Original Article

Diagnostic Performance of Cardiopulmonary Exercise Testing (CPET) in Chronic Obstructive Pulmonary Disease (COPD) at a Tertiary Hospital in Indonesia

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) remains a major global health burden. Spirometry as the diagnostic gold standard, still has limitations for functional assessment. The existence of cardiopulmonary exercise testing (CPET) provides a comprehensive evaluation of integrated cardiopulmonary and metabolic responses during exercise and may improve diagnostic and management decisions in COPD. This study determined the diagnostic quality of CPET parameters for COPD.

Methods: This observational analytic cross-sectional study used paired spirometry and CPET data from medical records at Universitas Sebelas Maret Hospital. Thirty-seven eligible records were analyzed after obtaining ethics approval. CPET parameters included maximal oxygen uptake (VO_2max), respiratory exchange ratio (RER), and the slope of the ratio between minute ventilation volume and carbon dioxide production volume (VE/VCO_2 slope). Discrimination was assessed using AUC, diagnostic performance was assessed using the chi-square test, and correlation with obstruction severity was assessed using the GOLD classification, with a value of $P<0.05$ being significant.

Results: Of 37 subjects, 62.2% had COPD. COPD status was significantly associated with older age and smoking (both $P<0.05$). VO_2max (sensitivity 73.9%; specificity 78.6%; AUC=0.795; P=0.002), RER (sensitivity 78.3%; specificity 78.6%; AUC=0.846; P=0.001), and VE/VCO_2 slope (sensitivity 78.3%; specificity 71.4%; AUC=742; P=0.003) showed useful discrimination. Among CPET parameters, RER correlated significantly with obstruction severity by GOLD ($P<0.05$), while VO_2max and VE/VCO_2 slope did not ($P>0.05$), though trends were worse with more severe disease.

Conclusion: The integration of CPET with spirometry provides a more comprehensive approach to the diagnosis and management of COPD.

Keywords: cardiopulmonary exercise testing, COPD, spirometry, VO_2max

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) remains a leading cause of morbidity and mortality worldwide, with a substantial and growing burden in low- and middle-income countries, where principal risk factors include male sex, cigarette smoking, and older age. Among adults aged ≥40 years, the global prevalence is 12.64% using the fixed-ratio (FR) criterion and 7.38% using the lower limit of normal (LLN) definition.[1] Further, global COPD cases are also projected to rise by ~23% by 2050 (≈600 million), especially in low-resource regions and among women, driven by aging, urbanization, and air pollution.[2]

Spirometry, used as the primary diagnostic criterion of COPD for confirming chronic airflow obstruction, does not fully capture integrated physiological constraints that determine symptoms and outcomes—particularly exertional dyspnea, exercise intolerance, and ventilatory inefficiency.[3–6] This limitation can lead to diagnostic and management uncertainty in cases with borderline spirometry or discordant symptom burden, where comorbid cardiovascular or metabolic factors may contribute to reduced functional capacity beyond what static ventilatory measures reveal.[7–9]

Meanwhile, cardiopulmonary exercise testing (CPET) provides a dynamic appraisal of respiratory, cardiovascular, and metabolic responses under physiologic stress, identifying mechanisms of exercise limitation to inform prognosis and rehabilitation planning.[10–13] Among commonly reported indices, maximal oxygen uptake (VO_2max) reflects global aerobic capacity, the respiratory exchange ratio (RER) gauges exercise effort and metabolic shift, and the ratio between minute ventilation volume and carbon dioxide production volume (VE/VCO_2 slope) quantifies ventilatory efficiency and dead-space ventilation.

Given the scale of COPD and the need for pragmatic, interpretable tools, this study evaluates the diagnostic performance of VO_2max, RER, and VE/VCO_2 slope for distinguishing COPD from non-COPD and examines their relationship with obstruction severity (GOLD). By estimating areas under the ROC curve, proposing operational cut-offs, and testing associations with GOLD stage, we aim to offer actionable thresholds for integrating CPET alongside spirometry in routine care.[10–13]

METHODS

This study was conducted as an observational analytic cross-sectional study at Universitas Sebelas Maret Hospital, Surakarta, Indonesia. The study population consisted of adult patients who underwent both spirometry and CPET within the same clinical period. Inclusion criteria were based on the GOLD diagnostic standards for COPD and standard CPET eligibility, while exclusion criteria included an inability to complete CPET safely or the presence of incomplete medical records. Consecutive sampling was used. Ethics approval was obtained prior to data collection.

