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ORIGINAL RESEARCH

Body Composition of Filipino Chronic Obstructive Pulmonary Disease (COPD) Patients in Relation to Their Lung Function, Exercise Capacity and Quality of Life

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Background and objectives: The loss of muscle or fat free mass (FFM) as a result of systemic inflammation and poor nutrition in Chronic Obstructive Pulmonary Disease (COPD), is recognized as an important factor that influences symptoms and disease-related outcomes. To date, there are no data on body composition among Filipino COPD patients and how it impacts COPD disease severity. This paper examined the relationship of Fat Free Mass Index (FFMI = FFM/height) and sarcopenia with COPD disease severity variables.
Methods: This was a cross-sectional analytic study comparing low and normal FFMI, sarcopenic and nonsarcopenic COPD patients, in terms of lung function, exercise capacity, and quality of life score. Filipino COPD patients older than 40 years were included. Patients performed six minute walking distance (6MWD), handgrip strength (HGS), and quality of life status evaluation using Filipino version of COPD Assessment Test (CAT). Body composition was measured using bioelectrical impedance analysis (BIA).
Results: A total of 41 patients were included. The mean age was 69.22 years. The prevalence of being underweight and having sarcopenia was 32% and 46%, respectively. Point biserial correlation showed that COPD patients with low FFMI had a statistically significant reduction in peak inspiratory flow (r= −0.5791, P value 0.0002), peak expiratory flow (r= −0.4475, P value 0.0055), and handgrip strength (r= −0.4560, P value 0.0027); and lower CAT score (r= −0.3422, P value 0.0285). Similar findings were observed among sarcopenic COPD patients.
Conclusion: The prevalence of being underweight and having sarcopenia was high. Low FFMI results in reduction of lung function and upper limb muscle strength among Filipino COPD patients.
Keywords: chronic obstructive pulmonary disease, nutrition, body composition, sarcopenia, lung function

Introduction

Chronic Obstructive Pulmonary Disease (COPD) remains among the top 10 leading causes of mortality in the Philippines.[1] Aside from lung involvement, COPD patients usually have extrapulmonary comorbidities, with cardiovascular, musculoskeletal, and psychologic conditions being the most prevalent.[2] The presence of oxidative stress and altered circulating levels of inflammatory mediators as reflected by acute-phase proteins give rise to a chronic inflammatory state in COPD, which can lead to weight loss, muscle wasting, and tissue depletion.[3]

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In COPD patients over 50 years of age, there is a 1–2% annual reduction of muscle mass, which was correlated to reduced exercise capacity, functional performance, and muscle strength.[4] This phenomenon, known as sarcopenia – a syndrome characterized by progressive skeletal muscle loss, reduced muscle strength and physical performance, has been shown to be twice as prevalent among COPD patients versus normal elderly population.[5] Furthermore, data[6] have shown that COPD patients with low muscle mass, as measured by Fat Free Mass Index (FFMI = FFM/height m^2) have lower quality of life scores,[7] and higher mortality.[8]

The body mass in a two-compartment model is divided in fat mass (FM), and fat-free mass (FFM), an indirect measure of muscle mass. Measurement of body weight or BMI does not accurately reflect body composition changes. For this reason, the European Respiratory Society (ERS) created a multidisciplinary task force for nutritional assessment,[9] where anthropometry, Dual Energy X-ray Absorptiometry (DEXA), and Bioimpedance analysis (BIA) were recommended for body composition evaluations in clinical practice. The widely used cut-off low FFMI values among COPD patients were based on American Thoracic Society (ATS) and ERS guidelines on Pulmonary rehabilitation[10] at FFMI <16 kg/m^2 and <15 kg/m^2, for males and females, respectively. However, a large European COPD cohort study by Vestbo et al[8] used the lowest 10th percentile of the general population in defining low FFMI instead.

In defining sarcopenia, European Working Group Society on Older People (EWGSOP) recommends the use of normative data derived from the study population, with equal to or below the mean minus two standard deviations.[11] A study done by Tee et al,[12] where FFMI from healthy young adult Filipinos was measured using BIA, and normality of the distribution of the data was assessed, determined the Philippine normative values for defining sarcopenia among normal elderly at FFMI values <12.50 kg/m^2 for males and <8.33 kg/m^2 for females.

Proper nutritional risk assessment and intervention are essential components of pulmonary rehabilitation, the cornerstone in the comprehensive management of COPD patients. However, the substantial differences in the current diagnostic cut-off points for low FFMI across populations are not reflective of race and environmental factors, and to date, there are no correlative data on body composition and cut-off values for low FFMI among Filipino COPD patients.

