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Original Article

Correlation of lung function and sarcopenia in elderly patients with chronic obstructive pulmonary disease and analysis of factors influencing sarcopenia

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Abstract: Objective: This study aims to investigate the correlation between lung function and sarcopenia in elderly patients with chronic obstructive pulmonary disease (COPD) and to analyze the factors influencing sarcopenia. The goal is to provide evidence for comprehensive management of COPD patients. Methods: A total of 294 elderly COPD patients admitted to Lanzhou City No. 1 People's Hospital from March 2022 to March 2024 were selected as study subjects. The patients were divided into a training group (n=205) and a validation group (n=89) in a 7:3 ratio. Lung function was assessed through pulmonary function tests, and sarcopenia was defined by evaluating muscle mass and muscle quality using bioelectrical impedance analysis. Based on the diagnostic criteria for sarcopenia, patients were categorized into a sarcopenia group (n=113) and a non-sarcopenia group (n=181). Basic information, lifestyle habits, and medical history were collected to analyze the correlation between lung function and sarcopenia, as well as influencing factors. Additionally, logistic regression analysis was conducted to identify independent risk factors, and a nomogram model was developed for risk prediction. Results: Multivariate logistic regression analysis revealed that age (P<0.001, OR=0.053), weight (P=0.032, OR=3.321), Cys-C (P=0.018, OR=0.283), Hb (P=0.001, OR=7.014), FVC (P=0.04, OR=3.605), FEV1 (P=0.001, OR=9.674), and CAT score (P<0.001, OR=0.085) were independent risk factors for sarcopenia in COPD patients. The nomogram model based on these independent risk factors demonstrated good predictive performance for sarcopenia in elderly COPD patients. ROC curve analysis showed that the area under the curve (AUC) of the nomogram model was 0.886 (95% CI: 0.819-0.932) in the training group and 0.809 (95% CI: 0.726-0.883) in the validation group, indicating a high predictive accuracy. Additionally, ROC curve analysis showed that the AUCs for age, BMI, and FEV1/FVC in diagnosing sarcopenia in elderly COPD patients were 0.710 (95% CI: 0.747-0.863), 0.647 (95% CI: 0.766-0.878), and 0.682 (95% CI: 0.701-0.833), respectively. Gene Set Enrichment Analysis (GSEA) revealed that pathways significantly enriched in the high Cys-C expression group included oxidative phosphorylation, fatty acid biosynthesis, the AMPK signaling pathway, the HIF-1 signaling pathway, and glycolysis/gluconeogenesis pathways, which may play important roles in energy metabolism and muscle function regulation in sarcopenic patients. Conclusion: Lung function decline in elderly COPD patients is closely associated with the occurrence of sarcopenia. Increasing age is an independent risk factor for sarcopenia in COPD patients, while higher BMI and FEV1/FVC are protective factors. The nomogram model based on these independent risk factors can effectively predict sarcopenia in elderly COPD patients.

Keywords: Chronic obstructive pulmonary disease (COPD), lung function, sarcopenia, gene set enrichment analysis (GSEA)

Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable condition characterized by persistent and typically irreversible airflow limitation, which is usually classified into acute exacerbation and stable phases [1]. Globally, COPD is one of the most prevalent and severe diseases, ranking among the top three causes of death and imposing a substantial economic and health burden on public health systems [2]. In recent years, the incidence of COPD in China has continued to rise, correlating with an aging population [3]. An epidemio-

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logical survey conducted in 2018 reported a COPD prevalence of 13.7% among individuals over 40 years old in China, marking a 5.5% increase compared to a 2007 survey [4, 5]. This upward trend underscores the urgent need for effective prevention and treatment strategies for COPD. Studies have confirmed that COPD is associated with various extrapulmonary comorbidities, including sarcopenia, osteoporosis, pulmonary heart disease, metabolic syndrome, and depression, which further complicate patient management and prognosis [6].

Sarcopenia is a syndrome characterized by progressive loss of muscle mass, decreased muscle strength, and impaired muscle function. It is commonly observed in the elderly and in patients with chronic diseases such as COPD, type 2 diabetes, and heart failure [7, 8]. Epidemiologic studies have shown that the prevalence of sarcopenia among Asian populations ranges from 5.5% to 25.7%, and among stable COPD patients, it is as high as 15% to 40% [9, 10]. Due to its insidious onset, sarcopenia initially presents as a reduction in muscle mass without obvious symptoms, making early detection challenging [11]. As the condition progresses, patients may develop complications such as cachexia, dysphagia, and fractures, leading to a poor prognosis [12]. Furthermore, sarcopenia significantly worsens patients' quality of life, with over 30% of affected individuals losing their ability to live independently. Additionally, patients with sarcopenia have a markedly higher risk of in-hospital mortality compared to those with normal muscle mass [13].

