International Journal of Chronic Obstructive Pulmonary Disease

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Impact of Nutritional Status and Sarcopenia on Acute Exacerbation Risk in Stable Chronic Obstructive Pulmonary Disease: A Retrospective Cohort Study

Haitao Pan, Meiqin Wang, Xiangfei Chen, Yanqing Wang

Department of General Practice, Jinling Hospital, Medical School of Nanjing University, Nanjing, 210002, People's Republic of China

Correspondence: Yanqing Wang, Department of General Practice, Jinling Hospital, Medical School of Nanjing University, No. 305, Zhongshan East Road, Xuanwu District, Nanjing, Jiangsu Province, 210002, People's Republic of China, Email qkyxwyq@163.com

Background: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) drive disease progression and mortality. This study aims to investigate whether nutritional risk and sarcopenia independently predict (AECOPD) in patients with stable COPD.

Methods: In this single-center retrospective cohort study, 264 hospitalized patients with stable COPD were followed for 12 months. Nutritional risk was assessed using the Nutritional Risk Screening 2002. Sarcopenia was defined according to the Asian Working Group for Sarcopenia 2019 criteria. Appendicular skeletal muscle index (ASMI), handgrip strength, gait speed, and five-repetition sit-to-stand (5STS) time were measured. Independent predictors of AECOPD were identified using multivariable logistic regression. Discrimination was evaluated using the area under the receiver operating characteristic curve (AUC).

Results: During follow-up, 102 patients (38.6%) developed AECOPD. Patients with AECOPD exhibited higher rates of sarcopenia (64.71% vs. 32.72%, $P < 0.001$) and nutritional risk (64.71% vs. 39.51%, $P < 0.001$), alongside lower ASMI, reduced handgrip strength, slower gait speed, and prolonged 5STS time (all $P < 0.01$). After adjustment for age, sex, smoking history, forced expiratory volume in 1 second (FEV_1)% predicted, and prior AECOPD, and comorbidity burden, both sarcopenia (OR 6.265, 95% CI 3.008–13.049) and nutritional risk (OR 3.016, 95% CI 1.571–5.793) remained independent predictors. ASMI demonstrated a protective association (OR 0.266, 95% CI 0.177–0.399), while TNF-α was positively associated with AECOPD risk (OR 1.175, 95% CI 1.044–1.322). The ASMI-based model achieved the highest discrimination (AUC 0.893).

Conclusion: Sarcopenia and nutritional risk independently increase AECOPD risk in stable COPD. Incorporating muscle mass parameters into risk stratification may improve predictive accuracy.

Keywords: chronic obstructive pulmonary disease, acute exacerbation, sarcopenia, nutritional risk, appendicular skeletal muscle index, predictive model, inflammatory markers

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation and chronic airway inflammation. Acute exacerbations of COPD (AECOPD) accelerate lung function decline, increase hospitalization rates and mortality, and impose substantial healthcare burdens worldwide.[1] Although prior exacerbation history represents the most robust predictors of future events, reliance on history and airflow limitation severity alone inadequately explains interindividual variability in the frequent exacerbator phenotype.[2] Therefore, identifying reproducible and modifiable systemic risk factors and incorporating them into a more clinically applicable risk stratification framework are critical priorities in the management of stable COPD.

COPD is increasingly recognized as a systemic disease with prominent extrapulmonary manifestations, particularly malnutrition and altered body composition. Systematic reviews have demonstrated high prevalence rates of malnutrition and nutritional risk among patients with COPD, both of which are associated with adverse clinical outcomes.[3] While

https://doi.org/10.2147/COPD.S605988
Received: 28 February 2026
Accepted: 2 May 2026
Published: 13 May 2026

body mass index (BMI) is widely utilized, it lacks sensitivity for detecting alterations in body composition. In contrast, the fat-free mass index (FFMI) more accurately reflects skeletal muscle and lean tissue depletion, correlating closely with disease phenotype and health-related quality of life.[4] Emerging evidence further suggests that nutritional assessment tools help identify high-risk individuals and are associated with the occurrence of AECOPD.[5] However, the independent predictive values of nutritional risk screening indices (eg, the Nutritional Risk Screening 2002 [NRS-2002]) and body composition parameters (eg, FFMI) for future exacerbations, and their interaction with muscle status, remain insufficiently clarified in stable COPD.

Sarcopenia, defined by progressive declines in muscle mass, strength, and physical performance, is highly prevalent in COPD. It may increase AECOPD susceptibility through reduced respiratory muscle reserve, impaired exercise capacity, and compromised immune defense. The 2019 consensus of the Asian Working Group for Sarcopenia (AWGS) provides standardized diagnostic algorithms and population-specific cut-off values, enhancing cross-study comparability.[6] Previous investigations have associated sarcopenia and related parameters with increased AECOPD risk and adverse outcomes during acute episodes,[7,8] with index-based sarcopenia assessments demonstrating prognostic value in hospitalized AECOPD patients.[9] Nevertheless, few studies on stable COPD have simultaneously incorporated multidimensional sarcopenia components, such as appendicular skeletal muscle index (ASMI), handgrip strength, gait speed, or five-repetition sit-to-stand (5STS), together with nutritional risk indicators within a unified predictive model. Comparative evaluation of their incremental predictive performance is still lacking.

