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The influence of underweight and dietary support on well-being in lung transplant candidates

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Summary
Background: Quality of life has been found to be a significant predictor of survival in lung transplantation candidates. The aim of this study was to investigate associations between underweight, dietary support and well-being.
Methods: A self-administered questionnaire for perceived well-being was administered to underweight ($n = 42$) and normal-weight ($n = 29$) candidates for lung transplantation before and after dietary intervention in which the underweight patients received dietary support for weight gain.
Results: Underweight compared with normal-weight, independent of lung function, was associated with low well-being in several of the measured dimensions. Improvements were observed after dietary intervention compared with baseline in the underweight patients, for scores in the dimension of tiredness 29.2 (4.2) vs. 26.2 (6.0), $P < 0.01$; general satisfaction 4.7 (1.5) vs. 4.0 (1.4), $P = 0.01$; social life 16.7 (3.9) vs. 15.0 (4.4), $P = 0.02$) (mean (SD) before and after dietary intervention respectively), but not in the normal-weight patients. The underweight patients achieved the goal for energy intake and protein intake and experienced a significant weight gain. Regression analyses showed that none of the well-being improvements was associated with weight gain or change in body composition. However, an association between less tiredness and an increase in protein intake was indicated ($b = -0.305$, $P = 0.055$).
Conclusion: Underweight compared with normal-weight was associated with more impaired quality of life in candidates for lung transplantation and some benefit from dietary support in terms of well-being was indicated.

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Introduction

The clinically adverse influence of weight loss in patients with chronic obstructive pulmonary disease (COPD) is indicated by a reduction in exercise performance,[1] an increase in morbidity, as evidenced by reports of increased frequency of hospitalisation,[2] and a reduction in survival.[3]

A few studies have reported on health-related quality of life in COPD patients in relation to nutritional depletion.[4,5] Mostert et al.[5] found impaired health-related quality of life associated with tissue depletion, independent of exercise capacity and dyspnoea. Most data in the literature on nutritional assessment and supplementation in pulmonary disease relate to COPD patients. Quality of life has increasingly been accepted as a supplementary outcome measure.[6] Weight gain has been shown to improve the prognosis in patients with COPD,[7,8] but has scarcely been studied in relation to quality of life.[9]

Because of the lack of organ donors, many candidates for lung transplantation are waiting for a long time for transplantation after acceptance and several patients die while waiting for transplantation. Several studies have examined health-related quality of life in candidates awaiting lung transplantation. Studies have shown that quality of life predicts survival in COPD patients[10] and in candidates for transplantation.[11] It appears from the study by Squier et al.[11] that higher health-related function may be associated with a better chance of survival both before and after lung transplantation. No attention has been paid to improvement of nutritional status and its relationship to quality of life in patients awaiting lung transplantation.

The purpose of this study was thus (1) to examine whether underweight was associated with impaired quality of life in a group of underweight and normal-weight candidates for lung transplantation and (2) to study well-being after dietary support for weight gain in the underweight patients.

Material and methods

Patients and study design

In this cross-sectional, prospective intervention study, we studied 71 underweight ($n = 42$) and normal-weight patients ($n = 29$), who were consecutively referred to the Department of Thoracic Medicine and assessed for lung transplantation between August 1993 and August 1998. In underweight and normal-weight patients, respectively, the majority had COPD ($n = 24$ and $n = 16$, including COPD with alpha-1 antitrypsin deficiency without liver affection ($n = 5$ and $n = 1$)), while other diagnoses (OTHERS) were fibrosing alveolitis ($n = 4$ and $n = 7$), sarcoidosis ($n = 2$ and $n = 4$), bronchiectasis ($n = 4$ and $n = 0$) and lymphangioleiomyelomatosis ($n = 3$ and $n = 1$). Patients with cystic fibrosis, pulmonary hypertension or overweight patients (body mass index (BMI) over 25 kg/m^2) were excluded.

The patients participated in a dietary intervention study for weight gain in the underweight patients and weight maintenance in the normal-weight ones.[12] Anthropometric measurements and lung function tests were performed after arrival at the hospital, when entering the study (first visit), and after intervention on the second visit to the hospital. The patients were contacted by telephone in their homes 3–4 weeks prior to their first and second admission to hospital. After obtaining the patient's informed consent, questionnaires for quality of life, a scale and a booklet for recording food were mailed to the patient. The questionnaires were self-administered. The patients recorded their food intake 3–4 weeks prior to their first admission to hospital. Food records were also kept during hospitalisation and at the end of the intervention period, 3–4 weeks prior to the second visit to the hospital.