The interaction between COPD and sarcopenia is complex, with shared pathophysiologic mechanisms including chronic inflammation, oxidative stress, and reduced physical activity [14]. As COPD progresses, patients experience a gradual decline in skeletal muscle mass and function, eventually leading to sarcopenia [15]. Impaired lung function in COPD patients is closely linked to the development of sarcopenia; reduced lung function not only increases patient mortality but also exacerbates sarcopenia symptoms, significantly diminishing quality of life [16]. Understanding the mechanisms underlying sarcopenia in COPD patients and identifying related factors are crucial for the early identification of high-risk populations and the development of targeted interventions to improve patient prognosis and quality of life.

Although previous studies have explored the association between COPD and sarcopenia, there remains a significant knowledge gap regarding the relationship between lung function and sarcopenia, specifically in elderly patients. The current literature lacks a comprehensive understanding of the mechanisms by which lung function impairment in COPD patients leads to sarcopenia, particularly among the elderly, and influencing factors were not thoroughly investigated. Therefore, the primary objective of this study is to examine the correlation between lung function and sarcopenia in elderly COPD patients and to analyze the factors influencing sarcopenia. By addressing this research gap, the study aims to provide new evidence to enhance the management of elderly COPD patients.

Methods and materials

Case collection

This retrospective study analyzed 294 elderly COPD patients admitted to Lanzhou City No. 1 People's Hospital between March 2022 to March 2024. According to the study design, patients were divided into a training group (n=205) and a validation group (n=89). The study was approved by the Lanzhou City No. 1 People's Hospital medical ethics committee.

Inclusion and exclusion criteria

Patients were eligible if they were diagnosed with COPD and met the diagnostic criteria for sarcopenia. Additionally, only those with complete clinical data were selected.

Patients were excluded if they had interstitial lung disease, pulmonary tuberculosis, peripheral edema, metabolic diseases, cardiac pacemaker implantation, severe liver or kidney dysfunction, limb infections, or a history of malignant tumors.

GEO database data collection

Gene expression profile data related to COPD (GSE76925) and sarcopenia (GSE111006) were obtained from the Gene Expression

Omnibus (GEO) database. The GSE111006 dataset comprises 40 samples, including 4 patients with sarcopenia and 36 controls. The GSE76925 dataset consists of 151 samples, with 40 COPD patients and 111 controls. These datasets were used for gene expression analysis and to explore molecular mechanisms associated with COPD and sarcopenia through Gene Set Enrichment Analysis (GSEA).

COPD diagnostic criteria

The diagnosis of COPD was based on the 2019 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [17]. The primary diagnostic criterion was a post-bronchodilator FEV1/FVC ratio of less than 0.70, confirmed by the presence of relevant symptoms and patient history.

Diagnostic criteria for sarcopenia

The diagnosis of sarcopenia adhered to the updated 2019 European Working Group on Sarcopenia in Older People (EWGSOP2) guidelines [18], which encompass the assessment of muscle mass, muscle strength, and physical performance. The criteria included reduced muscle mass as measured by Dual-Energy X-ray Absorptiometry (DXA) or Bioelectrical Impedance Analysis (BIA), accompanied by grip strength below the lower limit of the normal range for the respective gender and age group, or a walking speed below 0.8 m/s.

Clinical data collection

Clinical data were collected from patients' electronic medical records and outpatient follow-up records, categorized into clinical information, laboratory indicators, lung function indicators, and functional scores.

Clinical information included gender, age, disease duration, hypertension, coronary heart disease, diabetes, presence of two or more comorbidities, smoking history, alcohol abuse history, education level, and disease classification.

Laboratory indicators included serum creatinine (Scr), cystatin C (Cys-C), Scr to Cys-C ratio (Scr/Cys-C), total protein (TP), albumin (ALB), prealbumin (PAB), cholinesterase (CHE), total cholesterol (TC), triglycerides (TG), white blood cell count (WBC), neutrophils (NE), lymphocytes (LC), neutrophil-to-lymphocyte ratio (NLR), hemoglobin (Hb), platelet count (PLT), platelet-to-lymphocyte ratio (PLR), and C-reactive protein (CRP).

Lung function indicators included forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and the FEV1/FVC ratio (FEV1/FVC).