Systemic inflammation may represent a key biological pathway linking malnutrition, muscle wasting, and AECOPD susceptibility. Inflammatory markers predict AECOPD risk in stable COPD with moderate discriminative performance,[10] while nutritional supplementation and exercise-based interventions suggest that combined strategies improve body composition and functional status, thereby highlighting potentially modifiable risk factors.[11]

Given these evidence gaps, this study systematically evaluates associations among nutritional risk, sarcopenia, and their individual components with AECOPD risk in hospitalized patients with stable COPD. After adjustment for conventional risk factors, including age, smoking status, lung function, and prior AECOPD, we constructed and compared multivariable predictive models and further explored the potential role of inflammatory markers within this framework. These findings may provide evidence to support early identification of high-risk individuals, inform integrated nutrition-exercise intervention strategies, and optimize the management of stable COPD.

Methods

Study Design and Participants

This single-center retrospective cohort study included patients hospitalized with stable COPD at our institution between June 2024 and December 2025. Eligible participants were identified through the hospital electronic medical record (EMR) system. The study protocol was reviewed and approved by the Institutional Ethics Committee of Jinling Hospital, Medical School of Nanjing University (Approval No. DZQH-KYLL-24-11). Given the retrospective design and use of anonymized data, informed consent was waived. All procedures were conducted in accordance with the Declaration of Helsinki.

Inclusion criteria were as follows: (1) Age $\geq$ 40 years; (2) Diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (post-bronchodilator forced expiratory volume in 1 second/forced vital capacity [FEV_1/FVC] < 0.70); (3) Complete physical examination, laboratory, and sarcopenia assessment data available during hospitalization; (4) $\geq$ 12 months of follow-up data to determine the occurrence of AECOPD.

Exclusion criteria included: (1) Active malignancy or receipt of anti-tumor therapy within the previous 6 months; (2) End-stage liver or renal failure, or severe heart failure (New York Heart Association [NYHA] class III–IV); (3) Neuromuscular disorders or long-term immobility; (4) Death or discharge within 24 hours of admission; (5) Missing key variables required for analysis.

Sample Size Estimation

Given that multivariable logistic regression was employed to evaluate the predictive effects of sarcopenia and nutritional parameters on AECOPD risk, sample size estimation was based on the events-per-variable (EPV) principle. To ensure

model stability and minimize overfitting, at least 10 outcome events per predictor variable are generally recommended. With approximately 10 primary predictors anticipated, at least 100 AECOPD events (10 × 10) were required. Based on previous reports indicating an annual AECOPD incidence of 30–50% among patients with stable COPD,[12,13] an overall event rate of approximately 40% during follow-up was assumed. Therefore, to obtain at least 100 events, a minimum total sample size of 250 patients was required (100/0.40 = 250).

Considering potential missing data and loss to follow-up inherent in retrospective studies, the target sample size was increased by 10%, yielding a planned enrollment of approximately 275 patients. Ultimately, 264 patients were included, of whom 102 experienced AECOPD, meeting the requirements for regression analysis.

Data Collection

Baseline variables were extracted from the EMR system and included the following:

1. Demographic and Clinical Characteristics: Age, sex, BMI, smoking history, history of hypertension, coronary artery disease, diabetes mellitus, arrhythmia, pulmonary function parameter (FEV_1% predicted), GOLD stage, modified Medical Research Council (mMRC) dyspnea score, COPD Assessment Test (CAT) score, and number of prior AECOPD episodes. Comorbidity burden was assessed as the number of comorbidities, including history of hypertension, coronary artery disease, diabetes mellitus, arrhythmia.
2. Sarcopenia-Related Parameters: Sarcopenia and its components were assessed according to the AWGS 2019 criteria and the European Working Group on Sarcopenia in Older People (EWGSOP) criteria. ASMI (kg/m^2) assessed by bioelectrical impedance analysis (BIA), handgrip strength, physical performance indicators (gait speed and 5STS) were obtained.
3. Nutritional Status Indicators: BMI, serum albumin, prealbumin, lymphocyte count, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), NRS-2002 score, and FFMI. Nutritional risk was assessed using the Nutritional Risk Screening 2002 (NRS-2002), which is recommended by ESPEN for hospitalized patients and incorporates both nutritional status and disease severity. Other tools, such as MNA, MUST, and GLIM criteria, are also available; however, MNA is mainly used in older populations, MUST is more suitable for community settings, and GLIM requires additional data not consistently available in this retrospective study.
4. Follow-up Outcome: The primary outcome was the occurrence of AECOPD during follow-up.

Definitions

Sarcopenia was assessed according to the AWGS 2019 criteria[6] mass accompanied by decreased muscle strength and/or impaired physical performance. The AWGS guidelines recommend an integrated assessment of muscle mass, muscle strength, and physical performance for the diagnosis of sarcopenia. Muscle mass was evaluated using the ASMI, muscle strength via handgrip strength testing, and physical performance using gait speed or functional performance tests, such as 5STS or the Short Physical Performance Battery (SPPB) tests.

AECOPD was defined as an acute worsening of respiratory symptoms in a patient with underlying COPD, including increased cough, sputum volume or purulence, and/or worsening dyspnea, requiring treatment with antibiotics and/or systemic corticosteroids, or resulting in emergency department visits or hospitalization, in accordance with expert consensus criteria.[14]

Statistical Analysis

All statistical analyses were performed using SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). A two-sided P value < 0.05 was considered statistically significant. The normality of continuous variables was assessed using the Shapiro–Wilk test. Categorical variables are expressed as numbers (percentages). Normally distributed continuous variables are presented as mean ± standard deviation, while non-normally distributed variables are reported as median (interquartile range, IQR). Comparisons between groups were performed using the chi-square test for categorical variables and the independent-samples t-test for continuous variables. Variable selection for the multivariable analysis

followed a hierarchical approach, prioritizing clinical relevance in combination with statistical considerations, rather than relying solely on univariable screening.

