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Chronic obstructive pulmonary disease phenotypes and balance impairment

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Background/objective: Chronic obstructive pulmonary disease (COPD) is a respiratory disease that results in airflow limitation and respiratory distress, also having many nonrespiratory manifestations that affect both function and mobility. Preliminary evidence suggests that balance deficits constitute an important secondary impairment in individuals with COPD. Our objective was to investigate balance performance in two groups of COPD patients with different body compositions and to observe which of these groups are more likely to experience falls in the future.
Methods: We included 27 stable COPD patients and 17 healthy individuals who performed a series of balance tests. The COPD patients were divided in two groups: emphysematous and bronchitic. Patients completed the activities balance confidence scale and the COPD assessment test questionnaire and afterward performed the Berg Balance Scale, timed up and go, single leg stance and 6-minute walking distance test. We analyzed the differences in the balance tests between the studied groups.
Results: Bronchitic COPD was associated with a decreased value when compared to emphysematous COPD for the following variables: single leg stance (8.7 vs 15.6; $P<0.001$) and activities balance confidence (53.2 vs 74.2; $P=0.001$). Bronchitic COPD patients had a significantly higher value of timed up and go test compared to patients with emphysematous COPD (14.7 vs 12.8; $P=0.001$).
Conclusion: Patients with COPD have a higher balance impairment than their healthy peers. Moreover, we observed that the bronchitic COPD phenotype is more likely to experience falls compared to the emphysematous phenotype.
Keywords: body composition, obese, cachexia, falls, bronchtic, emphysematous, muscle wasting

Introduction

Chronic obstructive pulmonary disease (COPD) is a treatable and preventable disease with significant extrapulmonary effects, which can contribute to serious complications. The systemic component results in muscle weakness and weight loss, both of which contribute to the progression of the disease and deterioration in quality of life.[1] It has been shown that malnutrition in COPD patients is associated with increased morbidity and mortality and greater susceptibility to respiratory infections. Moreover, in stable COPD, it is a frequent problem that increases with the seriousness of the disease.[2] Loss of body cell mass is a common and serious problem for patients with COPD. However, skeletal muscle weakness is associated with wasting of extremity fat-free mass in COPD patients independent of airflow obstruction and COPD subtype.[3] Classical evidence about malnutrition being more common in patients with emphysema than in those with chronic bronchitis was endorsed by a recent study which included body composition measurement. Patients with emphysema had a lower body mass index (BMI), a lower fat-free mass index, and a lower fat index than patients with bronchitis or normal individuals.[4]

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Cachexia was, until recently, measured using BMI. Using BMI, cachexia in COPD is acknowledged to exist when BMI is <21 kg/m^2.[5] International classification of BMI identifies as obese if BMI >30 kg/m^2.[6] Often, the bronchitic COPD phenotype is linked with obesity and the emphysematous with chachexia.[7]

With aging, major risk factors for falls are related to physical activity and muscle impairment. Muscle weakness and gait and balance deficits increase the risk of falling three to four times.[8] While the literature suggests that malnutrition and falls in elderly populations are related, and a relation between muscle mass and falls seems realistic, there are only few studies that investigated the relationship between fall incidents and nutritional status in this population.

Roig et al[9] estimated in a prospective study that the incidence of falls in COPD patients is 1.2 persons per year, more than four times the incidence reported in the elderly. Postural control, balance, and stability are physical elements essential for the performance of activities of daily living. Maintenance of an upright stance while in motion or standing demands a rapid integration from the vestibular, visual, and proprioceptive sensory systems. These systems allow the involuntary activation of the lower limb muscles to counteract accelerating forces acting on the body, such as gravity. Falls have multiple precipitating causes, such as decreased strength, poor movement coordination, decline in balance, and gait and postural instability. A few studies investigating nutritional status and risk of falling have observed that patients at nutritional risk were more likely to experience falls than well-nourished patients.[10,11] Many pathophysiological features of COPD suggest that people who suffer from this disease have common risk factors that had been also identified in older individuals, such as multiple medications, polyneuropathy, and muscle weakness.[12] Based on these premises, we find it important to observe which of the two COPD phenotypes is more likely to experience falls.

Study aim

Given the fact that patients with COPD could have a higher incidence of falls than their healthy peers, our aims were to investigate balance performance in two groups of COPD patients with different body composition and the association among parameters of body composition, balance, and inflammatory markers.

