ORIGINAL ARTICLE

EFFECT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON BODY COMPOSITION PARAMETERS AND EXERCISE CAPACITY BY COMPARISON WITH AGE MATCHED HEALTHY CONTROLS

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ABSTRACT

Background & Objectives: Nutritional abnormalities are frequent systemic manifestation associated with COPD. The purpose of the present study was to compare the body composition parameters & exercise capacity between stable COPD patients and healthy controls, and to find the strength of association between exercise capacity, FMI and FFMI.

Methods: 100 subjects were recruited, and divided into two groups. Group I included stable COPD patients, and Group II consisted of age matched healthy controls respectively. The spirometric parameters recorded were FEV1 (Litres), FVC (Litres), FEV1/FVC ratio (% predicted), FEF 25%75% (Litres/sec). Anthrometric measurements included Body Weight, Height and BMI measurements. Body composition was assessed by four-frequency bioelectrical impedance analysis (BODY STAT, QUAD SCAN, USA). The following parameters were calculated: FFM, FFMI, FM and FMI. The exercise capacity was assessed by the six-minute walking distance test (6MWD). All the recordings were compared between groups and correlation was also computed between 6MWD, FMI & FFMI within groups. Results were analyzed using SPSS, version 16 & Pearson correlation coefficient.

Results: We found that COPD patients showed lower FFM, FFMI & exercise capacity as compared to healthy controls. And, great strength of association was found between FFMI and exercise capacity.

Conclusions: Thus, our study indicates that with COPD there is preferential loss of lean body mass evident from lower FFMI leading to decreased walking distance in these patients. Hence, it is prudent to include nutritional and exercise capacity assessment in patients of COPD, to better manage these patients and improve their quality of life.

Keywords: Chronic Obstructive Pulmonary Disease, body mass index, bioelectric impedance analysis, fat mass index, free fat mass index, six minute walking distance.

INTRODUCTION

COPD is a disease state characterized by progressive airflow limitation with many recognized systemic side effects[1]. Amongst these nutritional abnormalities like weight loss, depletion of FFM and to a lesser extent loss of FM is very common[2, 3].

However, very few studies have been conducted comparing body composition and exercise capacity of COPD patients with healthy controls. Thus, the aim of our study was:

- To compare the body composition parameters and exercise capacity in COPD patients with similar aged healthy control group.
- To study the strength of relationship between BMI, FFMI and exercise capacity in both the groups.

MATERIAL AND METHODS

Sample

The present study was conducted in outpatient clinic of department of Pulmonary Medicine, Indira Gandhi Medical College and Hospital, Shimla from August 2012 to November 2011. Institutional ethical clearance was obtained for the study by institutional review board. For this study we recruited hundred subjects, divided into two groups. A sample size of hundred subjects was calculated by PASS statistical software.

Group I consisted of fifty consecutive physician-diagnosed COPD patients & Group II included fifty healthy volunteers.

The COPD patients consisted of 28 males and 22 females (30-70years; mean age 64.8 years). All the patients were screened by a detailed history and physical examination as per inclusion and exclusion criteria. Enrolment criteria were:

1. Moderate to severe patients of COPD as per GOLD guidelines, 2013[4].
2. Stable patients of moderate to severe COPD with no acute exacerbation for the past six week according to GOLD guidelines, 2013[4].
3. COPD patients with baseline $SpO_2 \geq 90\%$.

Control group consisted of 35 males and 15 females (30-70 years of age; mean age 62 years), recruited on the basis of same criteria for age and smoking history. They were current or past smokers who did not suffer from pulmonary diseases either now or in the past. Neither lung symptoms nor physical examination deviations were stated in their cases. The results of spirometry tests in these subjects were normal.

The exclusion criteria for all the subjects were:

1. Those subjects with historic or clinical evidence of pulmonary diseases other than COPD.
2. Subjects with active or past diseases that could affect nutritional state disorders (diseases of heart, liver, kidney, diabetes, neoplasms) as well as those subjects using steroids, diuretics were excluded from the study.
3. Subjects who were symptomatic for neuromuscular, musculoskeletal, peripheral vascular diseases, cardiovascular diseases which limited their capacity to perform six minute walk test.

The purpose of the study was explained to the subjects and written consent was obtained thereof. Institutional ethical clearance was obtained for the study by institutional review board.

All the patients as well as controls were subject to detailed demographic history, occupational history, history of smoking habits, biomass exposure, history of disease with treatment history and history of any co-morbidities and complications.

All the selected patients & controls were subjected to thorough medical examination and various routine investigations such as complete blood count, lipid profile, blood sugar, serum protein, blood urea, serum creatinine, serum electrolyte profile, ankle brachial ratio. Plain chest radiograph, resting electrocardiogram and echocardiography were also performed to rule out any co morbidity and complications of COPD.