Based on prior literature and clinical knowledge, established risk factors for AECOPD, including age, sex, smoking status, severity of airflow limitation (FEV_1% predicted), and the number of AECOPD in the previous year, were entered as covariates in the multivariable binary logistic regression model. The primary exposure variables of interest, sarcopenia status (yes/no) and nutritional risk status (NRS-2002 $\geq$ 3), were subsequently entered into the model. Given potential collinearity among body composition and muscle-related parameters, ASMI, handgrip strength, gait speed, and FFMI were not entered simultaneously in the same model. Building upon the primary model, an extended model incorporating the inflammatory marker TNF-α was constructed to explore the potential mediating role of systemic inflammation in the relationship among nutritional status, sarcopenia, and AECOPD.

The discriminative ability of nutritional status and sarcopenia for predicting AECOPD was evaluated using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) with 95% confidence intervals (CI) was calculated. Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test.

Results

Comparison of Baseline Characteristics Between Patients with and without AECOPD

A total of 264 patients with COPD were included in the analysis. During the 12-month follow-up, 102 patients experienced an AECOPD, while 162 did not. Significant differences were observed between the two groups in age, BMI, smoking status, and disease severity. Patients in the AECOPD group were older than those in the non-AECOPD group (69.79 ± 7.57 vs. 67.00 ± 7.85 years, $P = 0.005$) and had a significantly lower BMI (21.05 ± 3.09 vs. 23.45 ± 3.41 kg/m^2, $P < 0.001$). The proportion of patients with a smoking history was higher in the AECOPD group (74.51% vs. 61.11%, $P = 0.025$). No significant differences were found in sex distribution or in the prevalence of comorbidities, including hypertension, coronary artery disease, diabetes mellitus, and arrhythmia (all $P > 0.05$).

Regarding pulmonary function and symptom burden, the AECOPD group exhibited more severe disease, characterized by significantly lower FEV_1% predicted (43.96 ± 13.75 vs. 55.04 ± 12.34, $P < 0.001$) and a higher proportion of patients with GOLD stage III–IV airflow limitation (GOLD stage III–IV: 66.67% vs. 37.04%, $P < 0.001$). Dyspnea severity was greater in the AECOPD group, as reflected by higher mMRC scores (median 3.00 vs. 2.00, $P < 0.001$) and CAT scores (18.22 ± 5.10 vs. 15.33 ± 6.19, $P < 0.001$). In addition, patients in the AECOPD group had a higher number of exacerbations in the previous year (median 3.00 vs. 2.00, $P < 0.001$). Detailed baseline characteristics are presented in Table 1.

Table 1 Comparison of Baseline Characteristics Between Patients with and without AECOPD

Variable		AECOPD Group (n = 102)	Non-AECOPD Group (n = 162)	$t/\chi^2/Z$	*P*
Age (years)		69.79 ± 7.57	67.00 ± 7.85	−2.856	0.005
Sex, n (%)	Male	71 (69.61%)	106 (65.43%)	0.494	0.852
	Female	31 (30.39%)	56 (34.57%)		
BMI (kg/m^2)		21.05 ± 3.09	23.45 ± 3.41	5.761	<0.001
Smoking history, n (%)	Yes	76 (74.51%)	99 (61.11%)	5.028	0.025
	No	26 (25.49%)	63 (38.89%)		
Hypertension, n (%)	Yes	40 (39.22%)	65 (40.12%)	0.022	0.883
	No	62 (60.78%)	97 (59.88%)		
Coronary artery disease, n (%)	Yes	15 (14.71%)	19 (11.73%)	0.495	0.482
	No	87 (85.29%)	143 (88.27%)		
Diabetes mellitus, n (%)	Yes	22 (21.57%)	33 (20.37%)	0.054	0.815
	No	80 (78.43%)	129 (79.63%)		
Arrhythmia, n (%)	Yes	7 (6.86%)	13 (8.02%)	0.121	0.728
	No	95 (93.14%)	149 (91.98%)		

(*Continued*)

Table 1 (Continued).

Variable		AECOPD Group (n = 102)	Non-AECOPD Group (n = 162)	t/χ^2/Z	*P*
Number of comorbidities		1.00(0.00–1.00)	1.00(0.00–1.00)	−0.244	0.808
FEV_1% predicted (n, %)		43.96 ± 13.75	55.04 ± 12.34	6.796	<0.001
GOLD stage, n (%)	I–II	34 (33.33%)	102 (62.96%)	20.830	<0.001
	III–IV	68 (66.67%)	60 (37.04%)		
mMRC score		3.00 (2.00, 3.00)	2.00 (1.00, 3.00)	−4.375	<0.001
CAT score		18.22 ± 5.10	15.33 ± 6.19	−3.944	<0.001
Number of prior AECOPD episodes		3.00 (1.00, 3.25)	2.00 (1.00, 3.00)	−4.690	<0.001

Abbreviations: BMI, body mass index; FEV_1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified Medical Research Council; CAT, COPD Assessment Test; AECOPD, acute exacerbation of chronic obstructive pulmonary disease.