Demographic and clinical variables (age, sex, smoking history, BMI, comorbidities) were abstracted from the medical records. Establishing a diagnosis of COPD and determining the severity of airflow obstruction according to GOLD criteria using spirometry. CPET was performed using institutional protocols, and the following parameters were extracted: VO_2max (mL/kg/min), peak RER, and VE/VCO_2 slope. Operational definitions and quality criteria were based on internationally recognized CPET guidelines. All spirometry and CPET procedures were conducted within a predefined time interval to ensure comparable clinical status.

Descriptive statistics summarized baseline characteristics by COPD status. Group comparisons used chi-square or Fisher's exact tests for categorical variables, and appropriate parametric or non-parametric tests for continuous variables, where $P<0.05$ was considered significant. Receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was calculated for VO_2max, RER, and VE/VCO_2 slope, with optimal cut-off values used to calculate sensitivity, specificity, predictive values, likelihood ratios, and accuracy with respect to the GOLD stage. The relationships between CPET parameters and the severity of airflow obstruction according to GOLD stage were examined using correlation analysis or trend tests, as appropriate.

RESULTS

A total of 37 subjects were analyzed, 62.2% were COPD and 37.8% were not (Figure 1). Whereas, in Table 1 shows baseline demographics and risk factors by COPD status. COPD patients were older and more likely to be smokers, while sex distribution, BMI, and major comorbidities were broadly similar between groups. Analysis shows COPD status was significantly associated with older age and a higher prevalence of smoking (both $P<0.05$).

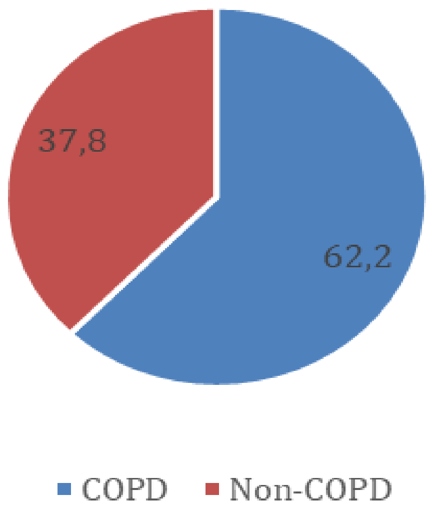

Figure 1. COPD patients' distribution

Table 1. Baseline Characteristics of Subjects

Variable	Non-COPD	COPD	Total	*P*
Sex				
Male	9 (64.3%)	19 (82.6%)	28 (75.7%)	0.255[a]
Female	5 (35.7%)	4 (17.4%)	9 (24.3%)	
Age, years (mean±SD)	46.86±3.66	55.78±11.05	52.41±9.94	0.040*
BMI, kg/m² (mean±SD)	25.63±4.25	23.96±5.50	24.90±5.07	0.339
Smoking Habit				
Non-smoker	9 (64.3%)	3 (13.0%)	12 (32.4%)	
Passive	0 (0.0%)	2 (8.7%)	2 (5.4%)	
Brinkman light	0 (0.0%)	4 (17.4%)	4 (10.8%)	0.021*[a]
Brinkman moderate	4 (28.6%)	10 (43.5%)	14 (37.8%)	
Brinkman heavy	1 (7.1%)	4 (17.4%)	5 (13.5%)	

Note: [a]Chi-square/Fisher's exact as appropriate; *P<0.05

Patients with COPD demonstrated significantly impaired exercise performance across all CPET parameters compared with non-COPD patients. The mean VO_2max was significantly lower in COPD (13.86±4.50 mL/kg/min) than in non-COPD (18.41±3.50 mL/kg/min; P=0.003), indicating reduced aerobic capacity. RER values were also lower (0.98±0.13 vs 1.15±0.11; P<0.001), suggesting submaximal effort, potentially related to ventilatory limitation.

In contrast, the VE/VCO_2 slope was higher in COPD (30.89±7.19) compared with non-COPD (26.00±3.26; P=0.008), consistent with increased ventilatory demand and reduced ventilatory efficiency of gas exchange. Table 2 summarizes these findings, showing that COPD is characterized by VO_2max ↓, RER ↓, and VE/VCO_2 slope ↑, with all differences reaching statistical significance (P<0.05).