The dietary intervention study consisted of inpatient dietary support,[13] followed by outpatient dietary intervention.[12] Following arrival at the hospital, the underweight patients were randomly allocated to two groups (Group A and Group B). Group A received intensified dietary support; while they were in hospital, they were offered an energy-rich diet with the addition of oral ready-made liquid nutritional supplements if they wanted them. Groups B and C (normal-weight patients) received the normal diet and regular support in hospital. Both groups A and B received outpatient dietary counselling, including meal planning and individual dietary suggestions. As outpatients, Group A received oral liquid nutritional supplements free of charge, while Group B received no supplements free of charge.

After the patients had been assessed for lung transplantation, they were put on a waiting list and re-admitted to hospital every 4–5 months for medical controls. All measurements were performed before transplantation. The regional ethics committee approved the study.

Anthropometric measurements

Normal-weight patients had a BMI (the ratio of body weight (kg) to height squared (m^2)) of between 19 and 25 and a weight loss equal to or less than 10%. The criteria for underweight were BMI below 19 kg/m^2 or BMI of between 19 and 25 kg/m^2 with a weight loss of more than 10% from the usual weight. This was because a weight loss of more than 10% in the terminal stages of COPD has shown to be associated with reduced survival.[14] In 1993, when the study started, we also considered general guidelines. The Norwegian guideline for underweight has been under or equal to 15% of IBW.[15] We chose a BMI of 19 kg/m^2 as the low cut-off point for underweight. Patients were asked for weight changes during the last 3 months and the last year before entering the study. Fat mass (FM) was determined by four skinfold measurements (bicipital, tricipital, subscapular and suprailiac) using the Durnin tables.[16] The fat-free mass (FFM) was assessed by subtracting the FM from the body weight. The fat-mass index and FFM index was computed by dividing FM and FFM, respectively, by the height squared.

Lung function

An automated pulmonary function unit (Gould 2400, Sensormedics, Bilthoven, the Netherlands) was used to measure spirometry variables; forced expiratory volume in 1 s (FEV_1). The reference values were those recommended by the European Respiratory Society.[17]

Quality of life questionnaires

Quality of life and subjective well-being was measured by items used and evaluated in general population surveys in Norway[18,19] and in clinical research.[20–22] The questionnaire evaluates several indexes:

Index (1): Time spent in bed over the last 14 days.
Index (2): Dimensions of tiredness or full of energy (six items each with 6step bipolar): (2a) At the present time, do you mostly feel strong and fit, or tired and worn out and, during the course of the last 14 days, (2b) Did you feel worn out, drained or exhausted, (2c) Did you feel that you had plenty of energy, (2d) Did you feel that you were full of "pep", (2e) Did you feel that you had enough initiative to do what you wanted to do, (2f) Did you feel tired.
Index (3): Would you say that you are usually cheerful or dejected (7step bipolar).
Index (4): Do you generally feel calm and good about yourself (4step bipolar).
Index (5): Considering how you feel these days, are you generally satisfied with your life or are you generally dissatisfied (7step bipolar).
Index (6): Cantril ladder for the best possible life or the worst possible life (10-rank).
Index (7): Present limitations in social and family activities (two items each with 15-cm linear scale), with high scores indicating poorer well-being.
Index (8): Present limitations in usual daily activities (10 tick-off items), and
Index (9): How often taken tranquillisers/sedatives or sleeping medication over the course of the last month? (4step frequency).

Indexes 3, 4, 5 and 9 have been validated in a Norwegian county survey, Nord-Trondelag Health Survey[19,21] while index 2 has been adapted from "vitality" dimension of the Short Form 36 (SF-36).[18] Index 6 has been used internationally, as well as with Norwegian patients.[20]

To characterise the patients, they were also asked whether they lived alone, the number of hospital stays last year and they were also asked: Do you have difficulty buying food? (yes/no), Do you have difficulty cooking? (yes/no), Who does the cooking? (patient/others/get ready-made) and Does eating make you tired? (yes/no).

Statistical analysis

The data were analysed using the SPSS program (SPSS for Windows, Release 9.0.0, SPSS Inc., Chicago, IL, 1998). The results are reported as *n* (%), mean (SD) and frequencies. Statistically significant differences were tested for dimensions of quality of life, weight change and FFM change. An independent-samples *t*-test or a Pearson χ^2-test was used to compare groups. Changes in quality of life were assessed by paired *t*-tests within groups. Internal consistency reliability for the multi-item indices was assessed by Cronbach's coefficient of alpha. Scales with an alpha above 0.70 are generally regarded as homogeneous and taken as evidence of good reliability for a scale. To ensure strict comparability between our multi-item index tiredness before and after intervention, factor (principal components) analysis was performed to evaluate factor score coefficients (i.e. the weights attached to each individual item). Pearson's correlation coefficient was used to estimate the association between changes in tiredness and changes in energy intake or protein intake. Multiple linear regression analyses were performed to test whether improvements in well-being measures after intervention were associated with weight change, change in FFM or protein intake, controlling for baseline values. *P*-values less than 0.05 were regarded as significant using a two-tailed test.