This paper aimed to describe body composition of Filipino COPD patients, compare and determine the appropriate cut-off values in defining low FFMI among Filipino COPD patients, and examine the relationship of low FFMI, presence or absence of sarcopenia with disease severity variables (lung function severity, exercise capacity, and quality of life score).

Methods

Study Population

Adult Filipino COPD patients older than 40 years attending Philippine General Hospital were included in this study. Diagnosis of COPD was made on the basis of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria:[13] history of chronic cough, sputum production and dyspnea, significant exposure to risk factors such as tobacco, and post-bronchodilator FEV1/FVC ratio < 0.70 on spirometry. Patients were recruited if they reported significant exposure to smoking or noxious gas (i.e, biofuel); had undergone pulmonary function testing with a spirometer; and had a post-bronchodilator FEV1/FVC ratio < 0.70. Exclusion criteria included: age <40 years, active infectious lung disease, medical conditions that can affect lean body mass or physical performance such as active neoplastic disease, hyperthyroidism, lower-leg trauma or severe muscle weakness, and conditions that will limit performing dual energy X-ray absorptiometry (DEXA) or conditions that would affect DEXA results such as recent barium intake, metallic instrumentation, and morbid obesity.

This study was conducted in accordance with the Declaration of Helsinki, and was approved by the Departmental Technical Review Board and Research Ethics Board, Philippine General Hospital, University of the Philippines Manila (Registration number 2018–270). Informed consent forms available in English and Filipino version were obtained from all subjects.

Data Collection Procedure

Participants were interviewed and examined to obtain relevant demographic and health information. Measurements for anthropometrics, body composition via BIA, hand grip strength and six-minute walking distance were performed and recorded as follows:

(A) Anthropometric measures

Subjects were weighed after they removed heavy outer garments, shoes, and emptied their pockets. It was recorded to the nearest 0.1 kg. Afterwards, height was recorded using a stadiometer to the nearest centimeter. BMI was calculated by dividing weight (Kg) by height (meter^2).

(B) Body composition

Fresenius Body Composition Monitor was used to determine lean tissue mass or Fat Free Mass. Standard manufacturer protocols were followed.

(C) Hang Grip Strength (HGS)

The subjects were asked to stand and hold the dynamometer in the hand to be tested, with the arm at right angles and the elbow by the side of the body. When ready, the subjects squeezed the dynamometer with maximum isometric effort, which was maintained for about five seconds. The assistant recorded the maximum reading in kilograms (kg). The subjects repeated the test three times, with 30 s rest in between. The assistant recorded the highest value to document each subject's performance.

(D) Six-minute walking distance

Subjects performed six-minute walking test according to international standards. Single personnel duly-trained from the section of Pulmonary Medicine conducted all six-minute walking tests.

(E) Quality of life

Filipino version of COPD assessment tool (CAT) was used to evaluate quality of life. This version of the questionnaire has already been validated. Appropriate permission for the use of the questionnaire was obtained. Cut-offs for low quality of life score is a value score <10, a criterion used patient stratification in 2018 GOLD guidelines.[13]

(F) Pulmonary Function Test

MIR spirolab III diagnostic spirometer was used for pulmonary function test. Personnel duly-trained from the section of Pulmonary Medicine conducted the tests. However, patients with spirometry results within one year from recruitment may not have repeat examination.

Low FFMI and Sarcopenia

Three cutoff values were compared to define low and normal Fat Free Mass Index (FFMI = FFM/height m^2):

1. ATS/ERS Criteria[10] for low FFMI: <16.0 kg/m^2 (M) and <15.0 kg/m^2 (F);
2. Philippine Normative Value[12] for sarcopenia: <12.50 kg/m^2 (M) and <8.33 kg/m^2 (F);
3. Extrapolated 10th percentile values based on Population specific cohort:[12] <13.8 kg/m^2 (M) and <10.5 kg/m^2 (F).

Sarcopenia was defined using EWGSOP definition of low muscle mass and either low muscle strength or low physical performance. Cutoff point specific for Filipinos:[12]

1. low muscle mass as defined by criteria 2;
2. low muscle strength defined as hand grip strength of <24.54 kg for males and <16.10 kg for females.[12]

Sample Size, Sampling and Data Analysis

Power analysis for a point biserial correlation was conducted in G*Power to determine a sufficient sample minimum sample size was computed using G*Power. At least 41 study participants are needed for a two-tailed point biserial correlation to achieve a power of 0.80, with a level of significance of 0.05, and a medium to large effect size (ρ = 0.41).[14] Pulmonary Medicine outpatient clinics were conducted twice per week; convenient sampling was used to achieve sample size.

