HEALTH SCIENCES QUARTERLY
Volume : 1
Issue : 2
2021
E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2021-05-21
Accepted: 2021-06-09

ORIGINAL ARTICLE

An evaluation of quantitative body composition on thoracic computed tomography and the effect on clinical severity in patients with chronic obstructive pulmonary disease

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Abstract

The aim of this study was to evaluate the effect on disease severity of the quantitative measurements of pectoral muscle area (PMA), pectoral muscle index (PMI), pectoral muscle density (PMD), subcutaneous adipose tissue (SAT) and mediastinal adipose tissue (MAT) taken on thoracic computed tomography (CT) of patients with chronic obstructive pulmonary disease (COPD), according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification. A retrospective screening was made of patients diagnosed with COPD and applied with thoracic CT and respiratory function tests. A record was made of height, weight, body mass index, and smoking history (packet/year). On thoracic axial CT images, the PMA, PMI, PMD, SAT, and MAT values at the aortic arch level were calculated quantitatively using OsiriX software (Pixmeo, Switzerland). The patients were grouped as A-B-C-D according to the GOLD 2018 guidelines. Then two groups were formed as mild-moderate COPD (GOLD A-B) and severe COPD (GOLD C-D). The relationship was evaluated between clinical severity and quantitative body composition values according to the GOLD classification. A total of 80 patients diagnosed with COPD were included in the study comprising 61 males and 19 females. The GOLD A-B group included 43 (53.75%) patients and the GOLD C-D group, 37 (46.25%) patients. No significant difference was determined between the two groups in respect of the PMA, PMI, and PMD values (p=0.001). A statistically significant difference was determined between the groups in respect of the SAT and MAT values (p=0.001, p=0.002, respectively). A cutoff value of <30.04 in PMD (0.964; 95%CI:0.928-1) showed the best performance in predicting the mild-moderate COPD patients (GOLD A-B) with 92% sensitivity and 93% specificity. The results of this study demonstrated that PMD showed the best quantitative body composition performance in the differentiation of mild-moderate and severe COPD disease.

Keywords: *Body composition, chronic obstructive pulmonary disease, quantitative analysis, thoracic computed tomography*

Citation: Kaya F, Ozgul E, Balci A, Bozkurt E, Atay E. An evaluation of quantitative body composition on thoracic computed tomography and the effect on clinical severity in patients with chronic obstructive pulmonary disease. Health Sci Q. 2021;2:75-81. https://doi.org/ 10.26900/hsq.1.2.04

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Introduction

Due to the heterogeneity of chronic obstructive pulmonary disease (COPD), there is a need for more descriptive biomarkers in diagnosis beyond pulmonary function tests [1]. Thoracic computed tomography (CT) has been used for many years for the visual diagnosis of emphysema and to obtain a precise evaluation of the presence of COPD [2]. It is thought that body composition, which may vary in COPD patients, is a marker of the clinical process of the disease. In this context, body mass index (BMI) is related to the increased mortality rate in COPD patients. It is known that in previous studies, lean muscle mass has been preferred to BMI in COPD patients [3-5]. There is also known to be clinical importance of different body components other than lean muscle mass and BMI. Skin fold thickness, bio-impedance, and dual-energy x-ray absorbancy are other methods used to determin body composition. Previous studies have suggested that CT measurements could provide additional information about the body composition of patients who smoke [6,7]. Evaluation of the cross-sectional area of the mid-thigh muscle has been shown to be a stronger predictor of mortality in COPD than BMI [6]. Quantitative body composition values such as pectoral muscle area (PMA), pectoral muscle index (PMI), pectoral muscle density (PMD), subcutaneous adipose tissue (SAT) and mediastinal adipose tissue (MAT) have been examined on thoracic CT images in COPD and several pulmonary diseases [8-13]. In previous studies, muscle mass has been reported to be significantly reduced in COPD patients and has shown a correlation with disease severity [10,11]. The aim of this study was to evaluate the relationship of the body composition values of PMA, PMI, PMD, SAT, and MAT, measured quantitatively on thoracic CT, with disease severity according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of COPD patients.

Materials and Methods

Patients diagnosed with COPD and applied with thoracic CT and respiratory function tests within the last year were identified from a retrospective screening of the hospital records system. Patients were excluded if there was an interval of more than one month between COPD diagnosis and respiratory function tests and CT scans, or if they had a known malignancy. A total of 80 COPD patients with non-contrast thoracic CT taken within the last year were included in the study. A record was made for each patient of height, weight, body mass index, and smoking status (packet/year).