Materials and methods

The study was approved by the ethics committee of the Clinical Hospital of Infectious Disease and Pneumology "Dr Victor Babes". Prior to inclusion in the study all patients who accepted to participate provided written informed consent. On admission day, blood sample and arterial blood gases were collected from all the COPD patients. On the same day, patients performed spirometry and all the balance tests and filled in questionnaires.

Subjects

We included 27 stable COPD patients (former smokers >10 packs-year) who met the criteria according to the international guidelines.[13] In addition, 17 healthy individuals with similar baseline characteristics, without COPD and with normal spirometry (forced expiratory volume in 1 second $\geq 80\%$ predicted, forced expiratory volume in the first second/forced vital capacity ≥ 0.7) volunteered to participate in the study. We separated the patients into two groups. Those with a low BMI formed the chachectic group and those with a high BMI made up the bronchitic group.

Exclusion criteria: use of medication that could have increased the risk of falls, postural orthostatic hypotension, musculoskeletal or neurological diseases that could account for possible falls and imbalance, serious cardiovascular problems, syncope, or lower-extremity joint replacement.

Balance measures

Patients first completed the activities balance confidence (ABC) questionnaire, which is a table designed to assess confidence levels in 16 daily activities and provides a confidence score. Respondents provide ratings on a 0%–100% continuous scale based on their confidence related to balance and stability.[14]

Patients afterward completed the balance tests. The Berg Balance Scale (BBS) is a 14-item scale for simple balance tasks that was developed to measure balance among older people with impairment in balance function by assessing the performance of functional tasks. The success in achieving each task is given a score of 0 (unable) to 4 (independent) and the final measure is the sum of all scores.[15] After completing the BBS test, patients performed the timed up and go test (TUG), which is a test of general mobility that requires both static and dynamic balance[16] and is a timed performance measure that includes gait maneuvers used in everyday life, and single leg stance (SLS), which is a task of static balance that records the time a participant is able to stand on one leg unassisted.[17] These two tests were performed three times with pause between repetitions and the best value was used. Functional exercise level was assessed using the 6-minute walking distance (6MWD) test which was performed according to the guidelines of the American Thoracic Society.[18] The global impact of COPD on the patient was evaluated using the COPD assessment test (CAT questionnaire).

Body composition was assessed using bioelectrical impedance analysis. This is a method for estimating body composition. The principle of bioelectrical impedance analysis is to determine the electric impedance for an electric current passing through the body. This analysis was performed using a Jawon IOI 353 body composition machine adopting the criteria established for bioelectrical impedance analysis.[19]

Statistical analysis

Data were collected and analyzed using the SPSS version 17 software suite (SPSS Inc., Chicago, IL, USA) and are presented as medians and interquartile range for continuous variables without Gaussian distribution or average ± standard deviation for continuous variables with Gaussian distribution.

To assess the significance of the differences between groups, Mann–Whitney *U* and Kruskal–Wallis tests (medians, non-Gaussian populations), respectively, unpaired Student's *t*-test and analysis of variance (ANOVA) (averages and Gaussian populations) tests were used. Continuous variable distributions were tested for normality using Shapiro–Wilk test. The correlation between studied variables was evaluated using Spearman's rank sum correlation coefficient (non-Gaussian distributed variables), its statistical significance being assessed using the *t*-distribution score test. In this study, a *P*-value of <0.05 was considered as the threshold for statistical significance.

Results

Patients enrolled in our study had comparable ages, the differences found between the three studied groups being nonsignificant ($P=0.087$). The presence of COPD was associated with differences regarding the BMI value (patients with bronchitic COPD having a significantly higher BMI when compared to controls, respectively, patients with emphysematous COPD had a significant lower BMI vs controls). The differences regarding the percentage of fat-free mass and the percentage of body weight were consistent with the results found for the BMI values; these differences being also significant.

While the differences between the two COPD groups for the respiratory parameters were nonsignificant, as expected, we found significant differences when compared to the control group (Table 1).

The presence of COPD in our study group was associated with an increased median CAT score. No significant differences were observed regarding the CAT values between the two COPD groups ($P=0.720$). Also, we observed a significant decrease of 6MWD values in patients with COPD compared to controls. Moreover, at the post hoc analysis, bronchitic COPD patients had a significantly lower median compared to the emphysematous patients (321.5 vs 420; $P=0.048$). Bronchitic COPD was also associated with a decreased value when compared to emphysematous COPD for the following variables: SLS (8.7 vs 15.6; $P<0.001$) and ABC (53.2 vs 74.2; $P=0.001$). Bronchitic COPD patients had a significantly higher value of TUG test compared to patients with emphysematous COPD (14.7 vs 12.8; $P=0.001$; Figure 1).