Results

Patient characteristics at entry for the underweight and normal-weight patients are shown in Table 1. Only a minority of the underweight patients had a recent significant weight loss ($\geqslant$5%). More underweight patients said that they had difficulties with cooking and were more tired by eating. The underweight patients had more stays in hospital during the last year (Table 1) and had spent more days in bed during the course of the last 14 days (Table 2). At baseline, the underweight patients also had more impaired quality of life than the normal-weight patients for several of the other measured scores: index 4 (generally feel calm and good about themselves); index 6 (for the dimension of the best possible life or the worst possible life); index 7 (for dimensions of present limitations in social and family activities) and index 9 (more often had taken tranquillisers/sedatives or sleeping medication over the course of the last month) (Table 2). The differences between underweight and normal-weight patients remained the same after controlling for FEV_1.

The mean intervention time was 21 weeks (range 13–44) in the underweight patients and 18 weeks (range 11–26) in the normal-weight ones. Thirty-one underweight patients and 23 normal-weight ones completed the whole intervention. Those who did not complete either died ($n = 8$ and $n = 2$, underweight and normal-weight, respectively) or were transplanted ($n = 3$ and $n = 4$). Three underweight patients were transplanted just before the

Table 1 Patient characteristics at baseline.

Variables	Underweight $N = 42$	Normal-weight $N = 29$
Age (years, range)	47 (25–60)	52 (26–60)
Male/female	20/21	12/17
FEV_1 (% predicted)*	23 (13)	26 (13)
Steroid therapy (*n*, %)	20 (48%)	23 (79%)
Steroid therapy (mg)*	8 (12)	7 (6)
Weight (kg)*	50.5 (7.5)	64.5 (8.3)
Weight change last 3 months (*n*, %)	†	
$\geqslant$5% weight loss	6 (15%)	4 (14%)
<5% weight loss	29 (71%)	19 (66%)
>5% weight gain	6 (15%)	6 (21%)
Weight change last year (*n*, %)		
$\geqslant$5% weight loss	20 (48%)	7 (24%)
<5% weight loss	17 (41%)	10 (35%)
>5% weight gain	5 (12%)	6 (41%)
Body mass index (kg/m^2)*	17.3 (1.8)	22.2 (1.5)
Fat free mass index (kg/m^2)*	14.4 (1.4)‡	15.7 (1.5)
Fat mass index (kg/m^2)*	3.1 (1.5)‡	6.5 (1.3)
Energy intake/REE predicted (%)*	150 (37)‡	130 (33)
Protein intake (g)*	67 (18)‡	75 (23)
Lived alone (*n*, %)	9 (22%)†	4 (14%)
Number of hospital stays last year (*n*)*	3.1 (2.3)†	2.0 (1.7) ($P = 0.035$)
Difficulties cooking (*n*, %)	30 (75%)†	12 (43%) ($P = 0.007$)
Difficulties buying foods (*n*, %)	6 (15%)†	3 (10%)
Who cooks (*n*, %)	†	
Patient	15 (37%)	15 (57%)
Others	22 (54%)	13 (45%)
Get ready-made food	4 (10%)	1 (3%)
Tired from eating (*n*, %)	29 (71%)†	12 (41%) ($P = 0.013$)

FEV_1 = forced expiratory volume in 1 s; REE = resting energy expenditure predicted by Harris and Benedict equation.
*Mean (SD).
†One value missing.

Table 2 Scores in dimensions of quality of life before and after dietary intervention.