Computed Tomography Technique

The images were acquired without contrast on a Toshiba Aquilion Prime (80x2) multi-slice CT device (Toshiba Medical Systems, Japan). After topogram acquisition, non-contrast images were taken during deep inspirium on two consecutive slices from the apexes as far as the bilateral adrenal glands, using tube voltage 120 kV, collimation 05x80 mm, image area 370mm, matrix 512 x 512, rotation speed 0.35 secs, table level 15 mm/sec, pitch factor 0.813 and helical pitch 65.0. The scanning time was 2-4 seconds.

GOLD Classification

Patients with post-bronchodilator FEV1/FVC<70% were accepted as having airway obstruction and were grouped as A-B-C-D according to the GOLD 2018 guidelines. In this classification system, GOLD A is defined as patients with low risk, few symptoms, 0-1 flare-ups, and mMRC grade 0-1 or CAT score <10, GOLD B as patients with low risk, more symptoms, 0-1 flare-ups, and mMRC grade ≥2 or CAT score ≥10, GOLD C as patients with high risk, few symptoms, ≥2 flare-ups, and mMRC grade 0-1 or CAT score <10, and GOLD D as patients with high risk, more symptoms, ≥2 flare-ups, and mMRC grade ≥2 or CAT score ≥10. For the evaluations in this study, two groups of patients were formed as mild-moderate (GOLD A-B) and severe (GOLD C-D).

Quantitative Computed Tomography Analysis

From a single axial slice thoracic CT image taken immediately over the aortic arch, measurements were taken of PMA, PMI, and PMD, and at the pectoral muscle level, measurements of SAT and mediastinal adipose tissue with OsiriX software (Pixmeo, Switzerland) in each patient (Figure 1). PMA was measured with threshold values of -50 to 90 Hounsfield Units (HU) [8,12], and SAT and MAT

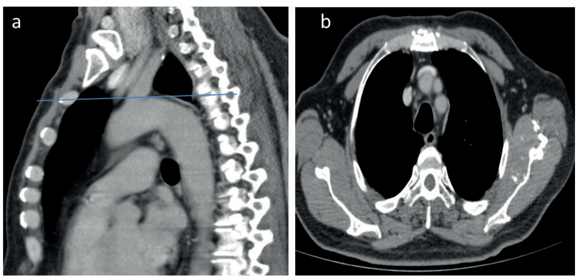

Figure 1. Determination of the cross-sectional area where quantitative body composition measurements were to be taken from the level of the aortic arch. (Blue line)

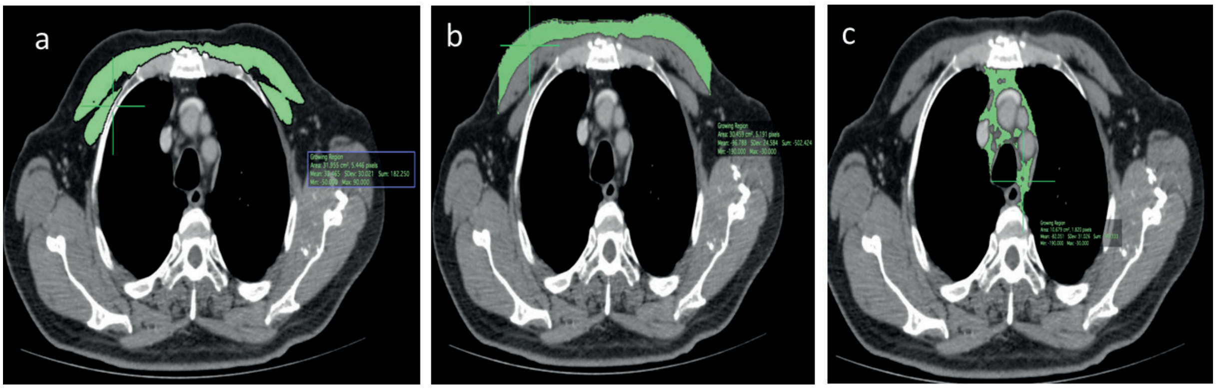

Figure 2. Measurement of PMA and SAT and MAT values from the same level

with threshold values of 190 to -30 HU (10). PMI (cm²/m²) was obtained as the ratio of height squared (m²) to muscle area (cm²) (Figure 2).

