Body composition and functional capacity in patients with chronic obstructive pulmonary disease

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Abstract. The systemic effects associated with Chronic Obstructive Pulmonary Disease (COPD), are related to alterations in body composition in these patients. The phase angle (PA) is the most extensively used parameter of electrical bioimpedance for the diagnosis of malnutrition since it is an indicator of water distribution, body cell mass (BCM) and cellular integrity. Therefore, the aim of this study is to compare the PA values of patients with COPD and healthy individuals and to study their relationship with parameters of lung function and functional capacity. Bioelectrical impedance analysis (BIA) was carried out in order to determine PA in 35 patients with COPD and 36 controls. In the group of women, the PA value was significantly lower in those who had COPD with respect to their controls. For both sexes, in patients with COPD the relationship with PA was inversely proportional to age and gait speed and directly proportional to weight, height, hand dynamometry and fat-free mass. We conclude that, in patients with COPD, the decrease in PA is related to impaired body composition and functional capacity. In particular, the PA could be a useful parameter for evaluating not only the body composition but also the functional capacity of these patients.

1. Introduction
The evaluation of body composition plays an increasingly important role in the diagnosis, assessment and treatment of COPD [1], since the loss of weight and muscle mass contribute to lower functional capacity, body mass index (BMI), FFM and fat free mass index (FFMI) [2]. This can cause adverse effects on health status, increasing the frequency or severity of exacerbations and being a strong predictor of mortality, independent of pulmonary function [3]. In accordance with this, the current recommendations of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) consider that nutritional monitoring is an important part of the routine assessment of these patients [4,5]. Consequently, it is necessary to improve the assessment of nutritional status and body composition in these patients through methods that enable the identification of the loss of FFM, BCM and extracellular mass (ECM) that can lead to physical impairment [6]. COPD is associated with extrapulmonary diseases that contribute to worsening the medical conditions of patients. The loss of FMM, weight and decreased muscle strength are common systemic effects associated with alterations in body composition in these patients. Various techniques are used evaluate body composition in COPD, where the choice will depend on their availability, the type of study and its applicability in clinical practice [3,7].

BIA is the most widely used method in clinical research for the estimation of body composition because it is portable, accessible, easy to use and non-invasive, can be frequently repeated, and it requires less patient collaboration [1,8]. It is a method that analyzes parameters such as impedance (Z),...
resistance (R), reactance (Xc) and phase angle (PA), which are used in predictive equations to estimate body composition [9]. However, this technique, as stated above, depends on the use of predictive equations, which are only valid for the specific population for which they have been developed [10]. Alternatively, the raw BIA data (Z, R, Xc and PA) can be accurate indicators of water distribution between intracellular and extracellular compartments and of cellular integrity [1,11].

PA is the parameter of bioimpedance most widely used for the diagnosis of malnutrition and the prognosis of different clinical conditions [12,13]. PA is an indicator of water distribution, BCM and cellular integrity [14,15], and may even be superior to other nutritional, biochemical and anthropometric indicators [12]. Despite the prognostic benefit of PA, its usefulness is limited in clinical situations due to the absence of reference values in healthy individuals and in specific diseases, which does not allow the individual deviations to be adequately evaluated in relation to the average population [10,13,14].

In patients with COPD, BIA has generally been used to estimate body composition from predictive equations and only some studies do so from net data compared with healthy subjects. Given the relationship between COPD and alterations in body composition in these patients, the general aim of this study is to compare the phase angle values between patients with COPD and healthy individuals and to study their relationship with lung function parameters and functional capacity.

2. Methodology
After excluding 2 people who did not meet the inclusion criteria, 71 patients over the age of 50 with a diagnosis of COPD, were selected from outpatient departments of internal medicine and pneumology and from different centers for the elderly in the city and evaluated between March and August 2018. Inclusion criteria were age >50 years, with diagnosis of COPD confirmed with spirometry, evidencing a FEV₁/FVC ratio < 70. The exclusion criteria included diagnosis of known respiratory disorders other than COPD, a history of significant inflammatory disease other than COPD, exacerbation of COPD within 4 weeks prior to inclusion, carrier of osteosynthesis material, partial or total amputation of an extremity and physical limitation for ambulation.

