Body Mass and Fat-Free Mass Indices in COPD*

Relation With Variables Expressing Disease Severity

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Background: **COPD primarily affects the lungs but also produces systemic consequences that are not reflected by the recent staging according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Body mass index (BMI) and fat-free mass index (FFMI) represent different aspects of nutrition abnormalities in COPD. We investigated whether BMI and FFMI could be related to parameters expressing airflow obstruction and limitation, exercise capacity, airway inflammation, and quality of life, and whether they would reflect the GOLD staging of the disease.**
Methods: **One hundred patients with clinically stable COPD equally classified into the five stages of the disease were evaluated for BMI, FFMI (measured by bioelectrical impedance analysis), airway obstruction and hyperinflation (FEV_1, FEV_1/FVC, inspiratory capacity), exercise capacity (6-min walk distance [6MWD], Borg scale before and after 6MWD]), chronic dyspnea using the Medical Research Council (MRC) scale, airway inflammation (sputum differential cell counts, leukotriene B_4 in supernatant), and quality of life (emotional part of the chronic respiratory disease questionnaire).**
Results: **6MWD was significantly associated with both BMI and FFMI values, while FFMI additionally presented significant correlations with MRC scale, percentage of predicted FEV_1, and FEV_1/FVC ratio. No association was observed between the two nutritional indexes. BMI was not statistically different among patients in the five stages of COPD, while FFMI reflected the staging of the disease, presenting the highest values in stage 0.**
Conclusions: **Nutritional status is mainly related to exercise capacity. FFMI seems to be more accurate in expressing variables of disease severity, as well as the current staging compared to BMI.**
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Key words: airway obstruction; body mass index; COPD; exercise capacity; fat-free mass index

Abbreviations: BMI = body mass index; ΔBorg = difference in breathlessness in Borg scale; CRQ = chronic respiratory disease questionnaire; FEV_1%pred = percentage of predicted FEV_1; FFM = fat-free mass; FFMI = fat-free mass index; GOLD = Global Initiative for Chronic Obstructive Lung Disease; IC = inspiratory capacity; LTB_4 = leukotriene B_4; MRC = Medical Research Council; 6MWD = 6-min walk distance

COPD is characterized by a range of pathophysiologic changes contributing to a highly variable clinical presentation as well as heterogeneity among the patients. One of the main consequences of the disease is the progressive loss of skeletal muscle mass and the presence of several bioenergetic abnormalities, mainly expressed by weight loss.[1] The above systemic effects might enhance significantly clinical symptoms, such as limitation of exercise capacity, and have a negative impact on quality of life.[2,3]

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Weight loss and low body mass index (BMI), as part of the BODE (BMI, airflow obstruction, dyspnea, and exercise capacity) index, are also negative prognostic factors for survival independent of other prognostic indexes based on the degree of pulmonary dysfunction.[4–6]

Nutritional status is mainly evaluated by BMI. The body mass is divided into two compartments, one called fat mass and the other fat free mass with the latter to contain the main metabolically active organs particularly skeletal muscle mass. However recent data suggests that fat-free mass index (FFMI) provides information beyond that provided by BMI.[5,7] This might be attributed to the fact that loss of skeletal muscle mass is the main cause of weight loss in COPD, whereas loss of fat mass contributes to a lesser extent, leading to the plausible theory that FFMI reflects better the muscle mass than BMI. Low FFMI is significantly correlated with severity of COPD.[7] Despite the fact that severity of the disease is assessed only with variables expressing airflow limitation and obstruction, parameters associated to weight loss are also considered powerful in assessing the disease prognosis.

We used data of COPD stable patients at all stages according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification in order to identify whether the above parameters are related to variables expressing airflow obstruction and limitation, exercise capacity, airway inflammation, and quality of life. As a secondary outcome, we investigated whether BMI and FFMI could equally be associated to the recent staging of GOLD classification.

