Determinants of exercise capacity in obese and non-obese COPD patients

Diego A. Rodríguez a,b,*, Judith Garcia-Aymerich c, Jose L. Valera d, Jaume Sauleda d, Bernat Togores d, Juan B. Galdiz e, Joaquim Gea b, Mauricio Orozco-Levi b, f, Antoni Ferrer b, Federico P. Gomez a, Joan Albert Barberà a, Ignasi Serra g, Josep M. Antó h, Josep Roca a on behalf of the PAC-COPD Study Group

a Servei de Pneumologia (ICT), Hospital Clinic, IDIBAPS, Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Universitat de Barcelona, Villarroel 170, 08036 Barcelona, Catalonia, Spain
b Muscle and Respiratory System Research Unit and Respiratory Medicine Department, IMIM-Hospital del Mar, Barcelona, Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Health and Experimental Sciences Department (CEXS), Universitat Pompeu Fabra (UPF), Passeig Maritim 25, 08003 Barcelona, Catalonia, Spain
c Centre for Research in Environmental Epidemiology (CREAL), Department of Experimental and Health Sciences, Universitat Pompeu Fabra, CIBER Epidemiología y Salud Pública (CIBERESP), Doctor Aiguader 88, 08003 Barcelona, Catalonia, Spain
d Hospital Son Espases, Carretera de Valldemossa 79, 07120 Palma de Mallorca, Spain
e Hospital Cruces, Universidad del País Vasco, Plaza de Cruces 12, 48903 San Vicente de Barakaldo, Vizcaya, Spain
f Respiratory Department, Fundación Cardiovascular de Colombia, Calle 155A No. 23–58, Urbanización El Bosque Floridablanca, Santander Floridablanca, Santander, Colombia

Received 29 September 2013; accepted 3 February 2014
Available online 12 February 2014

* Corresponding author. Servei de Pneumologia, Hospital del Mar, Passeig Maritim 25, 08003 Barcelona, Catalonia, Spain. Tel.: +34 93 2483138; fax: +34 93 2483425.
E-mail address: darodriguez@parcdesalutmar.cat (D.A. Rodríguez).

0954-6111/$ – see front matter © 2014 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.rmed.2014.02.004
Impaired exercise capacity is a cardinal feature of chronic obstructive pulmonary disease (COPD) because it is associated with poorer quality of life [1,2], increased use of healthcare resources [2–4] and worse prognosis [5–7]. The six-minute walking test (6MWT) [8] and the incremental cardiopulmonary exercise test (CPET) [9] are well accepted tests to evaluate exercise capacity in COPD (10–12). Yet, neither peak oxygen uptake (VO2 peak) determined during CPET [10–12] or the six-minute walking distance (6MWD) can be adequately predicted from the degree of airflow limitation [13–15] as an isolated factor, indicating that factors other than lung function impairment also modulate exercise capacity in COPD. Obesity [16] is often associated with COPD and it has the potential to contribute to exercise limitation [17,18], but its individual contribution to impaired aerobic capacity in these patients is unclear [18–21]. Different studies seem to indicate that obesity does not constitute a disadvantage during cycling exercise in COPD patients [18,21]. In contrast, Bautista et al. [22] reported that obese COPD patients had reduced 6MWD as compared with those with normal body weight. However, the mechanisms for the poorer walking performance in the obese COPD group were not fully established [23].

We hypothesized that the contribution of resting lung function, body composition and systemic inflammation to exercise capacity in COPD differs according to the obesity status. To test this hypothesis, we studied exercise capacity, as assessed by both 6MWT and CPET, in 251 clinically stable COPD patients with a wide range of airflow limitation severity included in the PAC-COPD cohort, a multi-center study conducted in 9 tertiary hospitals in Spain, some of whose results have already been reported elsewhere [20,24].

**Background**: The effects of obesity in combination with chronic obstructive pulmonary disease (COPD) on exercise capacity are receiving increased attention. But, a comprehensive analysis of factors associated with aerobic capacity in obese COPD patients has not been performed.

