight BMI $<20\,kg/m^2$ ($n = 10$)	Normal weight BMI 20–25 kg/m^2 ($n = 19$)	Overweight BMI $>25\,kg/m^2$ ($n = 12$)
Women	5 (50%)	13 (68%)	9 (75%)
Age (years)	68 ± 13	68 ± 9	66 ± 9
Pack years	21 ± 14¶	34 ± 13	29 ± 12
Weight (kg)	50 ± 5	62 ± 6	83 ± 18
BMI (kg/m^2)	17 ± 2	22 ± 2	30 ± 6
Admissions last year	1.2 ± 1.2¶	0.3 ± 0.6	0.2 ± 0.4
FEV_1(% of predicted)	28 ± 14±	38 ± 17	46 ± 19
Weight loss during follow-up	4 (40%)	6 (32%)	6 (50%)

¶$P<0.05$ compared with normal weight group.
±$P<0.05$ compared with overweight group.

Table 2 Energy demand, intake and energy deficiency patients divided into BMI categories (mean ± SD).

	Underweight BMI $<20\,kg/m^2$ ($n = 10$)	Normal weight BMI 20–25 kg/m^2 ($n = 19$)	Overweight BMI $<25\,kg/m^2$ ($n = 12$)
Energy demand (kcal)	1737 ± 161	2134 ± 244	2626 ± 569
Energy intake (% of needed)	91 ± 19	73 ± 13	56 ± 20
Energy intake (kcal)	1577 ± 347	1566 ± 357	1406 ± 261
Energy deficiency (kcal)	159 ± 324	567 ± 307¶	1220 ± 662±

¶$P<0.01$ compared with underweight group.
±$P<0.001$ compared with underweight group.

Changes in body mass during the 12-month period are shown in Table 1 and Fig. 1. There was a small decrease in body mass in the overweight group and a small increase in the under- and normal-weight patient groups. Eighteen patients had decreased body mass (range 0.5–12 kg). There was no significant difference in baseline BMI between patients that had a weight loss and patients with unchanged or increased weight (23.0 ± 5.7 vs. $24.0 \pm 6.3\,kg/m^2$, $P = 0.63$). The association between energy deficiency and weight change is presented in Fig. 2. No significant relationship between energy deficiency and weight change was found in the bivariate analysis (Fig. 2) or after adjusting for age, gender and BMI at baseline ($r = 0.24$, $P = 0.30$).

During the follow-up period, 24 of the 41 patients had an exacerbation. The time until an exacerbation in the three different BMI groups is shown in Fig. 3. The patients in the overweight group were less likely to have an exacerbation. Compared with the other two groups, this difference was of borderline significance ($P = 0.07$).

The group of patients that had a weight reduction during the follow-up had an increased likelihood of having an exacerbation compared with patients whose weight was either unchanged or increased ($P < 0.01$) (Fig. 4).

In a multivariate analysis using the Cox regression model, a low BMI at baseline and weight reduction during the follow-up period were found to be independent risk factors for acute exacerbations, whereas no significant associations were found for FEV_1, gender, age or pack years (Table 3). No significant correlation was found between energy deficiency and the risk of having an exacerbation.

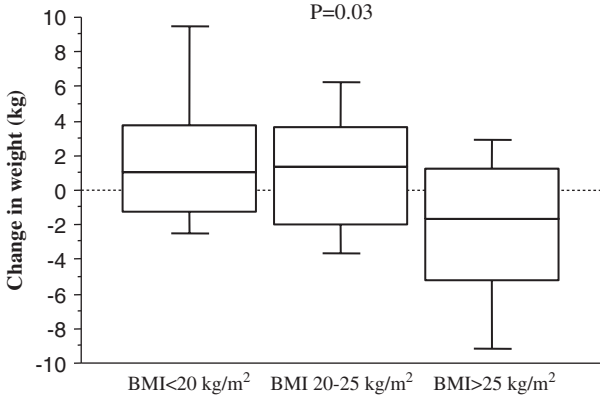

Figure 1 Change in weight during 12 months in COPD patients divided into BMI categories. The box plots show the values of the median, the 25th and 75th percentiles (box) and the 10th and 90th percentiles.

