

Original Article

Association between disease severity, nutritional status, body composition, and sarcopenia in patients with chronic obstructive pulmonary disease

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Abstract: Objective: To investigate the relationship between the severity of chronic obstructive pulmonary disease (COPD) and nutritional status, body composition, blood gas parameters, and the risk of sarcopenia, and to identify the independent influencing factors associated with sarcopenia. Methods: A total of 240 patients with COPD were retrospectively included in this study and divided into mild (n=80), moderate (n=66), severe (n=52), and extremely severe (n=42) groups according to disease severity. Differences in grip strength, nutritional status, serological markers, body composition characteristics, and blood gas parameters among the four groups were compared. According to the presence or absence of sarcopenia at the 1-year follow-up, patients were further divided into a sarcopenia group and a non-sarcopenia group for prognostic analysis. Results: With increasing severity of COPD, body weight, arm muscle circumference (AMC), handgrip strength, albumin (ALB), prealbumin (PA), retinol-binding protein (RBP), cholinesterase (CHE), fat-free mass (FFM), muscle mass (MM), skeletal muscle mass (SMM), skeletal muscle mass index (SMMI), fat-free mass index (FFMI), arterial partial pressure of oxygen (PaO_2), and arterial oxygen saturation (SaO_2) showed progressive decreases. In contrast, the Nutritional Risk Screening 2002 (NRS 2002) score, Subjective Global Assessment (SGA) score, hemoglobin (HGB), neutrophil-to-lymphocyte ratio (NLR), arterial partial pressure of carbon dioxide (PaCO_2), and prevalence of sarcopenia gradually increased (all $P<0.05$). Multivariate logistic regression analysis demonstrated that the NRS 2002 score and NLR were independent risk factors for sarcopenia, whereas ALB, handgrip strength, FFMI, PaO_2 , SMMI, RBP, and CHE were independent protective factors (all $P<0.05$). Conclusion: The severity of COPD is associated with impaired nutritional status, reduced muscle mass, and an increased risk of sarcopenia.

Keywords: COPD, severity of illness, nutritional status, body composition characteristics, sarcopenia

Introduction

Chronic obstructive pulmonary disease (COPD) is a global disease burden associated with high morbidity and mortality, and its impact extends beyond the respiratory system, often accompanied by various extrapulmonary manifestations [1, 2]. Among these, malnutrition is one of the most common and clinically significant comorbidities in COPD patients, with a high prevalence and it is recognized as an independent risk factor affecting patient prognosis [3]. The underlying mechanism involves an imbalance between insufficient energy intake and increased energy expenditure, which not only impairs physiological functions but also directly limits muscle protein synthesis and repair. Over

time, the body is compelled to break down muscle tissue to meet basal energy demands, ultimately leading to reduced muscle mass and impaired muscle function [4].

Sarcopenia is a syndrome characterized by the progressive loss of skeletal muscle mass, strength, and physical function. In patients with COPD, the prevalence of sarcopenia is significantly increased and is closely associated with reduced physical activity, compromised quality of life, and increased mortality [5]. More importantly, a vicious cycle exists between sarcopenia and malnutrition: muscle loss contributes to reduced physical activity, which further reduces nutritional intake and impairs nutrient absorption and utilization, thereby exacerbating mal-

nutrition and potentially triggering or aggravating immune dysfunction [6, 7]. Therefore, early identification and intervention of sarcopenia are of paramount clinical importance for delaying COPD progression, reducing the risk of acute exacerbations, and improving long-term survival.

Accurate assessment of patients' nutritional status and body composition is essential for implementing effective interventions. Traditional anthropometric measurements and serological markers (e.g., albumin and prealbumin) can reflect nutritional status to some extent; however, they cannot precisely quantify changes in body components, particularly muscle mass. In recent years, body composition analysis based on bioelectrical impedance analysis (BIA) has been increasingly used in clinical practice owing to its advantages of rapidity, simplicity, non-invasiveness, and high accuracy [8]. This technique enables quantitative assessment of body components, including fat mass, muscle mass, and body water, providing a powerful quantitative tool for comprehensive and dynamic assessment of the physical condition of COPD patients.

Although existing studies have demonstrated the presence of malnutrition and reduced muscle mass in COPD patients, large-scale and stratified investigations exploring how disease severity systematically affects multidimensional nutritional status, body composition characteristics, and the subsequent development of sarcopenia remain limited. Most existing studies have focused on single or limited parameters, while comprehensive analyses integrating nutritional risk scores, body composition parameters, and sarcopenia prevalence across different COPD severity categories are still insufficient.

Therefore, this study aimed to retrospectively analyze clinical data of COPD patients with varying severity levels, systematically evaluate differences in nutritional status, body composition, and sarcopenia prevalence, and identify independent factors influencing the development of sarcopenia. We hypothesized that increasing COPD severity would be associated with progressive deterioration in nutritional status, characterized by decreased body weight, reduced muscle mass, increased nutritional risk scores, and a higher prevalence of sarco-

penia. The findings of this study may provide a novel theoretical basis for stratified management and individualized intervention strategies in COPD patients.

Materials and methods

Study subjects

Clinical data from 240 patients with COPD who were treated at the Affiliated Hospital of Youjiang Medical University for Nationalities between March 2021 and March 2025 were retrospectively collected. This study protocol was approved by the Ethics Committee of the Affiliated Hospital of Youjiang Medical University for Nationalities. All study procedures were conducted in accordance with the principles of the Declaration of Helsinki. Given the retrospective nature of this study, the requirement for informed consent was waived by the Ethics Committee.

Inclusion criteria: (1) Age ≥ 40 years, with clear consciousness and the ability to cooperate with physical examinations and questionnaire surveys; (2) Meeting the diagnostic criteria outlined in the 2023 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report [9], defined as a post-bronchodilator ratio of forced expiratory volume in 1 second (FEV₁) to forced vital capacity (FVC) < 0.70 ; (3) Being in a stable disease phase, defined as no acute exacerbation within 4 weeks before treatment (i.e., no requirement for antibiotics or systemic corticosteroids); and (4) Availability of complete clinical data required for analysis, including anthropometric measurements, serological tests, body composition, and blood gas analysis.

