The Relationship between Body Composition and Clinical Parameters in Chronic Obstructive Pulmonary Disease

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Objective: *Identify a correlation between body mass index (BMI) and fat-free mass index (FFMI) to clinical parameters in chronic obstructive pulmonary disease.*

Material and Method: *The cross-sectional study was conducted at a single visit involving stable chronic obstructive pulmonary disease (COPD) patients at the outpatient chest clinic of the Chiang Mai University Hospital, Thailand. Eligible patients were evaluated for BMI, FFMI, lung function, modified medical research council (mMRC) dyspnea score, COPD assessment test (CAT) score, and number of acute exacerbation (AE) in the past year. The correlations of FFMI and BMI with other parameters were determined using Pearson correlation coefficient analysis. Body composition was categorized into four groups, normal, semi-starvation, muscle atrophy/sarcopenia, and cachexia based on BMI and FFMI. Statistical significance was accepted at p-value <0.05.*

Results: *One hundred twenty one stable COPD patients met study inclusion criteria. The FFMI showed a strong correlation with BMI (r = 0.792, p<0.001). The FFMI, but not BMI, was significantly correlated with mMRC, precentage of predicted forced expiratory volume in first second (FEV_1), and CAT score (r = -0.315, 0.214, and -0.278, respectively). Body composition was categorized into four groups: normal body composition (n = 62, 51.2%), semi-starvation (n = 4, 3.3%), sarcopenia/ muscular atrophy (n = 12, 9.9%), and cachexia (n = 43, 35.5%).*

Conclusion: *FFMI, but not BMI, was significantly correlated with dyspnea severity, lung function, and quality of life. Body composition category assignment is a useful clinical tool.*

Keywords: *Chronic obstructive pulmonary disease, Fat-free mass index, Body mass index, Quality of life, Correlation*

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Chronic obstructive pulmonary disease (COPD) is an important and growing cause of morbidity and mortality worldwide. Besides lung function impairment, multiple extra-pulmonary systemic effects and consequences leading to comorbid conditions are related to COPD, such as skeletal muscle wasting, osteoporosis, cardiovascular disease, and diabetes mellitus[1]. Decreased skeletal muscle mass is one of the most investigated extra-pulmonary features in COPD. Loss of body weight and depletion of fat-free mass (FFM) are common and important risk factors for mortality in COPD[2,3]. In addition, low FFM is associated with impaired health status[4,5].

Nutritional status is mainly evaluated using body mass index (BMI) measurement changes. However, recent data suggests that fat-free mass index (FFMI) is a more complete estimate of nutritional health than BMI[3,6,7]. This might be attributed to the fact that loss of skeletal muscle mass is the main cause of weight loss in COPD, whereas loss of fat mass contributes to a lesser extent, leading to the plausible theory that FFMI reflects the muscle mass better than BMI. Therefore, monitoring weight loss with particular evaluation of FFM depletion is essential for the assessment of nutritional status of COPD patients. Methods most commonly used include skin-fold anthropometry (SFA), bioelectrical impedance analysis (BIA), and bioimpedance spectroscopy (BIS). Recently, dual-energy X-ray absorptiometry (DXA) has been suggested as a gold standard method for the measurement of body composition including in COPD patients[8,9]. DXA is the most expensive method and the equipment is not commonly available in many hospitals. A previous study found no significant differences in mean FFM as determined by DXA, BIA, and SFA[10]. Although FFM assessment provides

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important information in COPD care and should be considered in the routine evaluation of patients with this condition[7], it is not widely utilized in clinical practice in Thailand. Therefore, we identify the correlation between BMI and FFMI and correlation of each index to clinical parameters.