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS 25 software. Conformity of the data to normal distribution was assessed with histogram analysis and the Kolmogorov-Smirnov test. Variables showing normal distribution were analyzed with parametric tests, and those not showing normal distribution with non-parametric tests. In the analysis of differences between categorical variables, the Chi-square test was applied, and comparisons of variables between groups were made using the Student's t-test, the Mann Whitney U-test, and the Kruskal-Wallis test. ROC analysis was applied to determine the cut-off values for successful subtraction models and determine these values' sensitivity and specificity. Results were stated in a 95% confidence interval and a value of $p<0.05$ was accepted as statistically significant.

Results

The evaluation was made of a total of 80 COPD patients, comprising 61 males and 19 females, with a mean age of 61.5±11.37 years and a mean BMI of 27.72±15.25.The smoking status of the patients was determined as a mean of 42.71±24.54 packet/year. No significant difference was determined between the genders in respect of weight, BMI, FVC%, and FEV1%. The GOLD classification groups were as follows; GOLD A: 22 patients (27.5%), GOLD B: 21 (26.3%), GOLD C: 19 (23.8%), and GOLD D:18 (22.5%). The mild-moderate COPD (GOLD A-B) group included 43 (53.75%) patients and the severe COPD (GOLD C-D) group, 37 (46.25%) patients (Table 1).

Evaluation of body composition on thoracic CT in COPD patients

In the COPD patients, PMA was measured as 40.41±12.51 cm², PMI as 14.10±4.18 cm²/m², PMD as 29.52±10.19, SAT area as 42.08±28.89 cm², and MAT area as 12.56±7.28 cm². (Table 1). A statistically significant difference was determined between the mild-moderate COPD group (GOLD A-B), and the severe COPD group (GOLD C-D) in respect of PMA, PMI and PMD values (p=0.001). A statistically significant difference was determined between the two groups in respect of the SAT and MAT values (p=0.001, p=0.002, respectively). No difference was determined between the groups in respect of cigarette smoking (p=0.265). A statistically significant difference was determined between the two groups in respect of BMI (p=0.01) (Table 2).

Table 1. Baseline characteristics of the patients with COPD

		COPD (n:80)
Sex	male	73(91.3%)
	female	7(8.8%)
Age, years		61.05±11.37
Height, cm		1.69±0.07
Weight, kg		79.61±15.25
BMI, kg/m²		27.72±15.25
Smoking history pack/years		42.71±24.54
GOLD stage	A	22(27.5%)
	B	21(26.3%)
	C	19(23.8%)
	D	18(22.5%)
FEV1 (% predicted)		67.51±16.51
FEV1/FVC		59.15±10.36
PMA (cm²)		40.41±12.51
PMI (cm²/m²)		14.10±4.18
PMD (HU)		29.52±10.19
SAT (cm²)		42.08±28.89
MAT (cm²)		12.56±7.28

PMA: Pectoral muscle area, PMI: Pectoral muscle index, PMD: Pectoral muscle density, SAT: Subcutaneous adipose tissue, MAT Mediastinal adipose tissue, BMI: body mass index

Table 2. Characteristics of the mild-moderate and severe COPD patients

	GOLD A-B (n:43)	GOLD C-D (n:37)	p
PMA (cm^2)	46.72±13.04	33.08±6.52	<0.001
PMI (cm^2/m^2)	15.91±4.22	11.99± 3.01	<0.001
PMD (HU)	36.79±4.62	21.07±8.17	<0.001
SAT (cm^2)	30.37±16.67	55.69±33.95	<0.001
MAT (cm^2)	10.31±5.54	15.17±8.22	0.002
BMI	26.43±4.14	29.23±5.32	0.01
Smoking history pack/years	40.21±18.29	45.62± 24.74	0.265

PMA:Pectoral muscle area, PMI:Pectoral muscle index, PMD: Pectoral muscle density, SAT: Subcutaneous adipose tissue, MAT: Mediastinal adipose tissue, BMI: body mass index

Table 3. ROC analysis of the diagnostic performance of BMI and quantitative body composition parameters according to the ROC analysis for the prediction of the clinical severity of mild-moderate and severe COPD patients according to the GOLD ABCD classification

AUC		Sensitivity (95% CI)	Specificity (95% CI)	Cut-Off
PMA	0.833(0.747-0.918)	67.4	79.4	<38.54
PMI	0.785 (0.685-0.885)	60.5	89.2	<15.06
PMD	0.964 (0.928-1)	93	92	<30.04
SAT	0.755 (0.648-0.862	64.9	79.1	>42.85
MAT	0.677 0.648-0.862)	56.8	76.7	>12.78
BMI	0.658 (0.537-0.780)	59.5	62.1	>29.05