Exclusion criteria: (1) Concurrent cardiovascular diseases; (2) Concurrent other pulmonary diseases; (3) Concurrent hepatic or renal dysfunction; or (4) Incomplete clinical data.

Based on the degree of FEV₁ reduction, COPD patients were categorized into: (1) Mild group (n=80), FEV₁% predicted $\geq 80\%$; (2) Moderate group (n=66), $50\% \leq$ FEV₁% predicted $< 80\%$; (3) Severe group (n=52), $30\% \leq$ FEV₁% predicted $< 50\%$; (4) Extremely severe group (n=42), FEV₁% predicted $< 30\%$. Patients were further divided into a sarcopenia group and a non-sarcopenia group according to the presence or absence of sarcopenia at the 1-year follow-up for prognostic analysis.

Sample size estimation: This retrospective study used the sample size calculation formula for cross-sectional studies. According to a previous meta-analysis [10], the prevalence of sarcopenia in COPD patients was approximately 27%. Assuming a significance level of $\alpha=0.05$ ($Z_{\alpha}=1.96$) and an allowable error of $d=0.08$, the minimum sample size was calculated using the formula: $n=Z_{\alpha}^2 \times P \times (1 - P)/d^2$, yielding an estimated minimum of 120 cases. Considering potential missing data and incomplete follow-up information in retrospective studies, the sample size was increased by approximately 20% from the original estimate, yielding a final required sample size of 144 cases. Ultimately, 240 COPD patients were included in this study, exceeding the estimated sample size requirement.

Clinical data collection

Baseline clinical data were retrospectively collected from the hospital electronic medical record system, including (1) General demographic data (age, sex, height, and disease duration); (2) Underlying comorbidities (e.g., hypertension, diabetes) confirmed according to diagnostic codes from the International Classification of Diseases, 10th Revision (ICD-10); (3) History of anti-COPD treatment (e.g., inhaled corticosteroids [ICS], long-acting β_2 -agonists [LABA], and long-acting muscarinic antagonists [LAMA] within the 3 months before treatment; long-term oxygen therapy [LTOT]).

Research methods

(1) **Basic physical measurements:** Height and weight were measured using an RGZ-120-RT scale (Wuxi Xiheng Measuring Instrument Co., Ltd., China). Arm circumference and triceps skinfold thickness (TST) were measured on the right upper arm using a skinfold caliper (Shanghai Hongkang Medical Instruments Co., Ltd., China). Arm circumference was measured at the midpoint between the acromion and olecranon, and TST was measured 2 cm above this point. All measurements were performed three times, and the mean value was recorded.

Arm muscle circumference (AMC) was calculated using the equation: $AMC = \text{Arm circumference} - 3.14 \times TST$.

(2) **Nutritional status:** All nutrition-related indicators were collected within 48 hours after

admission to establish a standardized baseline assessment. The Nutritional Risk Screening 2002 (NRS 2002) [11] was used to preliminarily screen nutritional risk at admission. In addition to assessing current disease severity, NRS 2002 incorporates recent nutritional changes by considering weight loss and changes in dietary intake within the preceding 1-3 months. An NRS 2002 score ≥ 3 was considered indicative of nutritional risk. Meanwhile, the Subjective Global Assessment (SGA) scale [12] was used to comprehensively evaluate weight changes, dietary intake, and gastrointestinal symptoms over the previous month, with higher scores indicating poorer nutritional status.

(3) **Serological markers:** Peripheral blood levels of hemoglobin (HGB), neutrophils, and lymphocytes were measured using a SE500 automated hematology analyzer (Sysmex Corporation, Japan), and the neutrophil-lymphocyte ratio (NLR) was calculated. Serum levels of albumin (ALB), prealbumin (PA), retinol-binding protein (RBP), and cholinesterase (CHE) were measured using a 7600 automated biochemical analyzer (Hitachi Instruments (Shanghai) Co., Ltd., China).

(4) **Grip strength analysis:** Handgrip strength was measured using a WCS-10000 electronic dynamometer (Shanghai Wanqing Electronics Co., Ltd., China). Participants were instructed to perform a steady and continuous grip, and the measurement accuracy was set at 0.1 kg.

(5) **Body composition analysis:** Body composition parameters were measured using a BCA-1B body composition analyzer (Beijing Tongfang Health Technology Co., Ltd., China). The measured parameters included fat mass, fat-free mass (FFM), mineral content, protein content, body water content, muscle mass (MM), and skeletal muscle mass (SMM).

The skeletal muscle mass index (SMMI) was calculated using the equation: $SMMI = SMM / \text{height}^2$.

The fat mass index (FMI) was calculated as: $FMI = \text{fat mass} / \text{height}^2$.

The FFM index (FFMI) was calculated as: $FFMI = FFM / \text{height}^2$.

(6) **Blood gas and oxygen therapy analysis:** Blood gas parameters were measured using a blood gas analyzer (Jinan Ailabao Instrument

Table 1. Comparison of baseline characteristics among groups

Indicator	Mild group (n=80)	Moderate group (n=66)	Severe group (n=52)	Very severe group (n=42)	χ^2/F	P
Age (years)	68.5 ± 9.3	69.1 ± 10.5	68.8 ± 9.5	70.3 ± 10.1	0.452	0.716
Sex (male/female)	52/28	40/26	32/20	28/14	0.387	0.943
Height (m)	1.70 ± 0.10	1.70 ± 0.10	1.70 ± 0.10	1.65 ± 0.10	1.855	0.148
Disease duration (years)	16.7 ± 13.6	17.2 ± 13.8	16.6 ± 15.2	17.0 ± 14.8	0.098	0.961
Complicated with hypertension [n (%)]	20 (25.0)	16 (24.2)	18 (34.6)	12 (28.6)	0.823	0.844
Complicated with diabetes [n (%)]	10 (12.5)	8 (12.1)	6 (11.5)	2 (4.8)	1.120	0.772
Inhalation medication plan [n (%)]					3.867	0.695
LABA or LAMA	0 (0)	0 (0)	0 (0)	0 (0)		
LABA + LAMA	12 (15.0)	12 (18.2)	6 (11.5)	4 (9.5)		
ICS + LABA + LAMA	30 (37.5)	28 (42.4)	28 (53.8)	24 (57.1)		
Not using inhaled medication	38 (47.5)	26 (39.4)	18 (34.6)	14 (33.3)		
Long-term home oxygen therapy [cases (%)]	0 (0)	8 (12.1)	16 (30.8)	28 (66.7)	62.341	0.001

Note: LABA, long-acting beta₂-agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroid.

