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Body composition by bioelectrical impedance predicts mortality in chronic obstructive pulmonary disease patients

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Summary Pulmonary rehabilitation is recommended in international treatment guidelines for chronic obstructive pulmonary disease (COPD). No one has however studied the effect on long-term mortality. The aim of the current study was to study the mortality in a sample of patients with severe COPD included in a 1-year multidisciplinary rehabilitation program. Body composition was assessed at baseline using bioelectrical impedance. Mortality was studied in 86 patients using the Cox proportional hazards model. Forty-seven (55%) of the patients died during the mean follow-up time which was almost 6 years. Risk of mortality increased with increasing age, increasing number of hospital days the year before inclusion and men had higher mortality risk than women. The mortality risk decreased with increasing % reference body weight, increasing fat-free mass index (FFMI), increasing FEV_1 and increasing 6-min walking distance. Gender, age and FFMI continued to be statistical significant predictors of mortality when controlling for the other baseline variables in a multivariate analysis. To conclude, body composition, measured by bioelectrical impedance and presented as FFMI, is an independent predictor of mortality in COPD patients.

Introduction

Chronic obstructive pulmonary disease (COPD) is the fifth leading cause of death in North America and its prevalence continues to increase, especially

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in women.[1,2] During the last decade, several studies have investigated factors affecting the mortality risk in COPD patients.[3–7] Common for most of these studies is that a low body weight or a low body mass index (BMI) is found to be a major mortality risk factor. Marquis et al.[7] however, in their study on 142 COPD patients, found that body composition, measured as midthigh muscle cross-sectional area obtained by computed tomography (CT) scan, was a better predictor of mortality than BMI. However this finding was not confirmed using body composition assessed by anthropometry. Studies using simpler and less expensive methods than CT to assess predictive effect from body composition were therefore asked for.[8]

Thomasset[9] was the first to report a relation between total body water and electrical impedance. The use of bioelectrical impedance is based on the principle that fat mass and fat-free mass (FFM) have different conductive and dielectric properties. This is due to the fact that FFM contains water and therefore has a lower resistance than fat mass.[10] An electrical current is sent through the human body and the bioelectrical impedance is measured. Relating the impedance to the conductor's (the human body) height gives an assessment of total body water and hence fat mass and FFM can be calculated.[11] The aim of the current study was to investigate the mortality in a sample of patients with severe COPD included in a 1-year multidisciplinary rehabilitation program in relation to body composition as evaluated by bioelectrical impedance.

Methods

Patients

The patients in this study were included from two prospective studies of multidisciplinary rehabilitation of COPD patients at the Department of Respiratory Medicine, Sahlgrenska University Hospital, Göteborg, Sweden. The rehabilitation program has been presented previously.[12] The first study comprised 50 patients randomized to a rehabilitation group and a control group. Subjects in the control group were given ordinary medical treatment, but no rehabilitation during the control period. All control subjects, however, went through an identical 1-year rehabilitation as the cases the year following the control period. The control subjects were added as cases in the current presentation with defining study start as the day they started the rehabilitation. The second study comprising 36 patients (to be published), compared the effect of the rehabilitation program supplemented by group psychotherapy. In both studies identical inclusion criteria were applied. Patients aged 40–75 with COPD with a forced expiratory volume in 1 s (FEV_1) $<$ 50% of predicted and with no demand of oxygen therapy were included. All of the patients were smokers or former smokers with a smoking history of at least 10 pack years. Exclusion criteria were other disabling or severe diseases and/or coexistence of other causes of impaired pulmonary function. Patients with a history that indicated asthma were excluded. None of the subjects had an acute exacerbation at the time of inclusion and they were included consecutively. The decision to make the present analysis was however retrospective.

Between March 1992 and June 1998, 86 patients were included in the studies. Patients that survived were followed from date of inclusion to 1 January 2003, and the ones who died from date of inclusion to their date of death. The subjects gave written informed consent to the study and the study was approved by the Ethics Research Committee of Göteborg University.

