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Physical performance, sarcopenia and respiratory function in older patients with chronic obstructive pulmonary disease

SIR—The aging process is characterised by a progressive decline of skeletal muscle (or sarcopenia) which, by closely interacting with chronic diseases, may predispose to the onset of physical disability [1]. Chronic obstructive pulmonary disease (COPD) is a highly prevalent condition associated with both depleted lean mass and impaired overall health status in older persons [2, 3]. Furthermore, lean mass has shown to be inversely associated with the Medical Research Council dyspnoea score [4] and the Activity component of the Saint George Respiratory Questionnaire [5], and directly related to pulmonary function parameters (including Forced Expiratory Volume in 1 second [FEV1]) [4].

Recently, Spruit et al. [6] reported the absence of relationship between fat-free mass and 6-minute walking test (6mWT) results in the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study. On the other hand, Ischaki et al. [4] previously reported a positive correlation between results at the 6mWT (the most commonly adopted and reliable physical performance measure in COPD [7]) and fat-free mass. The ECLIPSE investigators [6] explained their negative results by their analytical choices and the evaluation of a higher number of potential confounders.

To our knowledge, besides of these sparse data, the relationships existing among respiratory function, sarcopenia and physical performance have never been formally
Research letters

explored in literature, especially among older persons. Aim of the present study is to verify the respective strengths of associations between body composition (i.e. sarcopenia) and respiratory function (i.e. FEV1) with 6mWT results in older COPD patients.

Methods

For details about study methods, also see Supplementary data available in Age and Ageing online, Appendix S1.

Study participants

Data are from 71 subjects with COPD aged 65 years and older consecutively recruited among those attending the pulmonary medicine outpatient clinic of the University Hospital ‘Campus Bio-Medico’ in Rome (Italy) from December 2009 to April 2010. Diagnosis of COPD was ascertained according to the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines [8].

Six-minute walking test

All the study participants underwent the assessment of physical function through the administration of the 6mWT [9]. Oxyhaemoglobin desaturation during exercise was defined as a 4% or more decrease of oxyhaemoglobin saturation from baseline value occurred during the 6mWT performance.

Sarcopenia

Body composition was assessed in all the study participants by a dual-energy X-ray absorptiometry (DEXA), using a total-body scan performed with a QDR Explorer (Hologic Inc., Bedford, MA, USA).

For the present analyses, we used two definitions of sarcopenia [10, 11]. Appendicular lean mass (ALM) was calculated as the sum of lean mass (in kilograms) in arms and legs, assuming that all non-fat and non-bone tissue is skeletal muscle. The first measure of sarcopenia (i.e. fat-adjusted rALM), was defined by residuals of a linear regression model predicting ALM (in kilograms) from height (in metres) and total fat mass (in kilograms). The second definition was based on residuals of a linear regression model between the dependent variable ALM (in kilograms) and height (in metres).

Forced Expiratory Volume in 1 second

FEV1 (expressed in litres), the other independent variable of interest, was assessed using a spirometric evaluation performed by a bell spirometer (Biomedin, Padua, Italy) according to ATS/ERS guidelines [12].

Covariates

Clinical conditions were defined on the basis of the patients’ clinical documentation. Barthel Index was also assessed to measure physical disability [13]. The Mini Nutritional Assessment (MNA) screening score (ranging from 0 [severe risk of malnutrition] to 14 [no risk of malnutrition]) was used as a measure of nutritional status [14].

Statistical methods

The relationship of the 6mWT with sarcopenia and FEV1 was explored using multiple unadjusted and adjusted linear regression models. Each independent variable of interest (i.e. rALM, fat-adjusted rALM and FEV1) was entered separately from the other two in specific linear regression models (except as indicated, i.e. Models 4a and 4b). The existence of possible interactions of age or gender in the studied relationships was explored by including specific interaction terms (age or gender * independent variable of interest) in the unadjusted linear regression models. To exclude the relevant multicollinearities in the adjusted linear regression models, we estimated tolerances and variance inflation factors (VIFs). A P-value of <0.05 was considered as statistically significant. Analyses were performed using SPSS software package version 16.0 for Mac (SPSS Inc., Chicago, IL, USA).

