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Malnutrition and sarcopenia assessment in patients with chronic obstructive pulmonary disease according to international diagnostic criteria, and evaluation of raw BIA variables

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ABSTRACT

Background: Various criteria have been used so far for the diagnosis of malnutrition or sarcopenia in patients suffering from chronic obstructive pulmonary disease (COPD).
Objective: To determine the prevalence of malnutrition and sarcopenia in COPD, as defined by international diagnostic criteria, and determine their relationships with raw BIA variables.
Methods: Two-hundred and sixty-three COPD patients (185 males and 78 females) underwent both clinical examination and respiratory, anthropometric, bioelectrical impedance analysis (BIA raw variables: phase angle and impedance ratio), handgrip strength (HGS), 4 m gait speed and biochemical measurements. Malnutrition and sarcopenia were diagnosed based on European Society for Clinical Nutrition and Metabolism (ESPEN) criteria and European Working Group on Sarcopenia in Older People (EWGSOP) criteria, respectively.
Results: The overall prevalence of malnutrition and sarcopenia was 19.8% and 24.0% respectively, increasing with disease severity. The prevalence of sarcopenia was significantly higher in patients with malnutrition (71.2% vs 12.3%; $p < 0.001$), especially in those with systemic inflammation (cachectic patients) (85.7% vs 61.3%; $p < 0.001$). Malnourished patients with sarcopenia had a significant reduction in BMI, fat-free mass and HGS compared to non-sarcopenic patients. Finally, impedance ratio significantly increased and phase angle decreased in patients with severe sarcopenia and in cachectic patients.
Conclusion: A relatively high prevalence of malnutrition and sarcopenia was found in COPD patients applying international standard criteria, with some discrepancy between the two diagnoses. In addition, clear-cut changes in raw BIA variables were observed in malnourished patients with systemic inflammation and sarcopenic patients.

1. Introduction

Chronic obstructive pulmonary diseases (COPD) is a heterogeneous disease not only in terms of pulmonary characteristics but also with respect to systemic consequences (e.g weight loss and poor nutritional status) and comorbidities (e.g. cardiovascular diseases, osteoporosis, diabetes, etc.) [1] Specifically, the presence of malnutrition and/or sarcopenia is expected to have important clinical consequences, being relevant to stratification and management of the disease [2].

In general, defining the diagnostic criteria for malnutrition or sarcopenia is a commonly debated topic in clinical nutrition [3,4]. According to the latest and widely used criteria proposed by the European Society for Clinical Nutrition and Metabolism (ESPEN) in 2015 [3], malnutrition can be diagnosed based on low body mass index (BMI) or combining weight loss plus low BMI or low fat-free mass index (FFMI). In addition, the 2016 ESPEN consensus statement [4] further differentiated disease-related malnutrition with inflammation (or cachexia) from one without inflammation, depending on changes in biochemical inflammatory markers. A wide range of differences in the estimated prevalence of malnutrition in COPD has been reported in the literature, possibly due not only to the characteristics of patients (stages of the disease, exacerbations etc.) [5], but also to the use of different

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diagnostic approaches [6]. To the best of our knowledge, ESPEN criteria have been recently applied in hospitalized and other geriatric patients [7,8], but never in COPD.

Sarcopenia is another nutritional phenotype to consider in evaluating the nutritional status in COPD [2]. Widely accepted diagnostic criteria for sarcopenia have been developed by the European Working Group of Sarcopenia in Older People (EWGSOP), who have proposed an algorithm based on loss of skeletal muscle mass (SM) plus reduced strength and/or performance [4,9]. However, only few studies evaluating sarcopenia in COPD have so far considered muscle mass plus strength and performance [10,11], and other papers have just focused on the loss of muscle mass [12–20]. Finally, it is also worth underlining that no study has evaluated the simultaneous presence of sarcopenia and malnutrition in COPD (as assessed by ESPEN and EWGSOP criteria).

In the clinical setting, fat-free mass (FFM) and SM are commonly estimated in COPD patients using predictive equations that include bioimpedance analysis (BIA) data. Directly-measured raw BIA variables may also be of interest in the assessment of nutritional status [21]; for instance, impedance ratio (IR), i.e. the ratio between impedance (Z) at higher frequencies and Z at low frequencies, and phase angle (PhA) are both thought to be a proxy of extracellular water, body cell mass, and cellular integrity [22]. Few papers have shown that raw BIA variables were significantly altered in COPD [23,24], but no information is so far available on IR and PhA in malnourished and sarcopenic COPD patients whose diagnosis was based on international diagnostic criteria [4,9].

Against this background, using ESPEN and EWGSOP diagnostic criteria [3,4,9], the present study aimed to determine the prevalence of malnutrition and sarcopenia in COPD patients and their simultaneous presence in the same patient. As a further major objective, we assessed whether in malnutrition or sarcopenia there were significant changes in raw BIA variables such as IR or PhA.

