Body composition markers in older persons with COPD

ANGELA MARIE ABBATECOLA1,†, ALESSIA FUMAGALLI2,†, LIANA SPAZZAFUMO3, VALERIA BETTI1, CLEMENTINA MISURACA1, ANDREA CORSONELLO4, ANTONIO CHERUBINI5, ENRICO E. GUFFANTI2, FABRIZIA LATTANZIO1

1Scientific Direction – Italian National Research Center on Aging (INRCA), Via S. Margherita n. 5, Ancona 61000, Italy
2Unit of Pulmonary Rehabilitation, Research Hospital of Casatenovo, Italian National Research Center on Aging (INRCA), Casatenovo, Italy
3Statistic and Biometry Center, Department of Gerontology Research, Italian National Research Center on Aging, (INRCA), Ancona, Italy
4Unit of Geriatric Pharmacoepidemiology, Research Hospital of Cosenza, Italian National Research Center on Aging (INRCA), Cosenza, Italy
5Geriatric Hospital, IRCCS, Italian National Research Center on Aging (INRCA), Ancona, Italy

Address correspondence to: A. M. Abbatecola. Tel: +39 071 8004628; Fax: +39 071 35944.
E-mail: angela_abbatecola@yahoo.com

Abstract

Background: Body composition has been shown to be correlated with physical performance, but data in older persons with diverse chronic diseases are lacking.
Objective: We aimed at investigating the associations of body composition to gait speed and nutritional status of older people in different stages of chronic obstructive pulmonary disease (COPD).
Design, setting and subjects: Cross-sectional analysis of data from Pulmonary Rehabilitation Geriatric Unit at INRCA in Casatenovo, Italy including 132 consecutively admitted COPD patients (mean age: 75 years) with data on body composition, walking speed and respiratory parameters.
Methods: Body mass parameters were assessed using bioelectrical impedance analysis. Pulmonary function tests included spirometry and arterial blood gases. Differences among body composition markers were compared according to gender. Separate multivariate linear regression models with gait speed as the dependent variable were used to test for independent associations with body composition markers after adjusting for multiple confounders.
Results: Walking speed deteriorated with increasing severity of COPD. Men were heavier and had more lean mass than women. Participants in the fastest gait tertile were younger, had lower body mass index and fat mass (FM); higher lean-to-fat ratio and albumin levels and better respiratory function (FEV1, FVC) compared with those in the slower tertiles. Total body FM was an independent determinant of walking speed, while fat-free mass and lean-to-fat ratio were not.
Conclusions: Excess body fat may be harmful for physical functioning among elders with COPD.

Keywords: ageing, body fat, COPD, gait speed, indicators, older people

Introduction

Decreased skeletal muscle is one of the most investigated extra-pulmonary features in chronic obstructive pulmonary disease (COPD). Loss of body weight and depletion of fat-free mass (FFM) are common and severe risk factors for mortality in COPD [1, 2]. Population-based studies have shown higher COPD-related mortality rates in underweight and normal weight than in overweight and obese [3, 4]. Malnutrition along with the inability of respiratory muscles to
adapt to the increase in the ventilatory load [5] may contribute to exercise limitation [6]. Current COPD guidelines consider nutritional monitoring an important part of routine evaluation in patients [7].

While the role of low FFM seems to have a consistent impact on negative health outcomes, a potential role of fat mass (FM) on clinical functional parameters in older patients is highly contradictory. In middle-age adults, the relation between body mass index (BMI) and overall mortality is U-shaped with an increased risk in the lowest and highest percentiles [8]. In older hospitalised persons, the risk of mortality is lower with increasing body weight [9]. Fat tissue seems to have a different effect on physical function decline across age [10] and COPD [11].

Reduced gait speed is considered a determinant of disability and mortality in elders [12]. Considering that there is limited literature testing the association between body composition markers and gait speed in older COPD persons, we present data from a clinical study testing associations among nutritional parameters and anthropometric indexes on gait speed in older COPD patients.

