ORIGINAL ARTICLES

Prevalence of Malnutrition in Outpatients With Stable Chronic Obstructive Pulmonary Disease

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OBJECTIVE: To determine the prevalence of malnutrition in outpatients with stable chronic obstructive pulmonary disease (COPD) followed at a respiratory clinic.

MATERIAL AND METHOD: In this prospective study, we assessed the nutritional status of consecutive outpatients with stable COPD by investigating various anthropometric parameters. Patients were malnourished (low body weight) if their body mass index was within the bottom quartile of a reference population. Muscle mass was determined from the midarm muscle area and if this mass was at or within the bottom quartile, muscle wasting was present. Albumin and transferrin plasma concentrations were used as a measure of visceral protein stores. Fat stores were assessed from body fat and if this value was at or within the bottom quartile, calorific malnutrition was present. All patients underwent arterial blood gas sampling at rest and spirometry.

RESULTS: A total of 178 patients—one woman (0.6%) and 177 men (99.4%)—were enrolled in the study, with a mean (SD) age of 69 (9) years. We found low body weight in 19.1% of the patients, muscle wasting in 47.2%, visceral protein depletion in 17.4%, and fat depletion in 19.1%. Of the patients with normal weight, 62.9% showed muscle wasting. The proportion of patients with a body mass index or midarm muscle area at or within the bottom quartile increased significantly with increased bronchial obstruction (*P*<.001 and *P*=.015, respectively), though 35.7% of the patients showed muscle wasting even when COPD was mild.

CONCLUSIONS: Many patients with stable COPD suffer malnutrition. Nutritional state is worse with more severe COPD. Depletion involves both fat stores and muscle and visceral protein stores, but the greatest effect is seen in muscle wasting. A significant number of patients with normal weight also suffer muscle wasting. Although changes in body composition were common in our patients, low body weight was less prevalent than has been reported for populations in countries that are socially and economically similar to Spain.

Key words: *Chronic obstructive pulmonary disease (COPD). Malnutrition. Anthropometric measures.*

Prevalencia de la desnutrición en pacientes ambulatorios con enfermedad pulmonar obstructiva crónica estable

OBJETIVO: Determinar la prevalencia de la desnutrición en pacientes con enfermedad pulmonar obstructiva crónica (EPOC) estable, controlados en una consulta especializada de neumología.

MATERIAL Y MÉTODO: Se realizó un estudio prospectivo y consecutivo en pacientes con EPOC estable controlados de forma ambulatoria. Para valorar el estado nutricional empleamos diversos parámetros antropométricos. Se definió desnutrición global (bajo peso corporal) como la presencia de un índice de masa corporal inferior al percentil 25 del valor de referencia. Para valorar el compartimiento proteico muscular se determinó el área muscular del brazo y se definió la depleción muscular como un valor de área muscular del brazo igual o inferior al percentil 25. Como valoración de la proteína visceral se midieron las concentraciones plasmáticas de albúmina y transferrina. El compartimiento graso se estudió mediante la determinación de la grasa corporal total. Un valor de ésta igual o inferior al percentil 25 se utilizó como criterio de desnutrición calórica. Se realizaron a todos los pacientes espirometría y gasometría arterial en reposo.

RESULTADOS: Se incluyó en el estudio a 178 pacientes –una mujer (0,6%) y 177 varones (99,4%)–, con una edad media de 69 ± 9 años. Las prevalencias de bajo peso corporal, desnutrición proteica, muscular o visceral y depleción grasa fueron del 19,1, el 47,2, el 17,4 y el 19,1%, respectivamente. Entre los pacientes con normopeso, el 62,9% presentaba pérdida de masa muscular. La proporción de casos con índice de masa corporal igual o menor del percentil 25 o área muscular del brazo igual o inferior al percentil 25 aumentó de forma significativa a medida que empeoraba el grado de obstrucción bronquial (p < 0,001 y p = 0,015, respectivamente). No obstante, hasta un 35,7% de los pacientes con EPOC leve también mostraron depleción proteica muscular.

CONCLUSIONES: La desnutrición en pacientes con EPOC estable es un problema frecuente, que aumenta con la gravedad de la enfermedad. La depleción afecta tanto al compartimiento graso como al proteico muscular y visceral. No obstante, existe un cierto efecto preferencial sobre la pérdida de masa muscular. Una proporción significativa de pacientes con normopeso también sufre desnutrición proteica muscular. Pese a que las alteraciones en la composición corporal son frecuentes, nuestros resultados reflejan una prevalencia de bajo peso corporal menor que la de diversas series publicadas en países de nuestro entorno social y económico.