It is worth mentioning that our results point to a negative impact of the presence of COPD on all balance tests when compared to controls (Table 2).

In the correlation analysis, we found the presence of significant and positive relationships among the percentage of fat-free mass and 6MWD ($r=0.386$; $P<0.01$), SLS ($P=0.472$; $P<0.01$), and ABC ($P=0.404$; $P<0.01$; Figure 2); at the same time, the value of percentage fat-free mass was negative and significantly correlated with the score of the TUG test ($r=-0.408$; $P<0.01$). The detailed results are presented in Table 3.

Table 1 Comparison of studied parameters between the three groups

Parameter	A Controls (n=17)	B Emphysematous COPD (n=13)	C Bronchitic COPD (n=14)	*P*-value (A vs B vs C)§
Age§	61.3±4.0	64.1±2.6	63.9±1.9	0.087
BMI§	25.3±3.9	17.6±0.8	36.1±3.3	<0.001*
FFM (%)¥	77.1 (5.5)	87.2 (10.1)	58.9 (9.6)	<0.001*
Body fat (%)¥	18.2 (8.8)	10.2 (7.4)	37.3 (4.1)	<0.001*
FVC (%)¥	95 (15)	70 (10)	68 (9)	<0.001*
FEV_1 (%)¥	95 (18)	31 (2)	30 (4)	<0.001*
FVC/FEV_1¥	79 (9)	41 (7)	41 (8)	<0.001*

Notes: Values are presented as median and (interquartile range) – non-Gaussian distributions or average ± standard deviation – Gaussian distributions. *Differences are significant. §*P*-value was calculated using ANOVA test. ¥*P*-value was calculated using Kruskal–Wallis test.

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FFM, fat-free mass; FVC, forced vital capacity.

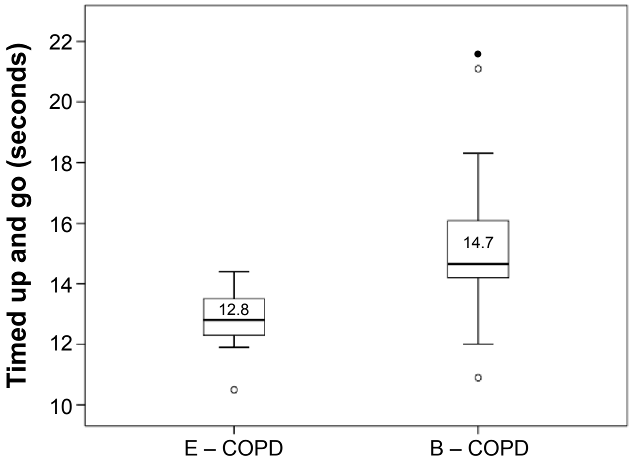

Figure 1 Comparison of timed up and go test between study subcohorts.
Abbreviation: COPD, chronic obstructive pulmonary disease.

Regarding the respiratory parameters, we found a significant and positive association between forced expiratory volume in 1 second and CAT (r=0.413; $P<0.05$), respectively, forced vital capacity and BBS (r=0.588; $P<0.01$).

Inflammation markers were significantly associated with CAT value: both C-reactive protein (CRP) (r=0.402; $P<0.05$) and fibrinogen (r=0.521; $P<0.01$), respectively, were negatively associated in the case of CRP and the values of the 6MWD test (r=–0.557; $P<0.01$).

The other pairs of correlations which were studied were not significantly correlated (Table 4).

Discussion

We observe that the bronchitic COPD patients have a more impaired balance compared to the emphysematous group.

The novelty of this study is that it evaluates balance impairment and correlates the data with the body composition, especially the fat-free mass of the lower limbs. Although individuals with COPD have many risk factors, limited information is available regarding the risk of falls in this population.[20]

Tinetti et al[21] defined a fall as "an event which results in a person coming to rest unintentionally on the ground or lower level, not as a result of a major intrinsic event or overwhelming hazard". From our experience, patients with COPD lose their ability to maintain balance thus having an increased risk of falls compared to their healthy peers.[22,23]

Extending the classical descriptions of the "pink puffer" and "blue bloater", recent statistical approaches support the concept that body composition and body weight discriminate pulmonary phenotypes and are predictors of outcome independent of lung function impairment.[24]

Beauchamp et al[25] demonstrated that a change of three points in the BBS represents a clinically important difference for measure. We observed that our patients approached the score of a very high risk of falls compared to the control group. This could be explained by the fact that 40% of patients with COPD have limited exercise capacity due to skeletal muscle alterations. Hypoxemia, systemic inflammation, and oxidative stress could cause muscle atrophy, which is an important risk factor for falls. No differences were observed between the two COPD groups. COPD is recognized as an inflammatory disease, whether or not originating in the lungs; evidence of systemic inflammation in COPD has been previously shown in several studies.[26] We found no significant evidence to demonstrate that inflammation can lead to balance impairment and risk of falls.