Methods

One hundred and thirty-two patients with COPD (mean age 75 ± 6 years) consecutively admitted to the inpatient Pulmonary Rehabilitation Geriatric Unit at INRCA in Casatenovo, Italy from 1 June to 30 September 2009 were enrolled. All patients were admitted for one cycle of physiotherapy and gave written informed consent approved by INRCA Institutional Review Board. All patients had the following characteristics: age ≥65 years, clinical stability of COPD and chronic treatment for COPD [7]. The exclusion criteria included pulmonary infection (<4 weeks), bronchial reversibility > 12% after administration of β-agonists, renal, hepatic or acute heart failure, cancer, drugs known to interfere with water–mineral homeostasis and/or any signs of oedema or dehydration. All patients underwent nutritional, body composition and respiratory evaluations (including arterial blood gas analysis of PaO2 and PaCO2) at the time of admission.

BODE index

The BODE index [13] is a multidimensional assessment score ranging from 0 to 10 (with higher values indicating greater COPD severity) based on the sum of cut-off scores for body-mass index (B), degree of airflow obstruction (O) [14, 15], functional dyspnoea (D) [16] and exercise capacity as measured by the 6-min walking test (6MWT) (E) [17]. The BODE index has been shown to be effective in predicting the mortality in patients with COPD [13]. The BODE score was calculated as the sum of scores assigned for each individual task. For BMI (kg/m²), patients were assigned a score 0 for BMI ≤ 21 or 1 for BMI > 21; airflow obstruction was assessed using FEV1 (% of predicted) [14, 15] and patients were scored 0 for FEV1 ≥ 65 = 0, 1 for FEV1 = 50–64, 2 for FEV1 = 36–49 and 3 for FEV1 ≤ 35; dyspnoea was assessed using the Modified Medical Research Council (MMRC) Dyspnea scale [16] and patients were assigned score 0 for MMRC = 0–1, 1 for MMRC = 2, 2 for MMRC = 3 and 3 for MMRC = 4; metres walked during the 6MWT were scored as follows [17]: ≥350 = 0, 250–349 = 1; 150–249 = 2 and ≤149 = 3.

Exercise capacity

6MWT was applied according to ATS criteria [17]. After the test, the distance in metres walked in 6 min was recorded for each patient. Gait speed (m/s) was calculated by dividing the distance walked during 6MWT by time [18].

Bioelectrical impedance analysis

Bioelectrical impedance analysis (BIA) was performed using a tetrapolar 101 System Analyzer (Akern, Florence, Italy) with the emission of a low electrical current (500–800 mA and 50 kHz). As previously described, patients were studied in the supine position with electrodes connected to the hands and feet [19]. The patient’s right side was standardised for the test. Resistance (R) and capacitance (Xc) were directly measured in ohms (V) at 50 kHz and 800 mA using the BIA (RJL Systems). Phase angle (PA) measures using the BIA reflect the relative contributions of fluid (resistance) and cellular membranes (capacitance) of the body. It was calculated using the following equation: PA: (resistance/capacitance) × (180/π). Sex-specific regression equations derived for COPD patients are lacking, but we employed the same sex-specific equations as previously reported in a validation study in Italy [19]. FM (kg) was calculated as total body weight (kg) minus FFM (kg). We also calculated the lean-to-fat ratio (FFM/FM) as reported in a previous study [20].

Pulmonary function tests

Function testing included spirometry and arterial blood gas analysis. Forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were measured with VMax Sensor Medics spirometer.

Global initiative for chronic obstructive lung disease

Global initiative for chronic obstructive lung disease (GOLD) staging system divides the severity of COPD into four stages (mild, moderate, severe, very severe) based on airflow limitation (obstruction) during pulmonary function tests. Based on FEV1, FEV1/FVC ratio, COPD severity was staged based on NHLBI/WHO GOLD criteria (Stages I–IV) [21].
Statistical analysis

Statistical analyses were performed using SPSS version 15.0 (SPSS, Chicago). Demographic and clinical characteristics were investigated across COPD stages according to GOLD stages I (less) to IV (very severe) with the analysis of variance (ANOVA)-based test for trend. Comparison of body composition markers between gender was performed using Student’s t testing. Clinical and anthropometric parameters were tested across tertiles of gait speed using ANOVA. Descriptive results of continuous variables are presented as means ± SD. Partial correlations investigated the relationship between walking speed and PA, body composition markers, respiratory function independently of age and weight in the entire study population. Separate multivariate linear regression models were used to test for independent associations between gait speed as the dependent variable and body composition parameters (FFM, FM, FFM/FM), age, gender, BMI, PA, albumin, FEV1 and the number of comorbidities. To avoid collinearity, we included body weight in our model testing the association with FFM and not in those with FM or FFM/FM as dependent variables. Albumin was included as a confounder because it is a widely known marker of malnutrition.

