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ORIGINAL RESEARCH

## Characteristics and Quality of Life of Patients with COPD with Different Degrees of Exercise-Induced Desaturation on Six-minute Walk Test

Beiyao Gao<sup>1,\*</sup>, Siyuan Wang<sup>1,\*</sup>, Li Zhao<sup>2-5,\*</sup>, Hongbin Liao<sup>6</sup>, Shiwei Qumu<sup>4,5,7</sup>, Peijian Wang<sup>1</sup>, Ting Yang<sup>4,5,7</sup>, Shan Jiang<sup>1</sup>

<sup>1</sup>Department of Rehabilitation Medicine, China-Japan Friendship Hospital, Beijing, People's Republic of China; <sup>2</sup>Department of Lung Transplantation, China-Japan Friendship Hospital, Beijing, People's Republic of China; <sup>3</sup>National Center for Respiratory Medicine, China-Japan Friendship Hospital, Beijing, People's Republic of China; <sup>4</sup>National Clinical Research Center for Respiratory Diseases, Beijing, People's Republic of China; <sup>5</sup>Institute of Respiratory Medicine, Chinese Academy of Medical Sciences, Beijing, China; <sup>6</sup>Department of Clinical Medicine, Peking University, Beijing, People's Republic of China; <sup>7</sup>Department of Pulmonary and Critical Care Medicine, China-Japan Friendship Hospital, Beijing, People's Republic of China

\*These authors contributed equally to this work

Correspondence: Shan Jiang; Ting Yang, Email landjiang@126.com; zryyyangting@163.com

**Objective:** To identify predictive factors for different exercise-induced desaturation (EID) severities and evaluate health-related quality of life six months later in chronic obstructive pulmonary disease (COPD) patients.

**Methods:** This retrospective study consecutively analyzed 116 COPD outpatients (male: 82.8% [96/116]; age:  $63.48 \pm 7.48$  years; disease severity distribution: GOLD 1/2/3/4 = 55.8%/34.6%/7.7%/1.9%). Patients were categorized into three groups based on oxygen desaturation (SpO<sub>2</sub>) during the six-minute walk test (6MWT): non-EID (n = 52), mild-EID (n = 42), and severe-EID (n = 22). EID was classified as follows: Mild EID: SpO<sub>2</sub> decrease  $\ge 4\%$  with nadir SpO<sub>2</sub>  $\ge 90\%$ . Severe EID: SpO<sub>2</sub> decrease  $\ge 4\%$  with nadir SpO<sub>2</sub>  $\ge 90\%$ . A six-month follow-up was conducted via telephone to record adverse events and assess quality of life using the Chinese version of the EQ-5D questionnaire, which includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, along with the EQ-VAS scale.

**Results:** Significant differences were observed across the three groups in peripheral blood oxygen saturation (SpO<sub>2</sub>, %), peak expiratory flow (PEF, L/s), PEF (%), forced expiratory volume in the first second (FEV1, L), FEV1 (%), 6MWT distance (6MWD, m), Borg dyspnea, and Borg fatigue scores. The optimal cutoff values for predicting EID severity was 54.45% for FEV1% (AUC=0.716), 450.5 m for 6MWD (AUC = 0.761), and 94.5% for resting SpO<sub>2</sub> (AUC = 0.737). Multivariate logistic regression analysis identified low FEV1%, reduced 6MWD, and low resting SpO<sub>2</sub> as risk factors for severe EID (FEV1%: p = 0.002; 6MWD: p = 0.008; SpO<sub>2</sub>: p = 0.018. Severe EID patients had significantly lower EQ-5D index and EQ-VAS scores (EQ-5D index: p = 0.002; EQ-VAS: P = 0.005), particularly in mobility and usual activities dimensions (mobility: p = 0.001; usual activities: p = 0.038). **Conclusion:** Low FEV1%, reduced 6MWD, and low resting SpO<sub>2</sub> are key risk factors for severe EID, provide practical thresholds for clinical management of EID in COPD patients.