Palabras clave: *Enfermedad pulmonar obstructiva crónica (EPOC). Desnutrición. Medidas antropométricas.*

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Introduction

Chronic obstructive pulmonary disease (COPD) has usually been considered limited to airway and parenchymal disorders that cause chronic airflow obstruction. Recent evidence suggests that the disease also has several systemic effects,[1] so interest in the nutritional aspects of the disease has been revived. Several studies have shown that malnutrition is common in COPD and a relevant concern that may even affect prognosis. Low body mass index (BMI) has been shown to be an independent marker of poor prognosis.[2,3] Nutritional disorders have also been associated with higher morbidity, with involvement of both respiratory and peripheral skeletal muscle,[4,5] lower exercise tolerance,[6,7] increased dyspnea,[8] and lower health-related quality of life.[9,10]

The exact prevalence of malnutrition in COPD is currently unknown because there is no diagnostic method that serves as a reference and no widely accepted definition. Body weight provides a simple indication of nutritional status. Repeated measurement of body weight can be used to monitor wasting, which is usually considered significant when it exceeds 5% to 10% per year. Previous studies have reported values for weight loss associated with COPD of 27%,[11] 33%,[12] and 47%.[13] However, interpretation of the changes in body weight can be difficult due to water retention, which is often observed in patients with respiratory failure. Attempts to improve the assessment of nutritional status have been made by way of comparison with reference values considered normal. Two methods have been used. The first compares actual body weight with the ideal weight derived from standard tables.[14] According to this method, malnutrition is arbitrarily considered to be present when the actual body weight is less than 90% of the ideal weight. The second method uses BMI, that is, weight divided by height squared. Malnutrition is considered to be present when BMI is less than 20 kg/m^2.[15] The prevalence of low body weight in 2 American series and a European series according to these definitions was similar—between 24% and 35%.[16-18] Few Spanish studies have investigated the prevalence of nutritional disorders in COPD.

The assessment of nutritional status by body weight is simple but subject to substantial limitations in that it does not provide qualitative information on body composition. Four different nutritional compartments can be identified: fat, skeletal, intracellular (also known as body cell mass), and extracellular. The latter 3 form the lean body mass. The body cell mass, which reflects metabolically active tissue (organs) and contractile tissue (muscle), is comprised of visceral protein and muscle protein. Approximately 60% of body cell mass is muscle. This variable cannot be directly measured by any method in clinical practice, thus the variable that best reflects nutritional status is lean body mass. Different methods are available for measuring body composition such as bioelectric impedance, dual energy x-ray absorptiometry, densitometry, measurement of total body water by deuterium dilution, or measurement of anthropometric variables. Anthropometric variables can be measured simply, cheaply, and quickly, and provide an indirect evaluation of nutritional status and body composition. For correct interpretation of such variables, reference values for the study population are required.

The objective of this study was to determine the prevalence of malnutrition in patients with stable COPD followed by specialists in a pneumology department. In addition to body weight, body composition was also assessed using a variety of measures.

Material and Method

In the first 6 months of 1999, a prospective study was carried out on consecutive patients with COPD followed by specialists in the outpatient respiratory medicine clinics in our hospital. Ours is a first-referral regional hospital responsible for all specialized care in Area 7 of the Autonomous Community of Valencia. The hospital caters for a population of approximately 58 000 people. Only patients diagnosed with COPD in accordance with the criteria of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) were included in the study.[19] Thus the patients had to have a forced expiratory volume in 1 second (FEV_1) below 80% of the reference value, a ratio of FEV_1/forced vital capacity (FVC) less than 70%, and a history of smoking. Patients with bronchial asthma, bronchiectasis, cystic fibrosis, upper airway obstruction, or bronchiolitis related to systemic diseases were excluded from the study. Patients with concomitant diseases that might alter nutritional status (heart failure, liver cirrhosis, uncontrolled diabetes, chronic renal failure, uncontrolled thyroid disease, neoplasms, uncontrolled chronic cor pulmonale, and sustained consumption of systemic corticosteroids) were also excluded. Patients had to be in a stable phase of the disease, that is, free from exacerbation in the 2 months prior to the study.

Nutritional Assessment

The nutritional status was assessed by measuring the following anthropometric variables: weight, height, triceps skinfold, subscapular skinfold, abdominal skinfold, and midarm circumference of nondominant arm. These variables were used to calculate BMI, midarm muscle circumference, midarm muscle area (MAMA), midarm arm fat area, fat-muscle index, and total body fat. Table 1 summarizes the equations used for these calculations. Total body fat was calculated with the Siri equation.[20] Two observers who had been trained in the use of skinfold calipers (Holtain, Cambridge, UK) measured the skinfolds with the standard method in nutritional studies.[21] All measurements were performed when the patient was relaxed. The final value was the mean of 3 consecutive measurements of each one of the skinfolds. The triceps skinfold was measured halfway along the arm between the olecranon and the acromion. The subscapular skinfold was measured below the lower vertex of the scapula with the skinfold caliper at 45º to vertical. The abdominal skinfold was measured halfway along an imaginary line joining the umbilicus and the anterosuperior

