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ORIGINAL RESEARCH

The relationship between anthropometric indicators and walking distance in patients with chronic obstructive pulmonary disease

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Background: Exercise intolerance is a major issue affecting many people with COPD. Six-minute walking distance (6MWD) is a widely used indicator of exercise capacity in patients with COPD. The process is strenuous and time-consuming, especially for patients who have muscle wasting. Anthropometric indicators that reflect body lean mass, such as body mass index (BMI), mid-arm circumference (MAC), and calf circumference (CC), may have value in predicting exercise intolerance.

Purpose: This study attempted to determine the abilities of simple anthropometric indicators including BMI, MAC, and CC in reflecting the exercise intolerance of COPD patients.

Methods: We recruited 136 nonhospitalized ambulatory COPD patients without acute conditions from a general hospital in Taiwan. Each subject's BMI, MAC, and CC were measured, and they were examined with pulmonary function tests and a 6-minute walk test.

Results: Among the three anthropometric indicators examined, CC showed the strongest correlation with the 6MWD, followed by MAC and BMI. CC was also strongly associated with functional capacity, followed by MAC, according to the receiver operating characteristic curves. CC and MAC, but not BMI, were significantly associated with exercise intolerance according to logistic regression models that controlled for potential confounders.

Conclusion: Among the three variables examined, CC and walking distance may have the strongest association in COPD patients. CC may have value in serving as an adjunct to 6MWD in evaluating exercise intolerance of patients with COPD.

Keywords: 6-minute walk distance, BMI, calf circumference, COPD, mid-arm circumference

Introduction

COPD is a major public health problem. In 2020, COPD is predicted to be the fifth leading cause of death in the world.[1] Exercise intolerance is a major disability in persons with COPD.[2,3] The disease severely affects their ability to perform activities of daily living and their quality of life.[3,4] The causes and mechanisms of exercise intolerance in these patients are complex and involve ventilator and respiratory mechanic impairments, gas exchange limitations, and muscle mass reductions in the extremities.[5] Thus, the ability to perform exercise is an important indicator of the severity of COPD, and an exercise test is an important component in routine clinical assessment of patients with this disease.

The 6-minute walk test (6MWT) is the most commonly used test for rating the functional capacity of persons with COPD. It is a reliable, valid, and responsive test measuring the functional exercise capacity of patients with COPD. To reduce

the variability between test subjects and to improve the reproducibility in a given individual, the test standard specifies that the 6MWT must be conducted on a 30 m straight path.[6] The 6MWT measures four functional indicators: 6-minute walking distance (6MWD), self-perceived dyspnea, oxygen saturation, and heart rate.[7] Among these indicators, 6MWD is probably the most frequently used or studied. A 6MWD <350 m is often considered the threshold for poor prognosis.[8,9]

In addition to the 6MWT space consideration, we should also consider that older patients with severe COPD and dyspnea with exercise have some limitations. Some studies found that the exercise capacity of COPD patients is related to lung function as well as anthropometric indicators such as body mass index (BMI), fat-free mass index, and status of systemic inflammation.[10] The 6MWD and dyspnea Borg scores are associated with fat-free mass index[11] and BMI and are positively associated with exercise capacity in COPD patients.[11,12] In non-COPD elderly population, mid-arm circumference (MAC) and calf circumference (CC) have been observed to be better indicators of physical functional ability than BMI.[13] Bonnefoy et al have suggested that circumferences of the extremities may provide valuable information on muscle-related disabilities and physical functional capacity in these patients.[14] Recent studies have also shown that circumferences of the extremities, such as CC and MAC, might be better indicators of exercise capacity.[15,16]

However, the ability of these anthropometric indicators to reflect exercise capacity in COPD patients has not been examined. Thus, this study attempted to examine the anthropometric indicators and 6MWT in relation to the assessment of exercise capacity in patients with COPD.