Functional scores included COPD assessment test (CAT score), modified medical research council dyspnea scale (mMRC score), body mass index (BMI), airflow obstruction, dyspnea, exercise capacity index (BODE index), and 6-minute walk distance grading (6MWD classification).

Indicator detection

Laboratory indicators: Serum biochemical values such as Scr, Cys-C, TP, ALB, PAB, CHE, TC, and TG were measured using a Siemens ADVIA 2400 biochemical analyzer. Complete blood counts, including WBC, NE, LC, Hb, and PLT levels, were determined using a Sysmex XE-2100 automated hematology analyzer, from which NLR and PLR were calculated. Additionally, CRP levels were measured using the same analyzer.

Lung function indicators: Pulmonary function tests were conducted using a Jaeger MasterScreen PFT automatic lung function analyzer, following GOLD standard procedures. The tests included FVC, FEV1, and FEV1/FVC to evaluate the patients' pulmonary ventilation function.

Functional scores

CAT [19] was conducted to assess the severity of COPD symptoms on a scale of 0-40 points, where higher scores indicate more severe symptoms and lower quality of life.

mMRC [20] was employed to evaluate the degree of dyspnea on a scale of 0-4 points, with higher scores indicating more severe dyspnea.

BODE index [21] is a comprehensive index assessing the severity of COPD on a scale of 0-10 points, where higher scores indicate a worse prognosis and higher mortality risk.

6MWD classification [22] was used to measure exercise tolerance based on the distance walked in six minutes, where lower scores indicate poorer exercise capacity.

GSEA analysis

GSEA [23] was employed to analyze gene expression data obtained from the GEO database, aiming to identify pathways and biological processes associated with COPD and sarcopenia. In this analysis, the four sarcopenic samples in the GSE111006 dataset were divided into high-expression and low-expression groups based on the mean Cys-C level. GSEA was then performed on these groups, including Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses, to identify enriched gene sets related to the diseases and to explore potential molecular mechanisms.

Outcome measurements

Primary outcome: Logistic regression analysis was utilized to identify independent risk factors for the coexistence of COPD and sarcopenia. A nomogram prediction model was developed based on these factors.

Secondary outcomes: Differences in clinical data between the training and validation groups were compared, and baseline differences within the training group were analyzed. Model stability was validated using receiver operating characteristic (ROC) curves, precision-recall (PR) curves, decision curve analysis (DCA), and calibration curves in both training and validation sets. Secondary outcomes also included analyzing nonlinear relationships between independent risk factors and the risk of COPD + sarcopenia using restricted cubic spline plots, conducting interaction analysis to assess the influence of factor interactions on COPD + sarcopenia risk, and interpreting GSEA results to elucidate biologic processes and pathways underlying gene expression differences.

Statistical analysis

All statistical analyses were conducted using R software (version 4.2.0) with specific R packages, including dplyr for data cleaning and organization, ggplot2 for data visualization, the glm() function from base R for logistic regression analysis, rms for constructing the nomogram prediction model and generating calibration curves, pROC for ROC curve plotting and analysis, PRROC for PR curve plotting, rmda for DCA analysis and plotting, splines for drawing and analyzing restricted cubic spline plots, and interactionR for interaction analysis. Continuous variables were expressed as mean ± standard deviation (mean ± SD) and compared between groups using independent samples t-test or Mann-Whitney U test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test. Logistic regression analysis was performed to identify independent risk factors for COPD + sarcopenia and to construct a nomogram prediction model based on these factors. The predictive performance of the model was evaluated using ROC curves, PR curves, DCA, and calibration curves. All statistical tests were two-sided, with $P<0.05$ considered significant.

Results

Clinical data of patients

The patient demographics and measurements were visualized using heatmaps (**Figure 1**). A total of 205 patients were allocated to the training group and 89 patients to the validation group in a 7:3 ratio. Chi-square test analysis indicated no significant differences between the training and validation groups regarding the presence of sarcopenia, gender, hypertension, coronary heart disease, diabetes, the presence of two or more comorbidities, smoking history, alcohol abuse history, education level, or disease classification ($P>0.05$, **Figure 2**). Additionally, independent samples t-tests and Mann-Whitney U tests revealed no significant differences between the training and validation groups in terms of age, height, weight, BMI, disease duration, Scr, Cys-C, Scr/Cys-C, TP, ALB, PAB, CHE, TC, TG, WBC count, NE, LC, NLR, Hb, PLT, PLR, CRP, FVC, FEV1, FEV1/FVC, CAT score, mMRC score, BMI, airflow obstruction, dyspnea, exercise capacity index, or 6MWD classification ($P>0.05$, **Figure 3**).