Equipment Co., Ltd., China). The recorded parameters included arterial partial pressure of oxygen (PaO₂), arterial partial pressure of carbon dioxide (PaCO₂), arterial oxygen saturation (SaO₂), and pH value. The number of patients receiving oxygen therapy was also recorded.

(7) Diagnosis and grouping of sarcopenia: According to the 2019 diagnostic criteria established by the Asian Working Group for Sarcopenia (AWGS) [13], sarcopenia was diagnosed in patients who met the criteria for low muscle mass (SMMI <7.0 kg/m² in males and <5.7 kg/m² in females) combined with either reduced handgrip strength (<28 kg in males and <18 kg in females), or reduced physical performance (gait speed <1.0 m/s). All patients completed a 1-year follow-up, and were classified into the sarcopenia group or non-sarcopenia group according to the occurrence of sarcopenia at the end of the follow-up period.

Statistical analysis

Statistical analyses were performed using SPSS 22.0. Continuous variables were expressed as mean ± standard deviation. Comparisons among multiple groups were performed using one-way analysis of variance (ANOVA). When ANOVA indicated a statistically significant difference ($P < 0.05$), the Student-Newman-Keuls (SNK-q) test was further performed for post hoc pairwise comparisons. Before performing the SNK-q test, Levene's test was conducted to assess homogeneity of variances, and all variables met the assumption of variance homogeneity ($P > 0.05$). Categorical variables were expressed as percentages (%) and compared using the chi-squared test. Multivariate logistic regression analysis was performed using the enter method, with entry criterion set at 0.05 and removal criterion at 0.10. Receiver operating characteristic (ROC) curve analysis were used to assess the predictive value of each independent factors for sarcopenia, with the area under the curve (AUC) values calculated. A two-sided P value < 0.05 was considered statistically significant.

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Results

Comparison of baseline characteristics among patient groups

As shown in **Table 1**, no significant differences were observed among the four groups in terms of age, sex, height, disease duration, or the prevalence of hypertension and diabetes (all $P > 0.05$), indicating good comparability among groups. Regarding treatment history, the proportion of patients receiving LTOT increased progressively with increasing disease severity (0%, 12.1%, 30.8%, and 66.7%, respectively; $P = 0.001$), whereas no significant differences were observed in the proportions of patients receiving ICS, LABA, or LAMA among the four groups (all $P > 0.05$).

Comparison of height, body weight, AMC, and handgrip strength among groups

There was no significant difference in height among the four groups ($P > 0.05$). However, as the severity of COPD increased, body weight

Table 2. Comparison of height, weight, upper AMC, and grip strength among groups

Indicator	Mild group (n=80)	Moderate group (n=66)	Severe group (n=52)	Very severe group (n=42)	F	P
Height (m)	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.6 ± 0.1	1.855	0.148
Weight (kg)	78.5 ± 8.2	74.2 ± 7.5 ^a	69.8 ± 6.9 ^b	63.5 ± 7.1 ^c	28.436	0.001
AMC (cm)	24.2 ± 2.5	22.5 ± 2.3 ^a	20.1 ± 2.1 ^b	17.8 ± 2.4 ^c	32.767	0.001
TST (cm)	14.5 ± 2.8	11.2 ± 2.5 ^a	9.1 ± 2.0 ^b	5.8 ± 1.5 ^c	35.124	0.001
Grip (kg)	13.8 ± 2.2	10.5 ± 2.0 ^a	8.2 ± 1.8 ^b	6.1 ± 1.5 ^c	29.876	0.001

Note: ^aP<0.05, compared with the mild group, ^bP<0.05, compared with the moderate group, ^cP<0.05, compared with the severe group. COPD, chronic obstructive pulmonary disease; AMC, arm muscle circumference; TST, triceps skinfold thickness; Grip, handgrip strength.

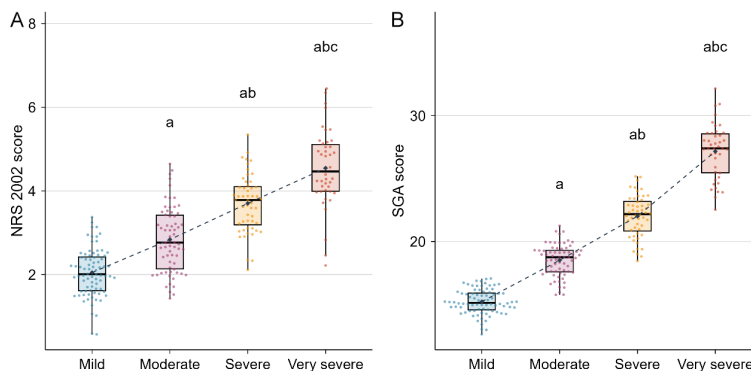


Figure 1. Comparison of nutritional status among groups. A. NRS 2002 score; B. SGA score; Notes: ^aP<0.05, compared with the mild group, ^bP<0.05, compared with the moderate group, ^cP<0.05, compared with the severe group. NRS-2002, Nutritional Risk Screening 2002; SGA, subjective global assessment.

gradually decreased, and the AMC, TST, and handgrip strength also progressively declined ($P<0.05$). Pairwise comparisons using the SNK-q test showed that body weight, AMC, TST, and handgrip strength all decreased sequentially between any two adjacent groups (mild vs. moderate, moderate vs. severe, and severe vs. very severe) (all $P<0.05$; **Table 2**).

