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ORIGINAL ARTICLE

Inspiratory fraction as a marker of skeletal muscle dysfunction in patients with COPD

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Abstract
Background: An inspiratory capacity to total lung capacity (IC/TLC) ratio of ≤25% has emerged as a better marker of mortality in chronic obstructive pulmonary disease (COPD) patients. The relationship among the IC/TLC ratio to lower extremity skeletal muscle function remains unknown.
Methods: Thirty-five men with moderate to severe COPD were divided into those with IC/TLC ≤ 25% ($n = 16$) and >25% ($n = 19$). The subjects were tested for thigh muscle mass volume (MMT), maximal strength, power output of the lower extremities, and physical activity.
Results: Total MMT in the IC/TLC < 25% group was significantly lower ($413.91 \pm 89.42\,cm^3$) ($p < 0.001$) than in the IC/TLC > 25% group ($575.20 \pm 11.76\,cm^3$). In the IC/TLC ≤ 25% group, maximal strength of the lower extremities and muscle peak power output of the lower extremities were 36–56% lower ($p < 0.01$) than among the patients in the IC/TLC > 25% group.
Conclusion: IC/TLC ≤ 25% is associated with reduced maximal strength and peak power output of the lower extremities. IC/TLC ≤ 25% may have an important clinical relevance as an index to determine peripheral muscle dysfunction.

Introduction

Skeletal muscle dysfunction has been postulated as one of the extrapulmonary effects in patients with chronic obstructive pulmonary disease (COPD), resulting in reduced peripheral muscle strength and muscle mass.[1,2] Reductions in muscle force production contribute to exercise intolerance and have been associated with an increased mortality risk and a decrease in quality of life.[3,4] Lower extremity muscle power has been also recently posited as a more discriminating variable for understanding the relationship between impairments, functional limitations, and

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resultant disability with aging.[5,6] Physical inactivity and systemic inflammation have been cited as factors responsible for muscle dysfunction in COPD.[7,8] Considering that reductions in peripheral muscle strength have important clinical and functional implications for COPD patients, the search for effective pulmonary indices to predict peripheral muscle function is of paramount importance.

Among the pulmonary parameters, forced expiratory volume in 1 second (FEV_1) is the most important spirometric indicator of the severity of airflow obstruction. However, several studies have shown the weak relationship between FEV_1 and mortality,[9,10] indeed, it cannot be used to detect abnormal skeletal muscle function. Recently, the inspiratory capacity-to total lung capacity (IC/TLC) ratio has emerged as a better marker of mortality and functional reserve and is associated with altered exercise capacity in COPD patients.[11,12] Recently, Ramon et al.[13] observed that the patients with COPD with lower IC/TLC experience a higher longitudinal decline in exercise capacity.

To date, only one study has investigated the role of IC/TLC ratio on the muscle function in the upper extremities in this population of patients. Its authors found that maximal hand grip strength was lower among IC/TLC $\leq$ 25% than among patients with IC/TLC > 25%.[14] However, no previous studies have established the correlation between the IC/TLC ratio and lower extremity muscle mass, maximal strength, and muscle peak power output in this patient population.

Accordingly, the primary aim of the present study was to determine whether the inspiratory capacity-to-total lung capacity ratio or inspiratory fraction would be useful in predicting skeletal muscle dysfunction in the lower and upper extremities. We hypothesized that patients with IC/TLC $\leq$ 25% would have less maximal muscle strength of the lower and upper extremities and peak power output of the lower limbs than IC/TLC > 25% patients.

Materials and methods

Subjects

Thirty-five men with stable COPD were recruited *via* an outpatient clinic through the local pulmonologist office to participate in the study. All patients had received a clinical and functional diagnosis of COPD according to the GOLD criteria (stages II and III). Patients presented with moderate-to-severe airways obstruction ($FEV_1/FVC < 0.7$ and FEV_1 < 80% but FEV_1 > 30% predicted). Inclusion criteria include: (1) dyspnea (mMMRC grades II and III); (2) non-smoker status; and (3) aged 60–80 yrs. Exclusion criteria include: (1) having never smoked; (2) exacerbation of symptoms in the preceding three months; and (3) cardiovascular, neuromuscular, musculoskeletal or arthritic problems that might limit exercise tolerance. The patients were informed carefully about the procedures and possible risks of the experiments, as well as the benefits of the project, and written consent was obtained. The Research Ethics Committees of the Public University of Navarre and Virgen del Camino Hospital approved the study.

Pulmonary functional and clinical assessments

Baseline assessment included: (1) spirometry, lung volumes by body plethysmography, maximal inspiratory and expiratory pressure according with recommended methods; (2) anthropometric variables; (3) 6-min, walk test (6MWT)[15]; and (4) BODE index.

Thigh muscle mass

Muscle mass (MM) of the thigh (T) were assessed using magnetic resonance imaging (MRI; 1.5 T; Siemens Magnetom, Germany). The length of the femur (Lf), taken as the distance from the intercondylar notch of the femur to the superior boundary of the femoral head was measured on a coronal plane. Subsequently, 15 axial scans of the thigh interspaced by a distance of 1/15 Lf were obtained from 1/15 Lf to 15/15 Lf. MR imaging of both thighs was obtained. Cross-sectional volumes (cm^3) of the thigh at 30% proximal, 50%, and 70% distal of the Lf were used for further analysis. The total volume (cm^3) of the MM_T was calculated as the combination of the 30, 50, and 70% of the Lf.[16]

Physical activity

Habitual physical activity was evaluated using accelerometry (TriTrac-R3D system; WI, USA). The TriTrac was worn around the waist. TriTrac monitoring was recorded on a minute-by-minute basis during two weekdays and two weekend days.

Lower extremity maximal strength and muscle peak power output

One repetition maximum (the heaviest load that could be lifted only once using the correct technique) was determined for the leg press exercise ($1RM_{LP}$) (Technogym, Gambettola, Italy). Three-to-four subsequent attempts were made to determine 1RM.[16]

The subjects were instructed to exert their maximal force as fast as possible.

Muscle peak power output of the leg extensor muscles was measured during the concentric phase of leg press using the load equal to 50 and 70% of 1RM. An optical encoder (Computer Optical Products Inc., CA, USA) was attached to weight plates to record the position and direction of the displacement to an accuracy of 0.2 mm at 1000 Hz. Subjects were instructed to displace the weights as fast as possible. Two testing trials were recorded and the best trial was taken for further analysis.

Upper extremity maximal strength

One repetition maximum (1RM) was determined for seated chest press ($1RM_{CP}$), shoulder press, and seated row (Technogym, Gambettola, Italy).[16]

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