Statistical analyses were performed using STATA (version 15.1; StataCorp, College Station, TX, USA). The quantitative variables age, BMI, post-bronchodilator FEV1, FEV1/FVC, PIF, PEF, 6MWD, and hand grip strength, were expressed as mean ± SD. The categorical variables gender, comorbidities, 2018 GOLD classification,[14] GOLD stage and CAT, were expressed as count (with proportion).

Point biserial correlation coefficients were computed to determine the relationship between the quantitative variables [pulmonary function (post-bronchodilator FEV1, FEV1/FVC, PIF, PEF); 6MWD; and CAT score] and the dichotomous variables [fat free muscle index (FFMI) low vs. normal; and presence or absence of sarcopenia]. Significant correlation coefficients ($r \neq 0$) were determined by evaluating p-values at $\alpha = 0.05$.

Results

Baseline Characteristics

Forty-three (43) patients were recruited and interviewed for this study, two (2) patients were excluded due to active lung infection, and history of neoplastic disease. The baseline characteristics, demographics, and body composition indices of the patients (n=41) are shown in Table 1. Majority of the subjects were elderly with mean age of 69.22 years, male, with GOLD III classification of airflow limitation and GOLD stage A. The prevalence of being underweight (WHO Asia Pacific criteria BMI <18.5 kg/m2) was 32% (13/41). 25% (7/28) of normal weight COPD patients had hidden muscle depletion (7/28).

Diagnosis of Low FFMI

The characteristics of patients with "low" and "normal" FFMI using three cutoff points are illustrated in Table 2.

Table 1 Baseline Characteristics, Demographics, and Body Composition Indices

Variable	Mean (SD)	Range
Age (years)	69.22 (6.78)	53–81
Gender (male/female)	37/4	
BMI (kg/m2)	20.79 (3.72)	12.11–26.44
Comorbidities		
Diabetes	3 (7.32%)	
Hypertension	13 (31.71%)	
Cardiovascular disease	10 (24.39%)	
GOLD classification of airflow limitation		
I/II/III/IV	1/16/19/5	
GOLD stage		
A/B/C/D	17/14/2/8	
Pulmonary Function		
Post-BD FEV1 (L)	1.08 (0.56)	0.53–1.64
FEV1 (% predicted)	47.53 (14.36)	23–91
PIF (L/min)	170.18 (53)	77–277
PEF (L/min)	172.81 (9.73)	73.2–284
6MWD (meters)	395 (100)	141–596
Hand grip strength (kg)	17.33 (7.13)	2–31
CAT score	10 (9)	9–30
Body composition indices		
Total body weight (kg)	54.24 (9.89)	
Fat mass (kg)	17.10 (10.15)	
Fat mass index (kg/m^2)	8.09 (3.36)	
Fat free mass/Lean tissue mass (Kg)	34.09 (7.75)	
Fat free mass index (kg/m^2)	12.53 (2.34)	

Abbreviations: BMI, body mass index; GOLD, global initiative for chronic obstructive lung disease; post-BD, post-bronchodilator; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; 6MWD, 6-minute walking distance; PEF, peak expiratory flow; PIF, peak inspiratory flow; CAT, COPD assessment test; DEXA, dual energy X-Ray absorptiometry; BIA, bioimpedance analysis.

The ATS/ERS criteria, extrapolated 10th percentile value and Philippine normative value for sarcopenia diagnosed 97%, 73%, and 48% of all COPD patients with low FFMI, respectively.

Using the Philippine normative value for sarcopenia cutoff point, COPD patients with low FFMI had statistically significant reduction in PIF (r= −0.5791, P value 0.0002), PEF (r= −0.4475, P value 0.0055), and hand grip strength (r= −0.4560, P value 0.0027), however low CAT score (r= −0.3422, P value 0.0285). Significant power was achieved in PIF (99%), PEF (88%), and HGS (89%) (Table 3).

Sarcopenic versus Nonsarcopenic COPD

As shown in Table 4, sarcopenic COPD patients had statistically significant reduced peak inspiratory flow (r= −0.6074, P value 0.0001), peak expiratory flow (r= −0.3993, P value 0.0144), hand grip strength (r= −0.3751, P value 0.0007), and CAT score (r= −0.3751, P value 0.0157) compared to non-sarcopenic patients.