Keywords: chronic obstructive pulmonary disease, exercise-induced desaturation, health-related quality of life

### **Background**

Chronic obstructive pulmonary disease (COPD) is a prevalent and debilitating respiratory condition characterized by irreversible airflow limitation, primarily resulting from chronic bronchitis and emphysema. It significantly impairs patients' quality of life and is a leading cause of morbidity and mortality worldwide, contributing to a substantial burden on healthcare systems. Despite advancements in pharmacological management and rehabilitation approaches, there

remains a critical need for comprehensive strategies that address the multifaceted nature of COPD, including its exerciseinduced symptoms and associated comorbidities.<sup>1,2</sup>

In particular, exercise-induced desaturation (EID) during physical activity is a common phenomenon among COPD patients, with studies indicating that approximately 20% or more of this patient population experiences significant oxygen desaturation during exertion.<sup>3–5</sup> Current literature highlights the importance of assessing EID as an indicator of disease severity and a predictor of adverse outcomes, such as increased hospitalization and mortality rates.<sup>6</sup> Nonetheless, the criteria for diagnosing EID are inconsistent across studies,<sup>7</sup> often relying on single assessments of resting  $SpO_2$  or subjective evaluations of exercise tolerance. This inconsistency underlines a significant gap in our understanding of how EID manifests in different COPD phenotypes and its implications for patient management.<sup>8</sup> Furthermore, dynamic monitoring of SpO<sub>2</sub> during standardized exercise tests, particularly the six-minute walk test (6MWT), is essential for accurately capturing EID and its physiological correlates.<sup>9</sup> The 6MWT has emerged as a widely accepted tool for evaluating exercise capacity in COPD patients, providing valuable insights into their functional status and prognosis.<sup>10</sup> It is not only straightforward to administer but also sensitive to changes in patient condition, making it a pivotal component of routine clinical assessments. Previous studies have demonstrated that a decline in SpO<sub>2</sub> during the 6MWT is associated with a higher risk of COPD exacerbations and mortality, reinforcing the need for continuous monitoring of oxygen levels during exertion.<sup>9,11-13</sup> However, the relationship between EID severity and health-related quality of life remains underexplored, with limited research investigating how varying degrees of desaturation impact patients' daily functioning and overall well-being. In summary, while the multifactorial nature of COPD necessitates a nuanced understanding of its clinical manifestations, existing literature provides a foundation for investigating the prevalence and implications of exercise-induced desaturation. This study endeavors to fill the current research void regarding EID characteristics and health-related quality of life among COPD patients, thereby advancing the knowledge base in this critical area of respiratory medicine. The present study adopts a retrospective design to address these gaps by analyzing data from 116 COPD patients who underwent the 6MWT. It aims to classify the severity of EID and evaluate its association with various physiological parameters, including forced expiratory volume (FEV1) and the distance walked during the test. Additionally, the research will assess the impact of EID on healthrelated quality of life, utilizing standardized measures such as the EQ-5D, to identify potential predictors of EID severity and their clinical implications. By elucidating these relationships, this study seeks to contribute to the development of targeted interventions for COPD patients, ultimately enhancing their management and quality of life.<sup>14-17</sup>

### **Materials and Methods**

### Data Collection

The study ethical approval was obtained from the China–Japan Friendship Hospital (2022-KY-141; clinical trial registration number: NCT04318912). Informed consent was obtained from all participants prior to their inclusion in the study. Patient data confidentiality was strictly maintained, and all procedures were in compliance with the Declaration of Helsinki. This study included 116 COPD patients diagnosed between May 1, 2023, and June 30, 2024, at the China–Japan Friendship Hospital. The cohort consisted of 97 males and 20 females. Inclusion criteria were based on the 2020 GOLD guidelines for stable COPD. Exclusion criteria included:

- 1. Resting SpO<sub>2</sub>  $\leq$  92%, HR > 120 bpm.
- 2. Systolic BP > 180 mmHg or diastolic BP > 100 mmHg.
- 3. Malignant arrhythmias.
- 4. Severe valvular disease.
- 5. Walking limitations due to neurological or musculoskeletal disorders.
- 6. Concurrent malignancy. Demographic data such as gender, age, baseline heart rate, and SpO<sub>2</sub> were extracted from electronic medical records.

### **Pulmonary Function Testing**

Pulmonary function tests were performed using the MasterScreen<sup>™</sup> PFT system (CareFusion Germany GmbH, Höchberg, Germany) following ATS/ERS guidelines. Parameters measured included forced expiratory volume in the

first second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, peak expiratory flow (PEF), and their respective predicted values.