Comparison of Sarcopenia-Related Parameters Between Groups

The prevalence of sarcopenia was significantly higher among patients who developed AECOPD compared with those who did not (64.71% vs. 32.72%, $P < 0.001$). ASMI was significantly lower in the AECOPD group [6.10 (5.16–6.76) vs. 7.07 (6.51–7.74) kg/m^2, $P < 0.001$]. Consistent differences were observed in measures of muscle strength and physical performance. Patients in the AECOPD group had lower handgrip strength (22.76 ± 6.29 vs. 25.52 ± 5.83 kg, $P < 0.001$) and slower gait speed (0.89 ± 0.28 vs. 0.98 ± 0.22 m/s, $P = 0.004$), while the 5STS time was significantly prolonged (14.61 ± 2.79 vs. 13.05 ± 2.60 s, $P < 0.001$). Sex-stratified analyses showed that the associations between sarcopenia-related parameters and AECOPD were generally consistent across male and female participants. In both sexes, patients with AECOPD exhibited a higher prevalence of sarcopenia, lower ASMI, slower gait speed, and prolonged 5STS time. Handgrip strength was significantly lower in male patients with AECOPD, while a similar trend was observed in female patients but did not reach statistical significance. Detailed comparisons are presented in Table 2.

Table 2 Comparison of Sarcopenia-Related Parameters Between Groups

Variable	AECOPD Group (n = 102)	Non-AECOPD Group (n = 162)	χ^2/Z/t	*P*
Sarcopenia, n (%)	66 (64.71%)	53 (32.72%)	24.596	<0.001
ASMI (kg/m^2)	6.10 (5.16–6.76)	7.07 (6.51–7.74)	−7.381	<0.001
Handgrip strength (kg)	22.76 ± 6.29	25.52 ± 5.83	3.625	<0.001
Gait speed (m/s)	0.89 ± 0.28	0.98 ± 0.22	2.93	0.004
Five-repetition sit-to-stand time (s)	14.61 ± 2.79	13.05 ± 2.60	−4.617	<0.001
Male participants				
Variable	AECOPD group (n = 71)	Non-AECOPD group (n = 106)	χ^2/Z/t	*P*
Sarcopenia, n (%)	57 (80.28%)	46 (43.40%)	23.778	<0.001
ASMI (kg/m^2)	6.07(5.10–6.56)	7.16(6.58–7.79)	−6.760	<0.001
Handgrip strength (kg)	22.49±6.52	25.54±5.93	3.219	0.002
Gait speed (m/s)	0.91±0.28	1.00±0.23	2.132	0.034
Five-repetition sit-to-stand time (s)	14.66±2.96	12.99±2.70	−3.876	<0.001
Female participants				
Variable	AECOPD group (n = 31)	Non-AECOPD group (n = 56)	χ^2/Z/t	*P*
Sarcopenia, n (%)	9(29.03%)	7(12.50%)	3.634	0.057
ASMI (kg/m^2)	6.17±0.96	6.93±0.98	3.503	<0.001
Handgrip strength (kg)	23.37±2.80	25.47±5.69	1.636	0.105
Gait speed (m/s)	0.83±0.25	0.95±0.21	2.299	0.024
Five-repetition sit-to-stand time (s)	14.49±2.39	13.16±2.41	−2.480	0.015

Abbreviation: ASMI, appendicular skeletal muscle index.

Comparison of Nutritional and Inflammatory Parameters Between Groups

Patients in the AECOPD group exhibited poorer nutritional status than those in the non-AECOPD group. Serum albumin levels were significantly lower in the AECOPD group (35.85 ± 4.29 vs. 37.23 ± 5.22 g/L, $P = 0.027$), as was the lymphocyte count (1.39 ± 0.50 × 10^9/L vs. 1.52 ± 0.52 × 10^9/L, $P = 0.043$). Although prealbumin levels showed a decreasing trend in the AECOPD group, the difference did not reach statistical significance ($P = 0.070$). NRS-2002 scores were significantly higher in the AECOPD group than in the non-AECOPD group [3 (1–4) vs. 2 (1–3.25), P = 0.007]. The prevalence of nutritional risk, defined as an NRS-2002 ≥ 3, was significantly higher in the AECOPD group (64.71% vs. 39.51%, $P < 0.001$). In addition, the FFMI was significantly lower among patients in the AECOPD group [15.24 (13.98–17.26) vs. 17.39 (15.70–19.27) kg/m^2, $P < 0.001$].

Regarding inflammatory markers, TNF-α levels were significantly elevated in the AECOPD group [6.39 (4.44–8.60) vs. 5.44 (3.52–7.62) pg/mL, $P = 0.003$], whereas no significant between-group difference was observed for IL-6 levels ($P = 0.608$). Detailed comparisons are shown in Table 3.

Multivariable Logistic Regression Analysis

Multivariable logistic regression analysis demonstrated that, after adjustment for demographic characteristics, smoking status, lung function, and prior exacerbation history, both nutritional risk (NRS-2002 ≥ 3) and sarcopenia were independently associated with an increased risk of AECOPD (Table 4). In the primary model (Model 1), sarcopenia was significantly associated with a higher risk of AECOPD (OR = 6.265, 95% CI 3.008–13.049, $P < 0.001$). Nutritional risk also remained an independent predictor (OR = 3.016, 95% CI 1.57–5.793, $P = 0.001$).

In the muscle composition model (Model 2), when ASMI was entered as a continuous variable in place of the categorical sarcopenia variable, ASMI was inversely associated with AECOPD risk (OR = 0.266 per 1 kg/m^2 increase, 95% CI 0.177–0.399, $P < 0.001$). In the inflammation-extended model (Model 3), elevated TNF-α levels were independently associated with AECOPD (OR = 1.175 per unit increase, 95% CI 1.044–1.322, $P = 0.008$). The associations of sarcopenia and nutritional risk remained statistically significant in this model, suggesting that systemic inflammation may partially contribute to, but does not fully explain, the observed associations. Comorbidity burden, expressed as the number of comorbid conditions, was not significantly associated with AECOPD in any of the models. Across all models, smoking, a higher number of prior AECOPD episodes, and lower FEV_1% predicted were consistently associated with increased AECOPD risk.