Methods
Study design and patients

We conducted a cross-sectional study in persons with COPD who were recruited from the pulmonary outpatient unit of a medical center in northern Taiwan from November 2009 to August 2011. The diagnosis of COPD and the stage of the severity of the disease were based on the 2007 version of the Global Initiative for Chronic Obstructive Lung Disease guidelines.[2] COPD patients with a forced expiratory volume in 1 second (FEV_1)/forced vital capacity ratio of <70% of the predicted value and aged 40–85 years were qualified to participate. Exclusion criteria included acute infection or acute exacerbation within 3 months prior to the study (no requirement for antibiotic or oral corticosteroid therapy and no change in respiratory symptoms), requirement for

oxygen therapy during exercise (because these patients were different at baseline on the 6MWT), and severe systemic disease (malignancy, systemic lupus erythematosus, end-stage renal disease, and severe liver cirrhosis). A total of 136 patients (131 men and five women) were qualified and agreed to participate. All participants were ambulatory, in stable condition, and undergoing standard pharmacological treatment for COPD. The study protocol was approved by the Ethics Committee of the Chang-Gung Memorial Hospital (98-3601B and 100-0002C), and all subjects gave written informed consent before participating in the study.

Procedures and measurements

Each patient was interviewed face-to-face by well-trained researchers (Ho and Hsu) to elicit demographic, lifestyle, and disease-related data. The participants' weight, height, MAC, and CC were measured, and all patients' physical functional capacity was evaluated by a well-trained therapist (Ho or Chen) with the 6MWT and pulmonary function tests.

Weight, height, MAC, and CC were measured according to standard methods.[17] Body weight was measured to the nearest 0.1 kg with the subjects standing barefoot with light indoor clothing. Height was measured to the nearest 0.1 cm. BMI was calculated according to kg/m^{2}. MAC and CC were measured to the nearest 0.1 cm with a flexible but non-stretching measuring tape.[17] MAC was measured at the midpoint of the nondominant arm (between the olecranon and acromion) and CC was measured at the largest point of the left calf in a sitting position.

Pulmonary function tests were performed with a Spiroanalyzer ST-250 (Fukuda Sangyo Co Ltd., Nagareyama City, Chiba, Japan) after a 10-minute rest. The best of at least three reproducible FEV_1 and forced vital capacity values (with a difference within 200 mL or less than 5%) were used.

Exercise capacity was assessed with the 6MWT according to the American Thoracic Society guidelines. The scale was validated[18] and shown to be reliable[19] in evaluating the exercise capacity of persons with COPD. All patients were instructed to walk as far as possible but were allowed to stop and rest during the test.[6] Oxygen saturation and pulse rate were recorded using a continuous finger-adapted pulse oximeter. Additionally, at the beginning and end of the 6MWT, the difference in exertion was assessed with the modified Borg scale[20] by rating perceived exertion based on breathlessness. We used a ten-point scale with a nonlinear scaling scheme using descriptive terms to anchor responses, which is a commonly used format.[21]

Statistical analysis

The results were statistically analyzed with SPSS for Windows 19.0 (SPSS Inc., Chicago, IL, USA). Descriptive data are expressed as the mean ± standard deviation or percentage. According to the Kolmogorov–Smirnov test, FEV_1, MAC, and CC were normally distributed ($P>0.20$), but BMI and 6MWD were not normally distributed ($P<0.05$). Spearman's correlation was used to evaluate the strength of the relationship between various anthropometric and pulmonary function indicators with the 6MWD. We used the sample size calculation for logistic regression with PASS 14 statistical software to retrospectively estimate the results of approximately 110 cases. The abilities of BMI, MAC, and CC in discriminating exercise capacity were analyzed with receiver operating characteristic (ROC) curves using the 6MWD (<350 m) as the reference standard. The areas under the curve (AUCs) of the ROC curves were determined. A larger AUC (maximum is 1) indicates better predictive ability. The association of BMI, MAC, and CC with the 6MWD was also analyzed with a multivariate logistic regression analysis. All models were controlled for possible confounders (age and FEV_1). Statistical significance for all evaluations was set at $\alpha=0.05$.

