



Value of cardiopulmonary exercise testing in the assessment of symptoms and quality of life in Asian patients with chronic obstructive pulmonary disease

Bora Lee[^], Yeon-Mok Oh[^], Sei Won Lee[^], Sang-Do Lee[^], Jae Seung Lee[^]

Division of Pulmonology and Critical Care Medicine, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Contributions: (I) Conception and design: JS Lee, B Lee; (II) Administrative support: JS Lee, B Lee, YM Oh, SW Lee, SD Lee; (III) Provision of study materials or patients: JS Lee, B Lee; (IV) Collection and assembly of data: JS Lee, B Lee; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Jae Seung Lee, MD. Division of Pulmonology and Critical Care Medicine, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea. Email: jsdoc1186@daum.net.

Background: The natural course of chronic obstructive pulmonary disease (COPD) is characterized by symptom exacerbation and quality-of-life reduction. Therefore, symptoms should be properly assessed. Some studies have demonstrated a weak correlation between cardiopulmonary exercise testing (CPET) parameters and symptoms in patients with COPD; however, data on Asian patients are lacking. We investigated the value of CPET parameters in assessing symptoms and quality of life in Asian patients with COPD.

Methods: Of 681 patients who underwent CPET at Asan Medical Center between January 2020 and June 2022, we analyzed 195 patients with COPD in this retrospective study. A cycle ergometer was used for the incremental protocol. The modified Medical Research Council (mMRC) dyspnea scale and COPD Assessment Test (CAT) were administered to assess the patients' symptoms.

Results: The mMRC grade was related to maximal oxygen uptake (VO_2 max, L/min) (Spearman's correlation coefficient $\rho=-0.295$, $P<0.001$) and physiological dead space/tidal volume ratio at peak exercise (V_D/V_T peak) ($\rho=0.256$, $P<0.001$). The CAT score was significantly correlated with VO_2 max (L/min) (Spearman's correlation coefficient $\rho=-0.297$, $P<0.001$) and V_D/V_T peak ($\rho=0.271$, $P<0.001$), but had no correlation with breathing reserve ($\rho=-0.122$, $P=0.089$). The optimal cut-off values of VO_2 max and V_D/V_T peak for predicting the onset of clinically significant dyspnea were 1.099 L/min and 0.295, respectively.

Conclusions: VO_2 max and V_D/V_T peak comprehensively reflect the symptoms and health-related quality of life of patients with COPD.

Keywords: Cardiopulmonary exercise testing (CPET); chronic obstructive pulmonary disease (COPD); modified Medical Research Council (mMRC); COPD Assessment Test (CAT); dyspnea; quality of life

Submitted Feb 06, 2023. Accepted for publication Jun 09, 2023. Published online Jul 18, 2023.

doi: 10.21037/jtd-23-185

View this article at: <https://dx.doi.org/10.21037/jtd-23-185>

[^] ORCID: Bora Lee, 0000-0003-1381-7506; Yeon-Mok Oh, 0000-0003-0116-4683; Sei Won Lee, 0000-0003-4814-6730; Sang-Do Lee, 0000-0001-8189-4509; Jae Seung Lee, 0000-0003-4130-1486.

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation (1) and many accompanying chronic respiratory symptoms (2). These symptoms worsen with disease progression, resulting in functional limitations and reduced quality of life (3). Therefore, it is important to evaluate the subjective complaints of patients with COPD. Several methods for assessing symptoms are available, among which the modified Medical Research Council (mMRC) dyspnea scale is mainly used to estimate the severity of dyspnea (1,4). The mMRC dyspnea scale is known to be strongly correlated with other methods of assessing the health status of patients (5) and is useful for predicting mortality (6). The COPD Assessment Test (CAT) is also a widely used method for evaluating symptoms (7). Rather than simply measuring breathlessness, CAT evaluates other respiratory symptoms and the ability to perform daily activities, thereby estimating the quality of life (8). The mMRC dyspnea scale and CAT are relatively simple measures that are included in the criteria for determining the treatment of COPD in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (1).

Cardiopulmonary exercise testing (CPET) is an important tool for diagnosis and functional evaluation

in patients with cardiopulmonary diseases (9-12). CPET parameters are used to evaluate integrative physiological responses during maximal exercise and help identify factors that may be causing exercise limitations (13). In many cases, multiple factors are involved, including cardiopulmonary, musculoskeletal, neurological, metabolic, and psychological factors (13). In particular, as multiple factors often contribute to exercise intolerance in patients with COPD (9,14), CPET can provide useful information that can guide the diagnosis and subsequent treatment of COPD.

Thus far, only a few studies have examined the relationship of CPET parameters to symptoms and quality of life in patients with COPD. Previous studies assessed symptoms and quality of life by using instruments such as the St. George's Respiratory Questionnaire (SGRQ) (15), 20-item Chronic Respiratory Disease Questionnaire (16), and Nijmegen Integral Assessment Framework (NIAF) (17), all of which are too complex to use in daily practice. In those studies, only maximal oxygen uptake (VO_2 max), breathing reserve, and VO_2 /work rate ratio were found to be correlated with some of the instruments used, and the degree of relationship were weak. Furthermore, no study has investigated the utility of CPET parameters in evaluating subjective complaints in Asian patients with COPD.

In this study, we investigated which CPET parameters can explain and reflect the symptoms and quality of life of Asian patients with COPD, as assessed using the mMRC grade and CAT score. We present this article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-185/rc>).