Comparison of nutritional status among groups

The nutritional risk and nutritional status scores of COPD patients with different COPD severity levels were compared (**Figure 1**). With the aggravation of the disease, the NRS 2002 and SGA scores of COPD subjects gradually increased. After pairwise comparisons using the SNK-q test, both NRS 2002 scores and SGA scores showed a sequentially increasing trend between any two adjacent groups (mild vs. moderate, moderate vs. severe, and severe vs. very severe) (all $P<0.05$).

Comparison of serum markers among groups

With increasing disease severity, the levels of ALB, PA, RBP, and CHE in the peripheral blood of COPD patients gradually decreased, whereas HGB levels and NLR gradually increased ($P<0.05$). Pairwise comparisons using the SNK-q test showed that NLR increased sequentially between any two adjacent groups (all $P<0.05$), while PA, RBP, and CHE decreased sequentially between any two adjacent groups (all $P<0.05$). ALB showed no

significant difference between the mild and moderate groups ($P>0.05$), but significantly decreased between the moderate and severe groups and between the severe and very severe groups (all $P<0.05$). HGB increased significantly only between the severe and very severe groups ($P<0.05$), while no significant differences were observed between the other adjacent groups (all $P>0.05$) (**Table 3**).

Comparison of body composition parameters among groups

No significant differences were observed in fat mass, mineral content, body water content, or fat mass index among the four groups ($P>0.05$). However, as COPD severity increased, FFM, protein content, MM, SMM, SMMI, and FFMI progressively decreased in the COPD patients (all $P<0.05$). Pairwise comparisons using the SNK-q test showed that FFM, protein, MM, SMM, SMMI, and FFMI all decreased sequentially between any two adjacent groups (mild vs. moderate, moderate vs. severe, and severe vs.

Table 3. Comparison of serum biomarker levels among groups

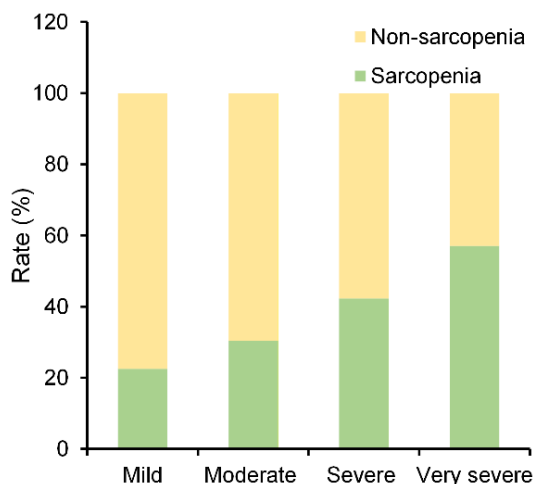
Indicator	Mild group (n=80)	Moderate group (n=66)	Severe group (n=52)	Very severe group (n=42)	F	P
HGB (g/L)	130.5 ± 15.2	134.2 ± 15.5	136.8 ± 15.8	149.5 ± 16.1 ^c	3.856	0.012
NLR	3.3 ± 0.8	4.3 ± 1.0 ^a	5.2 ± 1.2 ^b	7.2 ± 1.5 ^c	25.675	0.001
ALB (g/L)	39.9 ± 3.0	38.3 ± 3.2	35.7 ± 3.5 ^b	32.0 ± 3.8 ^c	4.823	0.003
PA (mg/L)	28.0 ± 4.0	24.0 ± 3.8 ^a	19.5 ± 3.5 ^b	15.0 ± 3.2 ^c	22.345	0.001
RBP (μg/L)	7.6 ± 1.0	6.5 ± 0.9 ^a	5.5 ± 0.8 ^b	4.2 ± 0.7 ^c	20.126	0.001
CHE (IU/L)	6017.5 ± 500.6	5500.6 ± 450.6 ^a	4802.6 ± 403.3 ^b	4057.7 ± 354.6 ^c	28.762	0.001

Note: ^aP<0.05, compared with the mild group, ^bP<0.05, compared with the moderate group, ^cP<0.05, compared with the severe group. HGB, hemoglobin; NLR, neutrophil-to-lymphocyte ratio; ALB, albumin; PA, prealbumin; RBP, retinol-binding protein; CHE, cholinesterase.

Table 4. Comparison of body composition parameters among groups

Indicator	Mild group (n=80)	Moderate group (n=66)	Severe group (n=52)	Very severe group (n=42)	F	P
Fat mass (kg)	20.5 ± 2.1	19.8 ± 2.0	19.5 ± 2.2	19.9 ± 2.1	0.879	0.485
FFM (kg)	52.0 ± 3.5	50.5 ± 3.2 ^a	49.0 ± 3.0 ^b	48.0 ± 2.8 ^c	12.568	0.001
Mineral salt (kg)	3.8 ± 0.5	3.7 ± 0.4	3.6 ± 0.4	3.5 ± 0.3	2.346	0.078
Protein (kg)	9.2 ± 1.0	8.8 ± 0.9 ^a	8.5 ± 0.8 ^b	7.5 ± 0.7 ^c	15.323	0.001
Water content (L)	36.0 ± 2.5	35.5 ± 2.3	35.0 ± 2.2	35.5 ± 2.0	2.563	0.056
MM (kg)	38.0 ± 2.8	36.5 ± 2.5 ^a	33.0 ± 2.2 ^b	28.0 ± 2.0 ^c	25.676	0.001
SMM (kg)	21.0 ± 2.2	18.5 ± 2.0 ^a	16.0 ± 1.8 ^b	14.5 ± 1.6 ^c	22.343	0.001
SMMI	9.5 ± 1.0	8.5 ± 0.9 ^a	7.5 ± 0.8 ^b	6.5 ± 0.7 ^c	20.126	0.001
Fat mass index	8.0 ± 0.8	7.8 ± 0.7	7.6 ± 0.7 ^b	7.7 ± 0.6	1.237	0.302
FFMI	20.5 ± 2.0	19.0 ± 1.8 ^a	17.5 ± 1.6 ^b	16.0 ± 1.4 ^c	18.765	0.001

Note: ^aP<0.05, compared with the mild group, ^bP<0.05, compared with the moderate group, ^cP<0.05, compared with the severe group. FFM, fat-free mass; MM, muscle mass; SMM, skeletal muscle mass; SMMI, skeletal muscle mass index; FFMI, fat-free mass index.