Table 2. CPET parameters by COPD status

Parameter	Mean±SD	Median (min–max)	*P*
VO_2max (mL/kg/min)			
Non-COPD	18.41±3.50	1.40 (11.90–24.79)	0.003*
COPD	13.86±4.50	13.11 (6.71–22.46)	
RER			
Non-COPD	1.15±0.11	1.19 (0.93–1.34)	<0.001*
COPD	0.98±0.13	0.98 (0.73–1.22)	
VE/VCO_2 slope			
Non-COPD	26.00±3.26	25.50 (20.90–33.90)	0.008*
COPD	30.89±7.19	29.60 (18.00–45.70)	

Note: *P<0.05 is significant, used an independent t-test

Analysis of ROC yielded AUCs of 0.795 for VO_2max, 0.846 for RER, and 0.742 for VE/VCO_2 slope. Optimal thresholds were: VO_2max <16.17 mL/kg/min; RER <1.08; VE/VCO_2 slope >26.75. All three CPET parameters showed useful discrimination for COPD. VO_2max <16.17 mL/kg/min had an AUC of 0.795, with sensitivity 73.9% and specificity 78.6% (P=0.002). RER <1.08 performed best (AUC=0.846), with sensitivity 78.3% and specificity 78.6% (P=0.001). VE/VCO_2 slope ≥26.75 showed moderate accuracy (AUC=0.742), with sensitivity 78.3% and specificity 71.4% (P=0.003). Among these, RER was the strongest predictor, while VO_2max and VE/VCO_2 slope still provided supportive diagnostic value.

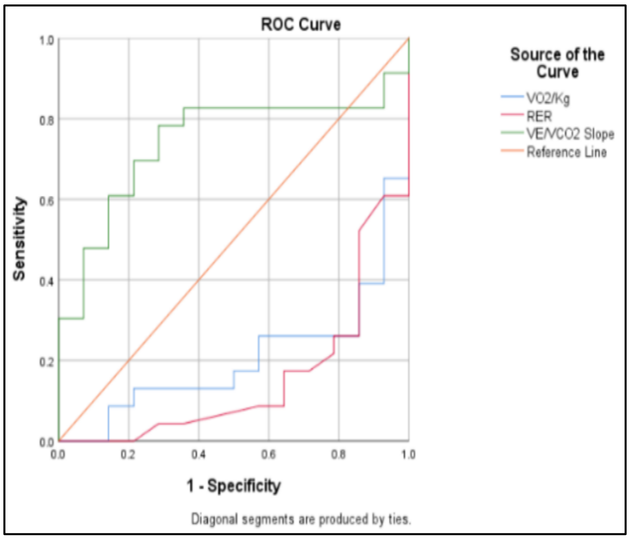

Figure 2. Receiver Operating Characteristic (ROC) curves of VO_2max, RER, and VE/VCO_2 for predicting COPD

Table 3 shows that RER demonstrated the highest discriminatory performance, while VO_2max and VE/VCO_2 slope also demonstrated meaningful diagnostic value. Together, these parameters suggest that CPET may provide complementary diagnostic information when spirometric findings are inconclusive.

Table 3. Diagnostic Performance of VO_2max, RER, and VE/VCO_2 for predicting COPD

Parameter	AUC	Optimal cut-off	*P*	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR–	Accuracy (%)
VO_2max (mL/kg/min)	0.795	< 16.17	0.002*	73.9	78.6	85.0	64.7	3.45	0.33	75.7
RER	0.846	< 1.08	0.001*	78.3	78.6	85.7	68.8	3.65	0.28	78.4
VE/VCO_2 slope	0.742	≥ 26.75	0.003*	78.3	71.4	81.8	66.7	2.74	0.30	75.7

Note: All metrics computed at the stated cut-offs; **P*<0.05

Table 4. CPET parameters vs GOLD obstruction severity

Variable	GOLD 1	GOLD 2	GOLD 3	GOLD 4	*P*
VO_2max					
>16.17	3 (60.0%)	1 (11.1%)	2 (28.6%)	0 (0.0%)	0.210
<16.17	2 (40.0%)	8 (80.9%)	5 (71.4%)	2 (100.0%)	
RER					
>1.08	3 (60.0%)	2 (22.2%)	0 (0.0%)	0 (0.0%)	0.015*
<1.08	2 (40.0%)	7 (77.8%)	7 (100.0%)	2 (100.0%)	
VE/VCO_2					
<26.75	1 (20.0%)	4 (44.4%)	0 (0.0%)	0 (0.0%)	0.182
≥26.75	4 (80.0%)	5 (55.6%)	7 (100.0%)	2 (100.0%)	

Note: *Mann–Whitney for ordinal obstruction; **P*<0.05

In Table 4, across GOLD categories, RER was the only CPET parameter that was significantly associated with obstruction, with the severity of airflow obstruction (*P*=0.015), with progressively lower values in GOLD 3–4 compared to GOLD 1–2. VO_2max and VE/VCO_2 slope did not reach statistical significance (*P*=0.210 and *P*=0.182), though both showed trends toward worse values in more severe GOLD stages. These findings indicate that while RER reflects severity-related effort limitation, VO_2max and VE/VCO_2 slope may still provide a supportive context for functional decline with increasing obstruction.