Discrimination and Calibration Performance of Multivariable Models for Predicting AECOPD

To compare the predictive performance of the three multivariable logistic regression models for AECOPD, ROC curve analyses were performed (Figure 1 and Table 5). The primary model (Model 1) demonstrated good discriminative ability, with an AUC of 0.8571 (95% CI 0.8104–0.9038), corresponding to a sensitivity of 71.57% and a specificity of 85.80%.

Table 3 Comparison of Nutritional and Inflammatory Parameters Between Patients with and without AECOPD

Variable	AECOPD Group (n = 102)	Non-AECOPD Group (n = 162)	t/Z/χ^2	P
Albumin (g/L)	35.85 ± 4.29	37.23 ± 5.22	2.226	0.027
Prealbumin (mg/L)	177.08 ± 59.11	189.66 ± 51.66	1.821	0.07
Lymphocyte count (×10^9/L)	1.39 ± 0.50	1.52 ± 0.52	2.036	0.043
IL-6 (pg/mL)	6.95 ± 3.01	6.76 ± 2.99	−0.513	0.608
TNF-α (pg/mL)	6.39 (4.44–8.60)	5.44 (3.52–7.62)	−2.961	0.003
NRS-2002 (score)	3(1–4)	2(1–3.25)	−2.703	0.007
NRS-2002 ≥ 3, n (%)	66 (64.71%)	64 (39.51%)	15.902	<0.001
FFMI (kg/m^2)	15.24 (13.98–17.26)	17.39 (15.70–19.27)	−5.798	<0.001

Abbreviations: FFMI, fat-free mass index; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; NRS-2002, Nutritional Risk Screening 2002.

Table 4 Multivariable Logistic Regression Analysis for Predictors of AECOPD

Variable	Model 1 OR (95% CI)	*P*	Model 2 OR (95% CI)	*P*	Model 3 OR (95% CI)	*P*
Age (per 1-year increase)	1.046 (1.003–1.091)	0.034	1.046 (1.000–1.095)	0.051	1.046 (1.003–1.092)	0.037
Male sex	0.445 (0.209–0.948)	0.036	1.057 (0.510–2.192)	0.882	0.459 (0.214–0.985)	0.046
Smoking	2.883 (1.413–5.884)	0.004	2.964 (1.357–6.472)	0.006	3.193 (1.533–6.652)	0.002
FEV_1% predicted (per 1% increase)	0.935 (0.911–0.960)	<0.001	0.930 (0.904–0.957)	<0.001	0.936 (0.912–0.962)	<0.001
Number of prior AECOPD episodes	1.547 (1.242–1.927)	<0.001	1.568 (1.228–2.002)	<0.001	1.579 (1.262–1.976)	<0.001
NRS-2002 ≥ 3	3.016 (1.571–5.793)	0.001	2.760 (1.358–5.610)	0.005	3.009 (1.547–5.854)	0.001
Sarcopenia	6.265 (3.008–13.049)	<0.001	–	–	6.290 (2.960–13.366)	<0.001
Comorbidity count (per 1-condition increase)	1.132 (0.735–1.743)	0.574	1.310 (0.834–2.058)	0.241	1.142 (0.734–1.777)	0.555
ASMI (per 1 kg/m^2 increase)	–	–	0.266 (0.177–0.399)	<0.001	–	–
TNF-α (per unit increase)	–	–	–	–	1.175 (1.044–1.322)	0.008

Notes: Model 1 (primary model) included age, sex, smoking status, FEV_1% predicted, prior AECOPD episodes, sarcopenia status, and nutritional risk (NRS-2002 ≥ 3), and comorbidity burden (expressed as the number of comorbid conditions). Model 2 (muscle composition model) replaced sarcopenia with ASMI. Model 3 (inflammation-extended model) further incorporated TNF-α into Model 1.
Abbreviations: OR, odds ratio; CI, confidence interval.

When ASMI was entered in place of the categorical sarcopenia variable in Model 2, discriminative performance further improved, yielding the highest AUC among the three models (AUC = 0.8934, 95% CI 0.8533–0.9334). This model achieved a sensitivity of 78.43% and a specificity of 88.27%, with the highest Youden index (0.6670). In the inflammation-extended model (Model 3), which incorporated TNF-α, the AUC was 0.8717 (95% CI 0.8258–0.9176), slightly higher than Model 1 but lower than Model 2. The sensitivity and specificity were 74.51% and 88.27%, respectively, with a Youden index of 0.6278. Overall, all three models demonstrated good predictive performance, with the ASMI-based model showing the best discrimination. In addition, the Hosmer–Lemeshow test indicated good calibration for all three models (Model 1: P = 0.124; Model 2: P = 0.674; Model 3: P = 0.272).

Discussion

This study systematically evaluated the associations of nutritional risk and sarcopenia-related parameters with 12-month AECOPD risk in hospitalized patients with stable COPD. The principal findings were threefold. First, both nutritional risk (NRS-2002 ≥ 3) and sarcopenia independently predicted an increased risk of AECOPD. Second, reduced muscle mass, quantified by ASMI, showed an inverse associated with AECOPD risk and demonstrated the highest discriminative performance among the predictive models. Third, elevated TNF-α levels independently predicted AECOPD, yet the associations of nutritional risk and sarcopenia remained significant after adjusting for inflammation, suggesting that systemic inflammation may partially, but not entirely, mediate these relationships. Collectively, these findings provide