**Figure 2.** Comparison of the incidence of sarcopenia among COPD patients of different disease severity. Note: COPD, chronic obstructive pulmonary disease.

very severe), and all differences were statistically significant (all $P<0.05$) (Table 4).

Comparison of sarcopenia prevalence among groups

The prevalence of sarcopenia in the mild, moderate, severe, and very severe groups were 22.5% (18/80), 30.3% (20/66), 42.3% (22/52), and 57.1% (24/42), respectively. The prevalence of sarcopenia increased significantly with increasing COPD severity ($P<0.05$). Pairwise comparisons using the chi-square partition method showed a sequential increase in the prevalence of sarcopenia between any two adjacent groups (mild vs. moderate, moderate vs. severe, and severe vs. very severe), with all differences being statistically significant (all $P<0.05$) (Figure 2).

Comparison of oxygen therapy among groups

With increasing COPD severity, the proportion of patients receiving oxygen therapy gradually increased ($P<0.05$). Pairwise comparisons using the chi-square partition method showed

Correlation between nutritional status, disease severity, and sarcopenia

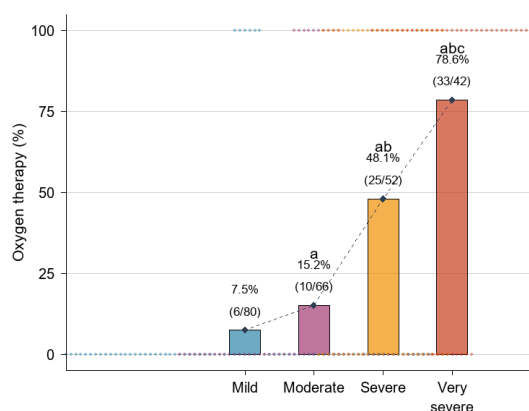


Figure 3. Comparison of oxygen therapy among COPD patients of different disease severity. Notes: ^a $P < 0.05$, compared with the mild group, ^b $P < 0.05$, compared with the moderate group, ^c $P < 0.05$, compared with the severe group. COPD, chronic obstructive pulmonary disease.

that the proportion of patients receiving LTOT increased sequentially between any two adjacent groups (mild vs. moderate, moderate vs. severe, and severe vs. very severe), and all differences were statistically significant (all $P < 0.05$) (**Figure 3**).

Comparison of blood gas parameters among groups

No significant difference was observed in pH values among the four groups ($P > 0.05$). However, as disease severity increased, PaO_2 and SaO_2 in COPD subjects progressively decreased ($P < 0.05$), whereas PaCO_2 gradually increased ($P < 0.05$). Pairwise comparisons using the SNK-q test demonstrated sequential decreases in PaO_2 and SaO_2 and sequential increases in PaCO_2 between adjacent groups (mild vs. moderate, moderate vs. severe, and severe vs. very severe), with all differences being statistically significant (all $P < 0.05$) (**Table 5**).

Analysis of factors associated with sarcopenia in patients with COPD

During the 1-year follow-up, sarcopenia occurred in 84 of the 240 patients. The patients were divided into a sarcopenia group ($n=84$) and a non-sarcopenia group ($n=156$), and clinical characteristics, nutritional status, body composition, and blood gas analysis indicators were compared between the two groups (**Table 6**). Patients with sarcopenia exhibited higher NRS-2002 and SGA scores and lower levels of

nutritional markers, including ALB, PA, RBP, and CHE (all $P < 0.05$). Additionally, fat mass, FFM, MM, SMM, and related indices were significantly reduced in the sarcopenia group compared with the non-sarcopenia group (all $P < 0.05$), along with lower PaO_2 , higher PaCO_2 , lower SaO_2 , and decreased pH values (all $P < 0.05$). No significant differences were observed between the two groups in terms of age, sex, height, prevalence of hypertension or diabetes, inhaled medication regimens, or proportion of patients receiving LTOT (all $P > 0.05$).

Based on univariate analysis, variables with $P < 0.05$ were subsequently included in the multivariate logistic regression analysis (**Table 7**). The results showed that NRS-2002 score (OR=2.489, 95% CI: 1.631-3.798, $P=0.001$) and NLR (OR=1.379, 95% CI: 1.121-1.694, $P=0.002$) were independent risk factors for sarcopenia, while ALB (OR=0.849), handgrip strength (OR=0.871), FFMI (OR=0.710), PaO_2 (OR=0.937), SMMI (OR=0.680), RBP (OR=0.998), and CHE (OR=0.999) were independent protective factors (all $P < 0.05$). **Figure 4** presents the ROC curves of individual indicators for predicting sarcopenia. The AUCs of all nine indicators were statistically significant (all $P < 0.05$).

Discussion

COPD is a chronic wasting disease, with approximately 60% or more of patients experiencing varying degrees of malnutrition [14]. Malnutrition is one of the major contributors to acute exacerbations and mortality in COPD patients. NRS 2002 is a widely used tool for nutritional risk screening. Studies have demonstrated that more than 55% of COPD patients are at risk of malnutrition, which is associated with reduced quality of life [15]. SGA is also a widely used method for nutritional status assessment, particularly among patients with tumors or undergoing dialysis. In this study, body weight gradually decreased, whereas NRS 2002 and SGA scores progressively increased with increasing COPD severity, indicating that COPD patients may experience varying degrees of nutritional deterioration. This may be attributed to chronic ventilatory impairment in COPD, which subsequently causes hypoxemia, CO_2 retention, or pulmonary hypertension, thereby impairing digestive dysfunction [16, 17]. Moreover, patients with severe or very severe COPD often