DISCUSSIONS

Of 37 subjects, 62.2% were COPD and 37.8% were non-COPD. Males predominated in both groups (COPD 82.6% vs non-COPD 64.3%), but the difference was not significant (*P*=0.255), consistent with evidence indicating that sex is not an independent risk factor for COPD when exposure patterns are controlled.[14] Other studies have reported a higher prevalence of COPD among men, likely reflecting heavier and longer cumulative smoking and greater occupational dust exposure.[15]

Age was higher in COPD (55.78±11.05 vs 46.86±3.66 years; *P*=0.040), consistent with epidemiological evidence indicating that COPD prevalence increases markedly with advancing age. BMI did not differ significantly (*P*=0.339), though extremes of BMI can influence COPD outcomes. Low BMI (≤21 kg/m^2) has been linked to worse lung function and survival.[16] Whereas, smoking exposure was significantly associated with COPD (*P*=0.021), mirroring the well-established dose–response relationship between tobacco exposure and COPD risk.[17]

Patients with COPD demonstrated lower VO_2max (*P*<0.05) and RER (0.98±0.13 vs 1.15±0.11; *P*<0.001), compared with a higher VE/VCO_2 slope (30.89±7.19 vs 26.00±3.26, though statistical distinction was not uniform across all subgroup strata). These patterns indicate impaired aerobic capacity, early exercise cessation, and ventilatory inefficiency in COPD.[18–21] Prior work also links lower VO_2max with worse prognosis in COPD.[22,23]

Analysis of ROC identified practical cut-offs, with VO_2max <16.17 mL/kg/min (AUC=0.795), RER <1.08 (AUC=0.846), and VE/VCO_2 slope ≥26.75 (AUC=0.742). At these thresholds, the associations were statistically significant—VO_2max (*P*=0.002), RER (*P*=0.001), VE/VCO_2 slope (*P*=0.003)—with sensitivity and specificity in the mid-70% range. In multivariable analysis, RER remained the strongest independent predictor of COPD (OR=13.47; *P*=0.003), highlighting its potential diagnostic utility alongside VO_2max and VE/VCO_2 slope as a pragmatic diagnostic adjunct when spirometry is borderline or discordant.[18,19,22–24]

Most COPD patients were GOLD 2 (39.1%) or GOLD 3 (30.4%), with smaller proportions in GOLD 1 (21.7%) and GOLD 4 (8.7%). RER correlated significantly with obstruction severity (P=0.015), whereas VO_2max (P=0.210) and VE/VCO_2 slope (P=0.182) showed non-significant but directionally consistent trends (worse values at higher GOLD stage). These findings are consistent with previous studies linking lower exercise capacity and ventilatory inefficiency to symptom burden and disease severity, though results vary across cohorts.[25–28]

Clinically, CPET complements spirometry by revealing functional constraints not fully captured by FEV_1 alone. Integrating RER, VO_2max, and VE/VCO_2 slope can refine diagnosis, gauge physiological limitation, and inform rehabilitation planning in routine care.[23,24]

LIMITATIONS

This study has several limitations that should be acknowledged. First, the cross-sectional design prevents conclusions about causality between CPET parameters and COPD outcomes, so that only associations can be described. Second, data were obtained from existing medical records, which may be incomplete or subject to documentation bias. The retrospective design also limited control, standardization of testing conditions and potential confounders, such as comorbidities or medication use, that could influence CPET performance. Third, the relatively small sample size from a single tertiary hospital restricts the generalizability of the findings to broader COPD populations. Finally, while VO_2max, RER, and VE/VCO_2 slope provided valuable diagnostic insights, other CPET parameters (e.g., oxygen pulse, ventilatory reserve, or lactate threshold) were not analyzed and may yield additional information in future research.

CONCLUSION

Cardiopulmonary exercise testing parameters, including VO_2max, RER, and VE/VCO_2 slope, complement spirometry for diagnosing COPD and gauging disease severity. RER demonstrated the strongest discriminative and severity-related signal. Integrating CPET with spirometry may enhance comprehensive COPD management in routine practice.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests, financial or otherwise, that could have influenced the conduct or reporting of this research.

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