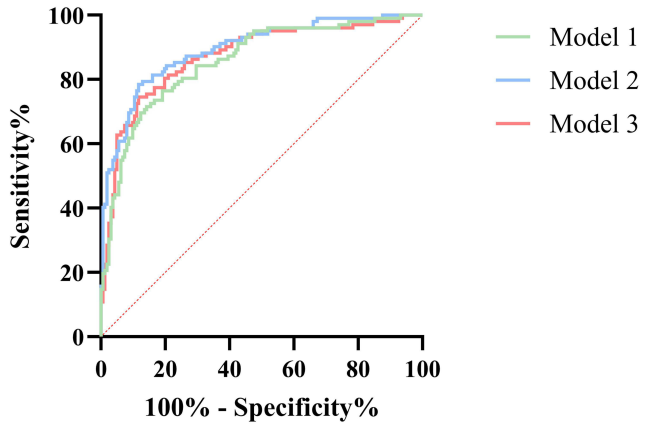

Figure 1 Comparison of ROC Curves of Three Models in Predicting AECOPD.
Notes: Model 1 includes age, sex, smoking status, FEV_1% predicted, number of prior AECOPD episodes, sarcopenia, nutritional risk (NRS-2002 ≥ 3), and comorbidity burden; Model 2 replaces sarcopenia with ASMI; Model 3 further incorporates TNF-α into Model 1.

https://doi.org/10.2147/COPD.S605988

Table 5 Discrimination and Calibration Performance of Multivariable Models for Predicting AECOPD

Factor	AUC	SE	95% CI	Youden's Index	Sensitivity %	Specificity %	HL Test (*P*)
Model 1	0.8571	0.0238	0.8104–0.9038	0.5737	71.57%	85.80%	0.124
Model 2	0.8934	0.0204	0.8533–0.9334	0.6670	78.43%	88.27%	0.674
Model 3	0.8717	0.0234	0.8258–0.9176	0.6278	74.51%	88.27%	0.272

Notes: Model 1 (primary model) included age, sex, smoking status, FEV_1% predicted, prior AECOPD episodes, sarcopenia status, and nutritional risk (NRS-2002 ≥ 3), and comorbidity burden (expressed as the number of comorbid conditions). Model 2 (muscle composition model) replaced sarcopenia with ASMI. Model 3 (inflammation-extended model) further incorporated TNF-α into Model 1.
Abbreviations: AUC, area under the curve, SE, standard error; 95% CI, 95% confidence interval; HL, Hosmer-Lemeshow goodness-of-fit test.

system-level evidence linking body composition, functional status, and inflammatory burden to the frequent exacerbator phenotype in COPD. Importantly, the novelty of this study lies in the integrated assessment of nutritional risk, multidimensional sarcopenia parameters, and inflammatory markers within a unified predictive framework, along with a comparative evaluation of their discriminative performance for future AECOPD.

Malnutrition is highly prevalent in COPD and has been associated with increased mortality, hospitalization, and impaired quality of life.[3,15,16] However, most investigations have focused on long-term outcomes rather than acute exacerbations as dynamic clinical events. In the present study, after adjustment for age, smoking status, lung function, and prior exacerbation history, NRS-2002 ≥ 3 conferred nearly a threefold increase in AECOPD risk. This finding suggests that nutritional risk may represent more than a mere severity marker and may function as an independent susceptibility factor.

This association aligns with prior evidence linking nutritional risk to adverse outcomes in COPD.[17] Malnutrition interacts with chronic low-grade inflammation, immune dysfunction, and muscle wasting, collectively driving disease progression and functional decline.[18,19] Several biological mechanisms may underlie this relationship between nutritional risk and exacerbation occurrence. Hypoalbuminemia and lymphopenia can impair mucosal immune defense and anti-infective capacity, increasing vulnerability to respiratory infections that trigger exacerbations. Concurrently, insufficient nutritional intake accelerates skeletal muscle catabolism and induces negative nitrogen balance, leading to respiratory and peripheral muscle weakness and diminished physiological reserve during inflammatory stress.[16] Recent studies corroborate our findings, demonstrating that nutritional assessment tools can identify individuals at high risk for AECOPD.[5]

Sarcopenia emerged as one of the strongest modifiable predictors, conferring approximately sixfold higher AECOPD risk. When ASMI was modeled continuously, each 1 kg/m^2 increase was associated with 72% lower exacerbation risk (OR = 0.266), and model discrimination improved substantially (AUC = 0.893). This suggests that reduced muscle mass may be the key structural basis underlying the sarcopenia-exacerbation relationship. COPD-related sarcopenia arises from chronic inflammation, oxidative stress, physical inactivity, and inadequate nutrition, all of which promote muscle protein breakdown and functional decline.[20,21] Muscle loss impairs not only peripheral performance but also respiratory muscle reserve, increasing susceptibility to ventilatory failure during inflammatory or infectious stress.[22] While previous studies have predominantly focused mainly on mortality or hospitalization,[8,23] our findings extend the prognostic relevance of sarcopenia to future exacerbations, consistent with prior evidence linking muscle impairment to adverse COPD outcomes.[7] Notably, ASMI outperformed the dichotomous sarcopenia definition, suggesting that continuous muscle mass assessment may better capture exacerbation susceptibility and enhance clinical risk stratification.

