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ORIGINAL RESEARCH

Physical activity and inactivity among different body composition phenotypes in individuals with moderate to very severe chronic obstructive pulmonary disease

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Abstract
Background: The phenotype profiling of individuals with chronic obstructive pulmonary disease (COPD) according to impairments in body composition and level of physical activity in daily life (PADL) needs to be determined.
Objective: To verify if individuals with COPD classified as physically active/inactive present different characteristics within different body composition phenotypes.
Methods: Individuals with COPD were cross-sectionally stratified into four groups according to fat-free and fat mass indexes: Normal Body Composition (NBC), Obese (Ob), Sarcopenic (Sarc), and Sarcopenic/Obese (Sarc/Ob). Additionally, individuals had their PADL level objectively assessed through activity monitoring during two weekdays for at least 10 h/day, and then were classified as physically active (Act) or inactive (Inact) according to international recommendations. Lung function (spirometry), exercise capacity (6-minute walking test [6MWT]) and peripheral muscle strength (1-repetition maximum [1RM]) were also assessed.

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Results: 176 individuals with COPD (mean ± standard deviation age: 67 ± 8 years, body mass index 26 ± 6 kg/m^2, FEV1 47 ± 16%predicted) were classified as: NBC + Act (17%), NBC + Inact (22%), Ob + Act (6%), Ob + Inact (10%), Sarc + Act (12%), Sarc + Inact (9%), Sarc/Ob + Act (8%) and Sarc/Ob + Inact (16%). The Sarc/Ob + Inact group presented lower 6MWT and 1RM for knee extension compared to NBC + Act, NBC + Inact, and Ob + Act groups ($p < 0.05$). The Sarc/Ob + Inact group also presented lower FEV1% predicted, 1RM for elbow flexion and elbow extension compared to the NBC + Act and NBC + Inact groups and lower 1RM for elbow extension compared to Ob + Inact group ($p < 0.05$).
Conclusion: The combination of sarcopenia, obesity, and physical inactivity was shown to be detrimental in individuals with COPD. Therefore, this profile is a main therapeutic target for improving PADL level and/or body composition.

Introduction

Persistent airflow limitation characterizes individuals with chronic obstructive pulmonary disease (COPD), resulting in symptoms such as dyspnea and fatigue. The association with reduced physical activity levels leads to worsening of the symptoms and characterizes a ''vicious circle'', which is related to the appearance of multiple extrapulmonary effects.[1–3]

The American College of Sports Medicine (ACSM) and the American Heart Association (AHA) recommend a minimum of 30 min of physical activity of moderate intensity (5 times per week) or 20 min of physical activity of vigorous intensity (at least 3 times/week) for an individual to be considered physically active; or even, to accumulate 3 bouts or more of 10 min of vigorous intensity.[4,5] Those individuals who do not reach these recommendations are considered physically inactive, and it is known that inactivity contributes to the increase of exacerbations' frequency and morbimortality in people with COPD.[6]

Individuals with COPD often present metabolic dysfunctions that may influence their body composition.[7,8] Furthermore, body composition abnormalities, may lead to impaired exercise capacity, more severe dyspnea and fatigue, worse health status, and higher mortality rate.[7,9–12] Sarcopenia is a body composition abnormality characterized by low fat-free mass index (FFMI), and this condition is associated with decreased physical activity in daily life (PADL), functional performance, and exercise capacity.[13,14] Obesity, another possible body composition abnormality, is also associated with decreased PADL, worse exercise capacity, and impaired lung function in individuals with COPD.[15,16] However, due to the ''protective effect'' present in the obesity paradox, obese individuals with COPD may present better disease prognosis than those with normal body mass index (BMI).[8,17,18] On the other hand, the combination of obesity and sarcopenia in this population is related to worse physical performance compared to other body composition phenotypes.[19,20]

Despite the array of important clinical complications involved, the phenotype profiling of individuals with COPD according to body composition abnormalities and the level of PADL has never been studied, and the present study focuses on the potential clinical implications of these phenotypes by hypothesizing that the combination of abnormalities in body composition and physical inactivity may further impair the physical functional characteristics of this population. Therefore, the aim of this study was to determine if individuals with COPD classified as physically active or inactive present different physical functional characteristics within different body composition phenotypes.