Results

The main characteristics of the study sample (n = 71) are reported in Table 1. No age or gender interaction was

<table>
<thead>
<tr>
<th>Table 1. Main characteristics of the study sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 71</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Gender (women)</td>
</tr>
<tr>
<td>Height (m)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Current smoking</td>
</tr>
<tr>
<td>Number of clinical conditions</td>
</tr>
<tr>
<td>MNA screening score</td>
</tr>
<tr>
<td>Risk of malnutrition (MNA &lt; 12)</td>
</tr>
<tr>
<td>Barthel index</td>
</tr>
<tr>
<td>C-reactive protein (mg/l)</td>
</tr>
<tr>
<td>FEV1 (l)</td>
</tr>
<tr>
<td>FEV1 (% of predicted value)</td>
</tr>
<tr>
<td>ALM (kg)</td>
</tr>
<tr>
<td>Total fat mass (kg)</td>
</tr>
<tr>
<td>6mWT (m)</td>
</tr>
<tr>
<td>6mWT (% of predicted value)</td>
</tr>
<tr>
<td>Patients experiencing relevant oxyhaemoglobin desaturation (≥4%) during exercise</td>
</tr>
</tbody>
</table>

Values are expressed as means (standard deviations), medians (interquartile range) or percentages.

MNA, Mini Nutritional Assessment; FEV1, Forced Expiratory Volume in 1 second; 6mWT, 6-minute walking test.
Formed considering:

Models (Models 4a and 4b).

Simultaneously included with FEV1 in fully adjusted variables, even when rALM or fat-adjusted rALM were consistently associated with the outcome. When potential confounders in the adjusted models (including inflammation), and consistent throughout the different operative definitions we adopted.

Consistently with previous studies [10, 11], the fat-adjusted definition of sarcopenia showed to slightly better predict physical function than the other one only considering lean mass. This confirms a role that fat mass may play in the development of the age-related muscle decline [11, 17, 18], especially in conditions (such as COPD) characterised by a body composition shift towards the adipose tissue gain [19, 20].

Although the spirometric exam was often considered difficult to performed and less reliable in older persons, its

Table 2. Results from separate linear regression models predicting 6mWT results (expressed in metres, dependent variable) from appendicular lean mass (rALM), fat-adjusted rALM or FEV1 (all per standard deviation increase) as independent variables (considered one per each model, except for Models 4a and 4b in which FEV1 is simultaneously included with one sarcopenia definition)

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4a</th>
<th>Model 4b</th>
</tr>
</thead>
<tbody>
<tr>
<td>rALM Beta coefficient (95% confidence interval)</td>
<td>9.42 (−18.75, 37.59)</td>
<td>51.57 (15.29, 87.85)</td>
<td>26.77 (−5.88, 59.41)</td>
<td>28.83 (−8.02, 65.67)</td>
<td>20.07 (−16.10, 56.24)</td>
<td>—</td>
</tr>
<tr>
<td>P-value</td>
<td>0.51</td>
<td>0.006</td>
<td>0.11</td>
<td>0.12</td>
<td>0.27</td>
<td>—</td>
</tr>
<tr>
<td>Fat-adjusted rALM Beta coefficient (95% confidence interval)</td>
<td>24.99 (2.15, 56.84)</td>
<td>42.51 (15.05, 69.98)</td>
<td>24.19 (−0.17, 48.55)</td>
<td>26.10 (−1.33, 53.53)</td>
<td>—</td>
<td>19.22 (−7.92, 46.37)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.04</td>
<td>0.003</td>
<td>0.052</td>
<td>0.06</td>
<td>—</td>
<td>0.16</td>
</tr>
<tr>
<td>FEV1 Beta coefficient (95% confidence interval)</td>
<td>65.82 (43.06, 88.58)</td>
<td>53.12 (29.38, 76.86)</td>
<td>30.83 (7.52, 54.14)</td>
<td>31.99 (6.60, 57.38)</td>
<td>30.61 (3.66, 57.57)</td>
<td>29.40 (2.55, 56.25)</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.01</td>
<td>0.02</td>
<td>0.03</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Standard deviations: rALM 2.64656; Fat-adjusted rALM 2.32896; FEV1 0.42624 l.

