ARTICLE ORIGINAL

COPD patients' body composition and its impact on lung function

Composition corporelle des patients atteints de BPCO et son impact sur la fonction respiratoire

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RÉSUMÉ

Introduction : Bien que l'indice de masse maigre (IMM) soit l'un des meilleurs facteurs prédictifs de survie lors de la broncho-pneumopathie chronique obstructive (BPCO), il existe un manque considérable d'information sur la composition corporelle chez les patients tunisiens souffrant de BPCO.

Objectifs : Décrire la composition corporelle des patients tunisiens suivis pour BPCO et examiner les relations entre la composition corporelle et la gravité de la maladie.

Méthodes : Etude transversale colligeant les patients atteints de BPCO à l'état stable. La composition corporelle a été évaluée par l'impédancemétrie bioélectrique. Les explorations fonctionnelles respiratoires (EFR) incluaient la spirométrie avec pléthysmographie et le test de marche de six minutes. La sévérité de dyspnée a été évaluée par l'échelle mMRC.

Résultats : Au cours de la période d'étude, 104 patients atteints d'une BPCO stable ont été inclus (âge moyen= 65,9 ans et VEMS moyen= 49,3%). Cinquante-quatre pourcent des patients étaient classés D à la classification du GOLD. Selon l'IMM, la malnutrition a été identifiée dans 20,2 % des cas. Les patients présentant un IMM bas étaient les plus symptomatiques, avaient une obstruction plus sévère aux EFR et une maladie plus grave. La distance de marche parcourue était plus courte chez les patients souffrant de malnutrition. Cependant, l'IMM n'a pas été significativement associé à la capacité d'exercice.

Conclusions : La malnutrition est très répandue chez les patients souffrant de BPCO et est corrélée à la gravité de la maladie, d'où l'intérêt d'inclure l'analyse de la composition corporelle lors de l'évaluation de ces patients.

Mots clés : Malnutrition, Masse maigre, Masse grasse, Analyse de l'impédancemétrie bioélectrique, Tunisie

SUMMARY

Introduction: Despite fat-free mass index (FFMI) is one of the strongest predictive factors of survival during chronic obstructive pulmonary disease (COPD), there is a considerable lack of information regarding body composition in Tunisian patients with COPD.

Aim: Describe the body composition of Tunisian patients followed for COPD and examine the relationship between body composition and the severity of the disease.

Methods: Cross-sectional study of patients with stable COPD. Body composition was assessed by bioelectrical impedance analysis. Pulmonary function tests (PFT) included spirometry with plethysmography and the six-minute walking test. The severity of dyspnea was assessed by the mMRC scale.

Results: During the study period, 104 patients with stable COPD were included (average age= 65.9 years and average FEV1= 49.3%). Fifty-four percent of patients were GOLD D stage. According to the IMM, malnutrition was identified in 20.2% of cases. Patients with low FFMI were the most symptomatic, had a more severe air flow limitation and a more severe disease. The walking distance was lower in malnourished patients. However, FFMI was not significantly associated with exercise capacity.

Conclusions: Malnutrition is highly prevalent in COPD patients and is correlated to the severity of the disease. Thus, body composition analysis should be considered in COPD patient management.

Key words: Malnutrition, Lean mass, Fat mass, Bioelectrical impedance analysis, Tunisia

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common chronic respiratory disease characterized by persistent air flow limitation that primarily affects the lung and leads to significant systemic effects, such as muscle dysfunction, impaired exercise performance and weight loss [1]. According to several studies, weight loss is particularly prevalent in patients with COPD [2,3]. Moreover, malnutrition affects pulmonary function, decreases quality of life, and increases the risk of exacerbations, hospital stay, and healthcare costs [4-6].Several studies have shown that low body mass index (BMI) is associated with worse outcomes in COPD [7,8]. Nevertheless, malnutrition can occur at any BMI, and important changes in body composition can occur in patients with COPD, even with a normal BMI [9,10]. Moreover, it has been recognized that fat-free mass (FFM), seems to be a stronger predictor of mortality and disease severity than does BMI [11,12]. All of these evidences are actually justifying the routine assessment of body composition during COPD. Single-frequency bioelectrical impedance analysis (BIA) is actually recognized as an appropriate measurement of body composition during COPD [13]. BIA is a simple, inexpensive, quick and non-invasive technique for assessing body composition and its changes over time. To the best of our knowledge, there is no previous published data regarding body composition in Tunisian patients with COPD. Thus, our study aims to describe body composition in patients with COPD referred to a pulmonary department of Tunis and to examine the relationships between FFM and the severity of the disease (dyspnea, air flow limitation and exercise capacity).