Spirometry

All the patients performed post-bronchodilator spirometry with an electronic portable PC based spirometer with printer (Vitalograph Compact Buckingham, England) which fulfilled the accuracy and precision criteria as per American Thoracic Society/ ERS[23]. The patients were staged as per GOLD guidelines, 2013[4] (post bronchodilator FEV1/FVC ratio<70% predicted), mild (FEV1≥ 80% predicted), moderate (50%≤FEV1<80% predicted), severe (30%≤FEV1<50% predicted), and very severe (FEV1<30% predicted) or FEV_1<50% predicted plus the presence of signs of chronic respiratory failure. Spirometric parameters were recorded as absolute measurements and percent predicted for race, age, gender and height. The spirometric parameters recorded were FEV1 (Liters), FVC (Liters), FEV1/FVC ratio (percent predicted), FEF 25%75% (Liters/sec).

Anthropometry

Body weight was measured on a calibrated balance to the nearest 0.1 kg while patients were barefoot and wearing light clothing. Body height was measured to the nearest 0.5 cm while patients were barefoot and standing with their backs and heels touching a vertical bar. BMI was calculated as weight divided by height squared (kg/m^2).

Body Composition

Body composition was assessed by four-frequency bioelectrical impedance analysis (BODY STAT, QUAD SCAN, USA). All body composition measurements were performed between noon and 2 p.m. The patients fasted on the day that the measurement was performed and did not ingest coffee, tea, chocolate or alcoholic beverages for 48 h prior to the measurement. During the measurement, patients lay in a supine position with their limbs slightly apart from their bodies. Two electrodes were positioned on the dorsal surface of the right hand, and two additional electrodes were positioned on the dorsal surface of the right foot. The FFM was calculated using an equation that has been specifically validated for patients with respiratory diseases. FM was calculated as total body weight minus FFM. FFM index (FFMI) and FM index (FMI) were calculated by dividing the body weight (in kg) of FFM and FM, respectively, by height (in m) squared in order to adjust for body surface area. Under these conditions, bioelectrical impedance analysis measurements are considered accurate and comparable to other techniques used to assess body composition. The following parameters were calculated: FFM (kg), FFMI (kg/m^2), FM (kg) and FMI (kg/m^2).

Exercise Capacity: The exercise capacity was assessed by the six-minute walking distance test (6MWD), which is validated and reliable for evaluation of the exercise capacity of patients with COPD. The 6MWT was performed according to the ATS guidelines, 2002[5]. Subjects were asked to walk as fast as they can, along a 30 m long and straight hospital hallway marked at intervals of meter each. All of the patients were familiarized with the test procedure prior to testing. Patients were instructed to walk as fast as possible, aiming to complete the longest possible distance in the allotted time. At each full minute during the test, the patients were verbally encouraged with a standardized incentive phrase. The patient was allowed to stop if symptoms of significant distress occurred, like severe dyspnea, chest pain, dizziness, diaphoresis, or leg cramps. However, the patient was asked to resume walking as soon as possible, if he or she could. At the end of six minutes, the patient was asked to stop. Each patient's result was expressed as an absolute value (meters).

Statistical Analysis: Statistical analysis was done using SPSS version 16, statistical software. Bivariate comparison between COPD patients and healthy controls was done by independent student t-test. The distribution of data is presented as Means ±Standard Deviation. Pearson correlation (parametric data) and Spearman rho test (non parametric data) were used to assess correlation of the FFMI and BMI with the exercise capacity. Statistical significance was accepted at a p value of <0.05. Statistical analysis was done using SPSS version 16, statistical software (SPSS, Inc., Chicago, IL, USA).

RESULTS

The spirometry, anthropometry, body composition & exercise capacity results are presented in Table 1, in which comparison is shown between the study and control group. There were no statistically significant differences among the groups in age, height and smoking history. As per inclusion criteria control group has normal spirometric data whereas most of the COPD patients fall in II & III stage according to Gold staging.

Table 1: Comparison of Socio-Demographic, BIA measurements and 6MWD in COPD patients with Healthy Controls

Variable	COPD patients (N=50)	Healthy controls (N=50)	p value
Age (Years)	64.8	62	0.08
Sex(M/F)	28/22	35/15	0.43
Education (1-6)	4	4	0.56
Smoking (Packs/yr)	39.95±18.46	36.45±14.48	0.06
BMI (kg/m2)*	19.68±1.28	20.13±0.74	0.01
FEV1(Liters)*	1.09±0.78	2.84±0.46	0.004
PEFR(Liters/min)	3.46±1.67	6.84±1.24	0.06
FVC(Liters)*	1.75±0.11	3.64±0.38	0.006
FEV1/FVC %*	60.52±6.352	73.04±4.288	0.003
Fat mass(kg)*	17.8±0.24	22.4±0.18	0.03
FMI (kg/m2)	6.992±2.4006	8.644±3.2236	0.84
FFMI (kg/m2)*	13.36±0.37	20.18±0.21	0.001
BCM(Kg)	23.67±0.13	29.48±0.18	0.09
Phase angle *	4.5±0.28	5.6±0.11	0.05
6MWD (meters)	392.30±124.856	425.20±224.122	0.84

*p<0.05 is statistical significant.