Table 5. Comparison of blood gas parameters among groups

Indicator	Mild group (n=80)	Moderate group (n=66)	Severe group (n=52)	Very severe group (n=42)	F	P
PaO ₂ (mmHg)	83.5 ± 4.2	70.2 ± 3.8 ^a	56.0 ± 4.6 ^b	44.0 ± 3.5 ^c	12.557	0.001
PaCO ₂ (mmHg)	38.3 ± 2.5	43.0 ± 2.1 ^a	51.0 ± 3.2 ^b	55.6 ± 3.2 ^c	15.498	0.001
SaO ₂ (%)	95.5 ± 1.1	91.7 ± 1.8 ^a	86.0 ± 2.5 ^b	83.4 ± 2.6 ^c	11.379	0.001
PH	7.4 ± 0.6	7.3 ± 0.3	7.3 ± 0.5	7.4 ± 0.3	0.673	0.181

Note: ^aP<0.05, compared with the mild group, ^bP<0.05, compared with the moderate group, ^cP<0.05, compared with the severe group. PaO₂, arterial partial pressure of oxygen; PaCO₂, arterial partial pressure of carbon dioxide; SaO₂, arterial oxygen saturation.

exhibit respiratory muscle dysfunction and swallowing impairment, which may further compromise oxygenation, induce dyspnea and anorexia, and consequently reduce food intake [18]. Ogan et al. [19] reported that malnutrition accounted for 48.8% of COPD patients in GOLD stage C-D, and that NRS 2002 scores were negatively correlated with upper AMC. Furthermore, this study demonstrated that upper AMC and handgrip strength progressively decreased with increasing disease severity. Malnutrition is often accompanied by insufficient energy intake, which may impair physiological functions, including muscle synthesis and maintenance. In addition, long-term insufficient nutritional intake in patients with COPD may promote muscle protein breakdown to provide energy substrates, ultimately leading to reduced muscle mass [20].

HGB is an important component of red blood cells and plays a critical role in transporting oxygen and carbon dioxide. Higher HGB levels may reflect stronger compensatory response to chronic hypoxia [21]. In this study, peripheral blood HGB levels gradually increased with increasing COPD severity. This may be explained by impaired ventilation caused by airway obstruction and airflow limitation in COPD, resulting in chronic hypoxia. As COPD progresses, worsening hypoxia and dyspnea may stimulate erythropoiesis, leading to increased HGB levels [22].

COPD can also induce a systemic inflammatory response. The release of multiple inflammatory mediators may contribute to autonomic nervous system dysfunction, including sympathetic-parasympathetic imbalance, thereby further aggravating pulmonary dysfunction. In addition, systemic inflammation may negatively affect other important organs, including the cardiovascular system [23, 24]. The results of

this study farther demonstrated that, as COPD severity increased, PaO₂ and SaO₂ progressively decreased, whereas PaCO₂ gradually increased. Meanwhile, the proportion of patients receiving oxygen therapy also increased. The decline in PaO₂ and SaO₂ reflects progressive impairment of oxygenation, whereas the elevation in PaCO₂ indicates worsening ventilatory dysfunction and impaired gas exchange, which may increase in the risk of respiratory failure. In response to these physiological changes, more patients require oxygen therapy to alleviate hypoxemia, improve symptoms, and maintain quality of life. These findings highlight the substantial impact of COPD progression on respiratory function and emphasize the importance of early identification, intervention, and the rational oxygen therapy in clinical management.

NLR is an important parameter to evaluate systemic inflammatory response and has been reported to be associated with disease severity, in-hospital mortality, and response to noninvasive mechanical ventilation in COPD patients [25]. In this study, NLR value increased progressively with increasing COPD severity.

Furthermore, with the aggravation of COPD, the peripheral blood levels of ALB, PA, and CHE gradually decreased. ALB is the predominant plasma protein and is widely used as an indicator of nutritional status. PA is involved in the transport of endogenous substances. Previous studies have suggested that PA levels may increase with resolution of inflammation and may serve as an early indicator for evaluating inflammatory responses during acute exacerbations of COPD [26]. Patients with COPD often experience malnutrition due to long-term dyspnea, reduced food intake, and increased energy expenditure, which may subsequently contribute to decreased ALB and PA levels.

Correlation between nutritional status, disease severity, and sarcopenia

Table 6. Comparison of clinical characteristics, nutritional status, body composition, and blood gas parameters between the sarcopenia group and the non-sarcopenia group

Indicator	Sarcopenia (n=84)	No sarcopenia (n=156)	t/χ^2	P
Age (years)	69.5 ± 8.3	69.2 ± 9.1	0.893	0.785
Male (n)	52 (61.9)	100 (64.1)	0.114	0.735
Height (m)	1.7 ± 0.4	1.6 ± 0.5	1.689	0.093
Weight (kg)	62.3 ± 6.8	78.5 ± 8.0	-16.530	<0.001
Combined hypertension [n (%)]	24 (28.6)	40 (25.6)	0.234	0.628
Combined diabetes [n (%)]	10 (11.9)	16 (10.3)	0.150	0.699
Inhalation medication plan [n (%)]			0.916	0.633
LABA or LAMA	30 (35.7)	66 (42.3)		
LABA + LAMA	34 (40.5)	56 (35.9)		
ICS + LABA + LAMA	20 (23.8)	34 (21.8)		
Long-term home oxygen therapy [n (%)]	22 (26.2)	30 (19.2)	1.569	0.211
AMC (cm)	21.5 ± 2.4	25.8 ± 2.6	-9.345	0.001
TST (cm)	8.1 ± 2.1	11.5 ± 2.3	-8.762	0.001
Grip (kg)	8.2 ± 4.5	18.6 ± 5.2	-12.038	0.001
NRS 2002 score	3.5 ± 0.7	1.6 ± 0.8	13.562	0.001
SGA score	24.2 ± 0.9	17.1 ± 1.2	16.894	0.001
HGB (g/L)	128.5 ± 15.2	138.2 ± 14.8	-2.498	0.014
NLR	6.8 ± 1.2	5.5 ± 0.8	7.216	0.001
ALB (g/L)	34.2 ± 3.5	41.5 ± 3.8	-11.251	0.001
PA (mg/L)	18.5 ± 5.2	28.3 ± 2.1	-11.893	0.001
RBP (μg/L)	5.5 ± 0.3	6.7 ± 0.5	-15.326	0.001
CHE (IU/L)	4800.0 ± 650.0	6200.0 ± 720.0	-11.569	0.001
Fat mass (kg)	15.2 ± 4.1	20.5 ± 5.2	-6.4527	0.001
FFM (kg)	57.1 ± 3.8	66.0 ± 4.5	-12.342	0.001
Mineral salt (kg)	3.2 ± 0.5	3.6 ± 0.6	-4.126	0.001
Protein (kg)	7.5 ± 1.1	9.8 ± 1.3	-10.898	0.001
Water content (L)	28.5 ± 3.2	35.2 ± 4.1	-10.233	0.001
MM (kg)	32.1 ± 3.5	40.5 ± 4.2	-12.567	0.001
SMM (kg)	14.4 ± 3.2	21.8 ± 4.0	-13.217	0.001
SMMI	5.2 ± 0.4	6.5 ± 0.5	-16.545	0.001
Fat mass index	5.6 ± 1.2	7.3 ± 1.5	-6.893	0.001
FFMI	17.5 ± 1.1	20.3 ± 1.2	-13.457	0.001
PaO ₂ (mmHg)	62.5 ± 8.3	78.4 ± 9.2	-10.256	0.001
PaCO ₂ (mmHg)	48.2 ± 6.5	42.1 ± 5.8	5.984	0.001
SaO ₂ (%)	90.2 ± 3.5	94.5 ± 2.8	-7.896	0.001
PH	7.1 ± 0.1	7.4 ± 0.1	-22.200	<0.001