Methods

Patients

This retrospective single-center study enrolled 681 adult patients who underwent CPET at Asan Medical Center (Seoul, Republic of Korea) between January 2020 and June 2022. Patients in whom COPD had been diagnosed on the basis of compatible clinical symptoms and confirmed using spirometry with a post-bronchodilator forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio of <0.7 were included. Patients were excluded for the following reasons: (I) lack of medical records, (II) presence of relevant comorbidities (stage IV lung cancer based on tumour-node-metastasis stage (18), heart failure, history of lung resection, interstitial lung disease, and neuromuscular disease), (III)

Highlight box

Key findings

- Among the parameters of cardiopulmonary exercise testing (CPET), maximal oxygen uptake (VO_2 max) and physiological dead space/tidal volume ratio at peak exercise (VD/VT peak) comprehensively reflect symptoms and quality of life in patients with COPD.

What is known and what is new?

- Previous studies assessed the correlation between CPET parameters and symptoms and quality of life by using complex instruments, and the correlation was weak. Also, no studies were conducted with Asian patients with COPD.
- We discovered that VO_2 max and VD/VT peak significantly correlate with the mMRC grade and COPD Assessment Test score. In addition, we proposed the optimal cut-off values of VO_2 max and VD/VT peak for predicting the onset of clinically significant dyspnea and poor quality of life.

What is the implication, and what should change now?

- VO_2 max and VD/VT peak are reliable indicators of symptoms and health-related quality of life in patients with COPD and would suggest when to consider more aggressive treatment.

presence of features of asthma, (IV) a submaximal test defined by a maximal respiratory exchange ratio of <1.15 , and (V) any COPD exacerbation within the previous two months. Clinical data, including age, sex, body weight, height, body mass index, and symptoms, were reviewed from medical records.

Assessment of symptoms

The mMRC dyspnea scale was administered to assess the degree of dyspnea. The mMRC scale categorizes patients into one of five grades (0–4) based on the degree of dyspnea (1). CAT was used to evaluate the patients' quality of life, including respiratory symptoms (e.g., cough and chest tightness), ability to perform daily activities, and sleep. Each item is scored from 0 to 5 points, with a higher score indicating a worse outcome. As the CAT questionnaire contains a total of eight items, the worst possible score is 40 points (8). Previous studies have demonstrated that CAT scores are strongly associated with SGRQ scores (7). Patients were stratified into two groups based on mMRC grade (either <2 or ≥ 2) and CAT score (either <10 or ≥ 10), differentiating those with less subjective and more subjective complaints.

CPET

CPET was performed using an electronically braked cycle ergometer (VIAsprint 150P; CareFusion Inc., San Diego, CA, USA) (19). A continuous incremental protocol based on the American Thoracic Society/American College of Chest Physicians guidelines on CPET was selected, and the test was performed under medical supervision (13,20). Inhaled and exhaled gas concentrations were measured through a face mask (V2™ Oro-Nasal Mask; Hans Rudolph Inc., Kansas City, MO, USA) and analyzed using the breath-by-breath method (13). All patients underwent spirometry before CPET on the same day. During CPET, electrocardiography, arterial saturation, heart rate, and blood pressure were monitored.

The test consisted of four phases: resting, warm-up, exercise, and recovery. During the resting phase, the patients rested for 2 min without pedalling and baseline data were collected. In the warm-up phase, the patients started pedalling without a load for 1 min and 30 s at a speed of 30–40 revolutions per minute (RPM). In the exercise phase, the patients pedalled at 65 RPM with increasing load at an individualized speed of 5–15 W/min, depending on fitness

and spirometry results. The patients were encouraged to exercise up to their maximum capacity, for >10 min if possible. However, even if the maximum capacity was not reached, the test was immediately terminated on the patients' request or in case of abnormal monitoring results. In the recovery phase, the patients pedalled at 30–40 RPM with no load until stabilization of vital signs.

Statistical analysis

Continuous variables are presented as means and standard deviations, and categorical variables are described as counts and percentages. The comparison of CPET parameters among groups stratified by symptom severity was conducted using Student's *t*-test. The Kolmogorov-Smirnov test was used to test data normality. For variables with a normal distribution, we used Pearson's correlation coefficients. For variables that did not follow a normal distribution, Spearman's correlation coefficients were employed. Receiver operating characteristic (ROC) analysis and the Youden index were used to determine cut-off values. In all analyzes, statistical significance was determined at $P<0.05$ and 95% confidence interval. IBM Statistical Package for the Social Sciences (version 24.0; SPSS Inc., Chicago, IL, USA) was used for data analysis.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board (IRB) of the Asan Medical Center (approval No. 2021-0915), and individual consent for this retrospective analysis was waived.

Results

Between January 2020 and June 2022, a total of 681 adult patients underwent CPET at Asan Medical Center. Of these patients, 268 had been diagnosed with COPD. The most common indications for CPET were pre-operative evaluation and investigation of dyspnea. Of the 268 patients with COPD, 73 patients were excluded according to the exclusion criteria. Finally, 195 patients were included in the analysis (*Figure 1*).

The patients' baseline characteristics, spirometry results, mMRC grades, and CAT scores are shown in *Table 1*, while CPET parameter values are summarized in *Table 2*.