TABLE 1
Equations Used for Calculating Anthropometric Parameters*

Parameter	Equation
Body mass index, kg/m^2	Weight/height^2
Midarm muscle circumference, cm	CA (cm)–(3.14×TSF [mm])
Midarm muscle area, cm^2	(CA [cm]–3.14×TSF[mm])^2 /(4×3.14)
Midarm fat area, cm^2	(CA^2/[4×3.14])–MAMA
Fat/muscle index	MAFA/MAMA
Total body fat, kg	([4.95/D]–4.5)×100
Body density	C–(M×log TSF[mm])

*CA indicates circumference of nondominant arm; TSF, triceps skinfold; MAMA, midarm muscle area; MAFA, midarm fat area; D, body density; C and M, linear regression constants to estimate body density (C=1.1114 and M=0.0618 for men, C=1.1278 and M=0.0775 for women).[20]

TABLE 2
Definition of Malnutrition*

Type of Malnutrition	Criteria Applied	
Overall malnutrition	BMI≤P25	
Mild	BMI: P11-25	
Moderate	BMI: P6-10	
Severe	BMI≤P5	
Muscle protein malnutrition	MAMA≤P25	
Mild	MAMA: P11-25	
Moderate	MAMA: P6-10	
Severe	MAMA≤P5	
Visceral protein malnutrition	Albumin (mg/dL) or transferrin (mg/dL)	
Mild	2.8-3.5	150-199
Moderate	2.1-2.7	100-149
Severe	<2.1	<149
Energy malnutrition	TBF≤P25	
Mild	TBF: P11-25	
Moderate	TBF: P6-10	
Severe	TBF≤P5	

*BMI indicates body mass index (kg/m^2); P, percentile; MAMA (cm^2), midarm muscle area; TBF, total body fat.

iliac crest. The circumference of the nondominant arm was measured halfway between the olecranon and the acromion with a tape measure. To determine the corresponding percentiles, we used the tables of Ricart et al[22] for the working population, and those of Esquius et al[23] for the elderly population. The percentiles of total body fat for the population under 65 years was calculated with the tables of Alastrué et al.[24]

Overall malnutrition (low body weight) was defined as BMI at or within the bottom reference quartile.[22,23] For comparison of the results with other populations, we also calculated the percentage of patients with actual body weight below 90% of ideal and the percentage of patients with BMI below 20 kg/m^2. We used the tables for ideal body weight recommended by the World Health Organization.[14] The muscle protein store was assessed by determination of MAMA. Plasma concentrations of albumin (mg/dL) and transferrin (mg/dL) were used to assess visceral protein. The body fat store was assessed by determining the total body fat. Table 2 presents the criteria used to define the severity of the different types of malnutrition.

Age, sex, smoking history, and associated comorbidity were also recorded in addition to the nutritional assessment. FEV_1 and FVC were measured with an Autospiro AS-600 spirometer (Minato Medical Science S.A., Osaka, Japan) in accordance with SEPAR guidelines.[25] The results for FEV_1 and FVC were expressed as percentages of reference values for adults.[26] Arterial blood gas was analyzed at rest with the method recommended by SEPAR.[27]

TABLE 3
Baseline Characteristics of the Patients in the Study (n=178; 99.4% Male)*

Age, years	69 (9)
Height, cm	162.1 (5.9)
Weight, kg	74.1 (13.2)
BMI, kg/m^2	28.2 (4.9)
FEV_1, L	1.16 (0.73)
FEV_1, %	44.6 (17.0)
FVC, L	2.18 (0.67)
FVC, %	67.1 (18.4)
PaO_2, mm Hg	66.7 (11.3)
$PaCO_2$, mm Hg	43.3 (6.1)

*BMI indicates body mass index; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.
Values are expressed as a mean (SD).

Statistical Analysis

A frequency distribution study was performed for each of the parameters studied, pooling values into 6 percentile (P) groups (≤P5, P6-10, P11-25, P26-75, P76-95, and ≥P76). The χ^2 test was used to compare percentages between 2 independent groups. Categorical variables were compared with the Mantel-Haenszel linear trend test. For percentages, 95% confidence intervals (CI) were constructed. The association between quantitative variables was analyzed by the Pearson correlation coefficient after testing for a normal distribution with the Kolmogov-Smirnov test. The value for alpha was set to 0.05.

Results

Study Sample

A total of 202 patients were studied consecutively in the 6-month study period. Twenty-four of these (11.8%) were excluded for the following reasons: 6 patients (3%) because of uncontrolled cor pulmonale, a further 6 (3%) because of liver cirrhosis, 4 (2%) because of neoplasms, 3 (1.5%) for sustained use of oral corticosteroids, 2 (1%) because of heart failure, and 3 (1.5%) for other reasons (uncontrolled diabetes, chronic renal failure, and malabsorption syndrome). Thus 178 patients were enrolled—1 woman (0.6%) and 177 men (99.4%). Table 3 shows the baseline characteristics of these patients. There were 139 patients (78.1%) over 65 years of age, of whom 21 (11.8%) were 80 years or over. All patients had been smokers and 30 (16.8%) were active smokers. COPD was mild in 28 patients (15.7%), moderate in 69 (38.8%), and severe in 81 (45.5%). Respiratory failure (PaO_2<60 mm Hg) was present in 53 patients (29.8%), of whom 39 (21.9%)

were receiving supplementary oxygen.