2. Materials and methods

2.1. Subjects

In this cross-sectional study, 263 consecutive COPD patients admitted to the Respiratory Medicine and Pulmonary Rehabilitation Section of the Clinic Center Private Hospital (Naples, Italy) were studied. The patients were admitted to undergo a 4–6 week comprehensive pulmonary rehabilitation protocol. All the patients met the following inclusion criteria: age > 50 years and a baseline post-bronchodilator forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) < 0.7. Exclusion criteria were related to diagnosis of known respiratory disorders other than COPD, known history of significant inflammatory disease other than COPD and a COPD exacerbation within 4 weeks of enrolment. The Ethics Committee of the “Federico II” University of Naples approved the research protocol and all patients gave their informed consent to participate in the study.

2.2. Lung function

All COPD patients performed a baseline post-bronchodilator spirometry and body plethysmography (QBOX® COSMED) according to American Thoracic Society (ATS)/European Respiratory Society (ERS) standardization [25]. FEV_1 and FVC were assessed in accordance with the latest GOLD guidelines [26].

Patients were classified into four stages according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. If $FEV_1 \geq 80\%$ of the predicted, patients were classified as GOLD stage I (mild), if $50\% \geq FEV_1 > 80\%$ as GOLD stage II (moderate), $30\% \geq FEV_1 > 50\%$ as GOLD stage III (severe), and if < 30% as GOLD stage IV (very severe).

2.3. Body composition

Body weight and body height were measured to the nearest 0.1 kg and 0.5 cm respectively, using a mechanical column scale and a stadiometer (SECA 711 and SECA 220, respectively; Hamburg - Germany), and BMI was calculated as body weight/height squared. Body composition was assessed by performing a multifrequency BIA in standardized conditions (i.e. ambient temperature between 23 and 25 °C, fast > 3 h, empty bladder, supine position for at least 10 min before starting the measurement), using a Human Im-Touch analyzer (© DS Medica S.r.l., Milan, Italy). In addition, after cleaning the skin surface, patients were asked to lie down with their legs and arms slightly abducted at 30° so there was no contact between the extremities and trunk.

A standard tetra-polar technique was used, with measuring electrodes placed on the anterior surface of the wrist and ankle, and injecting electrodes placed on the dorsal surface of the hand and foot, respectively. Z and phase angle were obtained at five frequency kHz for both dominant and non-dominant sides of the body with an imperceptible electrical current of 800 mA. The impedance ratio between high (250 kHz) to low (5 kHz) and phase angle at 50 kHz, expressed as a degree, provide information on hydration status, cellular mass and quality [21,27]. FFM and FFM index (FFMI kg/m^2 = $FFM/height^2$) were estimated from Z at 50 kHz using a disease-specific BIA equation [28]. Skeletal muscle mass (SM) was estimated using a BIA equation validated in a multiethnic sample [10,29]. Fat mass (FM) was calculated as total body weight minus fat free mass.

2.4. Diagnosis of malnutrition

Disease-related malnutrition was diagnosed according to the ESPEN consensus [3,4]. Patients were classified as malnourished when they had BMI < 18.5 kg/m^2 or between 18.5 and 22 kg/m^2, combined with low FFMI (< 17 kg/m^2 for men and < 15 kg/m^2 for females). The simultaneous presence of elevated serum CRP concentrations (CRP ≥5 mg/dL), and/or reduced serum concentrations of albumin (albumin < 3.5 g/dL), combined with malnutrition, was a criterion for the diagnosis of *cachexia* (or *disease-related malnutrition with inflammation,* i.e. systemic inflammation) [4]. Otherwise, the diagnosis was *disease-related malnutrition without inflammation*.

2.5. Diagnosis of sarcopenia

Sarcopenia was diagnosed in accordance with EWGSOP criteria [9], based on muscle mass, strength and performance. Patients were classified as *sarcopenic*, when affected by low muscle mass, plus low muscle strength or low physical performance. *Severe sarcopenia* was identified when all three criteria of the definition were met (low muscle and strength, and low physical performance).

Low muscle mass was assessed by BIA as described above; the cut-off values used were SMI ≤ 8.50 kg/m^2 for men and ≤5.75 kg/m^2 for women [30].

Low muscle strength was assessed by handgrip strength, a proxy index of overall muscle strength [31], measured at baseline with a digital hand-held dynamometer (Dynex, MD systems Inc. Ohio USA) and expressed in kg. Patients performed a maximum voluntary isometric contraction of finger flexor muscles. Three measurements were taken for both body sides (dominant and non-dominant). Mean value of the two body sides was indicated as whole body HGS (or HGS). The maximum values were considered for statistical analysis [32].

Physical performance was assessed by the 4-m gait speed test, as described by Kon et al. [33]. Participants were asked to walk down a 4 m flat, unobstructed course (marked out with an adhesive tape) at their usual speed. For the purpose of this analysis, low walking speed was defined as walking slower than 0.8 m/s [33].