Results

Our study population consisted of 132 persons (mean age 75 ± 6 years) with COPD in diverse stages I (n = 12), II (n = 59), III (n = 49), IV (n = 12). The mean walking distance and walking speed were lower across increased COPD severity (Table 1). We confirmed a significant decline in PA across COPD stages suggesting that lower PAs may be associated with decreased cell integrity (Table 1). Even though we used sex-specific regression equations (see methods), we tested for differences in body composition markers according to gender. In men versus women, we did not find any significant differences for FM (kg) (23.1 versus 24.8, P = 0.365), BMI (26.3 versus 26.1, P = 0.884) or FFM/FM (2.53 versus 2.79; P = 0.669), but men were significantly heavier (kg) (74.0 versus 63.8, P = 0.001) and had more FFM (kg) (50.8 versus 40.0, P = < 0.001) than women. In addition, there was not a significant difference in PA (5.05 versus 4.7, P = 0.096) between genders.

Table 2 describes clinical and anthropometric characteristics across tertiles of walking speed. Individuals in the fastest tertile of walking speed were younger, showed lower FM, higher FFM/FM and had better lung performance than those in slower tertiles.

Age- and body weight-adjusted correlations among walking speed and clinical parameters showed that walking speed correlated with PA (r = 0.180, P = 0.050), FM (r = -0.137, P = 0.035), pO2 (r = 0.384, P < 0.001), pCO2 (r = -0.192, P = 0.029), FVC (r = 0.265, P = 0.002) and FEV1 (r = 0.361, P < 0.001). There were no significant correlations between walking speed, FFM, FFM/FM and albumin.

The relationship between FM and walking speed independent of multiple confounders was tested in a multivariate linear regression model (Table 3). The same analysis was performed including FFM and FFM/FM separately (Table 3). With regard to body composition markers, we found that only FM was an independent determinant of walking speed. In all models, age and FEV1 continued to be independent determinants of walking speed (Table 3).

Discussion

In this study, we investigated the correlations of lean and FM on walking speed and gait speed in older COPD patients. We found that FM was an independent determinant for slower walking speed, while lean mass was not. The importance of limitation in mobility using diverse walking speed distances...
Body composition markers in older persons

Table 2. Clinical characteristics of the study group of older persons with COPD across body walking speed tertiles

<table>
<thead>
<tr>
<th></th>
<th>First tertile (n = 18)</th>
<th>Second tertile (n = 74)</th>
<th>Third Tertile (n = 40)</th>
<th>P (for trend)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking speed (m/s)</td>
<td>0.93 ± 0.13</td>
<td>1.10 ± 0.10</td>
<td>1.43 ± 0.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>75.8 ± 6.1</td>
<td>74.9 ± 5.9</td>
<td>73.4 ± 5.3</td>
<td>0.040</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>79.8 ± 16.7</td>
<td>70.7 ± 18.1</td>
<td>71.1 ± 15.1</td>
<td>0.123</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.0 ± 6.0</td>
<td>26.6 ± 5.9</td>
<td>25.0 ± 5.3</td>
<td>0.025</td>
</tr>
<tr>
<td>FM (kg)</td>
<td>27.6 ± 8.7</td>
<td>23.8 ± 9.3</td>
<td>22.9 ± 10.2</td>
<td>0.028</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>52.2 ± 13.0</td>
<td>46.8 ± 8.8</td>
<td>48.1 ± 8.8</td>
<td>0.143</td>
</tr>
<tr>
<td>Lean-to-fat ratio</td>
<td>1.89 ± 0.9</td>
<td>1.97 ± 0.9</td>
<td>2.10 ± 0.6</td>
<td>0.040</td>
</tr>
<tr>
<td>PA (°)</td>
<td>4.7 ± 1.0</td>
<td>5.2 ± 1.0</td>
<td>5.4 ± 0.9</td>
<td>0.004</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>47.7 ± 14.3</td>
<td>56.3 ± 16.1</td>
<td>57.8 ± 14.3</td>
<td>0.001</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>65.9 ± 15.9</td>
<td>74.4 ± 17.8</td>
<td>75.2 ± 15.2</td>
<td>0.007</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.7 ± 0.5</td>
<td>3.8 ± 0.4</td>
<td>4.0 ± 0.3</td>
<td>0.018</td>
</tr>
<tr>
<td>BODE index</td>
<td>6.7 ± 1.4</td>
<td>5.4 ± 1.6</td>
<td>3.5 ± 1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>3.0 ± 1.2</td>
<td>3.0 ± 1.3</td>
<td>2.8 ± 1.0</td>
<td>0.712</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation. BMI, body mass index; FM, fat mass; FFM, free fat mass; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity.