In our study, we observed that the bronchitic group had scored worse in the balance tests (TUG and SLS), had a greater fear of falling, and a reduced walking distance compared to the emphysematous group. This would suggest that those with a higher BMI could experience an increased risk of falls. The bronchitic group exceeded the cutoff score of ≥13.5 seconds for high risk of falls in the TUG test.

Table 2 Balance parameters in the three subgroups

Parameter	A	B	C	*P*-value
	Controls (n=17)	Emphysematous COPD (n=13)	Bronchitic COPD (n=14)	(A vs B vs C)§
CAT		20 (11)	18 (13)	<0.001
6MWD (m)	521 (92)	420 (148)	321.5 (193)	<0.001
BBS (points)	55 (2)	45 (14)	45.5 (9)	<0.001
TUG (seconds)	8.6 (2.5)	12.8 (1.25)	14.7 (2.5)	<0.001
SLS (seconds)	31.1 (16)	15.6 (6)	8.7 (6)	<0.001
ABC (%)	97.9 (4)	74.2 (12)	53.2 (20)	<0.001

Notes: Variables are not-Gaussian distributed. Values are presented as median and (interquartile range). §*P*-value was calculated using Kruskal–Wallis test.
Abbreviations: ABC, activities balance confidence; BBS, Berg Balance Scale; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; 6MWD, 6-minute walking distance; SLS, single leg stance; TUG, timed up and go.

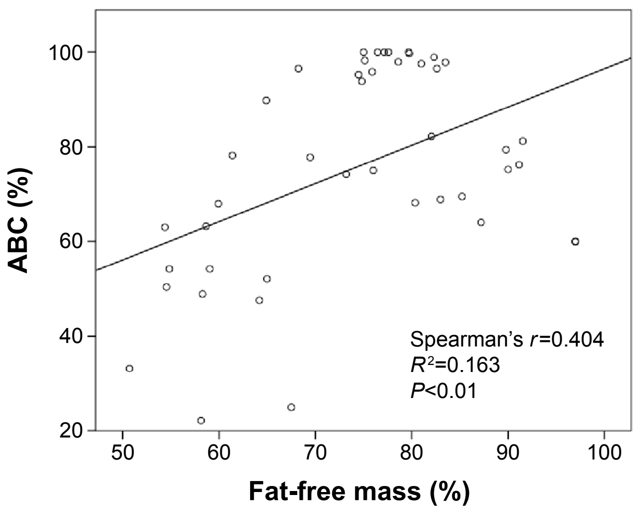

Figure 2 The interrelationship between the percentage of fat-free mass and ABC (%).
Abbreviation: ABC, activities balance confidence.

Table 4 Correlations among respiratory, inflammatory, and balance parameters

Studied parameters	FVC (%)	FEV_1 (%)	CRP	Fibrinogen
CAT	–0.243	0.413*	0.402*	0.521**
6MWD (m)	0.147	–0.035	–0.557**	–0.366
BBS (points)	0.588**	–0.346	–0.257	–0.242
TUG (seconds)	–0.145	–0.288	0.166	–0.017
SLS (seconds)	0.117	0.288	–0.241	0.075
ABC (%)	0.212	0.159	0.159	0.296

Notes: Correlations strengths were assessed using Spearman's rank sum correlation coefficient. *Correlation is significant at $\alpha<0.05$ level. **Correlation is significant at $\alpha<0.01$ level.
Abbreviations: ABC, activities balance confidence; BBS, Berg Balance Scale; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; 6MWD, 6-minute walking distance; SLS, single leg stance; TUG, timed up and go.