Material and Method

Study population

One hundred eighty COPD patients were screened at the outpatient chest clinic of Chiang Mai University Hospital, Chiang Mai, Thailand between April 2015 and July 2015. Recruitment criteria included: patients aged over 40 years with the diagnosis of COPD based on post-bronchodilator (BD) ratio of forced expiratory volume in first second (FEV_1)/forced vital capacity (FVC) <0.7[11], ex-smokers with a smoking history of more than 10 pack-years, no history of acute exacerbation (AE) for at least three months prior to the enrollment, and receiving standard pharmacological treatment for COPD. Patients meeting any of the following respiratory criteria were excluded; current diagnosis of asthma, current active respiratory disorders other than COPD, e.g., lung cancer, tuberculosis, or other significant chest radiographic findings not associated with COPD (documented within the past 1 year). Those with specific disease states such as chronic liver disease, diabetes mellitus, renal failure, clinically apparent heart failure, orthopedic disease, neurologic disease, as well as long-term use of systemic corticosteroids were also excluded.

BMI and FFMI assessment

BMI was calculated using the weight/height squared method. The FFM was measured by using a foot-to-foot BIA body composition analyzer system (Tanita SC-330P, Corporation of America Inc., Arlington Heights; IL, United States)[12]. The Tanita BIA system provides a valid measure of percent body fat in older adults, and could be a convenient and practical approach for assessment in public health settings[12]. The FFM was standardized for height and expressed as FFMI (FFM/height squared)[13]. Low BMI cut-off values were less than 18.5 kg/m^2 for men and women[14] and low FFMI values were less than 16 kg/m^2 in men and less than 15 kg/m^2 in women[15]. Body composition was divided into four categories: normal body composition [BMI >18.5 and FFMI >16 (men) or >15 (women)]; semi-starvation [BMI ≤18.5, and FFMI >16 (men) or >15 (women)]; muscle atrophy/sarcopenia [BMI >18.5, and FFMI ≤16 (men) or ≤15 (women)], and cachexia [BMI ≤18.5 and FFMI ≤16 (men) or ≤15 (women)][3,16].

Pulmonary function test

All subjects were evaluated for FVC, FEV_1, and ratio of FEV_1/FVC using a spirometer (Vmax series 22, Sensor Medics; Bilthoven, Holland) following the American Thoracic Society (ATS)/the European Respiratory Society (ERS) standard guidelines[17]. Values were calculated using the National Health and Nutrition Examination Survey III (NHANES III) reference equations[18]. However, for Asians, a correction factor of 0.88 was applied to the FVC and FEV_1 predicted[19].

Quality of life and dyspnea severity

The Thai version of COPD assessment test (CAT)[20] was administered to all subjects. Each item was scored from 0 to 5 resulting in a total score ranging from 0 to 40, corresponding to the best and worst health status in patients with COPD[21]. Dyspnea severity was classified using the modified Medical Research Council (mMRC) dyspnea scale[22].

Study procedures

The cross-sectional designed study was conducted during a single visit. All subjects underwent a medical history and medical examination by a pulmonologist, standard spirometry method measured FEV_1, FVC, and ratio of FEV_1/FVC was calculated for each patient. Eligible patients were then measured for BMI, FFMI, mMRC, and administered the CAT questionnaire for assessing quality of life. All patients were classified in the four COPD categories according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines[11]. The study was approved by the Ethics Committees of the Faculty of Medicine, Chiang Mai University [Institutional Review Board (IRB) approval number: MED-2558-02907, date of approval: March 26, 2015] and filed under the Thai Clinical Trials Registry (Study ID: TCTR20150407001, date of approval: April 6, 2015). Written informed consent was obtained from each patient prior to the study.

Statistical analysis

Data were presented as mean ± SD or n (%). The correlations of FFMI and BMI (dependent variables) with clinical parameters (independent variables including lung function, dyspnea scale, CAT score, and numbers of AE in the past year) were determined using Pearson correlation coefficient

analysis. We used the following cut-offs parameters: 0<| r |<0.3 = weak correlation; 0.3<| r |<0.7 = moderate correlation; | r | >0.7 = strong correlation[23]. Statistical significance of differences between groups stratified by body composition or disease severity was determined using the one-way analysis of variance (one-way ANOVA). Differences in proportions were determined using Chi-squared tests. Statistical significance was accepted at the *p*-value <0.05. All analyses were carried out with the SPSS statistical package, version 16 for Windows (SPSS; Chicago, IL).