Results

Table 1 shows the characteristics of the participants. The subjects averaged 72.4±7.5 years in age, 23.5±15.0 kg/m^2 in BMI, 26.4±3.5 cm in MAC, and 32.9±3.5 cm in CC. Over half of the subjects had mild or moderate COPD, approximately 1/3 of the subjects (31.6%) had severe COPD, and only 16.9%

Table 1 Characteristics of 136 patients with COPD

Variables	Mean ± standard deviation
Age (year)	72.41±7.47
Sex, M/F (n)	131/5
Body mass index (kg/m^2)	23.47±15.00
Mid-arm circumference (cm)	26.37±3.54
Calf circumference (cm)	32.94±3.48
FEV_1 (L/min)	1.02±0.39
FEV_1[a] (% of prediction)	51.68±20.82
Forced vital capacity (L/min)	2.43±5.48
Forced vital capacity (% of prediction)	70.60±19.22
6MWD (m)[b]	382.49±90.33
O_2 saturation at rest (%)	95.09±2.32
Borg score, at rest	0.82±1.23
Heart rate, at rest (bpm)	90.54±16.68

Notes: [a]According to the FEV_1 values, 23 (16.9%) subjects had very severe (FEV_1 <30%), 43 (31.6%) subjects had severe (FEV_1 >50% and ≤30%), and 70 (51.5%) subjects had mild-to-moderate COPD (FEV_1 ≥50%). [b]Ninety-five were 6MWD >350 m and 41 were <350 m.
Abbreviations: 6MWD, 6-minute walking distance; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; M, male; F, female.

Table 2 Spearman's correlation coefficients (r) of BMI, MAC, and CC with items in 6-minute walk distance and FEV_1 of 136 patients with COPD

Indicators	6MWD	FEV_1
BMI	0.252**	0.255**
MAC	0.301**	0.207*
CC	0.426**	0.171*
FEV_1	0.177*	–

Note: *$P<0.05$ and **$P<0.01$ based on Spearman's correlation test.
Abbreviations: 6MWD, 6-minute walk distance; BMI, body mass index; CC, calf circumference; FEV_1, forced expiratory volume in 1 second; MAC, mid-arm circumference.

of the subjects had very severe COPD. Approximately 2/3 of the subjects (95) had a 6MWD result of >350 m, and 41 of the subjects had a result of <350 m. The average O_2 saturation was 95.25% at rest. The average Borg score was 0.85±1.3 at rest. The average heart rate was 90.5±16.7 bpm at rest.

Table 2 shows Spearman's correlation coefficients of the anthropometric indicators (BMI, CC, and MAC) and FEV_1 with 6MWD; all were significantly correlated with BMI ($r=0.252$, $P<0.01$), MAC ($r=0.301$, $P<0.01$), CC ($r=0.426$, $P<0.01$), and FEV_1 ($r=0.177$, $P<0.05$). Similarly, the anthropometric indicators with FEV_1 were all significantly correlated with BMI, MAC, and CC.

Table 3 shows the logistic regression analysis of the association of various variables with 6MWD using 350 m as a threshold. Using a base model that controlled for age and FEV_1, model I explained between 10.4% (Cox & Snell) and 14.7% (Nagelkerke) of the variance in 6MWD in patients with COPD. BMI (odds ratio [OR] =0.89, 95% confidence interval [CI] =0.79–1.00, $P=0.050$) did not show a significant association with impaired 6MWD. Model II explained between 14.1% (Cox & Snell) and 19.7% (Nagelkerke) of the variance in 6MWD in patients with COPD. MAC (OR =0.82, 95% CI =0.71–0.93, $P=0.003$) showed a significant association with impaired 6MWD. Model III explained between 16.3% (Cox & Snell) and 23.0% (Nagelkerke) of the variance in 6MWD in patients with COPD. CC (OR =0.79, 95% CI =0.68–0.90, $P=0.001$) showed a significant association with impaired 6MWD.

Figure 1 shows the ability of BMI, MAC, and CC in differentiating impaired 6MWD (<350 m) with the ROC curves. The AUCs were 0.675 (0.514–0.776, $P=0.001$), 0.709 (0.616–0.802, $P=0.000$), and 0.758 (0.669–0.847, $P=0.000$) for BMI, MAC, and CC, respectively.