Body composition: Body weight: The study was conducted in Shimla (Himachal Pradesh), where due to difficult terrain & lifestyle it is very difficult to enroll overweight/ obese subjects for study (in control as well as study group). BMI: The calculated BMI in the study and control group were 19.68±1.28 & 20.13±0.74 respectively. The BMI (p<0.01) was significantly higher in control group. A comparison of the average BMI values in both groups is shown in Figure 1.

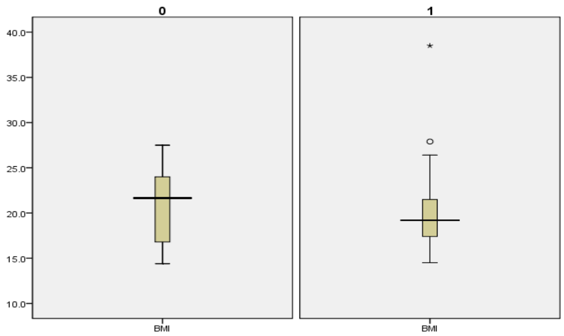

Figure 2: Comparison of mean BMI (in kg/m² on Y axis) indicators in study (COPD) and control group (0=COPD Patients, 1=Healthy Controls)

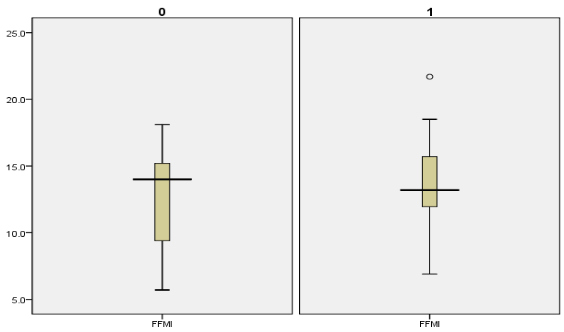

Figure 1: Comparison analysis of FFMI (in kg/m² on Y axis) in study (COPD) and control group (0=COPD Patients, 1=Healthy Controls)

Bioelectrical Impedance Analysis: FM, FFM, FMI & FFMI were found to be significantly lower in COPD patients as compared to healthy controls. Phase angle which is an indicator of nutritional state (used reference values: males>5.5, females >5) was also found to be lower in COPD patients (4.5±0.28) as compared to healthy controls (5.6±0.11).

FMI: The average fat mass index in both groups was calculated & compared. Mean FMI was 6.99±2.4in pts and 8.64±3.2 in control group. The control group had higher fat mass as compared to patients. (p<0.84)

FFMI: Average FFMI in the patients and control group were found to be13.36±0.37 & 20.18±0.21 respectively. Comparison analysis was made in both groups. A significant difference of FFMI between the groups was found. In the study group FFMI (p<0.001) was significantly lower than in controls. The results of this analysis are shown in Figure 2.

Exercise capacity: Exercise capacity was assessed using 6MWD test. Walking distance in absolute values (meters) was found to be 392.30±124.85& 425.20±224.12 respectively in the COPD & control group. Walking distance was found to significantly lower in the patients of COPD.

Table 2: Shows the Correlation in BMI, FFMI in the Study Population, COPD patients and Healthy Controls with 6MWD.

Variable	6MWD (COPD) (meters)	6MWD (Controls) (meters)
N	50	50
BMI (kg/m2)#	0.166	0.26
SIG. (2-Tailed)	0.001	0.01
FFMI (kg/m2)#,	0.266	0.146
SIG. (2-Tailed)	0.001	0.301

#Pearson (*r*) analyses were applied; * Correlation is significant at the 0.05 level (2-tailed); ** Correlation is significant at the 0.01 level (2-tailed).

Correlation data: Correlation data for the study group is presented in Table 2. As clear from the correlation coefficient, both BMI (r=0.166, p<0.001) & FFMI (r=0.266, p<0.001) show correlation with walking distance, but the strength of association was found to be significantly higher in case of FFMI.