The comparison of CPET results between groups

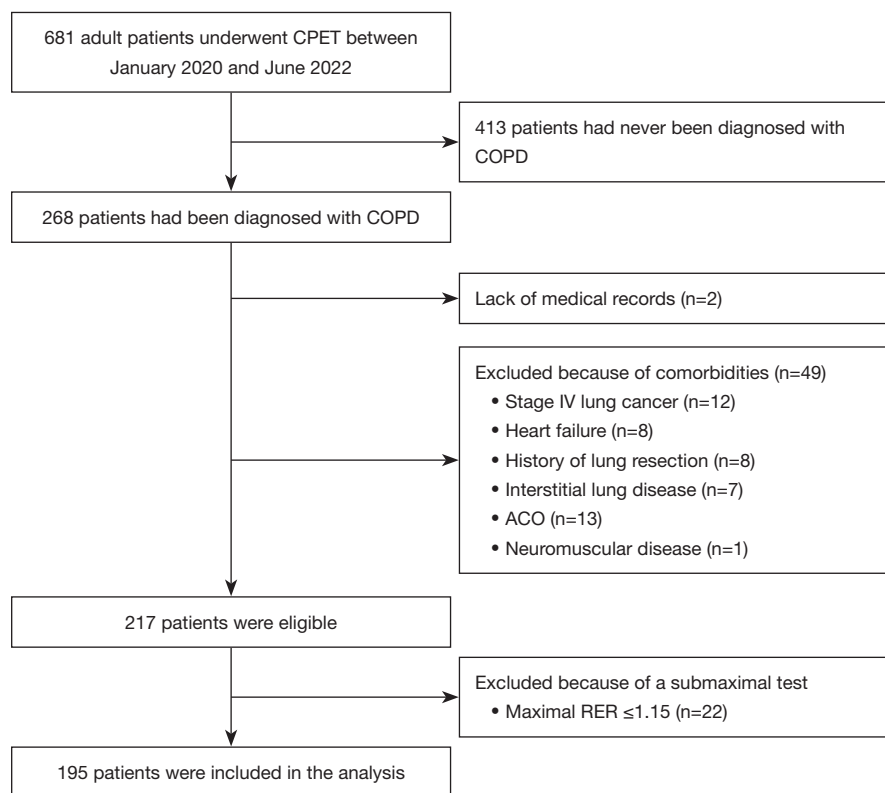


Figure 1 Study flowchart. CPET, cardiopulmonary exercise testing; COPD, chronic obstructive pulmonary disease; ACO, asthma-COPD overlap; RER, respiratory exchange ratio.

with less subjective and more subjective complaints are shown in *Tables 3,4*. Age did not differ between the two groups based on both mMRC grade and CAT score. In the comparison according to the mMRC scale, the group with higher mMRC grades showed significantly lower VO_2 max (1.15 ± 0.32 vs. 0.81 ± 0.30 L/min, $P < 0.001$), lower maximal minute ventilation (V_E max) (53.1 ± 14.7 vs. 39.4 ± 14.7 L/min, $P < 0.001$), and higher V_D/V_T peak (0.23 ± 0.04 vs. 0.27 ± 0.06 , $P = 0.006$). Further, no significant difference in breathing reserve and V_D/V_T at rest was found between the two groups divided according to mMRC grade. In the comparison according to the CAT result, the group with higher CAT scores showed significantly lower VO_2 max (1.18 ± 0.33 vs. 0.99 ± 0.33 L/min, $P < 0.001$), lower V_E max (53.6 ± 15.1 vs. 47.3 ± 15.0 , L/min, $P = 0.005$), higher V_D/V_T at rest (0.38 ± 0.07 vs. 0.40 ± 0.05 , $P = 0.002$), and higher V_D/V_T peak (0.23 ± 0.04 vs. 0.25 ± 0.05 , $P = 0.001$). CPET parameters exhibiting differences between the two groups were subjected to logistic regression analysis, and the findings are summarized in *Tables S1,S2*. Maximal voluntary ventilation (MVV) and V_D/V_T peak emerged as independent predictors

of severe dyspnea.

The correlations among mMRC grade, CAT score, CPET parameters, and FEV_1 are described in *Table 5*. A correlation between mMRC grade and VO_2 max (L/min) was observed (Spearman's correlation coefficient $\rho = -0.295$, $P < 0.001$), as well as between mMRC grade and V_D/V_T peak ($\rho = 0.256$, $P < 0.001$), as illustrated in *Figure 2*. Similarly, CAT score demonstrated a correlation with both VO_2 max (L/min) (Spearman's correlation coefficient $\rho = -0.297$, $P < 0.001$) and V_D/V_T peak ($\rho = 0.271$, $P < 0.001$), depicted in *Figure 3*. The mMRC grade and CAT score had no significant correlation with breathing reserve ($\rho = -0.108$, $P = 0.13$ and $\rho = -0.122$, $P = 0.089$, respectively).

Additionally, we analyzed whether FEV_1 has a correlation with VO_2 max and V_D/V_T peak. The results showed that FEV_1 (L) was correlated with VO_2 max (L/min) (Pearson's correlation coefficient $r = 0.450$, $P < 0.001$) and V_D/V_T peak ($r = -0.466$, $P < 0.001$).