Methods

A retrospective analysis was undertaken using available baseline-only data from a convenience sample of 176 individuals with COPD assessed during an initial evaluation at the Pulmonary Rehabilitation program at the University Hospital of Londrina (HUL, Brazil). The present sample combines participants from a previously published study[21] with those from an ongoing study (ClinicalTrials.gov number, NCT03127878), and all data were collected in the period of pre-rehabilitation assessments between 2006 and 2019. Both studies were approved by the Research Ethics Committee from the Universidade Estadual de Londrina, Paraná, Brazil (nos. 123/09 and 1.730.247) and all participants signed an informed consent form.

Inclusion criteria were the same as those for the two above mentioned related studies: COPD diagnosis according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria[2]; absence of any regular physical training in the preceding year; clinical stability defined as absence of exacerbations within the last month; and absence of severe comorbidities that could interfere in the assessment protocol (e.g. orthopedic, rheumatological, neurological, or cardiovascular conditions). Individuals were excluded from the present study's analyses in case of missing (unavailable) data concerning the complete assessments of body composition and PADL.

Assessments

Body weight and height were measured on a calibrated scale (Filizola modelo 21; Filizola, Brazil). Body mass index

(BMI) was calculated as weight divided by height squared (kg/m^2). Body composition was assessed by bioelectrical impedance [Biodynamics 310TM (Biodynamics Corp, USA)] according to Lukaski et al.[22] and the manufacturer's recommendations. Fat-free mass (FFM) was calculated from the impedance using a specific formula derived for individuals with COPD.[23] Fat mass (FM) was calculated subtracting FFM from body weight. FFM and FM were adjusted for differences in body surface by dividing them by height squared, and consequently FFM and FM indexes (FFMI and FMI, respectively) were calculated. FFMI values lower than 10th percentile and FMI values higher than 90th percentile were considered abnormal.[19,20] Individuals were classified into four metabolic phenotypes: normal body composition (NBC, FFMI $\geq$ 10th percentile and FMI < 90th percentile), obese (Ob, FMI $\geq$ 90th percentile and FFMI $\geq$ 10th percentile), sarcopenic (Sarc, FFMI < 10th percentile and FMI < 90th percentile), or sarcopenic–obese (Sarc/Ob, FFMI < 10th percentile and FMI $\geq$ 90th percentile).[19,20]

PADL was objectively assessed using a validated multisensor SenseWear® Armband (BodyMedia, USA).[24–27] All individuals were instructed to wear the device for two consecutive week days, 12 h/day. Consistent with the existing literature, an assessment day was considered valid when there was at least 10 h/day of wear time.[28,29] Individuals were divided into two groups according to PADL level, as recommended by the ACSM: actives (Act: individuals spending an average of more than 30 min/day in moderate-to-vigorous (MVPA) intensity activities, i.e., $\geq$3 MET); and inactives (Inact: individuals who did not meet the PADL recommendation).[4,5]

History of self-reported comorbidities (diabetes, hypertension, cardiopathy, among others) and demographic data were collected through self-report. Pulmonary function was assessed by spirometry with the Spirobank G® (MIR, Italy) following established protocol by the American Thoracic Society (ATS)/European Respiratory Society (ERS),[30] with reference values for the Brazilian population having been previously established by Pereira et al.[31] Exercise capacity was assessed with the 6-minute walking test (6MWT) according to international standardization,[32] and reference values were those for the Brazilian population established by Britto et al.[33] Peripheral muscle strength was assessed using a one-repetition maximum test (1RM) following international standardization[34] for knee extension, elbow extension, and elbow flexion (CRW 1000; Embreex, Brazil). The Medical Research Council (MRC) scale[35] was used to assess the level of limitation due to breathlessness in activities of daily living, with a minimal important difference (MID) of −1 point.[36] Functional status was assessed by the London Chest Activity of Daily Living (LCADL) scale,[37] and an absolute difference of −3 points represents the MID for its total score.[38] Symptoms of anxiety and depression were assessed using the Hospital and Depression Scale (HADS),[39] and its MID is 1.5 points.[40]

Statistical analysis

Data distribution was analyzed by the Shapiro–Wilk test. According to normality in data distribution, data were described as mean ± standard deviation or median [25–75% interquartile range]. Categorical variables were compared by the Chi-square test with Bonferroni post hoc test correction. Comparisons among physical (in)activity and body composition phenotypes were analyzed by two-way or three-way analysis of variance (ANOVA) or Kruskal–Wallis test with Bonferroni post hoc test. Statistical analysis was done using SPSS 22.0 (IBM, Armonk, NY, USA) and the significance level was set as $p < 0.05$.