**Methods**: Six-min walking test (6MWT) was performed in 251 COPD patients, and 159 of those also carried out an incremental cardiopulmonary exercise test (CPET) to evaluate exercise capacity. In all patients, anthropometrics, dyspnea and anxiety–depression scores, lung function, daily physical activity, co-morbidities and circulating inflammatory biomarkers were also assessed. Six-min walking distance (6MWD) and peak oxygen uptake (VO2 peak) during CPET were two primary outcome variables.

**Results**: 57% of the patients showed body mass index (BMI) < 30 kg/m2 (COPDn) and the remaining 43% were obese with a BMI ≥ 30 kg/m2 (COPDo). In patients with COPDn, 6MWD showed independent negative associations with age, dyspnea score, sedentarism, depression scores and a positive relationship with arterial oxygenation; whereas in COPDo, 6MWD showed an inverse relationship with BMI. In COPDn, VO2 peak showed a negative association with age and positive relationships with both FEV1 and DLCO. However, in COPDo the dyspnea score was the strongest determinant of VO2 peak.

**Conclusions**: Obese and non-obese COPD patients show different determinants of aerobic capacity, including pulmonary and non-pulmonary factors that are also dependent on the type of exercise protocol. These results could be considered in the evaluation of obese patients with COPD.

© 2014 Elsevier Ltd. All rights reserved.

---

**Introduction**

**Summary**

**Patients**

A total of 342 COPD patients were consecutively recruited from January 2004 to March 2006 during their first hospital admission for COPD exacerbation in 9 tertiary hospitals in Spain. The diagnosis of COPD was confirmed by forced spirometry after discharge, when the patient was considered clinically stable. The severity of airflow limitation was graded according to European Respiratory Society and the American Thoracic Society (ERS/ATS) criteria [25]. For the present study, we excluded 42 patients with missing data on exercise capacity or body composition. Additionally, and because the study focused on obese and normal weighted COPD patients, we also excluded patients with low Fat Free Mass Index (FFMI) [26] (men < 17 kg/m² and women < 14 kg/m²) (n = 47). Finally, two patients presenting simultaneously obesity and low FFMI they were also excluded from the study, giving a total of 251 subjects for the present analysis. There were no significant differences on main clinical and functional characteristics between included and excluded patients, except for BMI. The study protocol was approved by the Ethics Committees of the participating hospitals and written informed consent was obtained from all subjects. Detailed information on subject’s recruitment has been reported elsewhere [20,24,27].

**Measurements**

Patients were clinically stable for at least 6 weeks before the study and all of them were under optimal medical therapy. Exercise capacity was assessed by means of (i) the six-minute walking test (6MWT) following ATS guidelines

---

**KEYWORDS**

COPD; Exercise; Comorbidity; Obesity
Body mass index (kg/m²) was computed from weight and height in a physical examination, and composition was assessed using bio-impedance to obtain FFMI. Patients were classified in: obese COPD patients (body mass index, BMI ≥ 30 kg/m²) (COPD-O) and patients with BMI < 30 and normal FFMI (COPD-N) [26].

Laboratory lung function tests at rest, maximal inspiratory and expiratory pressures; peripheral muscle strength and several serum inflammatory biomarkers (Tumor Necrosis Factor [TNF] α, interleukin [IL]-6, IL-8, IL-10 and C-reactive protein [CRP]) in the blood were assessed at the same time during clinical stability. All patients answered an epidemiological questionnaire assessing among other variables: physical activity [using the Yale physical activity survey as validated in Spanish for COPD patients [28]], health related quality of life dyspnea [using the Modified Medical Research Council (MMRC) scale [29]], and anxiety and depression (HAD) scale [30]. Co-morbidities were evaluated by Charlson Index. Detailed information on measurements and procedures of the PAC-COPD study has been reported elsewhere [20,24].

Data analysis

The results are expressed as mean (SD), median (P25—P75) or number (percentages, %). Statistical analyses were done using SPSS package v. 14. Differences between groups were assessed by Chi-square test and unpaired t-test or Mann-Whitney U-test (for quantitative variables with normal and non-normal distributions, respectively) and Chi-squared or Fisher’s exact test (for qualitative variables).