Note: COPD, chronic obstructive pulmonary disease; LABA, long-acting β_2 -agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroid; AMC, arm muscle circumference; TST, triceps skinfold thickness; NRS-2002, Nutritional Risk Screening 2002; SGA, Subjective Global Assessment; HGB, hemoglobin; NLR, neutrophil-to-lymphocyte ratio; ALB, albumin; PA, prealbumin; RBP, retinol-binding protein; CHE, cholinesterase; FFM, fat-free mass; MM, muscle mass; SMM, skeletal muscle mass; SMMI, skeletal muscle mass index; FFMI, fat-free mass index; PaO₂, arterial partial pressure of oxygen; PaCO₂, arterial partial pressure of carbon dioxide; SaO₂, arterial oxygen saturation.

CHE reflects hepatic protein synthesis capacity and functional reserve. A greater reduction in CHE levels may indicate more severe disease and a higher risk of mortality [27]. Chronic hypoxia, infection, and systemic inflammation

in COPD patients may impair hepatic function, potentially leading to a decreased CHE level.

RBP is a protein essential for vitamin A transport in the blood and is also considered a nutri-

Table 7. Multivariate logistic regression analysis of factors associated with sarcopenia

Variable	B	SE	Wald χ^2	P	OR (95% CI)
NRS-2002 score	0.912	0.216	17.742	0.001	2.489 (1.631-3.798)
ALB (g/L)	-0.163	0.042	14.943	0.001	0.849 (0.783-0.921)
Grip (kg)	-0.138	0.032	18.538	0.001	0.871 (0.820-0.926)
FFMI (kg/m ²)	-0.342	0.091	14.051	0.001	0.710 (0.595-0.847)
NLR	0.321	0.105	9.364	0.002	1.379 (1.121-1.694)
PaO ₂ (mmHg)	-0.065	0.021	9.552	0.002	0.937 (0.899-0.977)
SMMI	-0.385	0.099	15.123	0.001	0.680 (0.565-0.819)
RBP (μg/L)	-0.001	0.001	9.218	0.002	0.998 (0.998-0.999)
CHE (IU/L)	-0.001	0.001	7.117	0.008	0.999 (0.998-0.999)

Note: NRS-2002, Nutritional Risk Screening 2002; ALB, albumin; Grip, handgrip strength; FFMI, fat-free mass index; NLR, neutrophil-to-lymphocyte ratio; PaO₂, arterial partial pressure of oxygen; SMMI, skeletal muscle mass index; RBP, retinol-binding protein; CHE, cholinesterase; β, regression coefficient; SE, standard error; OR, odds ratio; CI, confidence interval.

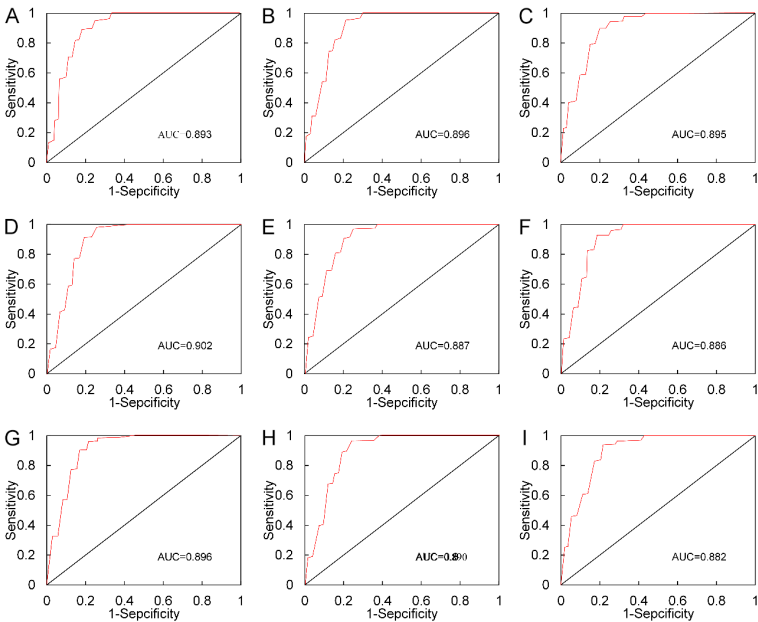


Figure 4. ROC curve analysis for independent predictive factors of sarcopenia in COPD patients. A. NRS-2002 score; B. ALB; C. Grip; D. FFMI; E. NLR; F. PaO₂; G. SMMI; H. RBP; I. CHE. Notes: NRS-2002, Nutritional Risk Screening 2002; ALB, albumin; Grip, handgrip strength; FFMI, fat-free mass index; NLR, neutrophil-to-lymphocyte ratio; PaO₂, arterial partial pressure of oxygen; SMMI, skeletal muscle mass index; RBP, retinol-binding protein; CHE, cholinesterase; ROC, receiver Operating Characteristic; COPD, chronic obstructive.