Prevalence of Low Body Weight

The numbers of patients in each percentile group for the anthropometric variables are shown in Table 4. Low body weight (BMI≤P25) was found in 19.1% of the patients (95% CI, 13.3%-24.9%). BMI was less than 20 kg/m^2 in 3.9% of the patients (95% CI, 1.1%-6.7%), and the actual body weight was less than 90% of ideal in 6.2% (95% CI, 2.6%-9.7%).

Analysis of Body Composition

Figure 1 shows the stratification of the patient series according to body composition. The muscle store was the most frequently affected compartment, though fat and visceral protein depletion was also seen in 20% of the patients. Somewhat more than half of the patients without low body weight had some sort of nutritional disorder.

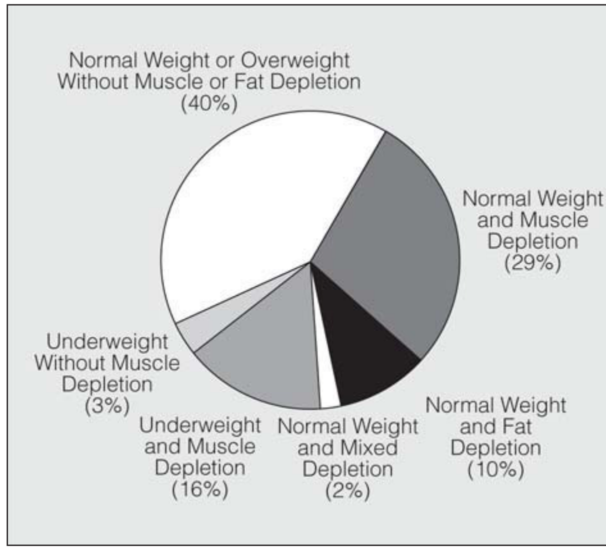

Figure 1. Stratification of patients with stable chronic obstructive pulmonary disease by body weight and composition.

Muscle Protein Store

As shown in Table 4, MAMA was at or within the bottom quartile for 47.2% of the patients (95% CI, 33.9%-54.5%). Muscle wasting was also seen in 62.9% of the patients (95% CI, 50.9%-74.9%) with normal BMI and in as many as 20.7% (95% CI, 11.9%-29.5%) of those who were overweight (Table 5).

Visceral Protein Store

A total of 31 patients (17.4%; 95% CI, 11.8%-23.0%) had low plasma concentrations of at least 1 of the visceral proteins (albumin or transferrin). The mean (SD) concentration of albumin was 4.04 (0.34) mg/dL. Sixteen patients (9.6%; 95% CI, 5.2%-13.8%) had mild hypoalbuminemia. Mean serum transferrin was 235 (36) mg/dL. Twenty-five patients (14%; 95% CI, 8.9%-19.1%) had mild transferrin deficiency and 3 (1.7%; 95% CI, 0.0%-3.6%) had moderate deficiency. Patients with low plasma concentrations of albumin all had associated transferrin deficiency with the exception of 3 (1.7%; 95% CI, 0.0%-3.6%).

Table 5 shows the percentage of patients with visceral protein deficiency according to BMI percentile. Of the patients with normal MAMA, 3 (1.7%; 95% CI, 0.0%-3.6%) had hypoalbuminemia and 6 (3.4%; 95% CI, 0.7%-6.1%) had mild transferrin deficiency.

Fat Store

Fat depletion was observed in 19.1% of patients (95% CI, 13.3%-24.9%) (Table 5). The abdominal

TABLE 4
Prevalence of Nutritional Disorders in Chronic Obstructive Pulmonary Disease by Anthropometric Parameters*

	Malnutrition				Normal	Overweight	
	Severe: P≤5	Moderate: P6-10	Mild: P11-25	ΣP≤5	P26-75	P76-95	P≥96
BMI	10 (5.6)	8 (4.5)	16 (9.0)	34 (19.1)	62 (34.8)	55 (30.9)	27 (15.2)
Muscle compartment							
MAMC	35 (19.7)	22 (12.4)	31 (17.4)	87 (49.9)	71 (39.9)	13 (7.3)	6 (3.4)
MAMA	32 (20.0)	26 (14.6)	26 (14.6)	84 (47.2)	71 (39.9)	15 (8.4)	8 (4.5)
Fat store							
TSF	21 (11.8)	13 (7.3)	24 (13.5)	58 (32.6)	71 (39.9)	26 (14.6)	23 (12.9)
SSF	11 (6.2)	8 (4.5)	21 (11.8)	40 (22.5)	72 (40.4)	38 (21.3)	28 (15.7)
ASF	33 (18.5)	15 (8.4)	30 (16.8)	78 (43.8)	58 (32.6)	20 (11.2)	22 (12.4)
MAFA	23 (12.9)	16 (9.0)	25 (14.0)	64 (35.9)	69 (38.8)	30 (16.8)	15 (8.4)
FMI	15 (8.4)	10 (5.6)	32 (18.0)	57 (32.0)	77 (43.2)	29 (16.3)	15 (8.4)
TBF	15 (8.6)	9 (5.1)	10 (5.6)	34 (19.1)	53 (29.8)	56 (31.5)	35 (19.7)

*ΣP≤25 indicates total number of patients at or below the bottom quartile; BMI, body mass index; P, percentile, MAMC, midarm muscle circumference; MAMA, midarm muscle area; TSF, triceps skinfold; SSF, subscapular skinfold; ASF, abdominal skinfold; MAFA, midarm fat area; FMI, fat-muscle index; TBF, total body fat. Values are numbers of patients with percentages between parentheses.