As both 6MWD and VO₂ peak were normally distributed, multivariate linear regression models were used to identify their determinants. Separate models were built for 6MWD and VO₂ peak. Potential determinants of 6MWD and VO₂ peak (mMRC dyspnea scale, BMI, FFMI, HAD depression scale, HAD anxiety scale, physical activity, SGRQ scores, severity of airflow limitation (FEV₁), gas trapping (inspiratory to total lung capacity), pulmonary diffusion impairment (DLco), arterial oxygenation (PaO₂), muscle force [handgrip, maximal inspiratory and expiratory pressures (MIP and MEP)], serum inflammatory markers (TNF-α, CRP, IL-6, IL-8, IL-10) and co-morbidities) as well as potential confounders of these associations (smoking status, gender, age) were tested in the multivariate models and finally included in the final models if (i) related to both the exposure and the outcome, or (ii) modified (>10% change in regression coefficient) the estimates of the remaining variables. Goodness of fit was assessed by means of normality of residuals, heteroscedasticity, linearity, collinearity and identification of influential data. The non-standardized β coefficient (β coeff.) and its 95% confidence interval of each covariate is reported to assess its relative independent effect on the outcome variable. All variables are reported as continuous variables except physical activity (Low < 3000 kcal/week versus Normal ≥ 3000 kcal/week) [31]. To assess whether the determinants of exercise capacity are different depending on obesity status, final linear regression models were stratified according to COPD-N and COPD-O. A p-value lower than 0.05 was considered statistically significant.

Results

Table 1 displays the main characteristics of the two groups of COPD patients by body composition. Overall, 57% of the patients showed a BMI below 30 kg/m² (COPD-O, n = 143) and 43% of them were obese (COPD-O, n = 108). The analysis of resting lung function testing showed that forced respiratory volume during first second (FEV₁), Carbon monoxide lung transfer capacity (DLco), maximal inspiratory pressure (MIP) and inspiratory to total lung capacity ratio (IC/TLC) were higher in the COPD-O group than the COPD-N patients, but no differences were observed in other lung function variables or handgrip strength (Table 1). Serum concentrations of the different inflammatory biomarkers measured in the study were not different between groups, except for IL-6 (Table 1).

Exercise capacity

6MWD was higher in COPD-N compared to COPD-O (Table 1). Of note, however, VO₂ peak (%predicted) and V̇e max were similar in two groups. In contrast, workload, oxygen pulse and the intensity of leg discomfort at peak exercise were higher in COPD-O (Table 1). Also COPD-O showed a lower V̇e peak/MVV ratio at peak of exercise than COPD-N. Likewise, both groups displayed similar cardiovascular response at peak exercise, as assessed by heart rate and heart rate reserve (p = 0.729) (Table 1). We did not observe significant differences on the reason for stopping (ie, breathlessness and/or leg fatigue) during incremental exercise test between groups (p = 0.387).

Determinants of exercise capacity by body composition

Table 2 presents the multiple regression analysis results. Age and dyspnea scores were inversely associated with 6MWD both in COPD-N and COPD-O. It is of note that dyspnea showed a stronger association with 6MWD in COPD-N than in COPD-O. By contrast, BMI was inversely associated with 6MWD only in COPD-O. Walking distance in COPD-N, in addition to age and dyspnea score mentioned above, also showed a negative association with depression score and positive relationships with both daily physical activity and arterial oxygenation. With respect to VO₂ peak, we found that it was related inversely with age and positively associated with FEV₁ both in COPD-N and COPD-O.

The most relevant characteristic of COPD-O was the extremely high negative association between dyspnea score and VO₂ peak, not seen in COPD-N, which accounted for a large proportion of the variance explained by the equation. Systemic inflammatory markers and respiratory and handgrip muscle force were not related to exercise capacity in this study group.