Elevated TNF-α levels independently predicted risk of AECOPD. After incorporating inflammatory markers, the effects of nutritional risk and sarcopenia were slightly attenuated but remained significant, suggesting partial mediation rather than full explanation. TNF-α promotes muscle protein degradation and inhibits muscle synthesis; its elevation accelerates muscle atrophy and impairs the physiological response to infectious stress.[24,25] Previous studies have similarly shown that inflammatory markers can predict future exacerbations in COPD,[10] underscoring the role of chronic systemic inflammation in risk stratification.[26] In contrast, IL-6 did not show a significant association in our analysis. This

discrepancy may be explained by the distinct biological roles of these cytokines. TNF-α is more directly involved in sustained systemic inflammation and muscle catabolism, whereas IL-6 exhibits context-dependent effects, functioning as both a pro-inflammatory cytokine and an anti-inflammatory myokine. In addition, IL-6 levels are more susceptible to short-term physiological fluctuations, which may reduce its stability as a predictive biomarker in retrospective analyses.

Our findings further suggested a mutually reinforcing interplay between systemic inflammation and body composition abnormalities. Inflammation accelerates muscle loss, whereas reduced muscle mass may weaken anti-inflammatory and immune regulatory capacity, thereby perpetuating a self-amplifying cycle. Although prior exacerbation history and airflow limitation remain the most robust predictors of AECOPD,[2] the incorporation of nutritional risk and muscle mass parameters substantially improved model discrimination (AUC > 0.89). These results underscore the need for COPD risk assessment to transcend traditional pulmonary function metrics and embrace a multidimensional framework that captures systemic health domains.

The present findings carry clear clinical implications. Unlike fixed airway obstruction, nutritional risk and reduced muscle mass represent potentially modifiable systemic phenotypes that may be improved through targeted nutritional support and pulmonary rehabilitation. Randomized controlled trials have demonstrated that combined nutritional supplementation and rehabilitation programs yield significant improvements in body composition and exercise capacity among patients with COPD.[11] Furthermore, integrating nutritional therapy with early rehabilitation has been shown to enhance muscle strength and preserve lean mass.[27] These findings suggest that combined nutritional and exercise-based interventions may also contribute to reducing the risk of future exacerbations by improving systemic resilience and respiratory muscle function.

In light of our demonstration that nutritional risk and low muscle mass independently predict future AECOPD, systematic assessment of nutritional status and body composition during the stable phase may facilitate early identification of high-risk individuals and provide actionable targets for individualized intervention. Should prospective studies establish that ameliorating nutritional and muscular deficits reduces exacerbation incidence, integrated nutrition–exercise strategies could be incorporated into secondary prevention paradigms, thereby shifting the therapeutic focus from functional optimization toward event prevention.

Several limitations merit acknowledgment. First, the single-center retrospective design, restricted to hospitalized patients with stable COPD, may introduce selection bias and limit generalizability to broader outpatient populations. Second, although bioelectrical impedance analysis offers clinical feasibility, its precision for body composition assessment is inferior to imaging modalities such as dual-energy X-ray absorptiometry. Third, our inflammatory assessment was confined to TNF-α, which may not fully capture the complexity of the inflammatory network operative in COPD. In addition, although NRS-2002 was used due to its applicability in hospitalized patients, other nutritional assessment tools such as GLIM may provide more comprehensive evaluation and warrant further investigation in prospective studies. Finally, an external validation cohort was absent, and the generalizability of the predictive models requires confirmation in multicenter prospective studies.

Despite these limitations, the associations among nutritional risk, sarcopenia, and AECOPD retained robustness after adjustment for potential confounders, and the constructed models demonstrated strong discriminative performance. These findings position nutritional and muscle status as important components of the COPD frequent exacerbator phenotype and highlight their potential utility as clinically meaningful targets for risk stratification and therapeutic intervention.

Conclusion

Nutritional risk and sarcopenia independently predict future AECOPD in stable COPD. Reduced muscle mass appears to constitute the structural foundation of this vulnerability, with systemic inflammation serving a partial mediating function. Integrating nutritional and muscle parameters into existing risk stratification models may improve prediction accuracy and inform individualized prevention strategies.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study protocol was reviewed and approved by the Institutional Ethics Committee of Jinling Hospital, Medical School of Nanjing University (Approval No. DZQH-KYLL-24-11). Given the retrospective design and use of anonymized data, informed consent was waived.

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.

Funding

There is no funding to report.

Disclosure

The authors declare no competing interests in this work.