Comparison of clinical data between COPD group and COPD with sarcopenia group in the training set

Patients were categorized into COPD and COPD with sarcopenia groups based on the presence

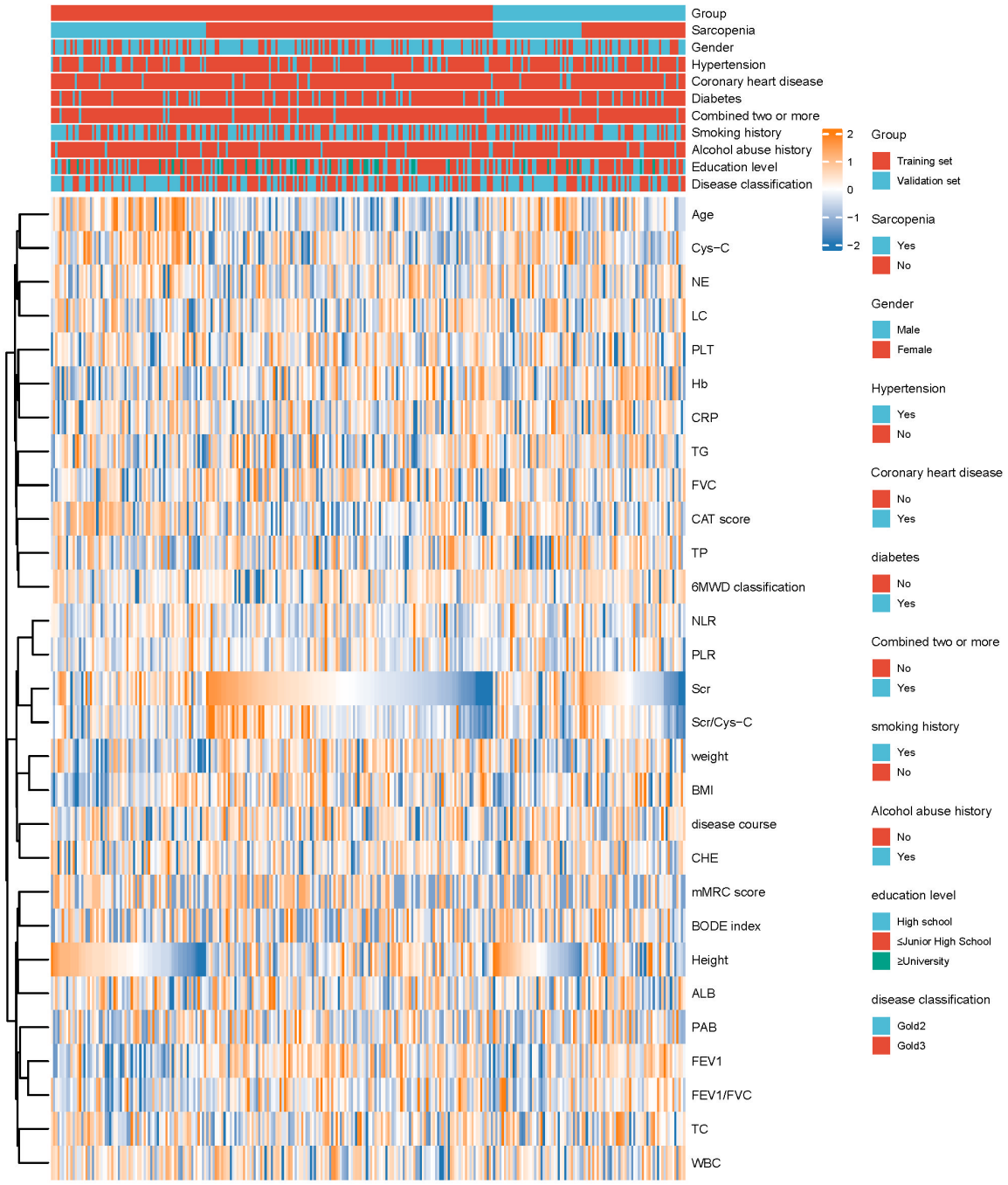

Figure 1. Heatmap showing clinical data of all patients. Note: Body Mass Index (BMI), Serum Creatinine (Scr), Cystatin C (Cys-C), Total Protein (TP), Albumin (ALB), Prealbumin (PAB), Cholinesterase (CHE), Total Cholesterol (TC), Triglycerides (TG), White Blood Cell count (WBC), Neutrophils (NE), Lymphocytes (LC), Neutrophil-to-Lymphocyte Ratio (NLR), Hemoglobin (Hb), Platelet count (PLT), Platelet-to-Lymphocyte Ratio (PLR), C-Reactive Protein (CRP), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, COPD Assessment Test (CAT), Modified Medical Research Council Dyspnea Scale (mMRC), Body Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index (BODE), and 6-Minute Walk Distance Grading (6MWD). To facilitate display, data were processed using the log (x+1, 2) method. Subsequent data analysis was performed using the original data.