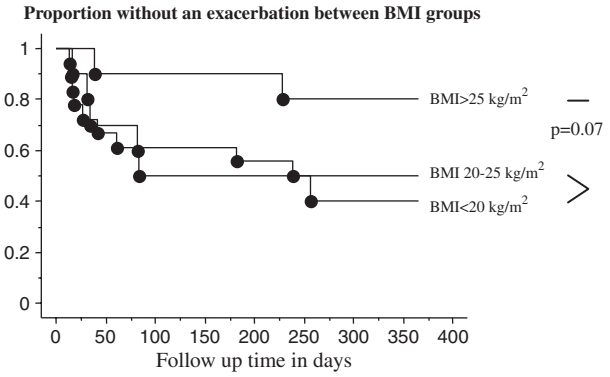

Figure 3 Kaplan–Meier cumulative survival plot for days until next COPD exacerbation in COPD patients divided into BMI categories.

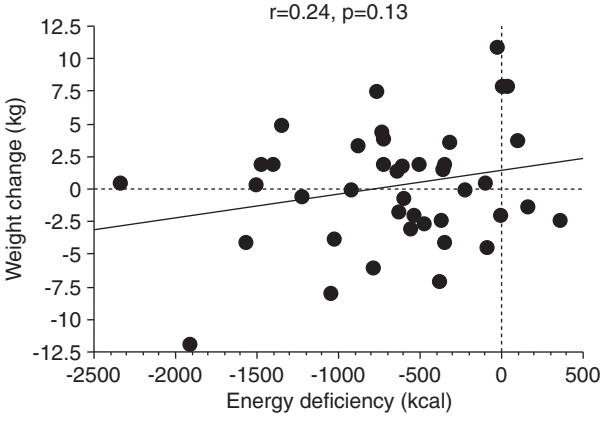

Figure 2 Relationship between energy deficiency and weight change.

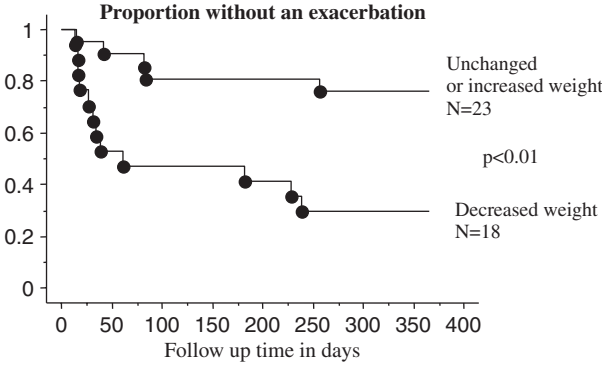

Figure 4 Kaplan–Meier cumulative survival plot for days until next COPD exacerbation in COPD patients with reduced or unchanged/increased weight during the follow-up period.

Table 3 Relationship between body mass index (BMI), weight change and covariates and the time to the next COPD exacerbation analysed with the Cox-regression model.

	Risk ratio*	95% confidence interval†
BMI at baseline	0.78	0.65–0.93
Weight change	0.76	0.63–0.93
FEV_1 at baseline (% of pred)†	0.90	0.60–1.34
Age (years)†	0.66	0.31–2.16
Male gender	0.72	0.22–2.38
Pack years†	1.34	0.82–2.16

*Adjusted for all the variables in the table.
†Per 10 units.

Discussion

The main finding in this prospective study of patients hospitalised with COPD is that underweight at baseline and weight loss during the 12-month observation period were independant risk factors of exacerbations. Our study also indicated that insufficient energy intake is common among patients with COPD, but we found no relationship between deficiency in energy intake and the risk of exacerbations.