Results

Correlation coefficients of BMI and FFMI with lung function, dyspnea, quality of life, and number of AE

One hundred twenty one stable COPD patients that met inclusion criteria were enrolled. The FFMI showed a strong correlation with BMI (r = 0.792, *p*-value <0.001; Fig. 1). Correlation data for all patients were summarized in Table 1. Briefly, FFMI was significant correlated with mMRC (moderate), FEV_1, and CAT. In contrast, BMI was not significantly correlated with all parameters being observed.

FFMI and BMI in the four GOLD classifications

The FFMI was statistically higher only in patients with GOLD-A classification when compared with GOLD classification D (*p*-value = 0.008, Fig. 2A). BMI was not statistically different among all GOLD classifications (*p*-value = 0.788, Fig. 2B).

GOLD classifications in the four body composition categories

The body composition was separated into four categories, normal body composition (n = 62, 51.2%),

Table 1. Correlation coefficients of BMI and FFMI with lung function, dyspnea, quality of life, and number of AE in the study group (n = 121)

Variables	Body composition			
	FFMI	*p*-value	BMI	*p*-value
FEV_1 (% predicted)	0.214	0.019*	0.041	0.661
mMRC score	-0.315	<0.001*	-0.110	0.230
CAT score	-0.278	0.002*	-0.113	0.219
No. of AE in the last year	-0.050	0.588	0.057	0.532

BMI = body mass index; FFMI = fat-free mass index; FEV_1 = forced expiratory volume in first second; mMRC = modified Medical Research Council scale; CAT = chronic obstructive pulmonary disease (COPD) assessment test; AE = acute exacerbation
Data are presented as Pearson correlation (r) and *p*-value
* Correlation is significant at the 0.05 level

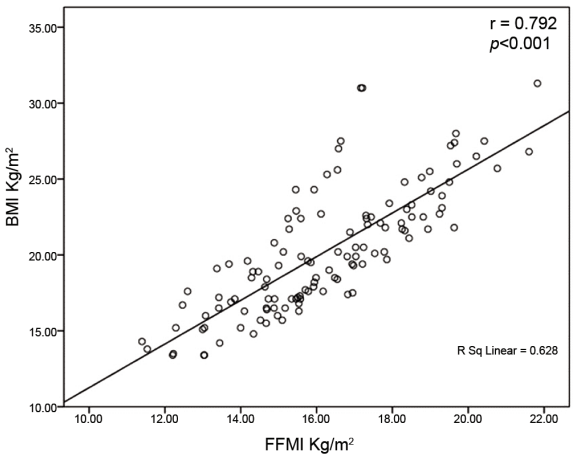

Fig. 1 Correlation between the FFMI and BMI in all COPD patients (r = 0.792, *p*-value <0.001).