Table 3. Multivariate linear regression models testing the association of gait speed as the dependent variable on body composition, nutritional and respiratory markers

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM</td>
<td>−0.009</td>
<td>0.004</td>
<td>0.025</td>
</tr>
<tr>
<td>Age</td>
<td>−0.014</td>
<td>0.005</td>
<td>0.006</td>
</tr>
<tr>
<td>FEV₁</td>
<td>0.007</td>
<td>0.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FM²</td>
<td>0.007</td>
<td>0.006</td>
<td>0.267</td>
</tr>
<tr>
<td>Age</td>
<td>−0.014</td>
<td>0.005</td>
<td>0.005</td>
</tr>
<tr>
<td>FEV₁</td>
<td>0.007</td>
<td>0.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FFM/FM</td>
<td>0.002</td>
<td>0.008</td>
<td>0.830</td>
</tr>
<tr>
<td>Age</td>
<td>−0.013</td>
<td>0.005</td>
<td>0.010</td>
</tr>
<tr>
<td>FEV₁</td>
<td>0.007</td>
<td>0.002</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

All models included BMI, gender, PA, number of comorbidities that did not reach statistical significance.
Model also included body weight that did not reach statistical significance.

has been shown to be important even if not attributable to specific disease stages in older persons [22]. Considering that there are contradicting data on the role of FM-related clinical outcomes in older persons especially with chronic diseases, this study adds important detail for future longitudinal perspectives. A previous community dwelling cohort of older persons suggested that the absolute amount of FM was negatively associated with physical performance, while lean mass is not as significant in absolute terms [23]. However, these authors did not aim at testing differences according to chronic diseases. With regard to studies performed in patients with COPD, an important impact of lean mass has been shown to have an important impact on negative clinical outcomes [2, 5]. Interestingly, a recent study found that the lean-to-fat ratio was associated with a greater walking distance in younger men, but not in women with COPD [20]. These same authors showed that higher measures of total adiposity (BMI) and central adiposity were related to functional limitation in both genders. However, these data were limited to a younger cohort of COPD patients (mean age of 58 years). We aimed at testing for differences in FM, lean mass (fat-free mass) and lean-to-fat ratio in a sample of older COPD patients (mean age of 75 years) admitted for respiratory rehabilitation on walking speed. This is a cross-sectional study from an ongoing protocol testing for performance outcomes in older persons with COPD, thus future findings will determine a predictive role of body composition measures on physical function in older persons. Our data also confirmed that older persons in a more severe state of COPD were more likely to walk slower.

Loss of lean mass is now recognised as a major comorbidity of COPD and causes functional impairment [2, 13, 24, 25]. Skeletal muscle wasting is a powerful predictor of mortality in COPD, independent of the lung function [11]. Clinically, rapid deteriorations in lean body mass have been described following an acute exacerbation of COPD, and particularly in more severe patients (FEV₁ is <50%) [26].