Variables	Underweight			Normal-weight			$P^{\dagger}$
	Baseline	After	P^{*}	Baseline	After	P^{*}	Underweight compared with normal-weight at baseline
Index number:	$N = 40$	$N = 30$		$N = 29$	$N = 22$		
1. In bed last 14 days (days)	3.8 (5.3)	3.0 (5.1)	0.6	1.7 (2,8)	0.7 (1.4)	0.1	0.041
2. Tired (6 items) 6 = never 36 = all the time	29.2 (4.2)	26.2 (6.0)	0.007	27.6 (5.0)	26.4 (4.2)	0.2	0.15
3. Depressed/happy 1 = extremely happy 7 = extremely depressed	3.4 (1.3)	3.8 (1.7)	0.3	3.3 (0.9)	3.2 (1.0)	0.3	0.6
4. Calm feeling 1 = almost all the time 4 = never	2.6 (0.9)	2.5 (1.0)	0.4	1.9 (0.8)	2.0 (0.9)	0.9	0.003
5. Life satisfaction 1 = extremely satisfied 7 = extr. dissatisfied	4.7 (1.5)	4.0 (1.4)	0.012	4.1 (1.4)	4.0 (1.3)	0.1	0.1
6. Worst/best life 1 = best possible 10 = worst possible	8.0 (1.9)	7.2 (1.7)	0.012	7.1 (1.9)	6.9 (2.2)	0.8	0.045
7. Limitation in family and social life (2 items) 2 = not at all 20 = seriously	16.7 (3.9)	15.0 (4.4)	0.021	14.2 (4.7)	14.6 (3.7)	0.8	0.020
8. Practical housework Less than usual of 10 activities	4.5 (2.0)	4.5 (2.0)	0.9	4.6 (1.8)	4.2 (2.1)	0.7	1.0
9. Medication last mo. (tranquillisers, sleep)							0.007
Daily	18 (44%)	13 (43%)		5 (17%)	4 (18%)		
Weekly, not daily	7 (17%)	3 (10%)		2 (7%)	2 (9%)		
More rare	1 (2%)	5 (17%)		6 (21%)	4 (18%)		
Never	15 (37%)	9 (30%)		16 (55%)	12 (55%)		

*By paired *t*-test.
†By *t*-test/χ^2.

planned end of the intervention period. Only weight and dietary assessment were available for the latter patients and are included in the data. After intervention, both Groups A and B improved their diet and gained weight with no differences between the groups. After intervention, the energy intake in all the underweight and normal-weight patients was mean (SD) 192 (55) % of resting energy expenditure predicted by Harris and Benedict equation (REE predicted) and 132 (31) % and change in protein intake, 11 (18) g and −6 (19) g, respectively. The underweight patients increased their weight significantly compared with the normal-weight ones, 2.6 (2.9) kg and 0 (2.1) kg ($P = 0.001$) and increased FFM, 0.7 (1.4) kg and −0.1 (1.5) kg ($P = 0.06$), respectively. Only one underweight patient lost more than 1 kg. For the underweight patients who completed the intervention, there was a significant improvement in four of the nine dimensions of well-being measurements repeated after dietary intervention, compared with baseline (Table 2). Regression analyses showed that none of the well-being improvements was associated with weight gain. Increases in FFM were associated with a reduction in tiredness ($r = -0.32$, $P = 0.027$), but the significance did not remain after controlling for baseline measurements. Changes in energy intake were not associated with

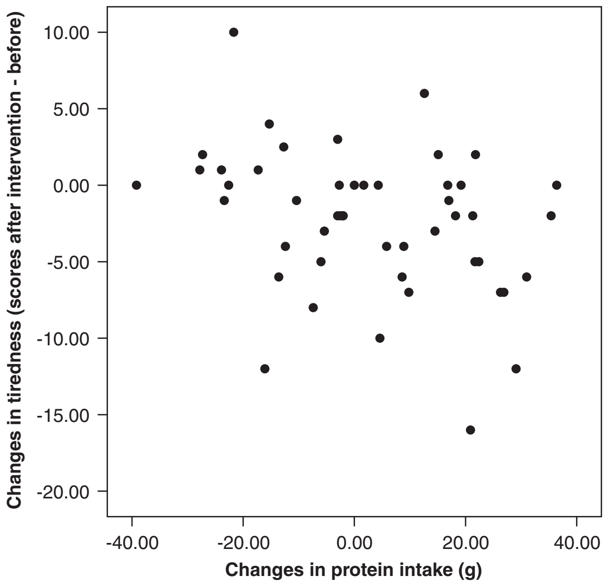

Figure 1 Correlation between changes in proteinintake and changes in tiredness (index 2) assessed in all patients ($r = -0.33$, $P < 0.02$).

changes in any of the well-being dimensions, but increases in protein intake after intervention were significantly correlated with a reduction in tiredness ($r = -0.33$, $P = 0.019$, Fig. 1) and displayed borderline significance after controlling for baseline measurements of protein intake and tiredness ($b = -0.305$, $P = 0.055$).

