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Nutritional state and exercise performance in patients with chronic obstructive lung disease

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ABSTRACT The relation between exercise performance and certain measures of nutritional state was investigated in 83 patients with stable chronic obstructive lung disease (mean age 62 (8) years). All patients had a forced expiratory volume in one second (FEV_1) less than 50% predicted, an arterial oxygen tension of more than 7·3 kPa, and no severe locomotor, cardiovascular, neurological, or endocrine disorders. Exercise performance was assessed from a 12 minute walking test; body weight (as a percentage of ideal weight), creatinine height index, and serum concentrations of albumin, transferrin, and prealbumin were assessed as measures of nutritional state. Mean values of the nutritional variables were within the normal range. The mean (SD) 12 minute walking distance was 686 (254) metres. Walking distance was positively associated with serum albumin concentration and creatinine height index but not with body weight, serum prealbumin, or serum transferrin concentrations. When patients were categorised into low, medium and high performance groups on the basis of their walking distance, a very low creatinine height index (mean (SD) 59% (19%)) was found in the low performance group. Albumin explained part of the variance in walking distance independently of pulmonary function in a stepwise regression analysis. The findings suggest that in patients with chronic airflow obstruction skeletal muscle mass and serum albumin concentration are positively associated with exercise performance as measured with a 12 minute walk.

Introduction

Chronic cough, expectoration, and dyspnoea are common symptoms in patients with chronic obstructive lung disease, many of whom are severely disabled by breathlessness and exercise impairment. Limitation of exercise is related to many factors, including abnormal pulmonary mechanics, impairment of pulmonary gas exchange and ventilatory control, abnormal perception of breathlessness, impaired cardiac performance due to pulmonary hypertension and ventricular failure, poor nutritional state, and the development of respiratory muscle fatigue.[1] Determination of the various factors and their relative importance in an individual patient is difficult and often impossible. The inability to characterise accurately the exercise limiting factors in individual patients has led to confusion and controversy in assessing the effectiveness of various forms of treatment designed to improve exercise performance.[2]

Over the past few years several studies have indicated that nutritional state is impaired in a high proportion of patients with chronic obstructive lung disease.[3–5] Weight loss is common with severe disease.[6] Malnutrition is a leading cause of impaired respiratory muscle contractility, affecting both strength and endurance.[7] In patients with severe malnutrition significant changes in respiratory and limb muscle contraction and relaxation characteristics and fatigability properties have been described.[8,9] The aim of our study was to evaluate the relation between some measures commonly used for assessing nutritional state and exercise performance in patients with stable chronic obstructive lung disease.

Methods

The study group consisted of 83 patients with chronic obstructive lung disease with severe airflow obstruction (forced expiratory volume in one second (FEV_1) less than 50% of predicted[10]) admitted to the pulmonary rehabilitation centre for physical training.

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Patients with cardiovascular, neurological, endocrine, and locomotor diseases and those with an arterial oxygen tension (Pa_{O_2}) below 7·3 kPa[11] were excluded from exercise testing. The patients were in a stable clinical condition. Maintenance medication in all patients included theophylline, $beta_2$ agonists, and inhaled or oral corticosteroids.

LUNG FUNCTION

FEV_1 and inspiratory vital capacity (IVC) were measured with a wet spirometer, the highest value from at least three spirometric manoeuvres being used. FEV_1 and IVC were expressed as percentages of the reference values.[10] Blood was taken from the brachial artery for blood gas analysis. Right ventricular hypertrophy was assessed by electrocardiography in 79 patients by two independent observers.

EXERCISE PERFORMANCE

Exercise performance was evaluated by a 12 minute walking test, performed in a level, enclosed corridor according to the method described by McGavin.[12] All tests were performed in the early afternoon and no encouragement was given. As learning effects have been noticed to occur quickly with repeated walking tests,[12 13] the patients performed one practice 12 minute walking test.

NUTRITIONAL STATE

Height and weight; 24 hour urinary creatinine excretion; and serum albumin, prealbumin, and transferrin concentrations were measured to assess nutritional state. Body weight was compared with a reference value based on height, sex, and frame size from the Metropolitan Life Insurance Company weight standards,[14] the ratio being expressed as a percentage of ideal weight. A fasting blood sample was drawn for measurement of serum protein concentrations. Serum albumin concentrations were measured by fractionation by standard electrophoresis and serum transferrin and prealbumin concentrations by radial immunodiffusion. Skeletal muscle mass was estimated from the creatinine height index (the 24 hour urinary creatinine excretion divided by a reference value based on percentage of ideal body weight).[15] All measurements were done immediately after admission to the centre.