METHODS

Subjects

A Cross-sectional study was performed in the pulmonary department of Rabta Teaching Hospital in Tunis from January to June 2019. Patients with mild-to-very severe COPD were considered for participation in the study. Patients were included according to the following criteria:

- Men patients aged over 40 years;
- Diagnosis of COPD confirmed according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [14].

The exclusion criteria were:

– A history of COPD exacerbation within the previous 2 weeks;
- Chronic respiratory failure with long term oxygen therapy;
- Serious organ failure, malignant tumor, or metabolic disease;
- Moderate to severe injury or recent surgery in the preceding month;
- Drugs known to interfere with water–mineral homeostasis and/or any signs of oedema or dehydration.

Severity of dyspnea was evaluated using the modified British Medical Research Council dyspnea scale (mMRC). Health status impairment was evaluated according to the COPD Assessment Test (CAT). COPD severity was assessed according to the GOLD guidelines [14]. The study protocol was approved by the local ethic committee. The aim of the study was fully explained to participants, and all gave informed consent.

Body composition measurements

Body composition was assessed using a single-frequency BIA analyzer with standard tetra polar lead placement and a low electrical current emission (900 mA and 50 kHz) (SC-240MA class III, Tanita coporation, Tokyo, Japan). BIA measurements were performed by one trained observer using the same equipment with recommended standard conditions. Before performing measurements on each participant, the BIA analyzer was calibrated using the manufacturer's recalibration device. Patients were studied in the supine position after an overnight fast. Height (H) was measured while standing erect. Parameters of body composition included: weight (W), body mass index (BMI), FFM, fat free mass index FFMI (FFM/height^2), percent of body fat (PBF), body fat mass (FM), skeletal muscle mass (SMM), and bone mass. Low BMI was defined as BMI<18.5 Kg/m^2, overweight as 25<BMI<30 Kg/m^{2}and obesity as BMI>30 Kg/m^2. A low FFMI was defined as FFMI <16 kg/m^2 in men, as reported previously [10]. The population study was divided in 2 groups according to the FFMI (G1: low FFMI, G2: normal FFMI).

Pulmonary function tests

Spirometry, whole body plethysmography measurements were performed according to the American Thoracic Society (ATS) and the European Respiratory Society (ERS) guidelines using a Medisoft Bodybox 5500 plethysmogrph that was calibrated daily [15,16]. Forced

vital capacity (FVC), mean forced expiratory volume in 1 second (FEV_1), FEV_1/FVC, total pulmonary capacity (TPC) and residual volume (RV) values were recorded.

6-Minute Walking Test (6MWT)

Patients performed the 6MWT according to the ATS guidelines [17]. The 6MWT was performed on a 30-meter indoor track while attempting to cover as much distance as possible in the allotted 6 minutes without supplementary oxygen. An experienced investigator timed the walk and recorded the distance traveled using standardized encouragement strategy. None of the patients used a walking aid in daily life or during the test. The expected walked distance was calculated according to the following formula: expected distance = 218 + [5.14 X height in cm] - [5.32 X age] - [1.8 X weight in kg] + [51.31 X sex] (0 : female, 1 : men). The ratio of walked distance/expected distance was then calculated (%).

Statistical analysis

A statistical software package was used for all measures (SPSS for Windows, version 11.0, Massachusetts, USA). Descriptive data were expressed as mean and standard deviation. Data comparison for descriptive data was performed by the Student's t test for independent series. Comparison of percentages was performed by the Pearson chi-square test. Correlation between 2 quantitative variables was performed by the Pearson correlation coefficient. A *p*-value of less than 0.05 was considered significant.