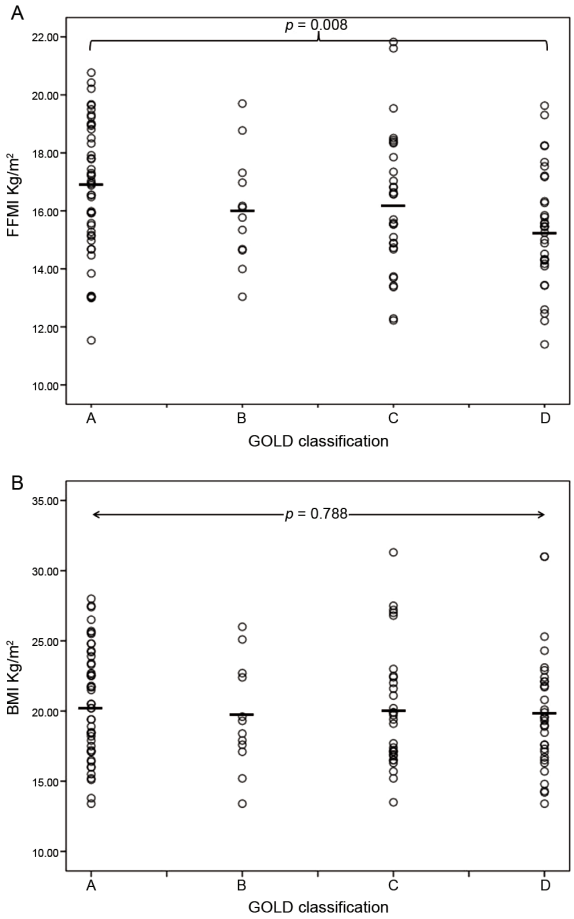

Fig. 2 FFMI and BMI in the four GOLD classifications (A, FFMI and B, BMI). Horizontal lines represent mean values.

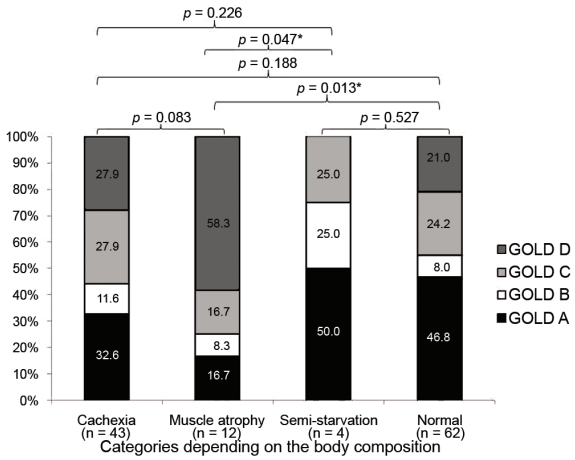

Fig. 3 GOLD classifications in the four categories depending on the BMI and FFMI. Data in graphs represent percentages of patients.

semi-starvation (n = 4, 3.3%), sarcopenia/muscular atrophy (n = 12, 9.9%), and cachexia (n = 43, 35.5%). In the normal composition and semi-starvation categories, about half of the patients were classified into the GOLD-A group. In the muscle atrophy/ sarcopenia category, almost of patients were classified as GOLD-D, which was significantly higher than normal (p-value = 0.013) and semi-starvation (p-value = 0.047) categories. In the cachexia category, the proportion of patients was equally distributed among GOLD A, C, and D groups (Fig. 3).

Discussion

The study result showed that FFMI was highly correlated with BMI and provided information beyond BMI regarding variables expressing disease severity, dyspnea severity, and quality of life. The BMI and FFMI represented different aspects of nutrition abnormalities in COPD. The distribution of the patients in the four categories of body composition in the present study was very similar to the data from a previous report[3]. The prevalence of cachexia was 35.5% in our study group, which was higher than the 22 to 27% reported by previous studies[16,24]. This study showed that the FFMI in GOLD-A group was significantly higher than GOLD-D group. This finding was not observed for BMI. The FFMI better reflected skeletal muscle mass; thus, an important issue is to explain why the skeletal muscle mass diminishes during late disease development, while it remains stable in early stages. This might be attributed to high rest energy expenditure due to increasing work of breathing in combination with inadequate dietary intake[25], physical inactivity due to exercise intolerance[26], excessive apoptosis of skeletal muscle due to increased systemic inflammation[27], the presence of hypoxia and the more frequent use of systemic corticosteroids[28]. The present study does not provide any data in order to confirm the above theories. Progressively increased dyspnea (as expressed by mMRC scale), more severe airway obstruction (as expressed by percentage of predicted FEV_1) may represent critical factors leading to the systemic consequences that affect the FFMI as disease progresses[29]. This is confirmed by our findings, where FFMI was significantly correlated with chronic dyspnea and airway obstruction in the whole study population. A previous study showed that alterations in skeletal muscle mass influenced health-related quality of life (HRQoL) mainly due to increased dyspnea[4,5]. Our finding confirms that FFM depletion affected HRQoL based on the CAT questionnaire responses. This finding indicated that nutritional status might be one of the critical factors affecting the quality of life.