The 6MWD provides a good estimate of overall functional performance and aerobic/endurance capacity. We found a significant reduced walking distance between the two COPD groups (a median value 420 vs 321 m). This test could be a useful tool to assess balance impairment and predict the risk of falls in patients with COPD. Although the bronchitic COPD patients had an increased muscle mass on the lower limbs compared to the control group (12.6 vs 10.2 kg), the walking distance in the 6MWD test was significantly reduced. This could be explained by the fact that they also had a significant increased fat mass thus being more difficult for them to walk. Our observation can be explained by Andersen's study who has shown that the loss of motor neurons results in an increase in the size of remaining motor units, but with greater preservation of type 1 fibers, resulting in conservation of mass with relatively fewer type 2 fibers, thus lower strength.[27]

Table 3 Correlations between FFM and balance parameters

Studied parameters	FFM (kg) – left leg	FFM (kg) – right leg	FFM (%)	BMI
CAT	–0.055	–0.066	–0.089	–0.127
6MWD (m)	–0.338	–0.319	0.386**	–0.355
BBS (points)	–0.079	–0.049	0.034	0.103
TUG (seconds)	0.608**	0.594**	–0.408**	0.621**
SLS (seconds)	–0.639**	–0.640**	0.472**	–0.681**
ABC (%)	–0.608**	–0.632**	0.404**	–0.586**

Notes: Correlations strengths were assessed using Spearman's rank sum correlation coefficient. **Correlation is significant at $\alpha<0.01$ level.
Abbreviations: ABC, activities balance confidence; BBS, Berg Balance Scale; BMI, body mass index; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; FFM, fat-free mass; 6MWD, 6-minute walking distance; SLS, single leg stance; TUG, timed up and go.

Previous studies on the relationship between BMI and falls indicate that increased BMI raises the risk of falls or adds on additional risks of falls.[28] In a study that analyses the relationship between increased BMI and falls, Sheehan et al[29] found that for an increase in BMI there was in fact a reduced risk of falling.[29] However, overweight and obese older adults have been shown to adopt a more tentative gait pattern, with slower velocity and increased base of support; as a result of these adaptations, stability is improved.[28] These alterations could inadvertently represent a protective effect against falls. Obese individuals are more likely to have reduced physical activity. This would suggest that healthy older adults with obesity are presenting fewer opportunities to fall as they are less physically active. Patients with COPD due to dyspnea avoid physical activities but although they are more inactive than healthy elders we observed in our study that they have an increased risk of falls.

Mitchell et al[30] has observed that obesity was associated with a higher risk of falls compared to individuals with healthy weight. Although both our COPD groups had decreased scores at the balance tests, the obese patients had even lower scores thus confirming the previous findings.

Fear of falling is frequently identified as a risk factor for falls. We can assume that reduced balance confidence measured with ABC questionnaire can be associated with an increased risk of falls. Lajoie and Gallagher[31] found that a score of 67% is a reliable mean to predict future falls. Our results are consistent with the findings of Beauchamp et al[25] and we observed that the bronchitic COPD group exceeded the cutoff score in the ABC test. Mitchell et al[30] observed that there were no significant differences in the fear of falling by BMI status. On the contrary, we found that obese COPD patients have a significant fear of falling compared to the malnourished COPD patients.

Several studies have demonstrated the association between malnutrition and functional damage in patients with COPD.[32] Malnutrition damages the normal functioning of the skeletal muscle, whether there is lung disease or not. A significant number of patients with COPD present involuntary weight loss during the disease. The numbers range between 20% and 30% in stable patients and can reach 50% in hospitalized patients with respiratory failure.[33] We observed that our malnourished patients had a reduced muscle mass in the lower limbs compared to their healthy peers (7.1 vs 10.2 kg). This could be explained by the fact that patients with severe COPD are very inactive; thus, extreme inactivity can play a role in malnutrition and balance impairment. Other explanations include hypermetabolism, diet-induced thermogenesis, tissue hypoxia, and the use of corticosteroids.[34,35]

Decreased muscle mass due to bed rest in older adults was associated with large reductions in strength, aerobic capacity, and amount of physical activity.[36] This increased loss of skeletal muscle, strength, and functional capacity is very likely to increase the balance impairment leading to a higher chance of falls. We observed that our studied COPD groups have a significant reduced walking distance compared to the control group.

Conclusion

This study has important implications for clinical practice and future research. Our research has demonstrated that patients with COPD have a higher chance of falls than their healthy peers. Moreover, we observed that the bronchitic COPD phenotype is more likely to experience falls compared to the emphysematous phenotype. Further research should explore the possible impact of mediating factors on fall risk for obese COPD patients.

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Disclosure

The authors report no conflicts of interest in this work.

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