ROC curves for VO_2 max and V_D/V_T peak were generated to determine the optimal cut-off values for predicting symptoms and quality of life in patients with

Table 1 Baseline characteristics of patients

Baseline characteristics	Values
No.	195
Age, years	68.3±9.0
BMI, kg/m ²	24.0±3.4
Height, cm	
Male	166.7±5.9
Female	153.9±5.3
Weight, kg	
Male	66.8±9.9
Female	55.4±13.8
Sex	
Male	185 (94.8)
Female	10 (5.2)
FEV ₁ , L	1.92±0.48
FEV ₁ , % predicted	64.1±13.2
GOLD 1	14 (7.2)
GOLD 2	147 (75.4)
GOLD 3	31 (15.9)
GOLD 4	3 (1.5)
FEV ₁ /FVC, %	57.1±10.5
DL _{CO} , % predicted	67.3±18.6
mMRC dyspnea scale	
Grade 0	115 (58.9)
Grade 1	55 (28.2)
Grade 2	17 (8.7)
Grade 3	4 (2.1)
Grade 4	4 (2.1)
CAT score	8.9±5.1
0–5	51 (26.2)
6–10	84 (43.0)
11–15	41 (21.0)
16–20	13 (6.7)
21–40	6 (3.1)

Continuous variables are presented as mean ± standard deviation, and categorical variables are described as counts and percentages. BMI, body mass index; FEV₁, forced expiratory volume in 1 s; GOLD, Global initiative for Chronic Obstructive Lung Disease; FVC, forced vital capacity; VC, vital capacity; DL_{CO}, diffusing capacity of the lung for carbon monoxide; mMRC, modified Medical Research Council; CAT, chronic obstructive pulmonary disease Assessment Test.

Table 2 Values of CPET parameters

CPET parameters	Values
VO ₂ max, L/min	1.11±0.34
VO ₂ max, mL/kg/min	16.8±4.7
AT, L/min	0.67±0.24
AT, % predicted VO ₂ max	39.9±13.9
WR max, W	87.5±28.8
HR max, beats/min	134.0±20.4
HRR, beats/min	25.4±17.7
O ₂ pulse max, mL/beat	8.84±4.93
O ₂ pulse max, % predicted	80.4±24.3
Systolic BP max, mmHg	200.8±32.69
V _E max, L/min	51.3±15.4
MVV, L/min	81.3±25.2
Peak P _{ETCO₂} , mmHg	36.8±5.3
Breathing reserve, %	34.1±17.8
V _D /V _T at rest	0.39±0.07
V _D /V _T peak	0.24±0.05

Data are presented as mean ± standard deviation. VO₂ max, maximal oxygen uptake; AT, anaerobic threshold; WR, work rate; HR, heart rate; HRR, heart rate reserve; BP, blood pressure; SpO₂, saturation of percutaneous oxygen; V_E, minute ventilation; MVV, maximal voluntary ventilation; P_{ETCO₂}, end-tidal P_{CO₂}; V_D, dead space volume; V_T, tidal volume.

COPD (Figure 4). VO₂ max =1.099 L/min and V_D/V_T peak =0.295 were optimal predictors of dyspnea assessed using the mMRC scale. VO₂ max =1.078 L/min and V_D/V_T peak =0.235 were also optimal thresholds for predicting quality of life estimated using the CAT score in patients with COPD.

Discussion

In this retrospective study, we evaluated the utility of CPET parameters in predicting symptoms and quality of life in Asian patients with COPD. To our knowledge, this is the first study to evaluate the correlation between CPET parameters and patients' symptoms using the mMRC scale and CAT. Among CPET parameters, VO₂ max (L/min) and V_D/V_T peak showed the most significant correlation with both mMRC grade and CAT score. Further, we determined the optimal cut-off values of VO₂ max and V_D/V_T peak for predicting clinically significant symptoms and poor quality

Table 3 Comparison of CPET parameters between mMRC grades <2 and ≥2

CPET parameters	mMRC grade <2	mMRC grade ≥2	P value
Age, years	68.3±7.8	68.0±15.0	0.895
VO ₂ max, L/min	1.15±0.32	0.81±0.30	<0.001
VO ₂ max, mL/kg/min	17.4±4.6	12.9±4.19	<0.001
AT, L/min	0.69±0.23	0.57±0.29	0.028
AT, % predicted VO ₂ max	40.5±13.3	36.2±17.1	0.163
WR max, W	91.8±26.6	58.1±26.7	<0.001
HR max, beats/min	135.5±20.8	124.0±13.3	0.001
HRR, beats/min	24.0±18.0	34.8±12.8	0.004
O ₂ pulse max, mL/beat	9.15±5.12	6.77±2.63	0.024
O ₂ pulse max, % predicted	82.1±24.0	69.0±26.7	0.011
Systolic BP max, mmHg	201.3±32.2	196.8±36.0	0.515
V _E max, L/min	53.1±14.7	39.4±14.7	<0.001
MVV, L/min	84.9±23.8	57.2±21.0	<0.001
Peak P _{ETCO₂} , mmHg	37.1±4.9	34.3±6.6	0.012
Breathing reserve, %	34.7±18.1	29.3±15.5	0.120
V _D /V _T at rest	0.38±0.07	0.39±0.05	0.483
V _D /V _T peak	0.23±0.04	0.27±0.06	0.006

Data are presented as mean ± standard deviation. CPET, cardiopulmonary exercise testing; mMRC, modified Medical Research Council; VO₂ max, maximal oxygen uptake; AT, anaerobic threshold; WR, work rate; HR, heart rate; HRR, heart rate reserve; BP, blood pressure; SpO₂, saturation of percutaneous oxygen; V_E, minute ventilation; MVV, maximal voluntary ventilation; P_{ETCO₂}, end-tidal P_{CO₂}; V_D, dead space volume; V_T, tidal volume.

of life.