Table 1 Characteristics of the participants.

Characteristics	n = 176
Sex (M/F)	(96/80)
Age (years)	67 ± 7.9
Height (m)	1.59 ± 0.85
Weight (kg)	67 ± 15.35
FVC (%pred)	73.4 [57.7–85.1]
FVC (L)	2.27 [1.72–2.93]
FEV_1 (%pred)	47.0 ± 16.2
FEV_1 (L)	1.14 [0.85–1.61]
FEV_1/FVC	53.9 ± 13.2
GOLD stage (I/II/III/IV)	(1/75/65/35)
Number of comorbidities (n = 159)	2 [1–2]
BMI (kg/m^2)	26.2 ± 5.6
FFMI (kg/m^2)	44.2 ± 8.7
FMI (kg/m^2)	9.2 [6.0–11.2]
6MWT (m)	461 ± 71.8
6MWT (%pred)	85.9 ± 13.0
Average energy expenditure/day (kcal)	1236 [1025–1498]
Average MET/day	1.6 [1.3–1.9]
Steps/day	5114 [3255–7846]
MVPA ($\geq$3MET) (min/day)	30.3 [10.3–70.8]
Lying time (min/day)	33.5 [0–69.2]
Sedentary time ($\leq$1.5 MET) (min/day)	444.0 ± 118.5
Sedentary time (% of the total time)	64.4 ± 17.0

Data are presented as mean ± standard deviation or median [interquartile range], according to normality in data distribution. M, male; F, female; FVC, forced vital capacity; FEV_1, forced expiratory volume in the first second; GOLD, global initiative for chronic lung disease; BMI, body mass index; FFMI, fat-free mass index; FMI, fat mass index; 6MWT, 6-minute walking test; MET, metabolic equivalent of task; MVPA, moderate-to-vigorous physical activity.

Results

One hundred and seventy six individuals with COPD, with mean age of 67 ± 7.9 years and moderate to very-severe airflow obstruction (47.0 ± 16.2%pred) were included. According to physical activity, the participants had a low PADL level (30.3 [10.3–70.8] min/day of MVPA) and relatively high sedentary time (444 ± 118.5 min/day of activities <1.5 MET) as shown in Table 1. Individuals were classified as NBC + Act (17%), NBC + Inact (21.6%), Ob + Act (6.3%), Ob + Inact (9.7%), Sarc + Act (12.5%), Sarc + Inact (8.5%), Sarc/Ob + Act (8.0%) and Sarc/Ob + Inact (16.5%).

Table 2 shows that the Sarc/Ob + Inact group presented lower 6MWT in % of the predicted value and 1RM for knee extension in comparison to NBC + Act, NBC + Inact, and Ob + Act groups and lower 6MWT in meters in comparison to the Ob + Act and Sarc + Act groups ($p < 0.05$ for all). The Sarc/Ob + Inact group also presented lower FEV_1, 1RM elbow

Table 2 Comparisons among different phenotypes for body composition and level of physical activity in daily life in individuals with COPD.