Skeletal muscle wasting is a powerful predictor of mortality in COPD patients, independent of lung function[30]. Clinically, rapid deteriorations in lean body mass was described following an acute exacerbation of COPD, and particularly in more severely diseased patients (FEV_1 is <50%)[31]. Our findings showed similar results to the previous study[31] that FFMI is significantly lower in GOLD-D than other GOLD classifications. Numerous reports showed an association between BMI and mortality risk in COPD[6,32]. Recently, FFMI was shown to predict three years COPD mortality in the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) cohort study[33]. The results of our study indicated that FFMI could be an even better independent predictor of systemic disease severity than BMI.

The present study had some limitations. Firstly, BIA may be less precise than other techniques, such as MRI and DXA, for the assessment of FFM. However, in recently published literature, FFMI has been assessed using BIA[3,16,34,35]. The BIA method is an easier method to estimate FFM without the need for an expensive apparatus, or highly skilled technicians. In a previous study[31], the correlation between BIA and magnetic resonance imaging-measured muscle mass was strongly significant. Another COPD study[36] showed that FFM assessed by BIA was significantly related to muscle fiber cross sectional area taken from a biopsy of muscle tissue from the vastus lateralis, which indicated that whole-body FFM also reflected

lower-limb muscle atrophy in chronic disease. The FFM estimation via BIA was also used in a recent analysis of NHANES III that identified skeletal muscle cut-offs associated with a high likelihood of physical disability[37]. Factors that could limit the use of BIA are apparent old age, severe underlying conditions such as cancer, insulin dependent diabetes, renal failure, and patients with heart failure. In the present study, we tried to diminish influence of the above limitations by excluding unstable patients, those with specific disease status, as well as those with clinically apparent heart failure. Secondly, our study did not measure the correlation between FFMI and exercise capacity such as a six-minute walk distance (6-MWD). A previous study showed a close relationship between 6-MWD and FFMI that should be involved in the routine daily assessment of COPD[29]. Furthermore, we believe that the next step for FFMI evaluation is to investigate whether a close relationship exists between FFMI initial values and disease progression. Thirdly, our study did not include pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), or C-reactive protein (CRP). Fourthly, we could not do further statistical analyses on the differences among the four subgroups of body composition since we had a relatively small sample size in the two subgroups; semi-starvation and sarcopenia/muscular atrophy group.

Conclusion

The FFMI, not BMI, is significantly related to lung function, dyspnea severity,quality of life and reflects skeletal muscle mass depletion. These findings support using FFMI as a screening parameter for characterization of body composition pattern in COPD patients.

What is already known on this topic?

Decreased skeletal muscle is one of the most investigated extra-pulmonary features in COPD. Loss of body weight and depletion of fat-free mass (FFM) are common and important risk factors for mortality in COPD[2,3]. Although FFM assessment provides important information in COPD care and should be considered in the routine evaluation of patients with this condition[7], it is not widely utilized in clinical practices in Thailand.

What this study adds?

This study added the information that the FFMI is a useful clinical screening instrument for characterization of body composition pattern in COPD. The FFMI is more significantly related to lung function, dyspnea severity, and quality of life compared to BMI.

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Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่างองค์ประกอบของร่างกายและลักษณะทางคลินิกในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง

ชายชาญ โพธิรัตน์, วราวุฒิ ไชยวงค์, นิตยา เพชรสุข, เฉลิม ลิ่วศรีสกุล, ชัยวัฒน์ บำรุงกิจ, อรรถวุฒิ ดีสมโชค, ธีรกร ธีรกิตติกุล, อติคุณ ลิ้มสุคนธ์

วัตถุประสงค์: *เพื่อศึกษาความสัมพันธ์ระหว่าง ดัชนีมวลกาย ดัชนีมวลกายส่วนที่ไร้ไขมัน และลักษณะทางคลินิกอื่น ๆ ในผู้ป่วยโรคปอดอุดกั้นเรื้อรัง*