## Six-minute Walk Test (6MWT) and SpO<sub>2</sub> Monitoring

The 6MWT was performed in a 30-meter indoor hallway following ATS guidelines as described previously,<sup>18,19</sup> supervised by two trained assessors. Continuous SpO<sub>2</sub> was monitored using a Multidimensional assessment system for 6-minute walk test with integrated wearable cardiopulmonary exercise test (Yiliankang Medical Technology Co., Zhejiang, China), with Bluetooth-enabled data acquisition at 3-second intervals from 1 minute pre-test to 4 minutes posttest. Subjective dyspnea and fatigue were assessed using the Borg scale post-test. EID was classified as follows: Mild EID: SpO<sub>2</sub> decrease  $\geq$ 4% with nadir SpO<sub>2</sub>  $\geq$ 90%. Severe EID: SpO<sub>2</sub> decrease  $\geq$ 4% with nadir SpO<sub>2</sub>  $\geq$ 90%.<sup>16</sup>

## The COPD Assessment Test (CAT)

The validated questionnaire was administered to evaluate symptom burden.<sup>20</sup> The CAT consists of 8 items (cough, cough sputum, chest tightness, shortness of breath climbing/walking up stairs, limitation of daily activities, confidence to go out, sleep quality, energy level), each using a 0–5 point Likert scale (0 = no effect, 5 = extremely severe).

### Hand Grip Strength

Measured using a Jamar Hydraulic Hand Dynamometer (KDG Grip Strength Tester, Bolingbrook, USA), with participants seated and elbow flexed at 90°.

## Quadriceps Strength

Assessed with an isokinetic dynamometer (MicroFET 2; Hoggan, West Jordan, UT), with participants positioned in 90° hip flexion and 60° knee flexion.

## Follow-Up

Patients were followed up six months post-clinic visit via telephone to record survival status, adverse events (acute exacerbations, complications, rehospitalizations), and quality of life using the Chinese EQ-5D-5L questionnaire.

## The EQ-5D-5L

EQ-5D-5L questionnaire includes five dimensions graded into five levels and a visual analog scale (EQ-VAS) for overall health evaluation.<sup>21</sup> Five dimensions of health included mobility, self-care, activities of daily living, pain/discomfort, anxiety/depression with 5 severity levels for each dimension. Health Status Codes: 5-digit codes (eg, "12345" for no difficulty with mobility, minor difficulty with self-care, etc), detailed information regarding the scoring system of the EQ-5D-5L questionnaire has been added to the <u>Table S1</u>. Indicator conversion was based on country/region-specific utility weights (eg, China). Conversion of 5-digit code to a single health utility index based on country/region-specific utility weights.

## Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics (version 26.0; IBM Corporation, Armonk, New York, USA). Measurement data following a normal distribution were expressed as mean  $\pm$  standard deviation (x<sup>-</sup> $\pm$ s). ANOVA was used to compare means across  $\geq$ 3 groups, justified by confirmed normality (Shapiro–Wilk test) and equal variance (Levene's test). Post hoc Bonferroni tests identified specific group differences if ANOVA was significant (\*p < 0.05\*). Count data were expressed as numbers or percentages and analyzed using the chi-square test. Significance testing of regression coefficients was performed at a significance level of 0.05. Multivariate logistic regression was used to analyze factors influencing severe EID in COPD patients. ROC curves were plotted to evaluate the predictive ability of influencing factors for the severity of EID.

## Results

### General Characteristics of Patients

A total of 116 COPD patients were included in the study, with an average age of  $63.32 \pm 7.99$  years. Among them, 44.8% patients had no EID, 36.2% had mild EID, and 19.0% had severe EID. There were no statistically significant differences in gender, age, BMI, grip strength, knee extension strength, or rest heart rate among the three groups (p > 0.05). Compared to patients with no or mild EID, those with severe EID had significantly lower levels of rest SPO<sub>2</sub> (%), PEF (L/s), PEF (%), FEV1 (L), and FEV1 (%) (SPO<sub>2</sub>: p = 0.002; PEF: p < 0.001; PEF (%): p < 0.001; FEV1: p = 0.026; FEV1 (%): p = 0.001). Severe EID patients also had shorter 6MWD (P < 0.001) and experienced more severe dyspnea and fatigue (Borg dyspnea: p = 0.040; Borg fatigue: p = 0.015). (See Table 1).