Discussion

Our study shows that sarcopenia negatively affects pulmonary function among COPD patients, and, as novelty, is the first attempt to describe body composition of Filipino COPD patients. We examined the relationship between body composition, lung function and exercise capacity, in individuals with "low" or "normal FFMI" according to standard versus population specific cutoff values using bioelectrical impedance analysis – an easy, safe, noninvasive, and convenient method of measuring lean and fat body compartments.

The results of this study showed 32% prevalence of being underweight, which is higher than Latin Americans[15] and other Asian populations (6–10%).[16,17] The disparities seen might be attributed to ethnic differences in body habitus, and perhaps, economic development of countries. Around 25% of normal weight/BMI COPD patients had nutritional depletion as evidenced by low FFMI. This finding is higher compared to other studies[17] where 9–10% of patients normal or high BMI can be associated with FFM depletion. Therefore, BMI can underestimate FFM depletion. Meanwhile, sarcopenia was observed in 35% of our COPD patients, which is again higher compared to another Asian COPD population (vs. 24–25%).[18]

The ATS/ERS criteria cut-off values over-diagnosed low FFMI, as evidenced by 97% diagnosis. These cut-off values were based on 5th percentile of the normative data of Caucasian population using electromagnetic scanning

Table 2 Pulmonary Function Test and COPD Disease Severity Variables According to Low versus Normal FFMI Using Three Cutoff Points

	ATS/ERS Criteria				Extrapolated 10th Percentile				Philippine Normative Value for Sarcopenia			
	Low FFMI (n=40, 97.56%)	**Normal FFMI (n=1, 2.44%)**	r_{pb}	***P value***	**Low FFMI (n=30, 73.17%)**	**Normal FFMI (n=11, 26.83%)**	r_{pb}	***P value***	**Low FFMI (n=20, 48.78%)**	**Normal FFMI (n=21, 51.22%)**	r_{pb}	***P value***
Post-BD FEV1 (L)	1.11 (0.33)	0.76 (–)	0.1648	0.3031	1.12 (0.34)	1.05 (0.32)	0.1039	0.5178	1.04 (0.33)	1.17 (0.33)	−0.2009	0.2080
PIF (L/min)	162.88 (59.55)	228 (–)	−0.1793	0.0878	155.31 (63.13)	189.1 (43.19)	−0.2536	0.1356	132.00 (49.76)	201.24 (48.15)	−0.5791	0.0002*
PEF (L/min)	168.08 (66.36)	180 (–)	−0.0295	0.8622	166.62 (70.56)	173.2 (52.18)	−0.0446	0.7931	139.88 (52.61)	198.50 (65.39)	−0.4475	0.0055*
6MWD (meters)	337.80 (89.88)	501 (–)	−0.2093	0.1891	385.27 (65.73)	368.64 (142.25)	0.0811	0.6140	388.70 (58.91)	373.29 (114.34)	0.0848	0.5979
Hand grip strength (Kg)	17.06 (7.01)	28 (–)	−0.2368	0.1361	16.57 (6.83)	19.41 (7.83)	−0.1767	0.2690	14.00 (5.67)	20.50 (7.02)	−0.4560	0.0027*
CAT score	11.48 (6.38)	22 (–)	−0.2495	0.1157	10.43 (6.44)	15.27 (5.50)	−0.3295	0.0354*	9.45 (5.63)	13.90 (6.66)	−0.3422	0.0285*

Note: *Indicates statistical significance.
Abbreviations: post-BD, post-bronchodilator; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; 6MWD, 6-minute walking distance; PEF, peak expiratory flow; PIF, peak inspiratory flow; CAT, COPD assessment test; r_{pb}, (point biserial coefficient).

instrument,[19] whose body habitus are larger and prevalence of obesity is higher. Therefore, these cutoff values were not applicable to our population. Hence, population specific cutoff values for defining low FFMI[12] were compared using the −2SD and 10th percentile values resulting in 48% and 78% diagnosis, in which the former has generally at close proximity of prevalence to another Asian COPD population.[16] The Philippine normative value cutoff for sarcopenia has proven its strength to show impact on clinically significant COPD related disease severity variables; nonetheless the authors support the use of the less stringent criteria, the extrapolated 10th percentile values, as screening cutoff for COPD patients. These criteria allow clinical interventions before the onset of clinically significant irreversible effects of muscle loss on pulmonary function and muscle strength.