STATISTICAL ANALYSIS

Descriptive statistics are given as mean (SD). Nutritional measures were correlated with exercise performance by means of the product moment correlation coefficient. As many biochemical variables are affected by age,[16] partial correlation coefficients were computed, adjusted for a possible confounding age effect. Patients were divided into low, medium, and high exercise performance groups, the medium performance group consisting of patients walking within one SD of the mean walking distance of the total group, and the low and high performance groups being more than one SD below and above the mean walking distance respectively. The three groups were compared for nutritional and lung function measures by one way analysis of variance. After the simple correlations had been completed a linear model was fitted to the data to enable the variables that contributed to the 12 minute walking distance to be determined by stepwise regression analysis.

Results

The study group consisted of 83 patients, 21 of whom had recently been discharged from hospital. Seven patients were currently receiving antibiotic treatment for a chest infection. The mean age of the 71 men and 12 women was 62 (8) years. Mean (SD) inspiratory vital capacity (IVC) and FEV_1 were 2·7 (0·6) and 0·9 (0·3) l respectively. Signs of right ventricular hypertrophy were found in 46 patients.

Although mean values of the nutritional variables were within the normal range, a substantial number of patients had a body weight less than 90% of ideal body weight (n = 21) or a creatinine height index less than 60% or both (n = 35). Twenty seven patients reported recent weight loss ($\geqslant$10% of previous body weight). None of the nutritional measures correlated significantly with age.

The mean 12 minute walking distance was 686 (254) metres. The mean difference between the test carried out during the study and the practice test was + 100·6 metres, with a 95% confidence interval of 72 to 129 metres.

The 12 minute walking distance showed a significant correlation with the serum albumin concentration and creatinine height index but no association with body weight or serum prealbumin or transferrin concentration (table 1). There were no

Table 1 *Partial correlation coefficients between nutritional measures, lung function, and 12 minute walking distance*

	12 minute walking distance	
	r	*p*
Percentage ideal body weight	0·19	NS
Creatinine height index	0·35	0·001
Serum concentrations of:		
albumin	0·44	0·001
transferrin	0·09	NS
prealbumin	0·10	NS
Inspiratory vital capacity	0·21	0·03
FEV_1	0·29	0·002
Arterial oxygen tension	0·42	0·001
Arterial carbon dioxide tension	0·21	0·03

IVC—inspiratory vital capacity; FEV_1—forced expiratory volume in one second; Pa_{O_2}, Pa_{CO_2}—arterial oxygen and carbon dioxide tension.

Table 2 *Nutritional and lung function variables (mean (SD)) categorised by 12 minute walking distance*

Walking (metres) performance	*<432, low*		*432–940, medium*		*>940, high*		*p*
Percentage ideal body weight	98	(12)	98	(16)	102	(10)	NS
Creatinine height index (%)	59	(19)	98	(18)	86	(25)	0·006
Serum concentrations (g/l) of:							
albumin	37·9	(4·7)	41·6	(4·3)	44·3	(3·6)	0·001
transferrin	2·5	(0·04)	2·6	(0·03)	2·6	(0·05)	NS
prealbumin	0·30	(0·05)	0·29	(0·08)	0·31	(0·07)	NS
IVC (% predicted)	62	(16)	69	(14)	74	(16)	NS
FEV_1 (% predicted)	31	(9)	31	(9)	36	(7)	NS
Pao_2 (kPa)	9·0	(0·9)	9·7	(1·4)	10·9	(2·0)	0·005
$Paco_2$ (kPa)	5·3	(0·7)	5·2	(0·7)	4·9	(0·6)	NS

IVC—inspiratory vital capacity; FEV_1—forced expiratory volume in one second; Pao_2, $Paco_2$—arterial oxygen and carbon dioxide tension.

significant differences in spirometric measures between the low, medium, and high performance groups (table 2). Pao_2 was significantly different between the three groups.