RESULTS

During the study period, 104 consecutive male patients with stable COPD met the inclusion and exclusion criteria and took part in the study. The mean age was 65.9 ± 8.9 years. Clinical characteristics and pulmonary function data of the patients are presented in Table 1. Comorbidities were found in 78 patients: diabetes mellitus (18 patients), hypertension (29 patients), renal failure (20 patients) and coronary artery disease (11 patients). COPD was classified GOLD A in 10 patients (9.6%), GOLD B in 17 patients (16.3%), GOLD C in 20 patients (19.2%) and GOLD D in 57 patients (54.8%). The mean exacerbation number during the previous year was 2.13 ± 1.9. The mean 6MWT distance was 454.4 ± 108.4 meters; it was on average

59.8±51.1% of the predicted value. Body composition parameters are resumed in table 2. According to BMI, 52 patients (50%) had normal weight, 30 patients had a low BMI (28.8%) and 27 patients were overweight or obese (26%). A low FFMI was noticed in 21 patients (20.1%) (G1). Patients with a low FFMI (G1) were more dyspneic (mMRC scale 2.2 in G1 vs 1.88 in G2; p=0.09) and has a worse heath status (CAT score 22.43 in G1 vs 19,5 in G2; p=0.08). However, there was no difference between the 2 groups regarding the number of exacerbations in the previous year (2.0 in G1 versus 2.08 in G2; p=0.8). FEV1, FEV1/FVC were significantly lower in G1 (p<0.05). Spirometric parameters of the 2 groups are summarized in table 3. Moreover, patients of G1 had a more severe disease. In fact, 90.5% of the G1 were classified at least GOLD C versus 68.8% of the G2. Comparison of mean walked distance showed no significant differences between the 2 groups (424.1 ± 117.2 m in G1 versus 461.7 ± 109.8 m in G2; p=0.47). However, the percentage predicted distance was significantly lower in G1 (55.9% ± 24.8% vs 66.7% ± 22.09% ; p=0.05).

Table 1. Clinical characteristics and pulmonary function data of the patients

Variable	Mean value	Standrad deviation	Range
Number of patients (n)	104	-	-
Male/female gender (n)	104/0	-	-
Age (years)	65.9	8.9	43 - 82
Dyspnea	1.96	0.86	0 - 4
Tobacco comsuption (package/year)	51.9	35.04	10 - 250
CAT score	20.35	9.91	8 - 40
FVC (l)	2.71	0.84	1.2 - 5.4
FVC (% predicted)	72.6	19	32 - 127
FEV_1 (l)	1.42	0.69	0.5 - 3.8
FEV_1 (% predicted)	49.3	21.5	17 - 85
FEV1/FVC	51.04	11.2	31 - 70
TLC (l)	7.37	1.44	4.31 - 11
TLC (% predicted)	113.16	23.3	60.8 - 170
RV (L)	4.7	1.52	1.5- 8.6
RV (% predicted)	194.3	61.4	83 - 369
RV/CPT	62.9	13.01	22.5 - 88.9

FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the First Second; FEV1/FVC = FEV1/FVC ratio; TLC = Total lung capacity; RV = residual volume.

Table 2. Body composition parameters of the study population.

Variable	Mean value	Standrad deviation	Range
Weight (Kg)	64.1	13.6	35 – 107
BMI (Kg/m²)	22.2	4.3	13.9– 32.8
PBF (%)	17.9	7.7	3 –42.2
BFM (Kg)	12.4	7.08	1.1– 34.2
FFM (Kg)	51.6	7.8	31.1– 75.3
FFMI (Kg/ m²)	17.9	2.28	13.03– 22,9
SSM (Kg)	49.2	8.5	32 –71
Bone mass (Kg)	2.6	3.4	1 – 26

BMI: body mass index, PBF: percent of body fat, BFM: body fat mass, FFM: fat free mass, FFMI: fat free mass index, SSM: skeletal muscle mass.

Table 3. Comparison of pulmonary function parameters in the 2 groups.

Variable	G1	G2	p
FVC (L)	2.45 ± 0.9	2.8 ± 0.81	0.108
FVC (% predicted)	66.45 ± 18.4	74.7 ± 19.1	0.08
FEV1 (L)	1.15 ±0.72	1.52 ± 0.76	0.03
FEV1 (% predicted)	39.7 ± 19.2	52.3 ± 21.6	0.01
FEV1/FVC	45.06 ± 8.5	52.9 ± 11.4	0.005
TPC (L)	7.45± 1.53	7.37 ± 1.44	0.83
TPC (% predicted)	117.7 ± 2.06	112.08 ± 24.5	0.35
RV (L)	5.01 ± 1.51	4.62 ± 1.55	0.31
RV (% predicted)	208.75 ± 62.3	190.5 ± 65.4	0.27

FVC = Forced Vital Capacity; FEV1 = Forced Expiratory Volume in the First Second; FEV1/FVC = FEV1/FVC ratio; TLC = Total lung capacity; RV = residual volume.