The study showed significant correlation between low FFMI, sarcopenia, and impaired lung function, expressed as PIF and PEF, but not FEV1. These findings showed that fat free mass affects respiratory muscle strength variables, and not airflow obstruction. These results validated a previous study by Engelen et al,[20] where nutritional depletion was correlated with decreased function of both muscle groups, preferentially peripheral muscles. The clinical utility of PIF and PEF as measures of a patient's inspiratory and expiratory effort, are useful to assess the patient's ability to do effective inhalation for inhaler medication[21] and for monitoring disease stability.[22]

Interestingly, our study showed that quality of life scores as measured by COPD assessment test (CAT) were lower among the low FFMI and sarcopenic group, which is contrary to other studies.[23,24] In the study of Shoup et al,[24] where St. Georges' Respiratory Questionnaire was utilized as measure of health-related quality of life, influence of nutritional depletion was mediated through increased levels of dyspnea. However, since the study was limited to information of patients' inhaler compliance (pharmacologic intervention to address dyspnea), its potential contribution to disparity of results is likely.

Lastly, our study was limited by its primary design as a relationship study between ordinal (low/normal FFMI) and continuous variables (COPD related disease severity variables), hence we recommend larger sample size for precise correlation between two continuous variables.

Conclusion

The prevalence of having sarcopenia and being underweight is higher among Filipino COPD patients than shown in other population studies. Low Fat Free Mass

Table 3 Power Analysis of Point Biserial Correlation

	ATS/ERS		Extrapolated 10th Percentile		Philippine Normative Value for Sarcopenia	
	Effect Size	**Achieved Power**	**Effect Size**	**Achieved Power**	**Effect Size**	**Achieved Power**
Post-BD FEV1 (L)	0.1648	18%	0.1039	10%	−0.2009	25%
PIF (L/min)	−0.1793	21%	−0.2536	37%	−0.5791	99%*
PEF (L/min)	−0.0295	5%	−0.0446	6%	−0.4475	88%*
6MWD (meters)	−0.2093	27%	0.0811	8%	0.0848	8%
Hand grip strength	−0.2368	33%	−0.1767	20%	−0.4560	89%*
CAT score	−0.2495	36%	−0.3295	59%	−0.3422	62%

Note: *Indicates significant power was achieved.
Abbreviations: post-BD, post-bronchodilator; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; 6MWD, 6-minute walking distance; PEF, peak expiratory flow; PIF, peak inspiratory flow, CAT, COPD assessment test.

Table 4 Pulmonary Function Test and COPD Disease Severity Variables According to Presence and Absence of Sarcopenia

Variables	Sarcopenic (n=19, 46.34%)	Nonsarcopenic (n=22, 53.66%)	r_{pb}	*P value*
Post-BD FEV1 (L)	1.04 (0.33)	1.16 (0.32)	−0.1800	0.2601
PIF (L/min)	128.44 (48.66)	200.94 (46.73)	−0.6074	0.0001*
PEF (L/min)	141.54 (53.62)	193.84 (66.71)	−0.3993	0.0144*
6MWD (meters)	388.89 (60.52)	373.82 (111.61)	0.0828	0.6068
Hand Grip Strength (Kg)	13.42 (5.18)	20.70 (6.92)	−0.5097	0.0007*
CAT score	9.11 (5.57)	14.00 (6.52)	−0.3751	0.0157*

Note: *Indicates statistical significance.
Abbreviations: post-BD, post-bronchodilator; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; 6MWD, 6-minute walking distance; PEF, peak expiratory flow; PIF, peak inspiratory flow; CAT, COPD assessment test; $r_{pb,}$ (point biserial coefficient).

Index and sarcopenia were correlated with reduced lung function and upper arm muscle strength. These findings shall serve as a foundation for future studies to establish appropriate rehabilitation and nutritional support to preserve lung function among COPD patients.

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Author Contributions

Study concept and design: JRC, ABA, MLT; COPD data acquisition: JRC, ABA; sarcopenia data acquisition: MLT; quality control of data and algorithms: JRC, ABA, MLT; data analysis and interpretation: JRC, ABA, MLT; statistical analysis: JRC, ABA, MLT; manuscript preparation: JRC, ABA, MLT; manuscript editing, review and final approval: JRC, ABA, MLT. All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The primary author has no conflict of interest in any form (financial, proprietary, professional) with the study, however the co-author (ABA) has acted as a paid freelance lecturer for Abbott and Nestle Philippines but did not receive funding for research carried out in this work. The authors report no other conflicts of interest in this work.

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