Right ventricular hypertrophy was not associated with impaired exercise performance. Weight loss was reported more often in the low (36%) and medium (67%) performance groups than in the high (7%) performance group. The creatinine height index was below normal in the low performance group. Serum albumin concentration was low in the low performance group and lower in the medium than in the high performance group. Albumin was positively associated with Pao_2 ($r = 0·28$, $p < 0·005$). In the regression analysis (table 3) serum albumin explained part of the variance in 12 minute walking distance after inclusion of spirometric measures and arterial blood gas tensions in the model.

Discussion

Many patients with chronic obstructive lung disease suffer from severe exercise impairment. The 12 minute walking test has been proposed as a simple and reproducible test to assess exercise performance in these patients.[12] Several studies have related exercise performance to spirometric measures. Small but significant correlations were found between walking distance and IVC and FEV_1 by some authors[17–20] but not by others.[13 21]

In this study we assessed whether impairment of exercise performance is associated with an impaired nutritional state. Only patients with an FEV_1 less than 50% of the predicted value were included, to increase the homogeneity of the study group. We established an association between 12 minute walking distance, creatinine height index, and serum albumin concentration.

In patients with chronic obstructive lung disease body weight as a percentage of ideal body weight is commonly used as an indicator of nutritional state. In our study, however, in agreement with the results of other authors using the six minute walking distance,[22 23] body weight expressed as a percentage of ideal body weight was not correlated with walking distance.

In patients with severe chronic obstructive lung disease muscle mass cannot be assumed to increase simultaneously with increasing body weight. Variability in body fat and extracellular fluid volume between patients may be quite large as a result of immobility and fluid retention. In addition to body weight we therefore assessed the creatinine height index.[24 25] Creatine and phosphocreatinine in muscle are non-enzymatically dehydrated to form creatinine, which is excreted in the urine. If the proportion of phosphocreatinine and creatine in muscle is constant, the production and excretion of creatinine in the urine over 24 hours provides a measure of muscle mass.[26] Creatinine excretion in healthy individuals correlates well with oxygen use and lean body mass.[24] In patients with wasting disease, however, the creatinine height

Table 3 *Determinants of variation in 12 minute walking distance*

Variable	*R^2 model†*	*F model‡*	*Df*	*F variable§*	*Df*
Albumin	17	16·9***	1·82	13·0***	1·79
Pao_2	28	15·4***	2·81	10·1***	1·79
Age	33	13·1***	3·80	6·4*	1·79

*p = 0·01; ***p = 0·001.
†R^2 = 100* (regression sum of squares)/(total sum of squares) for model consisting of current and preceding variables.
‡Model consisting of current and preceding variables.
§After adjustment for the remaining variables.
Pao_2—arterial oxygen tension.

index falls, and is no longer related to body weight. These changes presumably result from a distortion of body composition, especially the loss of protein.[27] It has been shown that fluid retention does not alter an abnormally low creatinine height index even when body weight is affected.[28] A 20% decrease in the creatinine height index between the ages of 65 and 74 years is considered to be a normal decline with advancing age. A value of less than 60%, however, is considered to indicate a severe deficit of muscle mass.[24] Further data, including serial values for the creatinine height index, need to be obtained to determine whether loss of muscle mass, as may happen with weight loss, is related to change in exercise performance.

Albumin, prealbumin, and transferrin concentrations are commonly used measures of visceral protein.[15] Prealbumin is more sensitive to short term nutritional depletion and repletion than albumin, because it has a very short half life; but there was no association between 12 minute walking distance and serum prealbumin concentration. This might be due to a large between day variability of prealbumin or sensitivity of the measurement to metabolic stress, such as bronchial infection or to chronic corticosteroid medication,[29] or to a combination of these. The low correlation coefficient between the 12 minute walking distance and serum transferrin concentrations could, in part at least, be explained by the fact that serum iron concentration in patients with chronic obstructive lung disease does not reflect iron stores as much as the adjustment of the body to hypoxaemia.[3]

Of three possible causes of the decrease in serum albumin, an excessive shift in body fluids is unlikely in the group under study, because of the inclusion criteria we used: all patients were in a stable cardiac and pulmonary condition. Serum albumin concentrations were also not different in the patients with right ventricular hypertrophy. The relative effects of malnutrition and the overall stress of the chronic disease process on serum albumin concentrations cannot yet be established. Albumin was not related to body weight expressed as a percentage of ideal body weight but was positively associated with arterial oxygen tension. In keeping with the findings of an earlier study, the results suggest that low serum albumin concentrations in patients with chronic obstructive lung disease may be due to chronic hypoxaemia.[30]

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