PMA:Pectoral muscle area, PMI:Pectoral muscle index, PMD: Pectoral muscle density, SAT: Subcutaneous adipose tissue, MAT: Mediastinal adipose tissue, BMI: body mass index

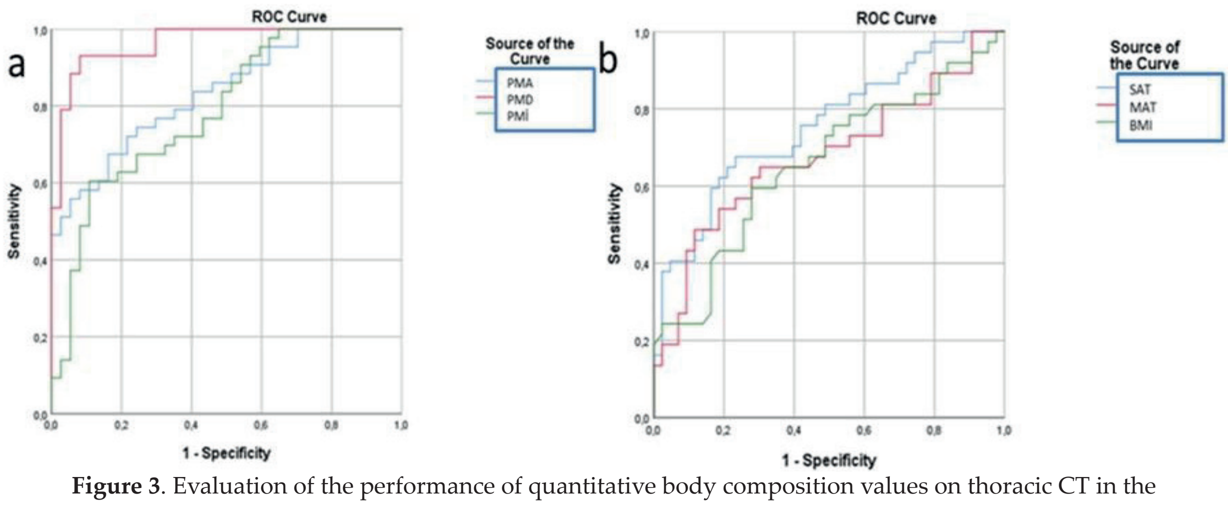

Figure 3. Evaluation of the performance of quantitative body composition values on thoracic CT in the Adifferentiation of mild-moderate (GOLD A-B) and severe (GOLD C-D) COPD.

Evaluation of the performance of the body composition values on thoracic CT according to GOLD ABCD

The best performance in predicting the mild-moderate COPD patients (GOLD A-B) was shown by PMD with a cutoff value of <30.04 (0.964; 95% CI:0.928-1) with a sensitivity of 92% and specificity of 93%, and the lowest performance was shown by PMI with a cutoff value of <15.06 (0.785; 95% CI:0.685-0.885) with 89.2% sensitivity and 60.05% specificity. The best performance in the prediction of severe COPD patients (GOLD C-D) was shown by SAT with a cutoff value of >42.85 (0.755; 95% CI:0.648-0.862) with 79.1% sensitivity and 64.9% specificity, and the lowest value was BMI with a cutoff value of >29.05 (0.658; 95% CI:0.537-0.780) with 62.1% sensitivity and 59.5% specificity (Table 3, Figure 3).

Discussion

The results of this study demonstrated that body composition measurements on thoracic CT can be used to differentiate mild-moderate and severe disease in COPD patients. A statistically significant difference was determined between mild-moderate and severe COPD patients in respect of the PMA, PMI, SAT, and MAT values measured at the level of the aortic arch ($p<0.05$). The PMD value showed the best performance in the prediction of mild-moderate COPD patients. The well-known simple approach used in this study was the measurement of single cross-sectional areas on thoracic CT scans to evaluate the pectoralis muscle and subcutaneous fat content [8]. Skeletal muscle mass is a lifetime predictor of outcomes related to COPD [5,13]. It has been reported that PMA determined with bio-electric impedance analysis (BIA) in healthy subjects on a single CT image is related to total skeletal muscle mass [14].