VO₂ max can predict 5-year mortality and is generally considered the most important CPET parameter (21). It is determined by how much oxygen the body actually uses through the process of receiving oxygen from respiration and transporting it to the tissues (22). Therefore, various factors are involved in this process, including arterial blood oxygen partial pressure, blood hemoglobin concentration, cardiac output, and tissue perfusion (13). As dyspnea and decreased exercise capacity in patients with COPD are frequently due to extrapulmonary factors, VO₂ max can be considered an important parameter in COPD (9).

A previous study reported that VO₂ max improved the prediction of self-reported function and health-related quality of life after controlling FEV₁ (16). Another study assessed the relationship between the NIAF health status and VO₂ max in patients with COPD, and found a weak correlation (17). In accordance with previous studies, our study showed that VO₂ max had a weak correlation with

mMRC grade and CAT score. Because most patients in this study had mild symptoms, the relationship may have been underestimated. Therefore, we divided the study population into two groups based on mMRC grade (<2 or ≥2) and CAT score (<10 or ≥10). We observed significant differences in VO₂ max between the two groups. This suggests that VO₂ max is not only an indicator of prognosis in patients with COPD but is also a valuable parameter reflecting actual symptoms and quality of life in these patients. We also created ROC curves of VO₂ max to determine the optimal cut-off value for predicting the onset of clinically significant symptoms and impaired quality of life. The extent to which CPET parameters vary as a disease progresses, and the clinical significance of such changes, remain inadequately understood compared to other objective measurements like FEV₁ in spirometry. This lack of data contributes to a reluctance to utilize CPET, despite its proven usefulness. A decrease in VO₂ max below the cut-off value during the patients' follow-up should prompt physicians to

Table 4 Comparison of CPET parameters between CAT scores <10 and ≥10

CPET parameters	CAT score <10	CAT score ≥10	P value
Age, years	68.3±7.7	68.3±11.0	0.994
VO ₂ max, L/min	1.18±0.33	0.99±0.33	<0.001
VO ₂ max, mL/kg/min	17.5±4.7	15.5±4.6	0.004
AT, L/min	0.70±0.23	0.62±0.24	0.023
AT, % predicted VO ₂ max	40.8±13.3	38.4±14.8	0.265
WR max, W	94.6±24.9	75.1±31.1	<0.001
HR max, beats/min	136.3±21.7	130.0±17.3	0.027
HRR, beats/min	22.8±18.2	29.7±16.1	0.009
O ₂ pulse max, mL/beat	9.35±5.83	7.96±2.54	0.058
O ₂ pulse max, % predicted	81.8±25.6	78.0±21.7	0.294
Systolic BP max, mmHg	202.4±32.6	198.0±32.8	0.365
V _E max, L/min	53.6±15.1	47.3±15.0	0.005
MVV, L/min	86.5±24.3	72.3±24.4	<0.001
Peak P _{ETCO₂} , mmHg	37.2±5.0	36.0±5.6	0.115
Breathing reserve, %	34.9±17.9	32.5±17.8	0.364
V _D /V _T at rest	0.38±0.07	0.40±0.05	0.002
V _D /V _T peak	0.23±0.04	0.25±0.05	0.001

Data are presented as mean ± standard deviation. CPET, cardiopulmonary exercise testing; CAT, chronic obstructive pulmonary disease Assessment Test; VO₂ max, maximal oxygen uptake; AT, anaerobic threshold; WR, work rate; HR, heart rate; HRR, heart rate reserve; BP, blood pressure; SpO₂, saturation of percutaneous oxygen; V_E, minute ventilation; MVV, maximal voluntary ventilation; P_{ETCO₂}, end-tidal P_{CO₂}; V_D, dead space volume; V_T, tidal volume.

Table 5 Correlations among mMRC grade, CAT score, CPET parameters, and FEV₁

Variables	mMRC grade		CAT score	
	ρ [†]	P value	ρ [†]	P value
VO ₂ max, L/min	-0.295	<0.001	-0.297	<0.001
VO ₂ max, mL/kg/min	-0.282	<0.001	-0.252	<0.001
FEV ₁	-0.387	<0.001	-0.299	<0.001
O ₂ pulse	-0.195	0.006	-0.142	0.047
Anaerobic threshold	-0.135	0.07	-0.194	0.009
Breathing reserve	-0.108	0.13	-0.122	0.089
ETCO ₂	-0.131	0.068	-0.145	0.043
V _E max	-0.248	<0.001	-0.232	0.001
V _D /V _T peak	0.256	<0.001	0.271	<0.001

†, Spearman's correlation coefficient. VO₂ max, maximal oxygen uptake; mMRC, modified Medical Research Council; CAT, chronic obstructive pulmonary disease Assessment Test; CPET, cardiopulmonary exercise testing; FEV₁, forced expiratory volume in 1 s; V_E, minute ventilation; V_D, dead space volume; V_T, tidal volume.