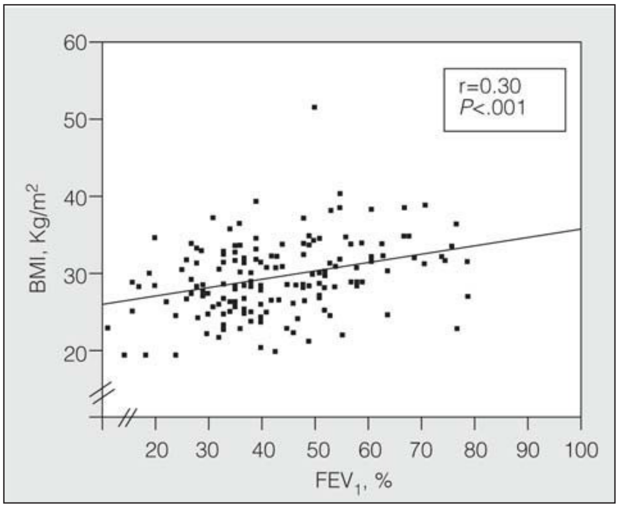

Figure 2. Correlation between body mass index (BMI) and forced expiratory volume in 1 second (FEV_1), expressed as a percentage of the reference value in patients with stable chronic obstructive pulmonary disease.

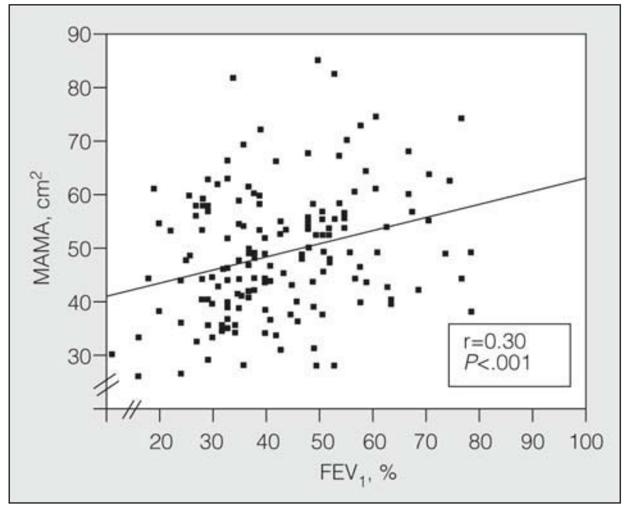

Figure 3. Correlation between midarm muscle area (MAMA) and forced expiratory volume in 1 second (FEV_1), expressed as a percentage of the reference value in patients with stable chronic obstructive pulmonary disease.

skinfold was the most affected, whereas the subscapular skinfold showed least fat depletion (Table 4).

Mixed Malnutrition

Nineteen patients (10.7%; 95% CI, 6.1%-15.2%) had mixed malnutrition (protein and energy malnutrition). This type of malnutrition occurred more often in the group of patients with BMI on or below the 10th percentile (44.4%; 95% CI, 37.1%-51.7%). Patients with mixed malnutrition are presented according to different BMI percentiles in Table 5.

Analysis by Subgroups of Severity

Table 6 shows nutritional status according to the degree of bronchial obstruction. The percentage of patients with low body weight increased significantly as the severity of disease increased (*P*=.001) (Table 6). There was a weak but significant correlation (r=0.30; *P*<.001) between FEV_1, expressed as a percentage of the reference value, and BMI (Figure 2). The percentages of patients with BMI less than 20 kg/m^2 and of patients with actual body weight less than 90% of ideal were similar for moderate and severe COPD. No patient with mild COPD showed a significant change in these parameters.