Study design

Assessment of diet, with the diet history method[13] and measurements of FEV_1, were performed at study start and after 12 months. Anthropometric measurements, bioelectrical impedance assessments, and 6-min walking distance tests were performed every third month. The 6-min walking distance test was performed by the same nurse at each occasion and all patients had one training test before the study started. Individualized dietary advice and follow-up by the dietitian were routinely done at study start and after 3, 6, 9, and 12 months and additional visits were individualized for each patient when judged needed by the dietitian. The patients trained on a bicycle under the supervision of a physiotherapist. Training also included breathing techniques and arm training. At study start patients trained twice a week. A home training program was introduced, which by time substituted supervised training. The time for changing from supervised to home based training was individualized after each patients needs. Further details of the training program is published by Engström et al.[12]

Body composition assessment

Height was measured to the nearest 0.5 cm and weight was measured on a Lindelltronic Scale to the nearest 0.1 kg with the subjects in light clothing. In addition to calculating the BMI, the weight of the patients was expressed as a percentage of the weight of a normal Swedish elderly population,[14] defined as % reference weight (% IBW). Single-frequency bioelectrical impedance assessment was performed in the morning after 10 min rest in the supine position. Impedance was measured by one single measurement of resistance (in Ohms) and reactance (in Ohms) with a BIA-101 equipment (Akern Florence, Italy). Short- and long-term reliability of resistance measurements indicate coefficient of variation between 2.7% and 4.0%.[15] The four electrodes were attached on the dorsal side of the foot and the ankle and on the dorsal side of the hand and the wrist at the right side of the body. FFM was calculated using manufacturer supplied equations, based on comparison with densitometry in a normal population. The fat-free mass index (FFMI) was calculated as FFM in kg divided by body height^2.

Physiological measurements

Routine spirometry was performed with a Vitalograph spirometer (Selefa, Buckingham, Ireland) before and 15 min after inhalation of 1 mg terbutaline to reach optimal standardization. The 6-min walking distance tests were performed following standardized instructions.[16]

Nutritional assessment and dietary intervention

A trained dietitian interviewed each patient with a diet history interview that constituted the background for the individual dietary advice given to the patients during the rehabilitation. One of the aims of the dietary advice was to give the patient an adequate intake of energy, in order to give maximal effect of physical training and reducing malnutrition. The normal weight patients were given dietary advice in order to stabilize the body weight. Overweight and obese patients were given individualized weight reducing advice (reduce energy intake, reduce fat intake, increase intake of fiber). The underweight patients were given advice intended to increase their body weight. They were also offered free availability of nutritional supplements containing energy and micronutrients. Effort was also made to correct imbalances between the energy-providing nutrients: fat, carbohydrates and protein.

Hospital days

The number of hospital days at Sahlgrenska University Hospital during the year before study start was recorded. So was the number of hospital days from study start to time of death or study end (1 January 2003).

Statistical analysis

Descriptive statistics were used to describe the study population at inclusion. Baseline information was used as independent predictors of mortality in a univariate analysis based on the Cox proportional hazards model where survival status at the 1 January 2003 was used as the dependent variable. Baseline variables that were associated with

Table 1 Patient characteristics at baseline and their prediction of mortality in an univariate analysis (mean (SD)), $n = 86$.

	All patients	Survivors ($n = 39$)	Non-survivors ($n = 47$)	*P*-value*	Hazard ratio	95% CI	*P*-value
Age (years)	65.9 (6.6)	63.6 (7.0)	67.7 (5.6)	0.0036	1.06	1.01–1.12	0.013
Sex (%F/%M)	49/51	59/41	40/60	0.13	1.64	0.92–2.94	0.096
Smokers (% of group)	29	36	23	0.24	0.85	0.43–1.68	0.65
Hospital days the year before inclusion	9 (24)	5 (18)	12 (27)	0.18	1.01	1.00–1.02	0.063
BMI (kg/m^2)	22.8 (4.1)	23.5 (3.5)	22.3 (4.4)	0.17	0.95	0.88–1.02	0.17
Reference body weight (%)	91.4 (16.3)	94.6 (14.1)	88.8 (17.7)	0.10	0.98	0.97–1.00	0.10
Fat free mass (kg)	48.6 (9.6)	50.1 (10.7)	47.3 (8.5)	0.18	0.98	0.95–1.01	0.20
FFMI (kg/m^2)	16.8 (2.3)	17.3 (2.4)	16.3 (2.2)	0.046	0.88	0.77–1.01	0.061
Body fat (%)	25.8 (7.2)	25.9 (6.3)	25.6 (8.0)	0.85	1.00	0.96–1.04	0.87
FEV_1 (% pred)	35 (11)	39 (11)	31 (10)	0.0013	0.96	0.93–0.99	0.0060
6 min walking distance (m)	329 (82)	354 (71)	307 (85)	0.0087	0.99	0.99–1.00	0.0031