Model 1, adjusted for age, gender, height, weight; Model 2, adjusted for Model 1 + current smoking, risk of malnutrition, number of clinical conditions, Barthel Index and oxyhaemoglobin desaturation during exercise; Model 3, adjusted for Model 2 + C-reactive protein (log value); Model 4a: adjusted for Model 2 + rALM and FEV1 (simultaneously added in the model); Model 4b, adjusted for Model 2 + fat-adjusted rALM and FEV1 (simultaneously added in the model).

Discussion

Our results show that respiratory function is a stronger independent predictor of 6mWT results compared with the body composition parameters. Such close association was confirmed even after the inclusion of a wide range of potential confounders in the adjusted models (including inflammation), and consistent throughout the different operative definitions we adopted.

Consistently with the above-mentioned findings from the ECLIPSE study [6] and by Ischaki et al. [4], our findings support a crude association between lean mass and physical performance, and at the same time demonstrate that other factors (in particular, respiratory function) may explain such relationship. The superiority of FEV1 in explaining physical function may be due to the inner nature of the variables definitions. In fact, sarcopenia is defined on the basis of one-point quantitative, and not qualitative, evaluation of the skeletal muscle, thus providing a static dimension of it. On the other hand, FEV1 is a respiratory parameter resulting from the dynamic interactions of a multitude of systems and apparatus. This is particularly true among the weakest and frailest subjects that may easily become dependent on muscle strength in the FEV1 production.

Consistently with previous studies [10, 11], the fat-adjusted definition of sarcopenia showed to slightly better predict physical function than the other one only considering lean mass. This confirms a role that fat mass may play in the development of the age-related muscle decline [11, 17, 18], especially in conditions (such as COPD) characterised by a body composition shift towards the adipose tissue gain [19, 20].

Although the spirometric exam was often considered difficult to performed and less reliable in older persons, its
Body composition still represents an important determinant of physical performance in older COPD patients. This does not mean that conclusions are poorly generalisable: a recent Spanish nutritional survey [23] reported a similar mean body mass index in a large cohort of stable COPD patients (i.e. 28 kg/m2) to our sample (i.e. 28.7 kg/m2). Moreover, the mean 6mWT results obtained in our population (i.e. 307.2 m walked) are consistent with those previously reported by Sciurba et al. [24] (i.e. 308.3 m walked, including a 10% reduction due to the methodological differences in the administration of the test) in a large multicenter trial. We assessed body composition by DEXA, a widely adopted method, but not the ‘gold standard’. Furthermore, we defined sarcopenia on the basis of pure quantitative parameters of body composition, thus unable to provide information about the qualitative dimension of sarcopenia (e.g. muscle strength). Third factors not considered in the present analyses (e.g. physical activity) might differently explain our findings. Finally, the cross-sectional design of the study does not allow to establish any cause-effect sequence among the studied relationships.

Body composition might be an important determinant of physical performance in older COPD patients, but FEV1 represents a stronger predictor. Research is needed to confirm this observation on larger samples with the aim of improving our understanding of determinants of physical performance in a complex population such as that with COPD.

Key points

• COPD is highly prevalent in the elderly, and significantly associated with both depleted lean mass and impaired overall health status.
• FEV1 is strongly associated with physical performance in older COPD patients, more than body composition parameters.
• Body composition still represents an important determinant of physical performance in older COPD patients.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in Age and Ageing online.

Conflicts of interest

None declared.

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