Materials and Methods

Patients

Four hundred twenty clinically stable COPD patients, all current smokers, were screened through the outpatient clinic of Veterans Hospital during a period of 1 year in order to select 100 patients and to form similar groups of each stage of the GOLD classification.[8] Inclusion criteria were medication according to the stage of their disease, no self-reported asthma or reversibility $> 12\%$ of airway obstruction after administration of a β_2-agonist, and no participation to a rehabilitation program for the last year. Patients were excluded if they had respiratory infection in the last 4 weeks, history of chronic liver and renal failure, malignancy, insulin-dependent diabetes mellitus, use of systemic corticosteroids, atopy, and clinical apparent heart failure. Additionally, they were not eligible to participate if they had abnormal electrolyte values at their initial visit, or they were not able to cooperate. The principal cause for exclusion in our initial sample was the use of COPD treatment not recommended according to the stage of the disease. Atopic status was assessed by the negative history and the negative skin-prick test results to six common aeroallergens.

BMI and FFMI Assessment

The main variables of interest were BMI and FFMI. BMI was calculated as weight/height squared. Fat-free mass (FFM) was measured as previously described by bioelectrical impedance analysis (BIA 101 System Analyzer; Akern; Florence, Italy) with an operating frequency of 50 KHz at 800 μA.[9] FFM was standardized for height and expressed the FFMI (FFM/height squared).[10]

Pulmonary Function Tests

FEV_1, FVC, and FEV_1/FVC ratio were measured with a dry spirometer (Vica-test, Model VEP2; Mijnhardt; Rotterdam, Holland).[11] Inspiratory capacity (IC) was determined as previously described.[12] Three trials were performed, and the two higher IC values had to agree within 5% or 60 mL. Arterial blood gases obtained in room air and were analyzed by a standard blood gas analyzer (Ecosys II, compact BGA; Eschweiler; Klel, Germany).

Sputum Induction and Processing

Sputum induction was performed with inhalation of hypertonic saline solution (3.5%) by an ultrasonic nebulizer (model 2696; DeVilbiss; Somerset, PA). Leukotriene B_4 (LTB_4) [Cayman Chemical; Ann Arbor, MI] was measured by enzyme-linked immunosorbent assay, with a lower limit of detection 13 pg/mL. Sputum cell counts were performed with standard procedures.[13]

Dyspnea and Exercise Capacity

Chronic dyspnea was assessed using the Medical Research Council (MRC) scale.[14] Exercise capacity was assessed with the 6-min walking distance (6MWD) according to the American Thoracic Society guidelines[15] in a walking cross of 50 m. All tests were supervised by an experienced pneumonologist. Oxygen saturation and pulse rate were recorded using a finger-adapted pulse oximeter. None of our patients experienced a desaturation $< 90\%$ during the test. All patients underwent a second test on a separate day with the highest value to be used in the study analysis. Additionally, the difference in breathlessness in the Borg scale (ΔBorg) before and after the end of 6MWD was assessed.[16]

Chronic Respiratory Disease Questionnaire

The emotional part of the chronic respiratory disease questionnaire (CRQ) validated for the Greek population was assessed in all patients.[17]

Study Protocol

On day 1, all subjects underwent a medical history and medical examination by an experienced pneumonologist, spirometry for measuring FEV_1 and FEV_1/FVC before and after bronchodilation, and biochemical blood tests for electrolytes, renal, and liver function. Patients eligible for the study were asked to come on a separate day (usually 2 days later) for measurement of BMI and FFMI. On the same day, blood gases, IC, MRC scale for dyspnea, and a questionnaire for assessing quality of life (CRQ, emotional part) were performed. On the following 2 days, exercise capacity was evaluated twice using the 6MWD in meters and the ΔBorg before and after the end of the test. Finally, 4 days after the initial visit, induced sputum was performed and analyzed for LTB_4 and sputum differential cell counts. All patients were classified in the five stages of COPD on the basis of FEV_1/FVC $< 70\%$ and FEV_1 percentage of predicted

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