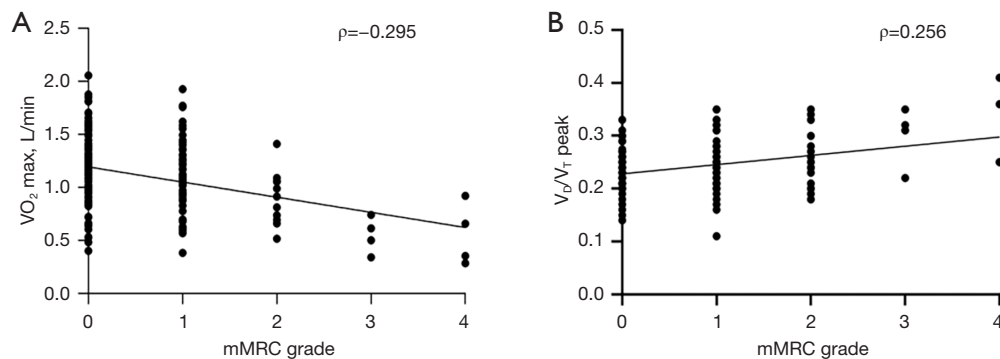


Figure 2 Correlation of VO_2 max (L/min) (A) and V_D/V_T peak (B) with mMRC grade. VO_2 max, maximal oxygen uptake; mMRC, modified Medical Research Council; V_D , dead space volume; V_T , tidal volume.

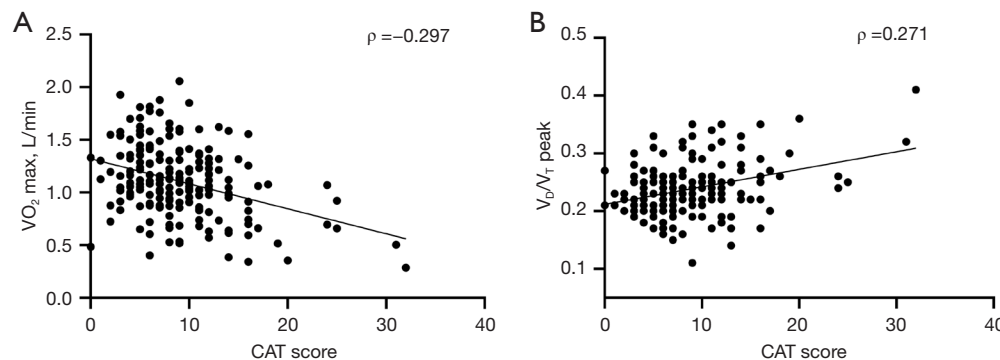


Figure 3 Correlation of VO_2 max (L/min) (A) and V_D/V_T peak (B) with CAT score. VO_2 max, maximal oxygen uptake; CAT, chronic obstructive pulmonary disease Assessment Test; ρ , Spearman's correlation coefficient; V_D , dead space volume; V_T , tidal volume.

consider more aggressive treatment, such as medication or rehabilitation, to control symptoms and ultimately improve quality of life. Additionally, improved interpretation of CPET results would facilitate its broader application in clinical practice.

In addition, we found that VO_2 max was closely correlated with FEV_1 , which is a well-established prognostic factor and an important parameter for evaluating lung function in patients with COPD (23). The significant correlation of VO_2 max with mMRC grade, CAT score, and FEV_1 suggests that VO_2 max can comprehensively reflect the lung function, symptoms, quality of life, and actual exercise capacity of patients with COPD.

In this study, V_D/V_T peak was more strongly correlated with mMRC grade and CAT score than other CPET parameters. COPD is characterized by airflow limitation, which becomes aggravated during exercise and leads to lung hyperinflation and increased dead space volume (24). When we compared V_D/V_T between the mMRC grade <2

and ≥ 2 groups, we observed a significant difference in V_D/V_T peak but not in V_D/V_T at rest between the two groups. This suggests that sudden hyperinflation of the lungs during exercise is one of the factors contributing to severe dyspnea during exercise, eventually causing exercise intolerance (25). The significant correlation of V_D/V_T peak with mMRC grade and CAT score implies that dyspnea and poor quality of life partially result from an increase in dead space during exercise.

V_D/V_T was also correlated with FEV_1 , with a stronger correlation between FEV_1 and V_D/V_T peak than between FEV_1 and V_D/V_T at rest. This suggests that air trapping during exercise and dynamic lung hyperinflation highly depend on the degree of airflow limitation.

In this study, we assessed dyspnea and quality of life in patients with COPD using the mMRC grade and the CAT score, both of which are readily available in clinical settings. The mMRC grade and CAT score demonstrated a significant correlation with VO_2 max and V_D/V_T peak, substantiating the validity of these two straightforward