In contrast to emphysema and small airway fibrosis, skeletal muscle wasting and functional impairment can be slightly improved by nutritional intervention, physical training and anabolic steroids, indicating that it is potentially reversible [27]. Considering the importance of physical performance prediction on COPD outcomes, we hypothesised that lower lean mass would have a negative association with gait speed. Our findings confirmed that the lean-to-fat ratio increased across walking speed tertiles even in COPD patients [23]. However, the lean-to-fat ratio was not an independent determinant of gait speed. These differences are most likely due to the fact that our study included only older patients (>65 years of age) with COPD, while the paper by Sternfeld et al. [23] included community dwelling individuals with ages ranging from 55 to 95 years (mean age of 69).

COPD individuals with less lean mass have been shown to have more negative outcomes [24, 25]. Surprisingly, we did not find that lower lean mass was an independent determinant of slower gait speed in older COPD patients. This finding indicates that other body composition factors may hold a greater impact on physical performance in older COPD patients. We found that absolute FFM levels and a higher lean-to-fat ratio were associated with faster walking speed. This finding to a certain extent reinforces that of previous studies showing that...
higher levels of fat were associated with a greater likelihood of disability, while lower levels of lean mass were not [20, 23, 28]. In a younger cohort of COPD adults, the accumulation of greater FM, not the loss of lean, was strongly associated with functional limitation in both sexes [20]. Our findings add insight to a potential role played by FM alone on functional decline in older COPD patients.

From the literature, it would appear that a decline in lean mass is an important precursor of functional limitation at an earlier age in COPD [20]; however, an increase in FM should not be underestimated. Our study also showed that even though nutritional parameters including albumin and PA were significantly lower across COPD stages and tertiles of gait speed, these same parameters were not independent determinants of impaired mobility in fully adjusted models.

Our study had some limitations. One cannot rule out a role played by increased inflammatory markers produced by fat tissue on gait speed. Unfortunately, our protocol did not include pro-inflammatory cytokines, such as interleukin-6 (IL-6) or tumour necrosis factor-alpha (TNF-α). The protocol did include C-reactive protein (CRP), but this was found not to be an independent determinant (data not shown). Recent data from the Health ABC study highlighted that excessive abdominal visceral fat contributes to increased plasma IL-6, which, in turn, was strongly associated with mortality in older persons with COPD [29]. Another important limitation is our relatively small sample size. The small number of participants in the first and fourth groups of the GOLD stages should be noted and may explain why FFM did reach statistical differences across COPD groups, but this was found not to be an independent determinant (data not shown).

Although fat tissue has been shown to hold a protective role against morbidity in elders, increased FM suggests a negative role on mobility in older COPD patients.

### Key points
- Analysing gait speed in older patients with COPD.
- Impact of body composition on gait speed in COPD.
- FM is a determinant on slower gait speed in COPD.

### Conflicts of interest
All authors declare no conflict of interest.

### References
BODE index or geriatric multidimensional assessment for the prediction of very-long-term mortality in elderly patients with chronic obstructive pulmonary disease? A prospective cohort study

Claudio Pedone1,2, Simone Scarlata3, Francesco Forastiere1, Vincenzo Bellia5, Raffaele Antonelli Incalzi6,7

1Cattedra di Geriatria, Università Campus Biomedico, Via dei Compositori 128, Roma 00128, Italy
2Fondazione Alberto Sordi, Rome, Italy
3Chair of Geriatrics, Unit of Respiratory Pathophysiology, Università Campus Bio Medico, Via A. del Portillo 200, Rome 00128, Italy
4Osservatorio Epidemiologico del Lazio, Rome, Italy
5Dipartimento di Medicina, Pneumologia, Endocrinologia, Fisiologia e Nutrizione Umana, Università di Palermo, Palermo, Italy
6Department of Geriatrics, University Campus Bio-Medico, Via dei Compositori 130, Rome 00128, Italy
7Fondazione ‘S. Raffaele – Cittadella della Cantà’, Taranto, Italy

Address correspondence to: S. Scarlata. Tel: +39 06 225411168; Fax: +39 06 22541456. Email: s.scarlata@unicampus.it

Abstract

Background: a multidimensional approach—the BODE index—has been proposed for prognostic purposes in chronic obstructive pulmonary disease (COPD) and theoretically seems to be well suited for elderly people, but there is a lack of data