# Multivariate Logistic Regression Analysis of Factors Influencing Severe EID in COPD Patients

Taking the severity of EID in COPD patients as the dependent variable (1 = severe EID, 0 = non-severe EID), variables with p < 0.05 from Table 1 were included as independent variables in the logistic regression analysis. Results showed that low FEV1(%), low 6MWD, and low blood SpO<sub>2</sub> were risk factors for severe EID in COPD patients (FEV1(%): p = 0.002; 6MWD: p = 0.008; blood oxygen: p = 0.018). (See Table 2).

## Analysis of FEVI (%), 6MWD, and Resting SpO<sub>2</sub> in Relation to EID Severity

The optimal cut-off values for predicting EID severity were as follows: FEV1(%): 54.45, with an AUC of 0.716. 6MWD (m): 450.5 m, with an AUC of 0.761. SpO<sub>2</sub> (%) at rest: 94.5%, with an AUC of 0.737. FEV1(%), 6MWD, and resting SpO<sub>2</sub> effectively distinguished patients with severe EID from those with non-severe EID. (See Figure 1 and Table 3).

### Health-Related Quality of Life in Patients with Different EID Severity

No deaths were reported during the follow-up period. Severe EID patients had significantly lower EQ-5D index and EQ VAS scores (EQ-5D index: p = 0.002; EQ VAS: p = 0.005). Among the five dimensions of the EQ-5D-5L scale, there were no significant differences in self-care, pain/discomfort, or anxiety/depression scores among groups (p > 0.05). However, patients with severe EID had significantly lower scores in mobility and usual activities compared to those with no or mild EID (mobility: p = 0.001; usual activities: p = 0.038). (Figure 2 and Table 4). Besides, there is no statistically significant difference in the frequency of acute exacerbations, emergency department visit or hospitalization rates, and Respiratory tract infection incidence rates among the different EID groups (p > 0.05) (Table 5).

## Discussion

The study highlights actionable thresholds (FEV1%, 6MWD, SpO<sub>2</sub>) and symptom metrics (Borg scores) that are clinically practical for EID management. By translating these findings into care pathways, clinicians can improve early diagnosis, tailor interventions, and optimize patient-centered outcomes.

Effective management strategies are critical, yet they often fall short of comprehensively addressing the multifaceted nature of the disease, particularly as COPD progresses and leads to exacerbations and comorbidities that further complicate patient care.<sup>4</sup> This study aims to investigate the characteristics of EID in COPD patients, identify predictive factors for varying degrees of EID, and evaluate the impact of EID on health-related quality of life (HRQoL). By analysis of clinical data from 116 COPD patients undergoing the six-minute walk test (6MWT), we aim to elucidate the relationship between physiological parameters and EID severity. In this study, approximately 55% of COPD patients exhibited EID. Research has shown that the severity of airflow limitation is associated with EID, with patients experiencing reduced FEV1 having a higher risk of EID.<sup>3</sup> Another study indicated that the decline in SpO<sub>2</sub> was significantly associated with reduced FEV.<sup>19</sup> This study demonstrated that pulmonary function parameters such as FEV1, and FEV1%value were associated with EID, suggesting that worsening EID is related to deteriorating pulmonary function, consistent with previous studies. However, some studies have indicated that pulmonary function alone may not sufficiently predict a reduction in 6MWD. The relationship between obesity and EID remains unclear. Some studies have