Variables	Normal body composition		Obese		Sarcopenic		Sarcopenic–obese	
	Active	Inactive	Active	Inactive	Active	Inactive	Active	Inactive
n (%)	30 (17.0)	38 (21.6)	11 (6.3)	17 (9.7)	22 (12.5)	15 (8.5)	14 (8.0)	29 (16.5)
Male sex (%)	21 (70.0)	12 (31.6)	10 (90.9)[#,##]	9 (52.9)	16 (72.7)	8 (19.4)	12 (85.7)	20 (68.9)
Age (years)	65.1 ± 8.3	66.2 ± 7.7	67.0 ± 8.4	67.6 ± 8	65.9 ± 9.3	68.6 ± 8.0	62.3 ± 8.4	65.8 ± 8.9
6MWT (m)	474 ± 55.6	444 ± 82.6	510 ± 75.4	424 ± 94.1	496 ± 49.1	425 ± 85.3	455 ± 120.6	415 ± 91.1[‡,¥]
6MWT (% pred)	88.7 ± 11.0	87.3 ± 16.2	93.9 ± 14.8	85.1 ± 15.9	87.5 ± 9.1	77.2 ± 16.8	81.2 ± 19.9	75.3 ± 16.6[*,‡]
1RM knee extension (kg)	19.1 (16.5, 21.7)	18.7 (16.4, 21.1)	20.7 (16.4, 25.0)	18.6 (15.1, 22.0)	16.9 (13.9, 19.9)	15.9 (12.4, 19.6)	16.9 (13.1, 20.8)	12.4 (9.8, 15.0) [*,†,‡]
1RM elbow flexion (kg)	13.6 (12.0, 15.1)	12.2 (10.7, 13.6)	13.1 (10.5, 15.7)	12.6 (10.5, 14.6)	10.8 (8.9, 12.5)	9.5 (7.3, 11.6)	11.0 (8.8, 13.3)	8.5 (6.9, 10.0) [*,†]
1RM elbow extension (kg)	15.1 (13.4, 16.8)	14.8 (13.3, 16.4)	13.9 (11.1, 16.7)	14.6 (12.4, 16.8)	13.2 (11.3, 15.2)	11.5 (9.1, 13.8)	11.8 (9.3, 14.3)	10.1 (8.4, 11.8)[*,†,§]
FEV_1 (%pred)	50.9 ± 15.8	51.1 ± 13.3	50.3 ± 17.3	45.8 ± 14.7	46.7 ± 14.6	36.9 ± 18.3	43.0 ± 13.9	38.0 ± 17.7 [*,†]
MRC scale	4.0 [2.0–4.0]	4.0 [2.0–4.0]	3.0 [2.0–4.0]	4.0 [2.25–4.0]	3.0 [3.0–4.0]	4.0 [3.0–4.0]	4.0 [2.0–4.0]	4.0 [2.0–4.0]
HADS anxiety (pts)	4.5 [3.0–8.5]	5.0 [2.0–9.0]	4.0 [3.0–9.0]	4.5 [1.0–7.3]	4.0 [3.0–7.5]	5.0 [1.0–7.5]	7.0 [3.0–8.0]	6.0 [3.0–7.0]
HADS depression (pts)	3.0 [2.0–6.8]	4.5 [1.3–7.0]	3.0 [1.0–6.0]	4.0 [0.3–9.0]	4.0 [1.3–6.0]	6.0 [3.0–9.0]	5.0 [3.0–10.0]	4.0 [1.0–8.0]
LCADL (pts)	20 [15.0–26.8]	21.5 [15.3–25.8]	15 [12.0–24.0]	21 [13.3–36.8]	18.5 [16.3–26.8]	27 [15.5–33.5]	25 [11.0–31.0]	19 [13.0–30.0]

Data are presented as mean ± deviation or median [interquartile range], according to normality in data distribution. 6MWT, 6-minute walking test; 1RM, 1 repetition maximum test; FEV_1, forced expiratory volume in the first second; MRC, Medical Research Council scale; HADS, Hospital Anxiety and Depression Scale; LCADL, London Chest Activity of Daily Living scale. All values of 1RM for knee extension and elbow flexion and extension were adjusted for sex and described as mean (95% confidence interval).

[*] $p < 0.05$ compared with NBC + Act.
[†] $p < 0.05$ compared with NBC + Inact.
[‡] $p < 0.05$ compared with Ob + Act.
[§] $p < 0.05$ compared with Ob + Inact.
[¥] $p < 0.05$ compared with Sarc + Act.
[#] $p < 0.003$ compared with NBC + Act.
[##] $p < 0.003$ compared with NBC + Inact.

flexion and elbow extension in comparison to NBC + Act and NBC + Inact groups, and lower 1RM for elbow extension compared to the Ob + Inact group ($p < 0.05$ for all), in addition to a near-significance for lower 1RM for elbow flexion compared to the Ob + Act group ($p = 0.07$). Although there were no statistically significant differences for MRC, LCADL, and HADS, some between-groups MIDs were reached in these instruments' scores (Table 2).

There was significant effect of body composition and PADL level on the 6MWT%pred ($p = 0.004$ and $p = 0.008$, respectively), as well as on the 1RM for elbow flexion ($p = 0.001$ and $p = 0.04$, respectively). As for the 1RM for knee extension, body composition presented a significant effect ($p = 0.01$), and PADL level presented a near-significant effect ($p = 0.09$).