Discussion

The results show that among the three anthropometric indicators examined, CC demonstrated the strongest association

Table 3 Multivariate binary logistic regression analysis of the association of various variables with impaired 6MWD (<350 m) in 136 patients with COPD

Variables	Model I: BMI		Model II: MAC		Model III: CC	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	1.06 (0.99–1.32)	0.064	1.05 (0.98–1.12)	0.162	1.04 (0.98–1.13)	0.219
FEV_1	0.97 (0.95–0.99)	0.029	0.98 (0.95–1.00)	0.056	0.98 (0.95–1.00)	0.080
BMI	0.89 (0.79–1.00)	0.050	–	–	–	–
MAC	–	–	0.82 (0.71–0.93)	0.003	–	–
CC	–	–	–	–	0.79 (0.68–0.90)	0.001

Notes: Model I: −2 likelihood log =151.55; Cox & Snell R^2=0.104; Nagelkerke R^2=0.147; Model II: −2 likelihood log =145.88; Cox & Snell R^2=0.141; Nagelkerke R^2=0.199; Model III: −2 likelihood log =142.28; Cox & Snell R^2=0.163; Nagelkerke R^2=0.2.
Abbreviations: 6MWD, 6-minute walk distance; BMI, body mass index; CC, calf circumference; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; MAC, mid-arm circumference; OR, odds ratio.

with the functional indicators, especially the 6MWD, compared to MAC and BMI. CC and MAC are the indicators that significantly predicted impaired 6MWD according to the regression analysis, and these factors may be capable to predict those with impaired 6MWD, according to the ROC analysis.

Association with exercise capacity

Enright et al established reference sex-specific equations to predict 6MWD in healthy adults: for men:

$$6MWD = (7.57 \times height_{cm}) - (5.02 \times age) - \qquad (1)^{22}$$
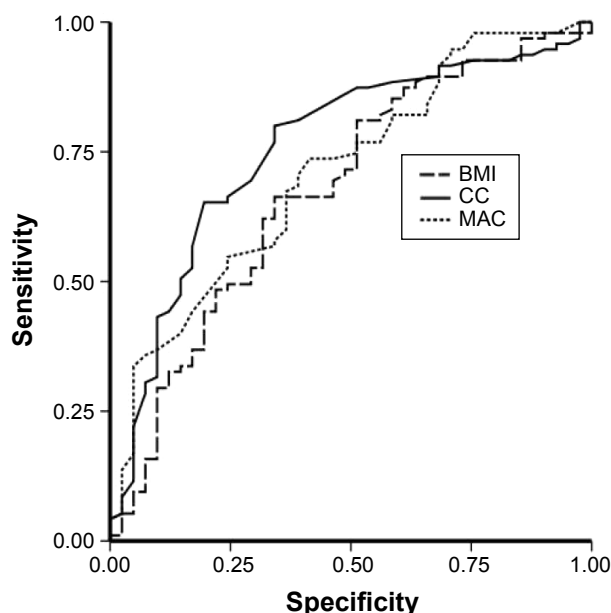$$(1.76 \times weight_{kg}) - 309 \text{ m}$$

Figure 1 The receiver operating characteristic curves for BMI, MAC, and CC in persons with COPD, using 350 m of 6-minute-walking distance as the reference.
Note: Areas under the curve for BMI, MAC, and CC were 0.675 (95% confidence interval =0.514–0.776, *P*=0.001), 0.709 (0.616–0.802, *P*=0.000), and 0.758 (0.669–0.847, *P*=0.000), respectively.
Abbreviations: BMI, body mass index; CC, calf circumference; MAC, mid-arm circumference.

and for women:

$$6MWD = (2.11 \times height_{cm}) - (5.78 \times age) - \qquad (2)^{22}$$
$$(2.29 \times weight_{kg}) + 667 \text{ m}$$

The 6MWD is reduced by several types of diseases, including obstructive lung disease, heart disease, and neuromuscular disease.[23] The determinants of poor 6MWD are complex and depend on both physical and psychological factors, and a poor 6MWD (<350 meters) result has prognostic value in identifying high-risk patients with COPD.[24] Therefore, in this study, we used the 6MWD (350 m) to define an impairment of functional capacity.