Characteristic	Non-EID	Mild-EID	Severe-EID	p Value	
	(n=52)	(n=42)	(n=22)	•	
Gender /Male	86.50%	76,70%	86 40%	0.413	
Age	63.48±7.48	62.16±8.83	65.18±7.39	0.350	
BMI (kg/m²)	24.07±3.50	24.07±3.39	24.20±4.06	0.987	
GOLD stage				0.082	
GOLD I	55.8%	35.7%	13.6%		
GOLD 2	34.6%	45.2%	40.9%		
GOLD 3	7.7%	16.7%	31.8%		
GOLD 4	1.9%	2.4%	13.6%		
Smoking Status					
Never smoker	30.8%	31.0%	31.8%		
Former smoker	34.6%	38.1%	36.4%	0.963	
Current smoker	34.6%	31.0%	31.8%		
Smoking Duration (years)	32.6 ± 8.5	34.1 ± 9.2	33.2 ± 7.8	0.423	
Cumulative Tobacco Exposure (Pack-years)	385.2 ± 108.7	398.5 ± 115.4	393.8 ± 110.2	0.682	
Whether regular inhaler use				0.997	
Regular use	13.5%	14.3%	15.0%		
Non-regular use	86.5%	85.7%	85.0%		
Grip strength (kg)	34.31±12.10	33.65±17.69	32.28±11.70	0.856	
Knee extension strength (kg)	28.69±25.98	28.82±12.17	29.67±13.86	0.980	
Heart rate (bpm)	82.37±11.62	83.71±14.08	86.14±13.28	0.516	
SpO <sub>2</sub> (%) at rest	95.46±1.74	95.74±2.20	93.91±2.11	0.002	
PEF (L/S)	5.31±1.86	5.56±2.33	3.22±2.11	<0.001	
PEF (%)	71.89±22.97	77.79±30.54	46.83±31.12	<0.001	
FVC (L)	3.10±1.40	3.26±1.21	2.83±1.82	0.514	
FVC predicted (%)	84.92±27.10	88.68±29.20	80.12±45.41	0.588	
FEVI(L)	2.06±0.97	1.92±0.88	1.41±0.97	0.026	
FEVI (%)	64.58±17.44	65.40±22.49	46.63±22.45	0.001	
FEVI/FVC (%)	57.77±29.20	56.31±22.61	38.21±52.66	0.055	
6MWD	489.92±72.70	512.52±90.61	416.73±91.63	<0.001	
Borg dyspnea scale level					
Not at all	2.10%	13.50%	0.00%	0.040	
Extremely light	18.80%	21.60%	0.00%		
Very light	22.90%	16.20%	15.80%		
Light	18.80%	18.90%	10.50%		
Heavy	18.80%	16.20%	31.60%		
Slightly severe	10.40%	10.80%	21.10%		
Extremely severe	8.30%	2.70%	21.10%		
Borg exertion level					
Very light	2.10%	5.40%	0.00%	0.015	
Light	14.60%	18.90%	0.00%		
Moderately light	31.30%	21.60%	5.30%		
Somewhat hard	25.00%	37.80%	47.40%		
Hard	22.90%	13.50%	26.30%		
Very hard	4.20%	2.70%	21.10%		

 Table I Basic Characteristic Information of Patients with Different Degrees of EID in Chronic Obstructive

 Pulmonary Disease

Note: Statistical significance (P<0.05) is highlighted in bold.

identified obesity as a positive predictor of EID, possibly because obese patients are more prone to dyspnea.<sup>3,12</sup> Waatevik et al<sup>13</sup> found a significant association between obesity and EID before incorporating the modified Medical Research Council dyspnea score into their model. However, other studies reported a negative correlation, with moderate obesity potentially mitigating hyperinflation and improving dyspnea in COPD patients.<sup>4</sup> Kim et al<sup>6</sup> found that patients with EID

		В	Standard Error	Wald Chi-Square Value	P value	OR	OR CI 95%
Model I	FEV1(%) Constant value	-0.047 1.171	0.013	12.215	<0.001	0.954	0.929~0.979
Model 2	FEV1(%) 6MWD (m) Constant value	-0.047 -0.01 5.945	0.015 0.003	9.996 10.483	0.002 0.001	0.954 0.99	0.927~0.982 0.983~0.996
Model 3	FEVI (%) 6MWD (m) SpO <sub>2</sub> (%) at rest Constant value	-0.05 -0.009 -0.362 39.756	0.016 0.003 0.153	9.736 7.059 5.599	0.002 0.008 0.018	0.951 0.991 0.696	0.985~0.998 0.922~0.982 0.516~0.94

 Table 2 Identifies the Factors Influencing Severe EID Through Logistic Regression and Establishes a Regression

 Model

had lower average BMI, with BMI reduction linked to increased mortality risk. In this study, obesity was not associated with EID, possibly due to the small sample size. The relationship and underlying mechanisms between obesity and EID require further exploration. Furthermore, some studies have indicated that advanced age and female sex are associated with an increased risk of EID.<sup>5</sup> However, in this study, neither age nor sex was related to EID, which may be attributed to selection bias in the sample.