The degree of muscle-protein malnutrition also increased with increasing severity of bronchial obstruction (*P*=.015). There was also significant correlation (r=0.30; *P*<.001) between MAMA and FEV_1

TABLE 5
Relationship Between Body Mass Index, Grouped by Percentiles, and Other Nutritional Parameters (Compartmental Analysis)*

	Malnutrition				
	Severe: BMI P≤5 (n=10)	**Moderate: BMI P6-10 (n=8)**	**Mild: BMI P11-25 (n=16)**	**Normal: BMI P26-75 (n=62)**	**Overweight: BMI P≥76 (n=82)**
Muscle protein malnutrition					
MAMA≤P25	9 (90)	7 (87.5)	12 (75)	39 (62.9)	17 (20.7)
Visceral protein malnutrition					
Albumin <3.5 mg/dL	3 (33.3)	1 (12.5)	3 (18.7)	10 (16.1)	0
Transferrin <200 mg/dL	2 (20.0)	1 (12.5)	4 (25.0)	8 (12.9)	13 (15.8)
Energy malnutrition					
TBF≤P25	4 (40.0)	5 (62.5)	4 (25.0)	13 (20.9)	8 (9.8)
Mixed malnutrition					
MAMA≤P25+TBF≤P25+VPM	3 (30.0)	–	1 (6.2)	–	–
MAMA≤P25+TBF≤P25	1 (10.0)	4 (50.0)	1 (6.2)	2 (3.2)	1 (1.2)
TBF≤P25+TBF	–		1 (6.2)	4 (6.4)	1 (1.2)
TBF≤P25+TBF	–		–	–	–

*BMI indicates body mass index (kg/m^2); P, percentile; MAMA, midarm muscle area; VPM, visceral protein malnutrition; TBF, total body fat. The values shown are numbers of patients with percentages between parentheses.

TABLE 6
Nutritional Parameters According to Severity of Bronchial Obstruction*

	Severity of COPD According to FEV_1			
	Mild (n=28)	Moderate (n=69)	Severe (n=81)	Significance
BMI				.001
≤P25	2 (7.2)	12 (17.4)	20 (24.7)	
P26-75	4 (14.3)	25 (36.2)	33 (40.7)	
≥P76	22 (78.5)	32 (46.4)	28 (34.5)	
BMI<20 kg/m^2	–	3 (4.3)	4 (4.9)	NS
BW<90%IBW	–	4 (5.8)	7 (8.6)	NS
MAMA				.015
≤P25	10 (35.7)	31 (44.9)	43 (53.1)	
P26-75	10 (35.7)	30 (43.4)	31 (38.3)	
≥P76	8 (28.6)	8 (11.6)	7 (8.6)	
Albumin (mg/dL)				NS
2.8-3.5	–	6 (8.7)	11 (13.5)	
2.1-2.7	–	–	–	
<2.1	–	–	–	
Transferrin (mg/dL)				NS
150-200	3 (10.7)	12 (17.4)	4 (12.3)	
100-150	–	–	3 (3.7)	
<100	–	–	–	
TBF				NS
≤P25	3 (10.7)	11 (15.9)	20 (24.7)	
P26-75	8 (28.6)	22 (31.9)	23 (28.4)	
≥P76	17 (60.7)	36 (52.2)	38 (46.9)	

*COPD indicates chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; BMI, body mass index (kg/m^2); P, percentile; BW<90%IBW, body weight <90% ideal body weight; MAMA, midarm muscle area; TBF, total body fat. Values are numbers of patients with percentages between parentheses.

(%) (Figure 3) but no significant differences were observed for visceral proteins or total body fat.

Of the patients who received continuous home oxygen therapy, 64.1% (95% CI, 57.0%-71.1%) had MAMA at or within the lower quartile, compared to 41.4% (95% CI, 34.2%-48.6%) of patients who received no such treatment (P=.009). There were no significant differences for BMI or total body fat between patients with continuous oxygen therapy at home and those who did not receive it. No significant differences were found for active smokers and ex-smokers for any of the 3 variables studied.

Discussion

Our study confirms that malnutrition in patients with stable COPD is a common problem that increases as disease severity increases. We found 19.1% of our patients had low body weight, defined as BMI at or within the bottom quartile of the reference population. Malnutrition was severe in 5.6% of our patients. The separate analyses for each nutritional compartment show that malnutrition affects both the fat store and the visceral protein store, but muscle mass is the compartment that is most affected. Almost half of the patients (47.2%) showed muscle wasting, and this was severe in 18% of the patients. Visceral protein malnutrition—seen in 17.4% of the patients—and body fat deficiency—seen in 19.1%—were also appreciable. Energy-protein (mixed) malnutrition was observed in 10.7% of the patients. Signs of muscle wasting were apparent in 62.7% of the patients with normal weight and also in 1 out of every 5 overweight patients.

Comparison of our findings with previous studies is difficult because the criteria for malnutrition are not universally accepted. We have opted for comparison of the anthropometric parameters of our patients with reference values for our population according to age group and sex.[22-24] We think that this approach allows the limits of normal nutrition to be better defined. In statistical terms, values between the 5th percentile and the 95th percentile define the normal state as they encompass 90% of all measured values for the parameter in a given population. Values outside the interquartile range (P25 to P75) may, however, also be indicators of an initial state of malnutrition or overweight, though with a marked loss of specificity.[23] We preferred to use the interquartile range in an attempt to include patients in the early stages of malnutrition but we also present the results for the extreme percentiles.