The increased risk of exacerbations in patients with underweight and weight loss found in our study is consistent with other reports, that have found an increased need of medical care and a higher mortality in underweight COPD patients.[9–13] In one study, Pouw and co-workers reported that patients, who lost weight during an exacerbation-related hospitalisation, had a higher risk of early non-elective re-admission.[10] In our study, we found that patients with a BMI of <20 had more exacerbations the year before inclusion. This patient group also had the lowest number of pack years, but, despite this, they also had also the lowest mean FEV_1. This may reflect the findings of Harik–Khan, that low-weight smokers are at a higher risk of developing COPD than normal and overweight smokers.[24] It is well known that having a low FEV_1, is a risk factor for exacerbations.[4,25] The association between underweight, weight change and exacerbation frequency was therefore investigated with adjustments for FEV_1 in the Cox-regression model. In the present study the risk of exacerbations increased with decreasing FEV_1 but the association was not statistically significant, probably due to the limited number of patients in the study.

Our food diary results suggest that an insufficient dietary intake is very common in COPD patients. In a recent study, Tang et al.,[26] found a significant negative energy balance due to insufficient intake, in seven out of ten patients. In one study, patients hospitalised for an exacerbation have been found to be in negative nitrogen balance, but some small gains were observed with increased energy intake.[27] In hospitalised patients in Iceland, the energy intake was 140% of the calculated needs, and this level was found to be sufficient to avoid protein losses, but a higher intake is needed to rehabilitate undernourished patients.[28] In our study we found no significant association between energy deficiency and weight loss and energy deficiency was lowest in the group of patients with a BMI of $<20\,kg/m^2$. This is probably explained by the more intensive information and use of food supplementation found in this group of patients. Another reason for the somewhat paradoxical relationship between body mass and energy deficiency may be that over weight patients tend to under-report their food intake. Energy expenditure was not measured, and calculation of energy demand were made using the Harris–Benedict equation and with a basal metabolic rate (BMR) of 140 kcal for ill yet mobile persons. In COPD patients the variation in total daily energy expenditure reflect differences in expenditures for activities but not for resting energy expenses (REE),[29,30] this may have affected the relation between energy intake deficiency and weight change, as the level of activity varies between patients.

This study has several limitations. The food diary was completed 1 year after inclusion in the study and covers only 1 week. The reported energy intake may therefore not reflect the whole study period in some patients. Weight loss was calculated from measured weight at inclusion and reported weight at the follow-up, which may also lead to some misclassification. Despite the fact that this is a prospective study, the causal relationship between weight loss and exacerbations remains unclear to some extent. Frequent exacerbations causes weight loss as a result of impaired energy balance due to reduced dietary intake and an increase in resting energy expenditure.[31] Systemic inflammation is another possible cause of weight loss during exacerbations [32] and is more pronounced during exacerbations.[14] It is therefore still difficult to know whether weight loss and low weight is a cause or a consequence of exacerbations.

Despite the limitations, this study highlights the prognostic implications of malnutrition in COPD. Even if weight loss is of multifactorial origin, energy intake is probably of importance. One cause

of low intake is the eating difficulties observed in many malnourished COPD patients and it has been suggested that this can be explained by, a cytokine-leptin link leading to increased levels of leptin. These increased leptin levels leads to reduced food intake and higher energy demand and therefore poor response to nutritional support.[27] Apart from systemic inflammation, elevated leptin levels are also related to exacerbations and presumably to corticoid treatment.[33] The most natural way of treating malnutrition in COPD is probably by nutritional support. At present, there is limited evidence to suggest that nutritional support has any impact on malnutrition in COPD patients.[34] Two recent reports did, however, show that nutritional supplementation therapy implemented in a pulmonary rehabilitation programme was effective in depleted patients with COPD.[35,36]

We conclude that underweight and weight loss during the follow-up period was related to a higher risk of exacerbations in patients with COPD. This study underlines the importance of examining nutritional status and monitoring weight changes in patients with severe COPD.

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