BMI has been demonstrated to influence walking distance in healthy subjects.[22] Previous studies have shown that patients with a low BMI have lower exercise capacity on submaximal and maximal exercise tests,[11,25,26] and that low BMI is an independent indicator of poor prognosis in persons with COPD. However, the present study showed that BMI is a much weaker indicator or functional indicator compared to MAC, particularly compared to CC in persons with COPD. Our finding confirms the findings of Ischaki et al[11] in which BMI was not effective in differentiating various COPD stages. Soler-Cataluña et al[27] also showed that in persons with COPD, mid-arm muscle area is a better predictor of mortality than BMI.[27] Villaça et al[28] found that an anthropometrically based method of estimating leg lean volume had high specificity and sensitivity in identifying peripheral muscle function in persons with depleted and nondepleted COPD. Patients with low leg lean volume had significantly lower exercise capacity and muscle performance than their normal counterparts. Lean body mass in legs has been observed to be a significant predictor of maximal exercise performance in patients with mild-to-moderate airflow limitation.[29]

The predictive ability of MAC is not as strong as CC. This difference is probably because the degree of functional impairment between the upper and lower limbs

is different in persons with COPD. Persons with COPD report more dyspnea during arm exercise compared to leg exercise.[30,31] A major cause of dyspnea is dynamic hyperinflation, which is caused by airflow limitations as well as an increase in ventilation.[30,32] Lower-limb muscles appear to be associated with muscle endurance and daily functional performance.[31]

In the present study, BMI, MAC, and CC were all significantly correlated with FEV_1. However, after adjusting for potential confounders, MAC and CC were not significantly associated with FEV_1 in multivariate logistic regression models. Our results support the findings of others,[33–35] suggesting that FEV_1 is not independently associated with 6MWD in COPD.

Significance of CC in COPD

After controlling for age and FEV_1, the results of three models using Nagelkerke measure of variance in 6MWD in patients with COPD were not high (0.147–0.23). However, in model III CC, R^2 was higher than that in model II MAC and model I BMI. The results of the present study may be affected because some important factors were not included in the models. In the study by Britto et al approximately 62% of the variance was explained by sex, age, height, and change in heart rate during the test to predict the 6MWD in Brazilian subjects.[36] The present study suggests that CC is more effective than BMI or MAC in predicting exercise tolerance in persons with COPD. Lower-limb muscle atrophy is relatively common in persons with COPD, ranging from 21% to 45%, depending on the population and its operational definition.[37,38] Muscle atrophy can even be found in persons with COPD with normal body weight.[37] Thus, it is conceivable that under some conditions, CC atrophy might be a factor limiting the exercise capability in persons with COPD. In non-COPD individuals, a larger CC is protective against physical functional decline.[39] CC is a pertinent nutritional marker compared to other anthropometric indicators.[40,41]

CC is a better indicator of body muscle mass because our legs contain over half of the muscle mass of the body and a decrease in walking activity can occur due to functional decline or long-term illness.[15] It is probable that long-term deconditioning could be caused by sedentary lifestyle in these patients as severe COPD is associated with greater dyspnea sensation and exercise-induced oxygen desaturation.[42]

Taken together, the results of the present study indicate that CC is highly associated with exercise tolerance in persons with COPD and it might be of value in predicting exercise intolerance in these patients. CC is highly accessible and simple to measure.

Limitations of the study

This study has some limitations. First, the study sample size was small and participants were drawn from one hospital; therefore, the results may not reflect the entire spectrum of patients with COPD. Second, there was a disproportionate number of men compared to women in this study. The applicability of study results to female subjects requires further investigation. Third, the present study involves only ambulatory patients with COPD. The applicability of the study results to persons with more severe COPD requires further investigation. Finally, the study could also benefit from using more elaborate body-composition measuring techniques, such as dual radiograph absorptiometry, to measure body lean mass.

Conclusion

The results suggest that among the three anthropometric indicators examined, CC is highly correlated with walking ability and can predict exercise capacity in persons with COPD. CC is accessible, non invasive, and easy to measure. It may serve as an alternative or adjunct to 6MWD in rating the physical functional capacity of persons with COPD.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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