Patients with COPD and control participants underwent an assessment of pulmonary function, body composition, functional capacity after previous corroboration of compliance with instructions. The study was approved by the ethics committee of the Universidad de Caldas and all the patients signed their informed consent to participate in the study.

2.1. Pulmonary function
To define the group of patients with COPD and the control group, all patients included in the study performed the spirometry test, pre- and post-bronchodilator, according to the standardization of the American Thoracic Society and the European Respiratory Society (ATS / ERS 2005) [16], in order to confirm the diagnosis of COPD with a FEV₁/FVC ratio < 70. The forced expiratory volume in the first second (FEV₁), the forced vital capacity (FVC) and the FEV₁/FVC ratio were measured according to the last GOLD. COPD was classified according to the severity of airflow limitation and the combined assessment of COPD from the COPD Assessment Test (CAT) [17].

2.2. Body Composition
During the assessment of anthropometry, body weight and height were measured with the Icob Detecto® digital scale with accuracy of ± 0.1 Kg and the Seca® digital stadiometer with accuracy of ± 0.1 cm respectively. The BMI was calculated as body weight/height$^2$. With the Skyndex II® adipometer, the value of the total percentage of body fat was obtained at the end of the measurement of the bicipital, triceps, subscapular and suprailiac folds. Three takes were made for each fold, determining as a result, the average between the registered values. To determine the average brachial perimeter, the patient was asked to perform 90° elbow flexion, then the midpoint between the acromion and the olecranon was marked. The measurement was made with the elbow extended and the arm in a neutral position, adducted to the thigh and with the arm relaxed, in the non-dominant hemi-body.
For the evaluation of BIA, a Xitron Technologies Hydra 4200® bioimpedance meter was used at a frequency of 50 kHz. The standard tetrapolar technique was used, with the distal current measuring electrodes on the dorsal surfaces of the hand and foot near the metacarpophalangeal and metatarsophalangeal joints and the voltage sensing electrodes on the pisiform prominence of the wrist and between the malleolus medial and lateral ankle [5], according to previously standardized protocols [18]. The FFM, FFMI and PA values were estimated. The FFM was obtained from predictive equations and the FFMI dividing the FFM over height\(^2\). The PA was calculated by the equipment software, obtained directly as its arc tangent: \((X_c/R) \times 180/\pi\) [8,12].

2.3. Functional Capacity
Handgrip strength was measured with a Baseline® digital dynamometer with an accuracy of ± 0.5 kg. The patients remained seated with both feet on the ground; they were asked to take the dynamometer with the dominant arm, adducted to the trunk, elbow flexed at 90 °, forearm in neutral position, wrist in dorsiflexion between 0 ° - 30 ° and ulnar deviation between 0 ° - 15 ° [19,20]. The evaluation of the gait speed was carried out over a distance of 4 meters, according to the instructions given in the protocol of the short test of Functional Physical Performance, recording the time used to travel this distance (SPPB) [21].

2.4. Statistical Analysis
The statistical analysis was performed with SPSS version 25.0. The values were reported as mean ± standard deviation (SD). The comparisons between patients with COPD and controls were made by Student's T-test for independent samples. The Pearson correlation coefficient was used to evaluate the link between the PA and the variables of lung function and functional capacity of both groups. Patients with COPD were stratified according to the mean value of the PA.

3. Results
After selecting patients who met the inclusion criteria, 35 patients with COPD (20 men and 15 women) and 36 controls (13 men and 23 women) participated in the study. The characteristics of body composition, lung function and functional capacity are shown in Table 1. Additionally, the characteristics of lung function and body composition that presented significant differences between patients with COPD and the control group, grouped by gender, are presented in Figure 1.

These patients had a mean FEV\(_1\) of 57.5 ± 20.6% and a FEV\(_1\)/FVC ratio of 54.2 of that predicted; the severity of COPD varied from mild to very severe (GOLD I/II/III/IV: 5.7% / 60% / 22.9 / 11.4%), predominantly the GOLD II and III subgroups.