DISCUSSION

To our knowledge, these are the first published data on body composition in Tunisian patients with COPD. Our study demonstrates that FFM depletion is frequent among our population. Moreover, it's correlated to air flow limitation, exercise capacity and severity of the disease.

During COPD, weight loss was initially being considered as an indicator of end-stage chronic respiratory failure. However, there is now convincing evidence that unintended weight loss is not an adaptive mechanism to decrease metabolic rate in advanced COPD but an independent determinant of survival [13]. Over the two

last decades, the recognition of the importance of nutrition status in COPD has led to an increasing interest in the management of malnutrition in these patients. Although BMI is the most used tool to assess nutritional status during COPD, weight changes and BMI classification do not take body compositional shifts, including fat and lean mass distribution into account. Using data from the epidemiologic Copenhagen City Heart Study [10], low FFMI was associated with an increased overall mortality and COPD mortality. Even in subjects with normal BMI, low FFMI was associated with increased overall mortality.

Dual-Energy X-ray absorptiometry (DEXA) is simple, non-invasive and considered as a reference method to assess body composition in COPD patients [18,19]. However, the disadvantages of this technique are currently its cost and accessibility. The DEXA is also difficult to perform in subjects with low autonomy. In comparison with DEXA, conventional BIA system, has satisfactory clinical accuracy in estimating body composition [20]. The BIA system, which is based on differential opposition to the electrical current among body tissues, has been used to assess body composition in COPD patients in various studies [21-23].

According to the BIA measurements, our results revealed that, according to FFMI, 20.1% of our patients were undernourished. This is consistent with other published data. In the Netherlands, the incidence of low FFMI, among COPD patients, was 27% [22]. Similarly, Norden J et al., found that 36% of COPD patients were malnourished [24]. In china, malnourishment seems to be more prevalent during COPD. This could be explained by differences in the ethnicity of the subjects, since Asians have often smaller body frames than whites [25,26]. According to Gologanu et al., malnourishment was less prevalent in Romanian population. This could be explained by the recruitment process in this study. Patients were admitted in a rehabilitation program which excluded from the beginning more severe patients who potentially have lower FFMI [27].

Data regarding the relation between FFMI, air flow limitation and symptoms during COPD are controversial. Some authors showed a significant correlation between FFMI, COPD stages and health status [12,27], while other studies failed to find a correlation between FFMI, FEV1 and dyspnoea scores [22]. Our study showed that patients with

low FFMI were more dyspneic and had a worse pulmonary function. Consistent with our findings, Krzystek-Korpacka et al. found that the FEV1 was significantly lower in malnourished subjects with COPD [28]. This is probably due to skeletal muscle apoptosis caused by inflammation and increased oxidative stress during COPD [29].

Unlike our findings, it has been demonstrated that nutritional status is correlated with acute COPD exacerbations [30]. Thus, improving the nutritional status through nutritional intervention can decrease the frequency of exacerbations and reduce hospitalization costs [29].

It has been also demonstrated that FFMI is correlated with exercise capacity. Malnourished COPD patients are particularly prone to exercise intolerance due to skeletal muscular cell atrophy [31]. Our study showed that malnourished patients had lower exercise capacity as demonstrated by the decrease in the percentage of predicted walking distance.

Our study has a few limitations. First, female subjects were not included in the present study. In fact morbidity of COPD is really rare in Tunisian women. However, since body composition may be different in women, future studies with more enrolled women should be done. Second, the number of enrolled subjects was relatively small. Further studies with a larger number are needed to reach statistical significance in some parameters.

CONCLUSION

Malnutrition is prevalent in Tunisian patients with COPD. Patients with low FFMI are more symptomatic and have significantly more severe air flow limitation and more severe disease. These findings highlight the need to focus on body composition assessment and on nutritional intervention and pulmonary rehabilitation in Tunisian COPD patients.

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