The prediction of EID can provide valuable guidance for clinical practice and prognostic management. Perez et al<sup>4</sup> reported that an abnormal reduction in resting  $SpO_2$  could serve as a predictor of EID. Andrianopoulos et al<sup>7</sup> identified the 6MWT as the preferred exercise test due to its simplicity and sensitivity to arterial oxygen desaturation. This study showed that FEV1%, 6MWD, and resting  $SpO_2$  could effectively predict the degree of EID, consistent with previous research. Additionally, some studies have suggested that diffusion capacity of the lung for carbon monoxide (DLCO) could predict the extent of oxygen desaturation. CT-defined emphysema has been found to outperform<sup>19</sup> and resting  $SpO_2$  in specific predictive contexts.<sup>13</sup> The current limitations of single-factor EID prediction emphasize the need for further research into multifactorial predictive models to more accurately predict EID and guide clinical and prognostic interventions.



Figure I ROC curve with FEVI, 6MWD, and resting blood oxygen can distinguish between severe EID patients and non-severe EID patients.

	AUC	Standard Error	P value	Cut-Off	Youden's Index
FEVI (%)	0.716	0.067	0.002	54.45	0.366
6MWD (m)	0.761	0.055	<0.001	450.5	0.447
SpO <sub>2</sub> (%) at rest	0.737	0.059	0.001	94.5	0.485

Table 3 Comparison of FEV1(%), 6MWD, and Resting  $SpO_2$  Between Severe and Non-Severe EID Patients

Furthermore, this study found that severe EID reduces HRQoL, primarily by impairing mobility and causing inconvenience in daily life. Patients with EID face a higher risk of dyspnea or fatigue during routine activities. Salant et al<sup>14</sup> reported that the mean utility value for assessing COPD patients using EQ-5D-5L in a meta-analysis was 0.676, compared to 0.780 for EQ-5D-3L. Moreover, longer timeframes in the EQ-5D scale can reduce ceiling effects and enhance reliability.<sup>17</sup> In this study, the timeframe for the EQ-5D scale was set as "today". Using a longer timeframe, such as "1 week" or "4 weeks", might better reflect the overall HRQoL of patients.

The findings will enhance our understanding of the predictors of EID and provide insights into how EID correlates with patients' functional status and overall quality of life, thereby guiding clinical management approaches tailored to individual patient needs. The innovation of this study lies in its comprehensive evaluation of EID in COPD patients through the lens of the 6MWT. Unlike previous research which primarily focused on static measurements of lung function,<sup>4,9,10,22</sup> our study highlights the dynamic nature of SpO<sub>2</sub> during exertion, filling a significant gap in the literature. While earlier studies, such as those by Chang et al,<sup>5</sup> indicated correlations between static pulmonary function metrics and EID, our findings suggest that factors such as the 6MWD and resting SpO<sub>2</sub> levels serve as critical predictive markers for EID severity. This research not only corroborates existing knowledge but also provides novel insights into the prognostic implications of EID for COPD patients, particularly in predicting long-term outcomes and guiding therapeutic interventions. The implications of our findings extend to clinical practice and policy-making. By identifying specific risk factors associated with EID, such as low FEV1% and diminished 6MWD, clinicians can implement targeted interventions for high-risk patients. This could include more personalized rehabilitation programs and the potential use of supplemental oxygen during physical activity to enhance exercise tolerance. Moreover, the identification of EID as a significant



Figure 2 The violin plot used to display the distribution of EQ-5D index across three groups, including statistical information such as density distribution, median, and quartiles. P-value \* < 0.05, \*\*\*< 0.001, ns >0.05.

	Non-EID (n=52)	Mild-EID (n=42)	Severe-EID (n=22)	P Value
EQ-5D index	0.87±0.22	0.93±0.13	0.72±0.33	0.002
EQ Vas	77.37±13.84	80.23±12.91	67.50±19.44	0.005
Mobility				
, No difficulty	57.70%	69.80%	27.30%	0.001
Slight difficulty	30.80%	25.60%	22.70%	
Moderate difficulty	5.80%	4.70%	31.80%	
Severe difficulty	5.80%	0.00%	18.20%	
Self-care				0.138
No difficulty	86.50%	95.30%	72.70%	
, Slight difficulty	7.70%	2.30%	9.10%	
Moderate difficulty	3.80%	0.00%	13.60%	
Severe difficulty	1.90%	0.00%	4.50%	
Unable to perform	0.00%	2.30%	0.00%	
Daily activities				
No difficulty	76.90%	79.10%	54.50%	0.038
Slight difficulty	9.60%	18.60%	13.60%	
Moderate difficulty	9.60%	2.30%	13.60%	
Severe difficulty	3.80%	0.00%	13.60%	
Unable to perform	0.00%	0.00%	4.50%	
Pain discomfort				
None	67.30%	83.70%	72.70%	0.340
Slight	23.10%	14.00%	13.60%	
Moderate	5.80%	0.00%	9.10%	
Severe	3.80%	0.00%	4.50%	
Very severe	0.00%	2.30%	0.00%	
Anxiety depression				
None	76.90%	83.70%	68.20%	0.391
Slight	15.40%	14.00%	13.60%	
Moderate	1.90%	2.30%	4.50%	
Severe	5.80%	0.00%	13.60%	
CAT total score	4.13±5.57	2.37±4.02	8.14±7.01	<0.001