References

1. Hogea SP, Tudorache E, Fildan AP, Fira-Mladinescu O, Marc M, Oancea C. Risk factors of chronic obstructive pulmonary disease exacerbations. *Clin Respir J*. 2020;14(3):183–197. doi:10.1111/crj.13129
2. Vogelmeier CF, Diesing J, Kossack N, Pignot M, Friedrich FW. COPD exacerbation history and impact on future exacerbations - 8-year retrospective observational database cohort study from Germany. *Int J Chron Obstruct Pulmon Dis*. 2021;16:2407–2417. doi:10.2147/COPD.S322036
3. Deng M, Lu Y, Zhang Q, Bian Y, Zhou X, Hou G. Global prevalence of malnutrition in patients with chronic obstructive pulmonary disease: systemic review and meta-analysis. *Clin Nutr*. 2023;42(6):848–858. doi:10.1016/j.clnu.2023.04.005
4. Shimada T, Chubachi S, Otake S, et al. Differential impacts between fat mass index and fat-free mass index on patients with COPD. *Respir Med*. 2023;217:107346. doi:10.1016/j.rmed.2023.107346
5. Di Raimondo D, Pirera E, Pintus C, et al. The impact of malnutrition on Chronic Obstructive Pulmonary Disease (COPD) outcomes: the predictive value of the Mini Nutritional Assessment (MNA) versus acute exacerbations in patients with highly complex COPD and its clinical and prognostic implications. *Nutrients*. 2024;16(14):2303. doi:10.3390/nu16142303
6. Chen LK, Woo J, Assantachai P, et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. 2020;21(3):300–307e302. doi:10.1016/j.jamda.2019.12.012
7. Wu JF, Jia J, Chen P, et al. Sarcopenia and its clinical correlation in elderly chronic obstructive pulmonary disease: a prospective cohort study. *Eur Rev Med Pharmacol Sci*. 2023;27(20):9762–9772. doi:10.26355/eurrev_202310_34150
8. Zhao X, Su R, Hu R, et al. Sarcopenia index as a predictor of clinical outcomes among older adult patients with acute exacerbation of chronic obstructive pulmonary disease: a cross-sectional study. *BMC Geriatr*. 2023;23(1):89. doi:10.1186/s12877-023-03784-7
9. Warnken-Miralles MD, Lopez-Garcia F, Zamora-Molina L, Soler-Sempere MJ, Padilla-Navas I, Garcia-Pachon E. [Sarcopenia index in hospitalized patients with chronic obstructive pulmonary disease exacerbation]. *Medicina*. 2021;81(3):323–328. Spanish.
10. Liu X, Ge H, Feng X, et al. The combination of hemogram indexes to predict exacerbation in stable chronic obstructive pulmonary disease. *Front Med*. 2020;7:572435. doi:10.3389/fmed.2020.572435
11. Aldhahir AM, Aldabayan YS, Alqahtani JS, et al. A double-blind randomised controlled trial of protein supplementation to enhance exercise capacity in COPD during pulmonary rehabilitation: a pilot study. *ERJ Open Res*. 2021;7(1):00077–2021. doi:10.1183/23120541.00077-2021
12. Whittaker H, Rubino A, Mullerova H, et al. Frequency and severity of exacerbations of COPD associated with future risk of exacerbations and mortality: a UK routine health care data study. *Int J Chron Obstruct Pulmon Dis*. 2022;17:427–437. doi:10.2147/COPD.S346591
13. Santus P, Di marco F, Braido F, et al. Exacerbation burden in COPD and occurrence of mortality in a cohort of Italian patients: results of the gulp study. *Int J Chron Obstruct Pulmon Dis*. 2024;19:607–618. doi:10.2147/COPD.S446636
14. Ritchie AI, Wedzicha JA. Definition, causes, pathogenesis, and consequences of chronic obstructive pulmonary disease exacerbations. *Clin Chest Med*. 2020;41(3):421–438. doi:10.1016/j.ccm.2020.06.007
15. Collins PF, Elia M, Stratton RJ. Nutritional support and functional capacity in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Respirology*. 2013;18(4):616–629. doi:10.1111/resp.12070
16. Shi G, Yue L, Tang Z, Wang Y, Hu X, Tong Y. Serum growth differentiation factor 15 as a biomarker for malnutrition in patients with acute exacerbation of chronic obstructive pulmonary disease. *Front Nutr*. 2024;11:1404063. doi:10.3389/fnut.2024.1404063
17. Shen X, Qian R, Wei Y, et al. Prediction model and assessment of malnutrition in patients with stable chronic obstructive pulmonary disease. *Sci Rep*. 2024;14(1):6508. doi:10.1038/s41598-024-56747-2
18. Hao X, Bu T. Clinical value of nutritional assessment tools in older adults with Chronic Obstructive Pulmonary Disease: an integrative review. *Clin Interv Aging*. 2025;20:2671–2683. doi:10.2147/CIA.S556215
19. Yao J, Wu P, Li Z, et al. Nutritional status and systemic inflammation in COPD: prognostic value of the advanced lung cancer inflammation index. *Front Nutr*. 2025;12:1550490. doi:10.3389/fnut.2025.1550490

20. Ma K, Huang F, Qiao R, Miao L. Pathogenesis of sarcopenia in chronic obstructive pulmonary disease. *Front Physiol*. 2022;13:850964. doi:10.3389/fphys.2022.850964
21. Nagano A, Wakabayashi H, Maeda K, et al. Respiratory sarcopenia and sarcopenic respiratory disability: concepts, diagnosis, and treatment. *J Nutr Health Aging*. 2021;25(4):507–515. doi:10.1007/s12603-021-1587-5
22. Yu Z, He J, Chen Y, Zhou Z, Wang L. Chronic obstructive pulmonary disease as a risk factor for sarcopenia: a systematic review and meta-analysis. *PLoS One*. 2024;19(4):e0300730. doi:10.1371/journal.pone.0300730
23. Choi YJ, Kim T, Park HJ, Cho JH, Byun MK. Long-term clinical outcomes of patients with chronic obstructive pulmonary disease with sarcopenia. *Life*. 2023;13(8). doi:10.3390/life13081628
24. Li X, Xu S, Zeng C, Wang X, Wang R, Feng Y. Research progress of sarcopenia index in chronic obstructive pulmonary disease: a review. *Cureus*. 2025;17(11):e97556. doi:10.7759/cureus.97556
25. Matera MG, Page C, Cazzola M. Sarcopenia as a treatable trait in COPD: from mechanisms to management. *Respir Med*. 2025;248:108401. doi:10.1016/j.rmed.2025.108401
26. Ellingsen J, Janson C, Broms K, et al. CRP, fibrinogen, white blood cells, and blood cell indices as prognostic biomarkers of future COPD exacerbation frequency: the TIE cohort study. *J Clin Med*. 2024;13(13):3855. doi:10.3390/jcm13133855
27. Oyama Y, Tatsumi H, Takikawa H, Taniguchi N, Masuda Y. Combined effect of early nutrition therapy and rehabilitation for patients with chronic obstructive pulmonary disease exacerbation: a prospective randomized controlled trial. *Nutrients*. 2024;16(5):739. doi:10.3390/nu16050739