Discussion

The results of the study indicate that: (1) COPD-O showed distinctive determinants of exercise capacity compared to COPD-N; (2) Dyspnea, was a stronger predictor of exercise capacity in COPD-O than in COPD-N, irrespective of
the protocol; (3) COPD₀ patients showed lower 6MWD and higher ventilatory requirements at peak cycling exercise compared to those with normal body mass composition; and, (4) the two exercise protocols, 6MWT and CPET, also showed differences in the type of determinants, namely: anxiety—depression, daily physical activity and arterial oxygenation played a significant role on exercise capacity (6MWD) in non-obese COPD patients, but not on VO₂ peak.

### Analysis of determinants of 6MWD and VO₂ peak

The 6MWT is increasingly recognized as an important test for clinical assessment and monitoring of COPD patients [32]. We found that in COPDₙ, 6MWD showed an inverse association with age together with a positive association with PaO₂. These observations are consistent with known physiological determinants of exercise capacity [9]. Likewise, the significant association of daily physical activity

---

### Table 1 Characteristics of the subjects by body composition.

<table>
<thead>
<tr>
<th>Clinical and functional variables</th>
<th>COPDₙ (n = 143)</th>
<th>COPD₀ (n = 108)</th>
<th>p-Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex:</strong> male, n (%)</td>
<td>142 (99)</td>
<td>102 (95)</td>
<td>0.087</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>67 (8)</td>
<td>68 (8)</td>
<td>0.948</td>
</tr>
<tr>
<td>Active smokers, n (%)</td>
<td>85 (59)</td>
<td>58 (54)</td>
<td>0.444</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.2 (2.2)</td>
<td>33.2 (2.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fat free mass index (kg/m²)</td>
<td>19.4 (1.6)</td>
<td>22.0 (2.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyspnea (mMRC scale)</td>
<td>2.0 (2−3)</td>
<td>2.5 (2−3)</td>
<td>0.312</td>
</tr>
<tr>
<td>Anxiety (HAD scale)</td>
<td>5.0 (1−8)</td>
<td>4.0 (1−7)</td>
<td>0.054</td>
</tr>
<tr>
<td>Depression (HAD scale)</td>
<td>3.0 (1−5)</td>
<td>3.0 (1−5)</td>
<td>0.969</td>
</tr>
<tr>
<td>Physical activity (kcal/week), median (P25–P75)</td>
<td>5373 (3243−8939)</td>
<td>6539 (3245−10,147)</td>
<td>0.247</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>1.5 (0.5)</td>
<td>1.7 (0.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV₁ (%predicted)</td>
<td>49 (16)</td>
<td>58 (8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DLCO (% predicted)</td>
<td>63 (20)</td>
<td>72 (20)</td>
<td>0.002</td>
</tr>
<tr>
<td>Total lung capacity (% predicted)</td>
<td>103 (19)</td>
<td>94 (17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inspiratory to total lung capacity</td>
<td>0.29 (0.09)</td>
<td>0.35 (0.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>75 (11)</td>
<td>73 (10)</td>
<td>0.197</td>
</tr>
<tr>
<td>MIP (% predicted)</td>
<td>66 (25)</td>
<td>59 (21)</td>
<td>0.029</td>
</tr>
<tr>
<td>MEP (% predicted)</td>
<td>64 (22)</td>
<td>65 (22)</td>
<td>0.598</td>
</tr>
<tr>
<td>Handgrip dominant (kg)</td>
<td>32 (7)</td>
<td>34 (8)</td>
<td>0.234</td>
</tr>
<tr>
<td>TNF α (pg/dl)</td>
<td>0.18 (0−0.9)</td>
<td>0.04 (0−0.5)</td>
<td>0.335</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>0.34 (0.1−0.9)</td>
<td>0.40 (0.2−0.7)</td>
<td>0.094</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>0.90 (0.4−1)</td>
<td>1.18 (0.6−2.0)</td>
<td>0.020</td>
</tr>
<tr>
<td>IL-8 (pg/ml)</td>
<td>4.19 (3.1−5.3)</td>
<td>4.30 (3.2−5.4)</td>
<td>0.980</td>
</tr>
<tr>
<td>IL-10 (pg/ml)</td>
<td>0.16 (0−1)</td>
<td>0.14 (0−1.1)</td>
<td>0.350</td>
</tr>
<tr>
<td>Charlson index</td>
<td>2.0 (1−2)</td>
<td>2.0 (1−2)</td>
<td>0.667</td>
</tr>
<tr>
<td><strong>6 MWD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance (meters)</td>
<td>452 (84)</td>
<td>423 (82)</td>
<td>0.008</td>
</tr>
<tr>
<td>SpO₂ fell &gt;4%, n (%)</td>
<td>22 (32)</td>
<td>33 (31)</td>
<td>0.590</td>
</tr>
<tr>
<td>Dyspnea at final (Borg scale)</td>
<td>3.3 (2.7)</td>
<td>3.5 (2.6)</td>
<td>0.598</td>
</tr>
<tr>
<td>Legs fatigue at final (Borg scale)</td>
<td>2.7 (2.7)</td>
<td>2.8 (2.8)</td>
<td>0.109</td>
</tr>
<tr>
<td><strong>Cycle-ergometer incremental exercise (n)</strong></td>
<td>96</td>
<td>63</td>
<td>0.033</td>
</tr>
<tr>
<td>Workload peak (watts)</td>
<td>74 (26)</td>
<td>84 (27)</td>
<td>0.033</td>
</tr>
<tr>
<td>VO₂ peak (L/min)</td>
<td>1.1 (0.3)</td>
<td>1.3 (0.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO₂ peak (% predicted)</td>
<td>61 (17)</td>
<td>59 (20)</td>
<td>0.528</td>
</tr>
<tr>
<td>V̇e peak (L/min)</td>
<td>42 (12)</td>
<td>48 (13)</td>
<td>0.101</td>
</tr>
<tr>
<td>V̇e peak/MVV</td>
<td>28 (9)</td>
<td>25 (6)</td>
<td>0.012</td>
</tr>
<tr>
<td>Heart rate peak (beats/min)</td>
<td>123 (19)</td>
<td>122 (22)</td>
<td>0.899</td>
</tr>
<tr>
<td>O₂ pulse peak (ml/beat)</td>
<td>9.2 (2.9)</td>
<td>11.1 (2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lactate at final (mEq/L)</td>
<td>4.9 (2.3)</td>
<td>4.9 (1.7)</td>
<td>0.967</td>
</tr>
<tr>
<td>Dyspnea at final (Borg scale)</td>
<td>5.0 (2.8)</td>
<td>5.6 (2.5)</td>
<td>0.981</td>
</tr>
<tr>
<td>Legs fatigue at final (Borg scale)</td>
<td>4.7 (2.8)</td>
<td>5.0 (2.8)</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Values are mean ± SD, median (P25−P75) or number (%).