Table 4	Follow-Up	EQ-5D	Data	of	COPD	Patients	with	Different	Degrees	of	EID	at	6
Months													

 Table 5 Follow-Up Data of COPD Patients with Different Degrees of EID During 6 Months

	Non-EID (n=52)	Mild-EID (n=42)	Severe-EID (n=22)	P Value
COPD Acute Exacerbations				
Never	92.30%	88.40%	86.40%	0.731
Once	1.90%	7.00%	4.50%	
Twice	3.80%	4.70%	9.10%	
≥3 times	1.90%	0.00%	0.00%	
Emergency department visit or hospitalization				
No	92.30%	86.00%	86.40%	0.574
Yes	7.70%	14.00%	13.60%	
Respiratory tract infection				
No	88.50%	86.00%	81.80%	0.747
Yes	11.50%	14.00%	18.20%	

predictor of adverse outcomes highlights the necessity for routine monitoring of  $SpO_2$  during physical exertion in COPD management protocols. These insights could influence health policy by advocating for integrated care approaches that prioritize exercise assessments alongside traditional pulmonary function tests, ultimately aiming to improve patient quality of life and reduce healthcare costs associated with COPD exacerbations.

Importantly, our previous study did examine the relationship between cardiovascular function and EID, despite evidence suggesting that conditions such as atrial fibrillation may increase the risk of EID during six-minute walk tests.<sup>16</sup> Chang et al<sup>5</sup> had found that atrial fibrillation was associated with EID, with COPD patients exhibiting higher risks of oxygen desaturation during the 6MWT. Mesquita et al<sup>23</sup> had reported that COPD patients with impaired left ventricular ejection fraction had significantly reduced 6MWD. But, the impact of left ventricular ejection fraction on six-minute walk distance was not investigated, despite existing literature indicating that compromised cardiac function could affect exercise capacity in COPD patients. In the future, the relationship between cardiovascular function and EID should be analyzed.

However, this study is not without limitations. The relatively small sample size may hinder the generalizability of the findings. Future research should aim to include larger, multicentric cohorts to validate our results further. Additionally, the proportion of patients who experienced exacerbations during the 6-month follow-up was relatively low, which may have reduced the statistical power to detect the association between EID and the risk of exacerbations. This limitation is partly due to the characteristics of the study cohort, which included stable COPD patients with good adherence to treatment and regular health management. Therefore, caution is needed when interpreting the relationship between EID and exacerbation risk based on our findings, and future studies involving cohorts with higher exacerbation rates are warranted to validate these results.

In summary, this study elucidates the clinical characteristics and predictive factors associated with EID in COPD patients, revealing a significant impact on their quality of life. The findings underscore the importance of early identification and management of EID to improve patient outcomes. By establishing the relationship between various physiological parameters and EID severity, this research provides a foundation for developing targeted interventions aimed at enhancing the quality of life for individuals with COPD. Future studies should focus on validating these predictive factors in larger, diverse populations and exploring the interplay between cardiovascular and pulmonary functions to further refine management strategies.

### Conclusion

This study highlights the necessity of a multifactorial approach to EID management, considering pulmonary function parameters, mobility, baseline oxygen saturation, and subjective patient experiences. These factors not only aid in identifying high-risk patients but also provide a basis for personalized treatment. Moreover, the relationship between EID and HRQoL underscores the importance of considering patient quality of life in COPD management. Monitoring parameters such as FEV1%, 6MWD, and resting SpO<sub>2</sub> can facilitate the effective assessment of EID in COPD patients, enabling earlier interventions to enhance patient outcomes and quality of life.

### **Data Sharing Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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### **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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