tional indicator. In this study, RBP levels gradually decreased with worsening COPD severity. Previous studies have reported that RBP levels are positively correlated with pulmonary function parameters (e.g., FEV1, FEV1/FVC) [28, 29]. Therefore, the progressive decline in peripheral blood RBP levels in more severe

COPD patients suggests that RBP may serve as a potential indicator for evaluating COPD severity.

Marinho et al. [30] reported that approximately 20% of COPD people exhibited muscle atrophy, accompanied by a significant reduction in FFMI. Lee et al. [31] further confirmed that MM varies with the severity of COPD. In this study, we observed that with the aggravation of the disease, the FFM, MM, SMM, SMMI, and FFMI of COPD patients gradually decreased. A decrease in protein content may contribute to the decline in FFM. Vestbo et al. [32] showed that the FFMI decreased in COPD patients and was associated with the severity of airway obstruction. Ahmadi et al. [33] also proposed that MM and SMMI were significantly lower in patients with severe COPD than in those with mild COPD. These findings suggest that substantial differences exist in body composition among patients with varying degrees of COPD severity, especially in MM. In the present study, the prevalence of sarcopenia among COPD patients ranged from 22.5-57.1%, and the incidence of sarcopenia increased with worsening COPD severity. Persistent oxidative stress and chronic inflammation in patients with COPD may contribute to skeletal muscle cell damage, resulting in decreased muscle mass and impaired muscle function. Previous studies have also demon-

strated that COPD patients commonly experience different degrees of malnutrition, which may further impair muscle protein synthesis and repair, ultimately contributing to the occurrence of sarcopenia. Both COPD and sarcopenia are associated with reduced exercise tolerance, which can impair respiratory muscle function

and aggravate the deterioration of lung function, resulting in reduced QoL. Moreover, sarcopenia may contribute to decreased multi-organ function and impaired immune function, subsequently increasing mortality risk in patients with COPD. Therefore, regular monitoring of nutritional status and changes in body composition is of great importance for improving QoL and long-term survival outcomes in COPD patients.

Univariate analysis in this study showed significant differences in nutritional status, body composition, and blood gas parameters between patients with and without sarcopenia. The NRS-2002 and SGA scores were significantly higher in the sarcopenia group, whereas nutritional biomarkers, including ALB, PA, RBP, and CHE, were generally lower, indicating that malnutrition may represent an important contributing factor in the development of sarcopenia [34]. In terms of body composition, core parameters, including fat mass, FFM, MM, SMM, SMMI, and FFMI, were significantly reduced in the sarcopenia group, further confirming the characteristic loss of muscle mass associated with sarcopenia. Moreover, lower PaO_2 and SaO_2 , along with increased PaCO_2 , indicated more pronounced hypoxemia and carbon dioxide retention in sarcopenic patients, which may provide an unfavorable physiological environment that promotes muscle catabolism and suppresses anabolic processes [35]. Multivariate logistic regression analysis further identified independent factors associated with the development of sarcopenia. In this study, the NRS-2002 score was identified as an independent risk factor for sarcopenia. An elevated NRS-2002 score reflects inadequate energy and protein intake, which may directly impair the availability of substrates required for muscle protein synthesis [36]. Additionally, a higher NLR, as a marker of systemic inflammation, suggests that chronic low-grade inflammatory status plays a key role in COPD-related sarcopenia; inflammatory cytokines may accelerate muscle protein degradation through activation of the ubiquitin-proteasome system (UPS) and inhibition of the IGF-1 signaling pathway [37]. Conversely, ALB, RBP, CHE, grip strength, FFMI, SMMI, and PaO_2 were identified as independent protective factors. Higher ALB and RBP reflects better nutritional status and protein synthetic function, which may contribute to the

maintenance of skeletal muscle mass [38]. Greater grip strength not only represents preserved muscle function but may also indicate better physical activity capacity and more favorable clinical outcomes. As objective quantitative indicators of muscle mass, declines in SMMI and FFMI represent fundamental characteristics and diagnostic components of sarcopenia. PaO_2 , as a critical determinant of tissue oxygen supply may influence skeletal muscle metabolism; reduced oxygen availability can lead to mitochondrial dysfunction and increased intracellular oxidative stress, thereby promoting muscle wasting and functional impairment. Additionally, although RBP and CHE were statistically significant independent protective factors in the multivariate analysis, their odds ratios were close to 1 (RBP: OR=0.998; CHE: OR=0.999), suggesting limited clinical significance. This finding may be partially attributed to the relatively small measurement units of these biomarkers.

This study does have some limitations. First, this was a single-center retrospective study with a relatively small sample size ($n=240$), including only 42 cases with very severe COPD, and the number of sarcopenia events was only 84. Second, the direct associations between nutritional risk scores and body composition parameters were not evaluated, and potential confounding factors, such as physical activity levels and medication adherence, were not fully adjusted for. Third, the follow-up period was only one year, which prevented an assessment of long-term clinical outcomes and prognosis. Therefore, future multicenter, prospective studies with larger sample sizes are warranted to further elucidate the complex interactions among COPD severity, nutritional status, body composition, and sarcopenia.

Conclusion

In patients with COPD, worsening disease severity is accompanied by an increased risk of malnutrition and a higher prevalence of sarcopenia. NRS-2002 score was identified as an independent risk factor for sarcopenia, whereas ALB, grip strength, and SMMI were identified as independent protective factors. However, these findings require further validation through prospective, multicenter studies with larger populations.

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Disclosure of conflict of interest

None.

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