Table 1. Characteristics of body composition and functional capacity of patients with COPD and controls studied.

| Characteristic                      | Men (n=33) | Women (n=38) |
|------------------------------------|------------|--------------|
|                                    | COPD (n=20) | Controls (n=13) | p-value | COPD (N=15) | Controls (n=23) | p-value |
| Age (years)                        | 70.4 ± 10.2 | 66.9 ± 8.9   | ns       | 64.5 ± 14.9 | 69.6 ± 10.6   | ns       |
| Height (cm)                        | 163.1 ± 8.0 | 164.9 ± 11.0 | ns       | 151.7 ± 7.7 | 152.8 ± 5.4   | ns       |
| Mean total body fat (%)            | 23.7 ± 7.0  | 25.4 ± 6.6   | ns       | 34.8 ± 5.3  | 37.7 ± 5.7    | ns       |
| Mid upper arm circumference (cm)   | 25.4 ± 4.1  | 27.0 ± 4.5   | ns       | 28.9 ± 13.4 | 28.2 ± 4.4    | ns       |
| FFM (kg)                           | 3.2 ± 3.5   | 25.1 ± 5.2   | ns       | 17.2 ± 2.6  | 18.6 ± 2.7    | ns       |
| FFMI (kg/m\(^2\))                 | 8.7 ± 1.1   | 8.9 ± 1.3    | ns       | 7.5 ± 1.0   | 8.0 ± 1.1     | ns       |
| Handgrip Strength (kg/f)           | 30.6 ± 8.4  | 32.3 ± 6.8   | ns       | 20.5 ± 4.5  | 20.2 ± 6.8    | ns       |
| Gait Speed (sec)                   | 5.8 ± 0.9   | 6.0 ± 0.9    | ns       | 5.3 ± 0.5   | 6.0 ± 1.2     | ns       |

Note: The data are shown as mean ± standard deviation.
Abbreviations: FFM, fat-free mass; FFMI, fat-free mass index; ns, not significant.
Figure 1. Characteristics of body composition and lung function that presented significant differences between patients with COPD and control group: weight (a), BMI (b), PA (c), FEV₁ (d), CVF (e) and FEV₁/CVF (f).

In the group of women, the PA value was significantly lower in those who had COPD with respect to their controls (5.3 ± 0.5 versus 6.1 ± 1.2, p < 0.05). For both sexes, in patients with COPD the relationship with PA was inversely proportional to age (r = -0.416, p < 0.05) and gait speed (r = -0.461, p < 0.005) and directly proportional to weight (r = 0.416, P < 0.05), height (r = 0.369, p < 0.05), handgrip strength (r = 0.584, p < 0.001) and FFM (r = 0.425, p < 0.01). The relationship between PA and the pulmonary function variables (FEV₁/FVC ratio (r = 0.164), FEV₁ (r = 0.330) and FVC (r = 0.116), were not significant.

According to the mean value of PA, patients with COPD were stratified, into those above and below it. Patients with lower PA values were associated with higher age and lower weight, BMI, FFM and FFMI. In the lung function variables (FEV₁, FVC and FEV₁/FVC ratio) there were no differences
between the two groups. 30.6% of the patients who were below the mean PA value belonged to the GOLD I and II stages (Table 2).

**Table 2.** Body composition, lung function and functional capacity of patients with COPD stratified according to the average value of the PA.

| Characteristic                        | Average value of the PA (5.5 ± 0.87°) |
|---------------------------------------|---------------------------------------|
|                                       | Under the middle value | Above the middle value | p - value |
| Age (years)                           | 71.9 ± 9.9               | 63.2 ± 14.1            | < 0.05    |
| Height (cm)                           | 155.2 ± 9.3              | 161.8 ± 9              | < 0.05    |
| Weight (kg)                           | 53.2 ± 9.1               | 68.5 ± 12.4            | < 0.001   |
| BMI (kg/m²)                           | 21.6 ± 3.6               | 25.7 ± 4.3             | < 0.005   |
| Mean total body fat (%)               | 27.8 ± 8.9               | 29.35 ± 7.9            | ns        |
| Mid upper arm circumference (cm)      | 26.5 ± 12.3              | 27.4 ± 3.7             | ns        |
| FFM (kg)                              | 18.5 ± 3.2               | 23.2 ± 4.2             | < 0.001   |
| FFMI (kg/m²)                          | 7.6 ± 1                  | 8.8 ± 1.2              | < 0.01    |
| FEV₁ (% of that predicted)            | 55.5 ± 22.4              | 59.8 ± 18.7            | ns        |
| CVF (% of that predicted)             | 77.6 ± 20                | 82.6 ± 18.4            | ns        |
| FEV₁/CVF (ml)                         | 53.2 ± 11.6              | 55.4 ± 9.3             | ns        |
| Handgrip Strength (kg/f)              | 21.89 ± 6.1              | 31.45 ± 8.3            | < 0.001   |
| Gait Speed (sec)                      | 6.6 ± 3.3                | 4.6 ± 1                | < 0.05    |