One of our most relevant findings is the confirmation that the prevalence of low body weight in stable COPD patients—near the Mediterranean coast at least—is lower than the figure published for other countries that are socially and economically comparable to Spain. In 779 patients enrolled in the National Institutes of Health Clinical Trial of Intermittent Positive-Pressure Breathing, 24% had an actual body weight less than 90% of ideal.[16] In the Netherlands, body weight was less than 90% of ideal in 35% of 255 patients enrolled in a rehabilitation program.[17] Finally, in a study performed in Cincinnati,[18] 29% of 126 stable patients followed in an outpatient clinic had a BMI less than 20 kg/m^2. In our series, the BMI of 19.1% of the patients was at or within the bottom quartile. However, on application of the same criteria used in the previous series, only 6.2% of the patients showed actual body weight less than 90% of ideal and the BMI of 3.9% of the patients was less than 20 kg/m^2. Similar results are obtained if we consider severe malnutrition only—the BMI of 5.6% of our patients was at or below the 5th percentile. These findings are similar to those of 2 previous Spanish studies.[28,29] In a study in Sagunto, Valencia, Pascual et al[28] found that the BMI of only 3 (6.6%) of 45 patients with severe COPD was less than 20 kg/m^2. Likewise, Coronell et al[29] also found the BMI of only 6.6% of the population to be less than 20 kg/m^2 in a large retrospective study of 3126 patients in Barcelona. The latter of these studies has generated some debate.[30,31] Coronell et al suggested that the prevalence of low body weight in patients with COPD is lower in the Mediterranean region,[30] but according to

Franssen et al,[31] the discrepancies may be due to lower severity of COPD in the sample (mean FEV_1: 51% [19%]) or to a different distribution of disease subtype (emphysema or chronic bronchitis). Regarding disease severity, our results provide support for the position of Coronell et al,[29,30] because the prevalence of low body weight was 4.9% among patients with severe COPD (FEV_1<40%). Unfortunately, we do not know the distribution of emphysema or chronic bronchitis in our patients, but given that all 3 Spanish studies agree on this point, a different distribution of emphysema and chronic bronchitis in the population does not seem a plausible explanation for the discrepancy.

The reasons that might explain the lower prevalence of low body weight in the Mediterranean region (for example, diet, genetic factors, etc.) are not well known. Coronell et al[29,30] propose that people who live in the Mediterranean region of Europe follow a different lifestyle to those of other regions who may be of a similar ethnic origin. For example, the French-speaking population in Quebec, Canada, has a higher prevalence of low body weight associated with COPD. Further specifically designed studies would be necessary to confirm this attractive hypothesis.

Although assessment of nutritional status through measurement of body weight is useful, it does not provide any quantitative information on body composition, which can also be affected in patients with COPD. In our study, the muscle store was the compartment most frequently affected. The MAMA of almost half our patients was at or within the bottom quartile, and 1 in 5 had severe muscle protein malnutrition (MAMA≤P5). These results suggest that malnutrition leads to muscle wasting rather than deficiency in the other body stores. In contrast, inanition mainly affects the fat store. This phenomenon has been mentioned by other authors[17,32] and is consistent with several studies that show deterioration of skeletal muscle function in malnourished patients.[4-7] Recently, Marquis et al[33] found that muscle mass is an even better predictor of mortality than body weight. They measured the cross-sectional area of the thigh of 142 patients by computed tomography and found that a cross-sectional thigh area of 70 cm^2 or less was independently associated with a 4-fold increase in the risk of death.

Body fat is also affected in patients with COPD, though to a lesser extent than muscle store.[17] Total body fat at or within the bottom quartile was observed in 19.1% of our patients. Deficiencies in the fat store have received less attention from a functional point of view, though recent results reinforce the role that this store plays in energy homeostasis. Body fat is not only an energy store but also participates in energy regulation through the production of leptin. This hormone, produced by adipocytes, acts as an afferent signal in the brain in a feedback mechanism that regulates deposition of fat.[34] Leptin also participates in glucose homeostasis[35] and seems to have some effect on immune response mediated by T cells.[36]

In our study, the percentage of patients with both low body weight and muscle wasting increased significantly with increasing severity of COPD. This relationship is well known[16,18] but it should be remembered that malnutrition also occurs in the early stages of COPD. In our study, 2 of the 28 patients with mild COPD had low body weight and 35.7% showed signs of muscle protein depletion. Few studies have addressed this point but we believe that it is a relevant finding that may even have pathogenic implications. The origin of malnutrition in COPD is not well established. Some possible causes seem to be related to the severity of the disease (tissue hypoxia, hypercapnia, dyspnea, etc) but not all (inflammation, leptin, smoking habit, etc). The study of these or other mechanisms not related to severity in malnourished patients with mild COPD might provide a better indication of the causes of malnutrition.