วัสดุและวิธีการ: *การศึกษาภาคตัดขวางในผู้ป่วยโรคปอดอุดกั้นเรื้อรังที่อยู่ในสภาวะคงที่ โดยผู้ป่วยจะได้รับการประเมินองค์ประกอบของร่างกาย (ดัชนีมวลกายและดัชนีมวลกายส่วนที่ไร้ไขมัน) รวมถึงลักษณะทางคลินิกอื่น ๆ ได้แก่ การตรวจสมรรถภาพปอด ระดับอาการหอบเหนื่อย ระดับคุณภาพชีวิต และจำนวนครั้งของการกำเริบเฉียบพลันในช่วงหนึ่งปีที่ผ่านมา ใช้การวิเคราะห์ค่าสัมประสิทธิ์สหสัมพันธ์เพียร์สันเพื่อหาความสัมพันธ์ระหว่างดัชนีมวลกาย ดัชนีมวลกายส่วนที่ไร้ไขมัน และลักษณะทางคลินิกต่าง ๆ นอกจากนี้แล้วยังได้แบ่งผู้ป่วยออกเป็น 4 กลุ่ม โดยใช้ค่าดัชนีมวลกายและดัชนีมวลกายส่วนที่ไร้ไขมันเป็นเกณฑ์ คือ กลุ่มที่มีองค์ประกอบของร่างกายปกติ กลุ่มขาดสารอาหาร กลุ่มกล้ามเนื้อลีบ และกลุ่มผอมหนังหุ้มกระดูก กำหนดค่าการยอมรับระดับนัยสำคัญทางสถิติไว้ที่ p-value <0.05*

ผลการศึกษา: *มีผู้ป่วยโรคปอดอุดกั้นเรื้อรังเข้าร่วมการศึกษาทั้งสิ้น 121 ราย ความสัมพันธ์ระหว่างดัชนีมวลกายและดัชนีมวลกายส่วนที่ไร้ไขมันอยู่ในระดับสูง (r = 0.792, p-value <0.001) ดัชนีมวลกายส่วนที่ไร้ไขมันมีความสัมพันธ์ในระดับปานกลางกับระดับอาการหอบเหนื่อย (r = -0.315, p-value <0.001) และมีความสัมพันธ์ในระดับน้อยกับปริมาตรของอากาศที่เป่าออกอย่างเร็วแรงในวินาทีแรกและระดับคุณภาพชีวิต (r = 0.214, p-value = 0.019 และ r = -0.278, p-value = 0.002 ตามลำดับ) ส่วนดัชนีมวลกายนั้นไม่มีความสัมพันธ์กับลักษณะทางคลินิกใด ๆ เลย นอกจากนี้เมื่อได้แบ่งผู้ป่วยออกเป็น 4 กลุ่มตามองค์ประกอบของร่างกายนั้นพบว่า มีผู้ป่วยจัดอยู่ในเกณฑ์ปกติร้อยละ 51.2 (62 ราย) กลุ่มขาดสารอาหารร้อยละ 3.3 (4 ราย) กลุ่มกล้ามเนื้อลีบร้อยละ 9.9 (12 ราย) และกลุ่มผอมหนังหุ้มกระดูกร้อยละ 35.5 (43 ราย)*

สรุป: *ดัชนีมวลกายส่วนที่ไร้ไขมันมีความสัมพันธ์อย่างมีนัยสำคัญกับสมรรถภาพปอด ระดับอาการหอบเหนื่อย และระดับคุณภาพชีวิต ส่วนดัชนีมวลกายนั้นไม่มีความสัมพันธ์กับลักษณะทางคลินิกใด ๆ เลย ดังนั้นการประเมินองค์ประกอบของร่างกายด้วยการวัดดัชนีมวลกายส่วนที่ไร้ไขมันนั้นถือเป็นวิธีการที่มีประโยชน์ในทางคลินิก*