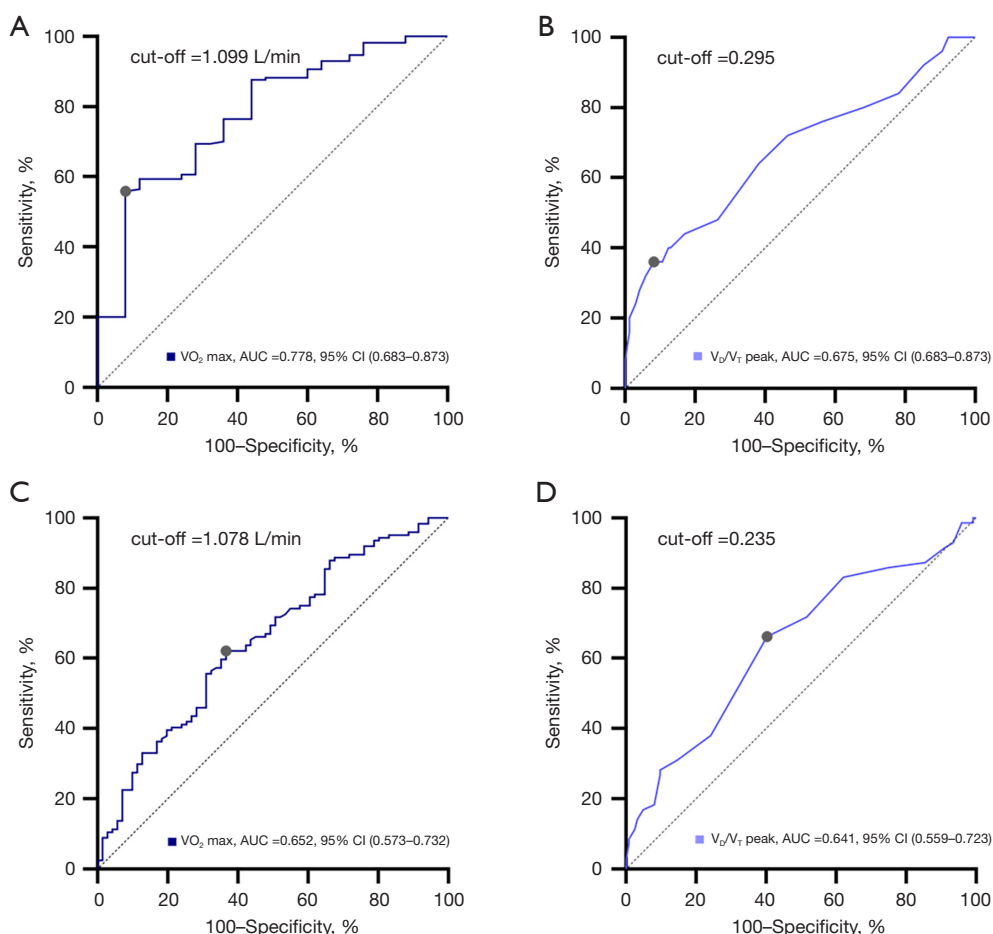


Figure 4 Receiver operating characteristic curves of VO_2 max and V_D/V_T peak in predicting mMRC grade and CAT score. VO_2 max (A) and V_D/V_T peak (B) for predicting mMRC, and VO_2 max (C) and V_D/V_T peak (D) for predicting CAT score. VO_2 max, maximal oxygen uptake; V_D , volume of dead space; V_T , tidal volume; AUC, area under the curve; CI, confidence interval; Mmrc, modified Medical Research Council; CAT, chronic obstructive pulmonary disease Assessment Test.

questionnaires. Therefore, we advocate for the increased utilization of these tools by physicians when assessing patients with COPD.

This retrospective study conducted at a single center is limited by the existence of relevant bias. Moreover, the generalizability of our findings is limited, as the majority of patients were male and the research was conducted exclusively on an Asian population. Also, the number of patients with severe symptoms (mMRC grade ≥ 2 or CAT score ≥ 10) was relatively small. Among patients with severe symptoms, few can undergo CPET and those who can frequently perform submaximal exercise owing to several reasons, including dyspnea and deconditioning. As the correlation is expected to be stronger if more patients with

severe symptoms are analyzed, a larger prospective study involving such patients is required.

Conclusions

In this study, among CPET parameters, VO_2 max and V_D/V_T peak demonstrated significant correlations with mMRC grade and CAT score. This suggests that VO_2 max and V_D/V_T peak are reliable indicators of symptoms and health-related quality of life in patients with COPD.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-185/rc>

Data Sharing Statement: Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-185/dss>

Peer Review File: Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-185/prf>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-185/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the Asan Medical Center (approval No. 2021-0915) and individual consent for this retrospective analysis was waived.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Global Initiative for Chronic Obstructive Lung Disease. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2022 report [Internet]. c2022 [cited 2022 28 November]. Available online: https://goldcopd.org/wp-content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf.
2. Ahmed MS, Neyaz A, Aslami AN. Health-related quality of life of chronic obstructive pulmonary disease patients: Results from a community based cross-sectional study in Aligarh, Uttar Pradesh, India. *Lung India* 2016;33:148-53.
3. Rennard S, Decramer M, Calverley PM, et al. Impact of COPD in North America and Europe in 2000: subjects' perspective of Confronting COPD International Survey. *Eur Respir J* 2002;20:799-805.
4. Hajiro T, Nishimura K, Tsukino M, et al. Analysis of clinical methods used to evaluate dyspnea in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;158:1185-9.
5. Bestall JC, Paul EA, Garrod R, et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999;54:581-6.
6. Nishimura K, Izumi T, Tsukino M, et al. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. *Chest* 2002;121:1434-40.
7. Karloh M, Fleig Mayer A, Maurici R, et al. The COPD Assessment Test: What Do We Know So Far?: A Systematic Review and Meta-Analysis About Clinical Outcomes Prediction and Classification of Patients Into GOLD Stages. *Chest* 2016;149:413-25.
8. Jones PW, Harding G, Berry P, et al. Development and first validation of the COPD Assessment Test. *Eur Respir J* 2009;34:648-54.
9. ERS Task Force; Palange P, Ward SA, et al. Recommendations on the use of exercise testing in clinical practice. *Eur Respir J* 2007;29:185-209.
10. Ferrazza AM, Martolini D, Valli G, et al. Cardiopulmonary exercise testing in the functional and prognostic evaluation of patients with pulmonary diseases. *Respiration* 2009;77:3-17.
11. DeCato TW, Haverkamp H, Hegewald MJ. Cardiopulmonary Exercise Testing (CPET). *Am J Respir Crit Care Med* 2020;201:P1-2.
12. Laveneziana P, Di Paolo M, Palange P. The clinical value of cardiopulmonary exercise testing in the modern era. *Eur Respir Rev* 2021;30:200187.
13. American Thoracic Society; American College of Chest Physicians. ATS/ACCP Statement on cardiopulmonary exercise testing. *Am J Respir Crit Care Med* 2003;167:211-77.
14. Franssen FM, Rochester CL. Comorbidities in patients with COPD and pulmonary rehabilitation: do they matter? *Eur Respir Rev* 2014;23:131-41.
15. Mirdamadi M, Rahimi B, Safavi E, et al. Correlation of cardiopulmonary exercise testing parameters with