Discussion

The present study investigated whether individuals with COPD classified as active or inactive present different physical and functional characteristics within different body composition phenotypes and its results showed that worse exercise capacity, muscle force, and lung function are found when physical inactivity is added to the combination of sarcopenia and obesity. Moreover, while benefits of being physically active in this population are well-established in the literature, the present study suggests that individuals with a profile of physical inactivity added to body composition abnormalities should be seen as primary therapeutic targets. These results are consistent with those from Machado et al.[20] who showed that individuals classified as sarcopenic/obese were most debilitated, considering their worse exercise capacity, PADL, and peripheral and respiratory muscle strength.

The novelty of adding the burden of physical inactivity to the body composition phenotype of sarcopenia and obesity highlights the importance of the physical activity level in this population. In contrast to the Sarc/Ob + Inact group, obese and sarcopenic individuals showed no differences in any outcome when compared to the NBC group, regardless of PADL level. To counteract inactivity, some ''strategies'' are known, such as having an active partner, going out to walk the dog, playing with grandchildren, and participating in behavior change coaching activities, among others.[41–43]

Poulain et al.[44] previously showed that obese individuals with COPD are characterized by a higher FFM. This observation is important because, as already shown in previous studies, muscle mass predicts survival better than BMI.[7,12,45] Moreover, exercise capacity is also a strong predictor of survival in individuals with COPD.[46] Individuals with COPD who are obese appear to present with an advantage due to ''obesity paradox'', that is associated with higher survival and functional outcomes, but in contrast also associated with increased risk of metabolic and cardiovascular disease.[47] Groups Ob + Act and Sarc + Act had better exercise capacity than Sarc/Ob + Inact, and this is consistent with previous studies that showed a relationship between FFM and exercise capacity, as a negative energy balance (e.g. loss of muscle mass) may affect the individual's tolerance to exercise.[14,19,47]

There were no significant differences in MRC scores among groups possibly due to the fact that all groups presented median score of 3 or 4, therefore all of them fitting in the most impaired groups of the GOLD classification.[2] As for the LCADL, there were also no significant differences among groups, although some of them presented differences greater than the MID of 3 points; this may indicate differences in functional limitation among them, despite the lack of statistical significance.[38] For the HADS, although differences greater than the MID of 1.5 points,[40] was present between some groups, these individuals were unlikely severely affected by anxiety and depression, because the scores were generally relatively low.

One of the novelties and strengths of the present study is that it is the first to our knowledge in the scientific literature to analyze differences in clinical features of individuals with COPD classified according to their body composition phenotypes and level of physical (in)activity. The clinical implication of the present results is that individuals combining sarcopenia and obesity with inactivity need more attention from health professionals. Furthermore, another strength of the study is that the accelerometer used to assess PADL is valid and accurate specifically for individuals with COPD,[24–27] a population known to be mostly inactive, sedentary, and composed of slow-walking individuals.

Some study limitations to take into account were: the cross-sectional design (not allowing to infer causality); the results cannot be extended to individuals classified as GOLD I, because our sample had only one individual in this category; the reference values for FMI and FFMI, as well as the formula used to estimate FFM, were not developed specifically for the Brazilian population; the PADL assessment being performed over only two days, while sufficient for reliable measurements in more severe individuals, may require more days in individuals with milder impairment[28,48]; and the unavailability of important information to describe the sample of participants, such as information on socioeconomic status, educational level, and climatic conditions during the PADL assessment. Lastly, the use of bioelectrical impedance may present limitations related to hydroelectrolytic abnormalities and the choice of the appropriate population, age, or disease-specific equations.[49]

Moreover, new and interesting scientific possibilities may unfold from the present results. Future studies should investigate whether increasing PADL level, associated or not with changes in body composition phenotypes, at least in borderline individuals, may result in improvements in physical function of individuals with COPD.

Conclusion

Worse exercise capacity, muscle force, and lung function are found when physical inactivity is added to the combination of sarcopenia and obesity in individuals with moderate to very severe COPD.

Conflict of interest

The authors declare no conflicts of interest.