With the patients in this study, Cronbach's alpha coefficient at both points in time for dimensions of tiredness/full of energy and for dimensions of limitations in social and family activities ranged from 0.83 to 0.89. Because attempts with other multi-item indices (indexes 3 and 5, indexes 5 and 6) produced a Cronbach's alpha of < 0.70, these measures were reported separately.

Discussion

Quality of life is important for candidates for lung transplantation.[23] Quality of well-being may be a significant predictor of survival.[11] Even in these patients with severe limitations in functional ability, there appears to be potential for improved quality of life, as indicated in a pilot study that examined the impact of exercise programmes.[24] The results from our study showed that at baseline, underweight was associated with more impaired quality of life compared with the normal-weight patients for several of the measured dimensions and some improvements were observed after dietary intervention in the underweight patients but not in the normal-weight patients. Underweight patients who achieved the goal for energy and protein intake and experience a significant weight gain,[12] but the improvements in their well-being were not associated with the weight gain or change in body composition. In spite of this, achieving positive energy balance and nitrogen retention even without substantial weight gain could possibly have contributed to the patients feeling less impaired. Our data indicated an association between an increased intake of protein and a reduction in tiredness. Protein supplementation has been shown to be associated with a better clinical outcome in elderly patients with hip fractures,[25] but few studies have examined the question of dietary intake and quality of life.[26] The suggestion that improving nutrient intake per se may play a valuable role was also suggested in severely malnourished head and neck cancer patients.[27] In these patients, preoperative enteral nutritional support improved quality of life, even though their nutritional status was not improved.

As in the study by Squier et al.,[11] our measures of quality of life did not focus on disease-specific, health-related quality of life. Even though general well-being is influenced by the severity of disease, it allows for an overall impact of illness and reflects the patients' perceived well-being. Both lung-specific and general (SF-36) measures of quality of life have been shown to be sensitive in candidates for lung transplantation.[28] One potential advantage of measuring overall well-being, however, is that it includes the impact of interventions and non-disease-specific effects that may not be anticipated.[29]

At baseline, the most striking difference between underweight and normal-weight patients was that the underweight patients, independent of lung function, felt less calm compared with the normal-weight patients. This is consistent with the observation that the underweight patients used more tranquillisers and sleeping medication and is in agreement with the general view that psychological distress is associated with malnutrition.[30]

Having a terminal lung disease and being given the opportunity for treatment would most probably have a substantial emotional impact on patients. There is some uncertainty as to whether the improvements in well-being were achieved by the nutritional support or the extra medical attention the patients were given. However, we have no evidence to support the hypothesis that the feeling that something positive had happened differed between the underweight and normal-weight patients or that the medical attention the patients received was perceived differently by the underweight patients compared with the normal-weight ones.

Both underweight and normal-weight patients experienced substantial limitations in their family and social life and this was more marked in the case of the underweight patients. In spite of practical difficulties, several of the underweight patients improved their food intake. Our questionnaire was aimed at different dimensions of well-being, where some items would also be related to dietary behaviour, such as items in our index of tiredness and family and social activities. A change in dietary behaviour could potentially explain improvements in quality of life, because cooking and eating are important aspects of everyday life. Self-efficacy and perceived behaviour control are important, changeable determinants of dietary behaviour.[31,32] If the patients are confident that they are able to maintain a certain food intake, they will be more motivated to try and their attempts will be more persistent.[31] Goal-directed behaviour is supposed to be influenced by an evaluation of the belief in the positive or negative consequences of the behaviour.[33] Short-term positive benefits of this kind, such as being stronger before the transplantation, could probably have influenced motivation and shaped behaviour in our patients. Short-term effects are usually more effective than long-term effects[34] and this is relevant in our patients with end-stage pulmonary disease aiming for transplantation.

Some of our patients who were struggling with weight loss were satisfied if they could stop the weight loss. Patient satisfaction with maintaining a stable weight and avoiding further weight loss could explain the lack of association between weight gain and improvements in well-being. In a previously published study of COPD patients, improved quality of life was found after dietary intervention and weight gain.[9] However, in the study by Creutzberg et al.,[9] dietary intervention was implemented in a rehabilitation programme which also included physical training. In other patient groups, in contrast to our results, the restitution of body weight during nutritional support was shown to be associated with significant improvements in quality of life indices in patients with chronic illness.[35] In these patients, the mean weight gain was 4.2 kg, which is higher than in our patients. The higher weight gain could have made a difference to the impact on quality of life.

In conclusion, our results reveal that being underweight is associated with more impaired quality of life in candidates for lung transplantation. Benefits from dietary support on well-being, which was not associated with weight gain, were indicated.

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