*Survivors compared with non-survivors.

mortality with a $P<0.15$ were further on included in a multivariate analysis based on the Cox proportional hazards model. To examine differences between survivors and non-survivors, an unpaired t-test was used for continuous variables, and Fisher's exact test for comparison of proportions. Data were analyzed using the SPSS 11.5 for Windows statistical package (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of the patients (42 women and 44 men) are presented in Table 1. During the rehabilitation year three of the patients died, one patient received oxygen treatment, two patients underwent major surgery and one patient was diagnosed for cancer and they are included in the further analysis. Table 1 show that the survivors were younger, had a higher FFMI and FEV_1 and performed better on the 6 min walking distance. In total there were 47 deaths (55%) and the causes of death are presented in Table 2. The causes of death included in "other" were stroke, mediastinitis, pulmonary embolism and drug overdose. Mean follow-up time for the survivors was 7 years and 3 months. For the patients who died, it was 4 years and 3 months. The Cox proportional hazards model presented in Table 1 and Fig. 1, shows that the mortality risk increased with increasing age, increasing number of hospital days during the year before inclusion and that men had higher mortality risk than women. The mortality risk decreased with increasing percentage reference body weight, increasing FFMI, increasing FEV_1 and increasing 6-min walking distance. In addition to gender and age, FFMI continued to be a statistically significant predictor of mortality when controlling for the other baseline variables in the multivariate analysis (Table 3). Changes in some variables from baseline to end of the rehabilitation year are presented in Table 4. The results for the total patient group is presented earlier[13] showing slight, but uniform, indications of positive effects of the rehabilitation. A larger proportion of the non-survivors were prescribed nutritional supplements while the survivors had more visits at the physiotherapist.

Table 2 Main cause of death, $n=47$.

Respiratory failure	19
Chronic obstructive pulmonary disease	9
Heart failure	8
Lung cancer	5
Cancer, other than lung	2
Other	4

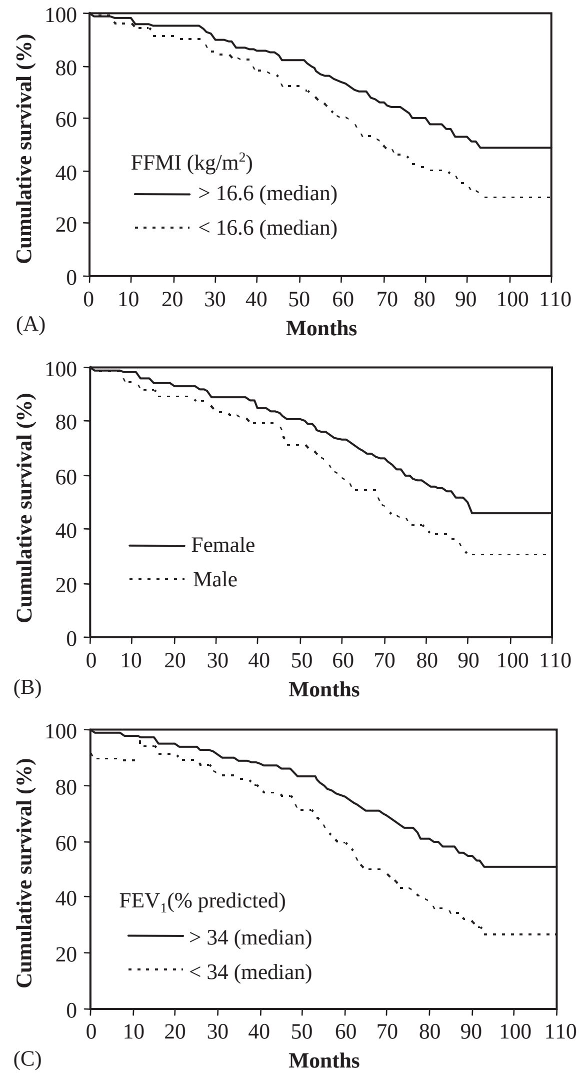

Figure 1 Cumulative survival in a group of COPD patients categorized by FFMI (panel A), gender (panel B), and FEV_1 (panel C) ($n=86$).