Note: The data are shown as mean ± standard deviation.

Abbreviations: BMI, body mass index; FFM, fat-free mass; FFMI, fat-free mass index; PA, phase angle; FEV₁, forced expiratory volume in the first second; FVC, forced vital capacity; ns, not significant.

Finally, with respect to the functional capacity variables, a significant difference was observed in the values obtained from manual dynamometry, with approximately 10 kg/f more in those patients who had higher PA results. Patients with PA values below the average took more time in the 4-meter walk.

4. Discussion

The results of this study showed that women with COPD had decreased weight and BMI compared to controls (p < 0.05), whereas no significant differences were observed in percentage of fat, FFM and FFMI for men and women in both groups. Among both men and women with COPD, FEV₁ and FEV₁/FVC ratio was reduced compared to controls.

The alteration in the nutritional status is a systemic effect associated with COPD and can be evaluated using different methods [1,7]. BIA is the most widely used method in clinical research to estimate body composition by using predictive equations [5]. Alternatively, from raw BIA data, such as PA, body composition can be estimated [11] and, regarding this, there are few studies that record data in patients with COPD.

This is how PA has been considered as a global health marker that depends on the Xc associated with cellularity and R, mainly related to the hydration of tissues [9,10,18]. In this way, PA could provide information on the function of the cell membrane through the distribution of intra- and extracellular water [8].

The current study showed that, in patients with COPD, the decrease in PA is related to impaired body composition and functional capacity.

As far as we know, this is one of the few studies that offers data on the body composition of patients with COPD and that compares PA in patients with COPD and controls. In Colombia, no evidence of similar studies was found. With regards this, the current study showed significant differences in PA among women with COPD and their control group, which did not happen in the group of men. These
results differ from those in a study [23] in which it was found that a decreased value of PA was associated with a higher BMI. On the contrary, women in the control group of the current study had a higher PA associated with higher weight and BMI. This could suggest that a slight increase in the total percentage of fat, with the consequent increase in weight, could represent a protective factor [22] expressed by a greater PA.

Our results are coincident with those of other studies [6,13], that show that PA is reduced in patients with COPD, suggesting a deterioration in cell integrity related to the disease [4]. On the other hand, as far as we know, there are still no PA reference values for the specific case of COPD [12].

The study by Maddocks M, et al., [11] evaluated the relationship between PA and COPD severity and prognosis markers in 502 stable outpatients. The authors found only a positive correlation of PA with FFM; while we found that patients with low PA values were also associated with lower FFMI, weight and BMI. These results are similar to those found in the study by Satish Kumar, et al., [23] but they differ from another study in which a decreased PA value in patients with higher BMI is described [12].

Previously, it had been shown that PA correlates directly with functional capacity variables [4]. In the study by Norman K, et al., [8] in which they described the measurement of PA in patients with COPD. The authors that PA positively correlated with the results of functional capacity tests and disease severity and that the results obtained in the present study, in which patients with PA values below the mean, also had lower results in handgrip strength and longer duration during the 4-meter walk.

One limitation of this study was that the composition of the sample is not uniform, with a greater proportion of women in the control group and a greater proportion of men in the group with COPD, which may have had an effect on the general comparison between the control group and the group with COPD.

5. Conclusion
Patients with COPD who had lower functional capacity and a more altered body composition also had the lowest PA values. Additionally, differences were found between PA in women with COPD in relation to their controls. In men this difference was not significant. That is why it is suggested that additional studies be carried out to corroborate these findings and contribute to the recognition of the PA as a useful parameter for the assessment of these patients.

Conflict of interest
No conflicts of interest are declared by authors.

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