Definition of abbreviation: COPDₙ = BMI < 30 and normal FFMI; COPD₀ = Obese; COPD₁ = low FFMI; FEV₁ = forced expiratory volume in one second; DLCO = diffusing lung capacity; MMRC = Modified Medical Research Council; HAD = hospital anxiety and depression scale; MIP = maximal inspiratory pressure; MEP = maximal expiratory pressure; VO₂ = oxygen uptake; VE = minute ventilation; 6MWD = six-minute walking distance; CRP = C-reactive protein; TNFα = tumor necrosis factor alpha.

<sup>a</sup> Chi-square tests and unpaired t-tests or Mann-Whitney U-tests significant between groups.
with 6MWD and the negative association with the anxiety–depression score confirm previous data [31,33]. By contrast, our study provides novel data with respect to the effects of body composition on 6MWD in COPD patients. We observed that, the regression equation for 6MWD is different between COPDO and COPDN. In the former, COPDO, the equation includes a negative association with BMI indicating that increased BMI determines a higher work rate during the test that leads to lower walking speed and lower distance [18,34]. As mentioned above, obese COPD patients show an increase in the weight of the dyspnea score as compared to COPDN [21,35].

Common determinants of VO2 peak in the two regression models were the negative association with age and MMRC and the positive weight of lung function measurements. It is of note, however, that in COPDO (Table 2, last column), dyspnea score emerged as the major covariate of VO2 peak, due to higher ventilatory requirements at a given work rate [17,18] compared to COPD patients with normal body mass composition. But, recent studies seem to challenge that constraints in respiratory mechanics due to obesity significantly contribute to increased dyspnea during exercise [17,36].