Discussion

We have shown that body composition, measured by a non-invasive and relatively simple method, is an independent predictor of mortality in COPD patients. The present study supports the findings of Marquis et al.[7] that suggested that body composition would be a significant predictor of mortality in COPD patients. In this study we used bioelectrical impedance assessment, which is a non-invasive, simple and relatively non-expensive method of body composition assessment. Body composition results were presented as FFMI as recommended by VanItallie et al.[17] It is important that techniques for body composition analysis are standardized. We have previously shown that measurements of bioelectrical impedance used for body composition assessment need to be highly standardized.[18,19] In the current study, the subjects were measured in the morning after 10 min rest in the supine position.

However, we could not confirm previous findings that BMI or body weight are predictors of mortality.[3,4,7] This is in consistency with the findings of Marquis et al.,[7] who found a body composition measure to be a better predictor of mortality than BMI. The lack of this relation in the present study could be due to a limited group size. Except body composition, old age and male gender also were found to be independent predictors of mortality in this study. Age is a natural risk factor for death. The effect of gender is complicated. In the current study, men did not differ from women in disease severity (FEV_1). Even if the men were older than the women ($P<0.05$), the effect of gender on mortality is shown independently of age. There are indications from epidemiological studies, that women are more susceptible than men to develop COPD,[20] but the risk of developing COPD might not be identical with the severity of the disease when it has been established. The results of the present study, however, is in line with other studies investigating the prognosis in groups of patients with established COPD, in which poor prognosis in male patients was shown.[1,21–23]

The mortality rate in this study is well in line with results from comparable studies of similar patient groups performed the last decade. In this study, 55% of the patients died during the mean follow-up time of 5.6 years, which gives an annual death rate of 9%. In the study of Marquis et al.[7] 18% of the patients died during the 3.4 years of follow-up, resulting in an annual death rate of 5%. The patients in that study had however somewhat less severe disease (mean FEV_1 was 42% predicted compared with 35% predicted in the current study). In a Canadian study[24] 47% of the patients died during the follow-up of almost 3 year, giving an annual death rate of 16%. In that study, mean FEV_1 was 27% predicted, and they also included patients receiving oxygen treatment, indicating a lower pulmonary function and hence a higher mortality rate would be expected. Thus approximately 50% of patients with severe COPD included in rehabilitation programs can be expected to die within 5 years. Thus the prognosis in advanced COPD is worse than for most forms of malignant diseases.[25]

Table 3 Baseline predictors of mortality: multivariate analyses, $n = 86$.

	Hazard ratio	95% CI	*P*-value
Age (years)	1.06	1.00–1.12	0.037
Sex (F/M)	3.52	1.27–9.78	0.016
Hospital days the year before inclusion	1.01	0.99–1.02	0.30
Reference body weight (%)	1.05	0.99–1.10	0.11
FFMI (kg/m^2)	0.65	0.44–0.96	0.030
FEV_1 (% pred)	0.98	0.95–1.02	0.28
6 min walking distance (m)	1.00	0.99–1.00	0.54

Table 4 Patient characteristics during the rehabilitation year (mean (SD)), $n = 86$.

	All patients	Survivors ($n = 39$)	Non-survivors ($n = 47$)	*P*-value*
ΔBMI (kg/m^2)	0.0 (1.2)	+ 0.1 (1.1)	−0.2 (1.2)	0.25
ΔFFM (kg)	−0.1 (2.3)	0.0 (2.4)	−0.2 (2.4)	0.69
ΔFFMI (kg/m^2)	0.0 (0.8)	0.0 (0.8)	−0.1 (0.8)	0.61
ΔFEV_1 (% pred)	+ 3 (8)	+ 3 (8)	+ 3 (8)	0.77
Δ6 min walking distance (m)	+ 17 (58)	+ 27 (56)	+ 6 (59)	0.12
Cortisone treatments, *n*	1.9 (2.2)	1.4 (1.5)	2.4 (2.6)	0.069
Visits at the dietitian, *n*	8.5 (5.0)	7.6 (4.7)	9.3 (5.1)	0.10
% of group prescribed nutritional supplements (%)	51	36	64	0.017
Visits at the physiotherapist, *n*	25.8 (14.2)	29.2 (13.0)	23.0 (14.7)	0.042

*Survivors compared with non-survivors.

In this study we have shown that body composition, measured by bioelectrical impedance and presented as FFMI, is an independent predictor of mortality in COPD patients.

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