Muscle wasting and, to a lesser extent, fat depletion also occur in patients with normal weight and even in some overweight patients. In our series, as many as 62.9% of the patients with normal BMI and 20.7% of those who were overweight showed muscle protein malnutrition. This interesting observation had already been noted by Schols et al[17] in a study of 255 patients with stable COPD enrolled in a rehabilitation program. These authors, using bioelectric impedance, found that 24 out of 162 patients (14.8%) with normal weight, defined as a body weight at least 90% of ideal, had low lean body mass values. These patients had weakened respiratory muscles and covered smaller distances in the walking test compared to patients with normal weight and normal lean body mass values. Our study shows a very different proportion of the patient series with muscle wasting. Two circumstances may explain this discrepancy. First, the definitions used in the 2 series to define low body weight and muscle wasting are different. In the Dutch series, 35% of the patients had low body weight (actual body weight less than 90% of ideal) whereas in our study the BMI of only 19.1% of the patients was at or within the bottom quartile. If the definition for normal weight is extended to encompass more patients in the group with low body weight, the number of patients with muscle wasting probably increases. In addition, lean body mass and MAMA are not interchangeable terms so the parameters used to define muscle wasting are not directly comparable. Second, we think that the method used to study body stores also affects the results. According to Scholl et al,[37] measurement of anthropometric variables overestimates the lean body mass when compared to bioelectric impedance.

Anthropometric parameters are simple, cheap, and quick measures, but they do have certain shortcomings when used to estimate nutritional status and body composition. First, the changes in body composition associated with aging lead to changes in anthropometric values that have nothing to do with the state of malnutrition. Thus, it is necessary to use reference anthropometric parameters for the study population. We have used the reference values most recently published in Spain, namely, those of Ricart et al[22] for the working population and those of Esquius et al[23] for the elderly population. Second, reproducibility of the anthropometric values from one observer to another is lower. To reduce this source of error, we repeated the measurement of each parameter 3 times in succession and then took the final value to be the arithmetic mean of the 3 measurements in accordance with recommended practice.[21] Even with the adoption of these precautions, agreement between anthropometric measurements and other methods for assessing nutritional status is not satisfactory. Heymsfield et al,[38] using computed tomography, showed that anthropometric measurements overestimated arm muscle area by 20%-25%. Between 10% and 15% of this overestimation comes from assuming that the muscle store is circular. Moreover, the calculation of the midarm muscle circumference, and subsequently the MAMA, is based on the assumption that the measurement of the fat layer represents a constant fraction of total body fat. This is not entirely true for elderly patients, in whom fat tends to be preferentially deposited in the central and internal parts of the body. For this reason, total body fat tends to be underestimated and lean body mass overestimated in COPD.[39]

The remaining techniques used to measure body composition are usually more precise and reproducible. In a recent study, Steiner et al[40] compared bioelectric impedance and various anthropometric measures with dual energy x-ray absorption as the reference standard. Bioelectric impedance had a sensitivity of 86% and a specificity of 88% for detecting nutritional alterations, whereas anthropometric measures had a sensitivity of 74% and a specificity of 98%. The prevalence of malnutrition, defined as BMI of 21 kg/m^2 or less and a fat-free index (lean body mass/height^2) less than 15 (for women) or 16 (for men), was 49% for absorptiometry, 48% for bioelectric impedance, and 38% for anthropometric measures.

Although these techniques offer a more reliable diagnosis, their application is limited for a number of reasons. First, they are expensive techniques so they are not widely available. Second, confusion arises because there is no reliable technique of reference. Finally, most of these techniques lack reference values, particularly for the elderly population (78.1% of our patients were over 65 years). We therefore think that use of anthropometric parameters adjusted to our reference values is appropriate, at least for the time being. This approach provides a better definition of normality and everything that lies outside the limits of normality. Nevertheless, further studies are needed to assess the relationship of these parameters with different diseases and mortality to better define the actual importance of abnormal values.

Our study is subject to limitations which have been mentioned in the preceding discussion but which we think appropriate to highlight. First, the sample size was small and data were collected from a single center. Larger, multicenter studies should therefore be performed. Second, the diagnostic method used in our study (measurement of anthropometric variables) is less sensitive than other more precise measures (bioelectric impedance, dual energy x-ray absorption, etc).[40] Future studies should, in our opinion, use these other techniques. First, however, they should be tested in the general Spanish population to establish the appropriate reference values. In fact, the anthropometric reference tables used in our study might constitute another limitation. We used the latest reference values published for Spain[22-24] but these values were taken from studies performed 10 years ago and so the values might have changed since then. If we had used the values of Alastrué et al,[41] published in the 1980s, the results would have been slightly different. Finally, we have no data on subtypes of COPD because, when the study was performed, high resolution computed tomography was not available at our center and we did not have the possibility of measuring carbon monoxide diffusion. Previous work points to a higher prevalence of low body weight among patients with emphysema.[42]

In conclusion, our results reinforce the hypothesis that there is a lower prevalence of low body weight in patients with COPD in Spain, at least near the Mediterranean coast. Although body weight is less affected, our patients do show frequent alterations in body composition, affecting both the muscle store and the fat and visceral protein store. Of particular note is a preferential depletion of muscle mass. This depletion is more marked for more severe COPD, though patients with mild COPD also show a certain degree of muscle wasting.

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