The current study indicates that the determinants of exercise performance vary with the type of protocol, either constant load sub-maximal exercise (6MWT) or incremental exercise (VO2 peak) [13], but we confirmed the strong relationship between dyspnea score and exercise performance in COPDO patients, independently to the exercise protocol.

It is of note that VO2 peak was similar between COPDO and COPDN, expressed either in absolute terms or as % predicted (Table 1). In this line, several studies demonstrated that mild to moderate obesity does not alter exercise performance measured by endurance and/or incremental exercise testing on cycle-ergometer [36]. In the current study, COPDO patients have shown significantly higher IC/TLC values than COPDN patients indicating their potential advantage to perform exercise from a mechanical standpoint [21]. However, studies comparing treadmill and cycling exercise are needed to determine if putative mechanical advantages of obesity during cycling exercise are also evident during weight-bearing exercise and to better elucidate the complex and multifactorial nature of dyspnea in obese COPD patients [36].

### Exercise capacity and systemic inflammation

Low-grade chronic systemic inflammation has been observed in different chronic diseases, including COPD and ageing [37]. The current study, however, did not show consistent relationships between exercise capacity and systemic inflammation, consistent with previous reports [38]. However, the complexities of the interplay between COPD and their co-morbidities [39] indicate the need for further longitudinal and integrative research in this field [40].

### Strengths and limitations

The analysis of a large cohort of clinically stable patients (n = 251) recruited after the first hospital admission due to an exacerbation of COPD is a unique feature of the current research because it provides a picture of exercise performance and its determinants at a very specific and important time point during the natural course of the disease. Yet, our
study has some limitations that deserve comment. Although peripheral muscle strength was not an important determinant, in our study it was only assessed by handgrip strength. Quadriceps strength might have provided different results.

It is of note that 6MWD and VO2 peak could not be determined in all patients, but we demonstrated that this does not constrain our conclusions. Finally, we acknowledge that our cross-sectional report cannot generate prognostic information on longitudinal changes of exercise capacity as disease progresses.

Conclusions and future perspectives

Taken together the findings of the study indicate that dyspnea is a significant limiting factor of exercise in obese COPD patients independently of the degree of airflow limitation and co-morbidities. Obesity has a relevant role limiting 6MWD and, consequently, it may have an impact on daily physical activities [41]. Future COPD strategies should include reduction of obesity as a key therapeutic objective [18,42]. Moreover, the results highlight an independent association of lung function and body composition on exercise capacity in these patients indicating that body composition shall be taken into account in the clinical interpretation of exercise testing in COPD patients.

Conflict of interest

Supported by: Fundació Marató TV3-042010 Fondo de Investigaciones Sanitarias (FIS-PI061510); CIBERESP (CB-06/06) and European Commission (FP6) BIOBRIDGE (LSHG-CT-2006-037939). The PAC-COPD study is funded by grants from Fondo de Investigación Sanitaria (FIS PI020541), Ministry of Health, Spain; Agència d’Avaluació de Tecnologia i Recerca Mèdiques (AATRM 035/20/02), Catalonia Government; Spanish Society of Pneumology and Thoracic Surgery (SEPAR 2002/137); Catalan Foundation of Pneumology (FUCAP 2003 Beca Maríà Rava); Red RESPIRA (RTIC C03/11); Red RCESP (RTIC C03/09); Fondo de Investigación Sanitaria (PI052486); Fondo de Investigación Sanitaria (PI052302); Fundación La Marató de TV3 (Num. 041110); DURSI (2005SGR00392); and an unrestricted educational grant from Novartis Farmacéutica, Spain. CIBERESP and CIBERES are funded by the Instituto de Salud Carlos III, Ministry of Health, Spain.

DAR, JGA, JLV, JS, BT, JBG, JG, MOL, AF, FPG, JAB, IS, JMA, JR have no conflict to declare.

References

Exercise in obese COPD patients 751