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References

1. Garcia-Aymerich J, Lange P, Benet M, et al. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: a population based cohort study. *Thorax*. 2006;61(9):772–778.
2. Singh D, Agusti A, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. *Eur Respir J*. 2019;53(5), http://dx.doi.org/10.1183/13993003.00164-2019.
3. Ramon MA, Ter Riet G, Carsin AE, et al. The dyspnoea-inactivity vicious circle in COPD: development and external validation of a conceptual model. *Eur Respir J*. 2018;52(3), http://dx.doi.org/10.1183/13993003.00079-2018.
4. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43(7):1334–1359.
5. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007;116(9):1081–1093.
6. Pitta F, Troosters T, Probst VS, et al. Physical activity and hospitalization for exacerbation of COPD. *Chest*. 2006;129(3):536–544.
7. Schols AM, Broekhuizen R, Weling-Scheepers CA, et al. Body composition and mortality in chronic obstructive pulmonary disease. *Am J Clin Nutr*. 2005;82(1):53–59.
8. Sava F, Laviolette L, Bernard S, et al. The impact of obesity on walking and cycling performance and response to pulmonary rehabilitation in COPD. *BMC Pulm Med*. 2010;10:55, http://dx.doi.org/10.1186/1471-2466-10-55.
9. Rutten EP, Calverley PM, Casaburi R, et al. Changes in body composition in patients with chronic obstructive pulmonary disease: do they influence patient-related outcomes? *Ann Nutr Metab*. 2013;63(3):239–247.
10. Steuten LM, Creutzberg EC, Vrijhoef HJ, et al. COPD as a multicomponent disease: inventory of dyspnoea, underweight, obesity and fat free mass depletion in primary care. *Prim Care Respir J*. 2006;15(2):84–91.
11. Vanfleteren LE, Spruit MA, Groenen M, et al. Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2013;187(7):728–735.
12. Vestbo J, Prescott E, Almdal T, et al. Body mass, fat-free body mass, and prognosis in patients with chronic obstructive pulmonary disease from a random population sample: findings from the Copenhagen City Heart Study. *Am J Respir Crit Care Med*. 2006;173(1):79–83.
13. Jones SE, Maddocks M, Kon SS, et al. Sarcopenia in COPD: prevalence, clinical correlates and response to pulmonary rehabilitation. *Thorax*. 2015;70(3):213–218.
14. Schols AM, Ferreira IM, Franssen FM, et al. Nutritional assessment and therapy in COPD: a European Respiratory Society statement. *Eur Respir J*. 2014;44(6):1504–1520.
15. Monteiro F, Camillo CA, Vitorasso R, et al. Obesity and physical activity in the daily life of patients with COPD. *Lung*. 2012;190(4):403–410, http://dx.doi.org/10.1007/s00408-012-9381-0.
16. Sahin H, Naz I, Varol Y, et al. The effect of obesity on dyspnea, exercise capacity, walk work and workload in patients with COPD. *Tuberk Toraks*. 2017;65(3):202–209.
17. Landbo C, Prescott E, Lange P, et al. Prognostic value of nutritional status in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1999;160(6):1856–1861.
18. Schols AM, Slangen J, Volovics L, et al. Weight loss is a reversible factor in the prognosis of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1998;157(6 Pt 1):1791–1797.
19. Joppa P, Tkacova R, Franssen FM, et al. Sarcopenic obesity, functional outcomes, and systemic inflammation in patients with chronic obstructive pulmonary disease. *J Am Med Dir Assoc*. 2016;17(8):712–718.
20. Machado FVC, Schneider LP, Fonseca J, et al. Clinical impact of body composition phenotypes in patients with COPD: a retrospective analysis. *Eur J Clin Nutr*. 2019;73(11): 1512–1519.
21. Rodrigues A, Camillo CA, Furlanetto KC, et al. Cluster analysis identifying patients with COPD at high risk of 2-year all-cause mortality. *Chron Respir Dis*. 2019;16, 1479972318809452.
22. Lukaski HC, Bolonchuk WW, Hall CB, et al. Validation of tetrapolar bioelectrical impedance method to assess human body composition. *J Appl Physiol (1985)*. 1986;60(4):1327–1332, http://dx.doi.org/10.1152/jappl.1986.60.4.1327.
23. Steiner MC, Barton RL, Singh SJ, et al. Bedside methods versus dual energy X-ray absorptiometry for body composition measurement in COPD. *Eur Respir J*. 2002;19(4):626–631.
24. Cavalheri V, Donaria L, Ferreira T, et al. Energy expenditure during daily activities as measured by two motion sensors in patients with COPD. *Respir Med*. 2011;105(6):922–929.
25. Hill K, Dolmage TE, Woon L, et al. Measurement properties of the SenseWear armband in adults with chronic obstructive pulmonary disease. *Thorax*. 2010;65(6):486–491.
26. Langer D, Gosselink R, Sena R, et al. Validation of two activity monitors in patients with COPD. *Thorax*. 2009;64(7):641–642.
27. Patel SA, Benzo RP, Slivka WA, et al. Activity monitoring and energy expenditure in COPD patients: a validation study. *COPD*. 2007;4(2):107–112.
28. Demeyer H, Burtin C, Van Remoortel H, et al. Standardizing the analysis of physical activity in patients with COPD following a pulmonary rehabilitation program. *Chest*. 2014;146(2):318–327.
29. Mesquita R, Meijer K, Pitta F, et al. Changes in physical activity and sedentary behaviour following pulmonary rehabilitation in patients with COPD. *Respir Med*. 2017;126:122–129.
30. Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. *Eur Respir J*. 2005;26(1):153–161.
31. Pereira CA, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. *J Bras Pneumol*. 2007;33(4):397–406.
32. Holland AE, Spruit MA, Troosters T, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J*. 2014;44(6):1428–1446.
33. Britto RR, Probst VS, de Andrade AF, et al. Reference equations for the six-minute walk distance based on a Brazilian multicenter study. *Braz J Phys Ther*. 2013;17(6):556–563.
34. Brown L, Weir J. ASEP procedures recommendation I: accurate assessment of Muscular strength and Power. *J Exerc Physiol*. 2001;4:1–21.