Several studies in the literature have examined the relationship between low muscle mass and mortality in different populations with different pulmonary diseases including COPD, cancer, idopathic pulmonary fibrosis and surgical outcomes [15-27]. The majority of measurements derived from CT show a correlation with the severity of the health status. It is important that both qualitative and quantitative skeletal muscle loss is referred to with the term sarcopenia in these studies. However, muscle quality shows information much more relevant to the prediction of patient health and outcomes than the amount of muscle [16-18]. Lipid accumulation in muscles is seen on CT as low muscle density, and fatty accumulation in muscles is known to decrease strength independently of muscle mass [28]. Bak et al. [29] evaluated the effect of PMA and PMD to determine correlations between COPD severity and changes in longitudinal lung function in COPD patients. A relationship was determined between parameters derived from CT and initial pulmonary function and the severity of emphysema ($p<0.05$). In a study by Park et al. [15], CT histogram analysis was used to obtain quantitative measurements from the intercostal muscles and the latissimus dorsi muscle to show fatty infiltration within the muscle. These analyses were correlated with the severity of COPD, and it was determined that intercostal muscle mass decreased and intercostal fatty tissue increased associated with worsening COPD severity. In the same study, intercostal muscle mass adjusted according to BMI was observed to be significantly higher in GOLD A than in GOLD C and D patients, and thus it was reported that intercostal muscle mass could be a marker of COPD severity. A moderate level correlation was also shown in that study between COPD severity and intercostal muscle fat content [15]. McDonald et al. evaluated the relationship between PMA on CT and COPD morbidity. A significant relationship was determined between PMA and parameters related to COPD such as spirometric measurements, shortness of breath, and walking distance [13]. Similarly, in the current study, PMA, PMI, and PMD were determined to be related to COPD severity. When the patients were grouped according to the GOLD classification; PMA, PMI, and PMD were observed to be statistically significantly lower in the severe COPD group (GOLD C-D) than in the mild-moderate COPD group (GOLD A-B) ($p<0.001$). However, as there was no long-term follow up of these patients, the relationship with morbidity and mortality could not be evaluated.

In the study by McDonald et al. [13], PMA was related to the GOLD grade, and there was evidence of a more statistically significant relationship of COPD severity with these measurements than with BMI. In the current study, PMD and PMA showed the best performance in the differentiation of mild-moderate and severe COPD patients. In a study by Furutate et al, the SAT value was reported to be negatively correlated with emphysema progression over a 6-year period ($p<0.01$). In the same study, visceral adipose tissue did not decrease with the severity of emphysema, and showed a positive correlation with the degree of dyspnea [30]. Grace et al. [31] reported that increased subcutaneous thoracic adipose tissue was less related to the progression of emphysema over time in smokers, and increased mediastinal adipose tissue volume was related to a decreased walking distance and increased interleukin-6 (IL-6) levels. In the same study, there was reported to be no significant correlation of IL-6 and C-Reactive Protein (CRP) levels with the longitudinal change in the percentage of pulmonary emphysema or pulmonary function, and walking test. In the current study, the SAT and MAT values were observed to be statistically significantly higher in severe COPD patients than in the mild-moderate group ($p=0.001$, $p=0.002$, respectively). However, biomarkers such as IL-6 and CRP were not evaluated in this study. To be able to evaluate changes occurring in MAT, it can be considered necessary to evaluate inflammatory changes associated with COPD severity or changes associated with smoking together. Therefore, there is a need for further studies.

There were some limitations to this study, primarily the retrospective design and the low number of patients. A second limitation was the lack of a control group, and the third, comorbidities other than COPD that could affect body composition were not known. In addition, as there was no long-term follow-up, the mortality risk could not be investigated. Finally, in the SAT measurement in female patients, breast fatty tissue in the cross-sectional area could have caused a higher measurement of SAT in some patients.

Conclusion

In conclusion, body composition can be evaluated quantitatively in routine follow-up on thoracic CT in COPD patients without any additional radiation. In addition, the results of this study showed that that the quantitative body composition values measured with thoracic CT can be used in the differentiation of mild-moderate and severe disease in COPD patients. The results also demonstrated that PMD showed the best quantitative body composition performance in the differentiation of mild-moderate and severe COPD patients. Nevertheless, there is a need for further prospective, long-term studies of the use of thoracic CT in the evaluation of body composition.

Funding
The authors declared that this study has no financial support.

Conflict of interest
The authors have no conflicts of interest declared.

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