DISCUSSION

Although COPD is primarily a disease reflecting lungs, it produces wide ranging systemic consequences such as nutritional changes, skeletal muscular dysfunction, cardiovascular and neurological effects.[6] Malnutrition is a frequent complication in COPD and an important predictor of functional capacity, mortality and morbidity. [7]Malnutrition is associated with structural and metabolic changes in peripheral and respiratory muscles, thereby aggravating preexisting dyspnoea and exercise intolerance. [7, 8] Exercise intolerance is a hallmark of chronic obstructive pulmonary disease (COPD). Although exertional symptoms may be mild at the outset, exercise limitation is the most disabling and consequence of COPD for majority of the patient. Considering the key role of exercise intolerance in the pathophysiology and course of COPD, the evaluation of exercise tolerance should now be included in the assessment of this disease [9] especially for the evaluation of the response to pharmacological and nonpharmacological interventions [10].

Several studies have confirmed lower values of body composition parameters (BMI, FMI, FFMI) in COPD patients and the change in these parameters keeps on increasing with increased severity of disease.[11] But, loss of skeletal muscle mass is described not only in patients with COPD and other consuming diseases,[12] but also in healthy elderly. [13]Thus, the main goal of our study was to compare the body composition parameters & exercise capacity of COPD patients with age matched healthy controls. In the present study we used body weight, BMI, FMI, FFMI as indicators for assessment of body mass & 6MWD for assessment of exercise capacity.

We found significant difference in body mass of subjects on basis of body weight and BMI assessment between the study and control group. In other studies, malnutrition estimated by BMI assessment was seen in 3.9% ([14]), 6.6 %([15]) & 23 %([16]) patients. In several studies BMI in range of 18.5- 25 kg/m2 is considered normal, consequently the % of subjects with malnutrition decreased in these studies.

Surrogate measures such as BMI alone give no indication of body composition, muscle mass or nutritional state. Thus, malnutrition requiring intervention can exist in spite of normal to high BMI. [17] In a study by Spanish researchers (Soller & colleagues), in 62.9%of patients without loss of complete body mass (20.7% of them with over nutrition & obesity), nutritional status disorders were confirmed.[14] In a study by Schols. et al, 14.8% of patients with normal body mass , had significant FFMI loss.[18]

Analysis of body composition by BIA is simple, quick & non- invasive technique which provides the assessment of body composition by division into components (FM& FFM). [17] BIA provides qualitative information on body composition that is it can detect where loss is occurring (fat/muscle) & pathogenesis of weight loss.[19] In current study, the body composition parameters FM& FFM showed well defined differences of nutritional status between the two groups. Significant difference was found in FFMI (p<0.001) between COPD patients and control group. COPD patients more frequently lost muscle mass, whereas for those from control group greater muscle was characteristic.

Although BMI was lower in COPD patients as compared to controls, we found significantly worse results concerning muscle mass and body composition among the study group compared to controls. These results suggest that BMI alone does not allow conclusions to be drawn regarding body composition/ nutritional state of these patients.

The mechanisms leading to muscle wasting in COPD are still uncertain. Accelerated muscle proteolysis is considered the primary cause of the loss of lean body mass, not only in COPD, but also in many other chronic disorders.[12] Physical inactivity, hormonal dysfunction, increased levels of cytokines play important roles in muscle wasting.[14]

In current study, we found that exercise capacity (p<0.84) assessed by 6MWD was lower in COPD patients as compared control group. A significant strength of association was also found between decreased exercise capacities, FMI &FFMI. But, the association was stronger for FFMI. Whether loss of skeletal muscle mass leads to decreased exercise capacity or it is a multifactorial process, because of severe obstruction (exercise intolerance), airflow limitation (dyspnoea) or high resting energy expenditure is debatable. FFMI (r=0.266, p<0.001) , (r=0.146, p<0.301) which depicts lean body mass showed a stronger association with 6MWD as compared to BMI (r=0.166, p<0.001), (r=0.26, p<0.01) in both study and control groups. Some studies show that body mass composition is a determining factor of maximal exercise tolerance. Schols et al[20] found that FFMI correlated with distance walked in 12 minutes. Various studies have shown that patients with low FFM, show lower exercise capacity on sub maximal and maximal exercise tests.[21, 22]

Today, COPD is a multisystem disease with rising prevalence and is reported as the leading cause of death and physical incapacity.[23] Amongst systemic changes, COPD influences aspects related to body composition & muscle structure also. And both these factors adversely affect the exercise capacity. Severe depletion of FFM affects peak O_2 consumption, ventilator response, O_2 pulse and anaerobic energy metabolism.[24]

However, only few studies have compared findings of COPD patients with similar age matched healthy controls. Our, findings suggest that COPD patients show a significant decrease in BMI, FFMI and exercise capacity as compared to healthy controls.

In conclusion, the current study findings and rising prevalence of COPD as a major public health problem with heavy economic burden, point to the need to consider body composition & exercise capacity analysis as a part of routine assessment of COPD patients. So, that nutritional intervention & increase use of load bearing capacity through increase in physical exercise can be incorporated in treatment regimen of COPD patients, to improve body functionality, quality of life in these patients.

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