35. Kovelis D, Segretti NO, Probst VS, et al. Validation of the Modified Pulmonary Functional Status and Dyspnea Questionnaire and the Medical Research Council scale for use in Brazilian patients with chronic obstructive pulmonary disease. *J Bras Pneumol*. 2008;34(12):1008–1018.
36. de Torres JP, Pinto-Plata V, Ingenito E, et al. Power of outcome measurements to detect clinically significant changes in pulmonary rehabilitation of patients with COPD. *Chest*. 2002;121(4):1092–1098.
37. Pitta F, Probst VS, Kovelis D, et al. Validation of the Portuguese version of the London Chest Activity of Daily Living Scale (LCADL) in chronic obstructive pulmonary disease patients. *Rev Port Pneumol*. 2008;14(1):27–47.
38. Almeida Gulart A, de Araujo CLP, Bauer Munari A, et al. Minimal important difference for London Chest Activity of Daily Living scale in patients with chronic obstructive pulmonary disease. *Physiotherapy*. 2020;107:28–35.
39. Botega NJ, Bio MR, Zomignani MA, et al. Mood disorders among inpatients in ambulatory and validation of the anxiety and depression scale HAD. *Rev Saude Publica*. 1995;29(5):355–363.
40. Puhan MA, Frey M, Buchi S, et al. The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. *Health Qual Life Outcomes*. 2008;6:46.
41. Arbillaga-Etxarri A, Gimeno-Santos E, Barberan-Garcia A, et al. Socio-environmental correlates of physical activity in patients with chronic obstructive pulmonary disease (COPD). *Thorax*. 2017;72(9):796–802, http://dx.doi.org/10.1136/thoraxjnl-2016-209209.
42. Mesquita R, Nakken N, Janssen DJA, et al. Activity levels and exercise motivation in patients with COPD and their resident loved ones. *Chest*. 2017;151(5):1028–1038.
43. Sallis JF, Linton LS, Kraft MK, et al. The Active Living Research program: six years of grantmaking. *Am J Prev Med*. 2009;36(2 suppl.):S10–S21.
44. Poulain M, Doucet M, Drapeau V, et al. Metabolic and inflammatory profile in obese patients with chronic obstructive pulmonary disease. *Chron Respir Dis*. 2008;5(1):35–41.
45. Marquis K, Debigare R, Lacasse Y, et al. Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2002;166(6):809–813.
46. Oga T, Nishimura K, Tsukino M, et al. Analysis of the factors related to mortality in chronic obstructive pulmonary disease: role of exercise capacity and health status. *Am J Respir Crit Care Med*. 2003;167(4):544–549.
47. van de Bool C, Rutten EP, Franssen FM, et al. Antagonistic implications of sarcopenia and abdominal obesity on physical performance in COPD. *Eur Respir J*. 2015;46(2):336–345.
48. Watz H, Pitta F, Rochester CL, et al. An official European Respiratory Society statement on physical activity in COPD. *Eur Respir J*. 2014;44(6):1521–1537.
49. Kyle UG, Bosaeus I, De Lorenzo AD, et al. Bioelectrical impedance analysis – part I: review of principles and methods. *Clin Nutr*. 2004;23(5):1226–1243.