- quality of life in stable COPD patients. *J Thorac Dis* 2016;8:2138-45.
16. Berry MJ, Adair NE, Rejeski WJ. Use of peak oxygen consumption in predicting physical function and quality of life in COPD patients. *Chest* 2006;129:1516-22.
 17. Verhage TL, Vercoulen JH, van Helvoort HA, et al. Maximal exercise capacity in chronic obstructive pulmonary disease: a limited indicator of the health status. *Respiration* 2010;80:453-62.
 18. Deterbeck FC, Boffa DJ, Kim AW, et al. The Eighth Edition Lung Cancer Stage Classification. *Chest* 2017;151:193-203.
 19. Jeong D, Oh YM, Lee SW, et al. Comparison of Predicted Exercise Capacity Equations in Adult Korean Subjects. *J Korean Med Sci* 2022;37:e113.
 20. Myers J, Buchanan N, Walsh D, et al. Comparison of the ramp versus standard exercise protocols. *J Am Coll Cardiol* 1991;17:1334-42.
 21. Oga T, Nishimura K, Tsukino M, et al. Analysis of the factors related to mortality in chronic obstructive pulmonary disease: role of exercise capacity and health status. *Am J Respir Crit Care Med* 2003;167:544-9.
 22. Albouaini K, Egred M, Alahmar A, et al. Cardiopulmonary exercise testing and its application. *Heart* 2007;93:1285-92.
 23. Qaseem A, Wilt TJ, Weinberger SE, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med* 2011;155:179-91.
 24. Díaz O, Villafranca C, Ghezzi H, et al. Breathing pattern and gas exchange at peak exercise in COPD patients with and without tidal flow limitation at rest. *Eur Respir J* 2001;17:1120-7.
 25. O'Donnell DE, D'Arsigny C, Fitzpatrick M, et al. Exercise hypercapnia in advanced chronic obstructive pulmonary disease: the role of lung hyperinflation. *Am J Respir Crit Care Med* 2002;166:663-8.

Cite this article as: Lee B, Oh YM, Lee SW, Lee SD, Lee JS. Value of cardiopulmonary exercise testing in the assessment of symptoms and quality of life in Asian patients with chronic obstructive pulmonary disease. *J Thorac Dis* 2023;15(7):3662-3672. doi: 10.21037/jtd-23-185

Supplementary

Table S1 Multivariate odds ratios (ORs) from logistic regression with severe dyspnea (mMRC ≥ 2)

CPET parameters	Adjusted OR (95% CI)	P value
VO ₂ max, L/min	0.426 (0.003–60.408)	0.736
WR max, W	0.991 (0.961–1.023)	0.591
HRR, beats/min	1.027 (0.989–1.067)	0.168
O ₂ pulse max, mL/beat	1.018 (0.872–1.189)	0.821
V _E max, L/min	0.970 (0.872–1.079)	0.573
MVV, L/min	0.930 (0.890–0.973)	0.002
Peak P _{ETCO₂} , mmHg	0.827 (0.684–1.000)	0.05
V _D /V _T peak	0.000 (0.000–0.818)	<0.001

CPET, cardiopulmonary exercise testing; mMRC, modified Medical Research Council; VO₂ max, maximal oxygen uptake; WR, work rate; HRR, heart rate reserve; VE, minute ventilation; MVV, maximal voluntary ventilation; P_{ETCO₂}, end-tidal PCO₂; V_D, dead space volume; V_T, tidal volume.

Table S2 Multivariate odds ratios (ORs) from logistic regression with poor quality of life (CAT ≥ 10)

CPET parameters	Adjusted OR (95% CI)	P value
VO ₂ max, L/min	0.232 (0.016–3.470)	0.290
WR max, W	0.986 (0.968–1.005)	0.151
HRR, beats/min	1.010 (0.990–1.030)	0.320
V _E max, L/min	1.029 (0.971–1.090)	0.336
MVV, L/min	0.982 (0.963–1.002)	0.071
Peak P _{ETCO₂} , mmHg	1.019 (0.920–1.128)	0.719
V _D /V _T rest	114.720 (0.226–58,235.092)	0.136
V _D /V _T peak	0.012 (0.000–753.646)	0.433

CPET, cardiopulmonary exercise testing; CAT, COPD Assessment Test; VO₂ max, maximal oxygen uptake; WR, work rate; HRR, heart rate reserve; V_E, minute ventilation; MVV, maximal voluntary ventilation; P_{ETCO₂}, end-tidal P_{CO₂}; V_D, dead space volume; V_T, tidal volume.