of sarcopenia. Further analysis revealed that a significantly higher number of patients in the COPD with sarcopenia group were classified as grade three COPD compared to the COPD group

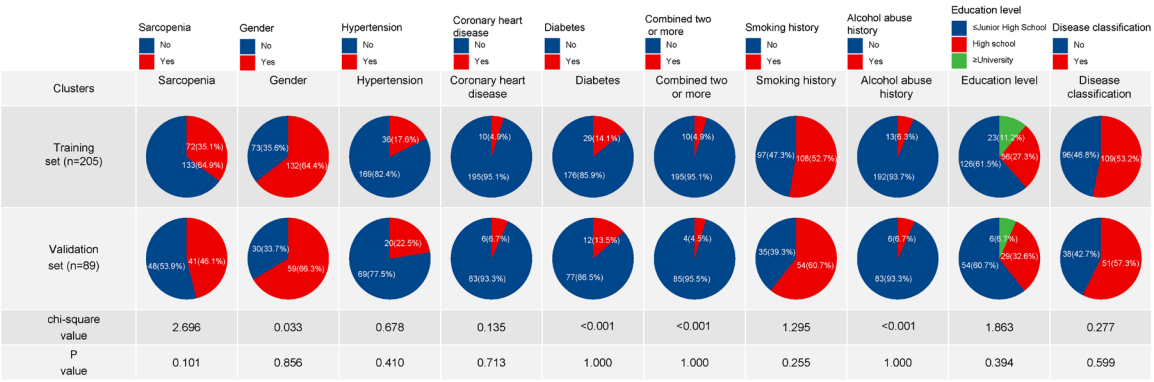

Figure 2. Comparison of counted data between training and validation sets.

(P<0.001, **Figure 4**). Measured data comparisons showed (**Table 1**) that the COPD with sarcopenia group was significantly older than the COPD group (P<0.001, **Figure 5A**), while their weight (P<0.001, **Figure 5B**) and BMI (P=0.001, **Figure 5C**) were significantly lower. Additionally, the level of Cys-C in the COPD with sarcopenia group was significantly higher than in the COPD group (P<0.001, **Figure 5D**), whereas Hb levels were significantly lower (P<0.001, **Figure 5E**). In terms of lung function, FVC (P=0.005, **Figure 5F**), FEV1 (P<0.001, **Figure 5G**), and FEV1/FVC (P=0.005, **Figure 5H**) were significantly lower in the COPD with sarcopenia group compared to the COPD group. Furthermore, the CAT score was significantly higher in the COPD with sarcopenia group than in the COPD group (P<0.001, **Figure 5I**).

Clinical value of quantitative data in evaluating COPD with sarcopenia

ROC curve analysis was used to evaluate the diagnostic performance of various clinical values in distinguishing between COPD and COPD with sarcopenia patients. Age demonstrated the highest evaluative value with an area under the curve (AUC) of 0.86 and a cutoff value of 65.5 years (P<0.001), achieving a sensitivity of 87.22%, specificity of 66.67%, accuracy of 80.00%, positive predictive value of 82.86%, negative predictive value of 73.85%, and a Youden index of 53.88%. Similarly, the CAT score exhibited high evaluative ability with an AUC of 0.86 and a cutoff value of 9.5 (P<0.001), yielding a sensitivity of 75.19%, specificity of 69.44%, accuracy of 73.17%, positive predictive value of 81.97%, negative predictive value of 60.24%, and a Youden index of 44.63%. Other indicators, including FEV1, weight, Cys-C, Hb, FVC, and BMI, showed moderate evaluative efficacy with AUCs of 0.77, 0.72, 0.71, 0.66, 0.60, and 0.58, respectively (**Figure 6A**). A radar chart further illustrated the performance of each parameter in terms of sensitivity, specificity, accuracy, positive predictive value, negative predictive value, and Youden index, highlighting the clinical value of different laboratory values in evaluating COPD with sarcopenia (**Figure 6B**).

Logistic regression for identifying independent risk factors for COPD with sarcopenia

Initially, data were dichotomized based on the cutoff values derived from the ROC curve analysis. Univariate logistic regression analysis identified age (P<0.001, odds ratio [OR] =0.073), weight (P<0.001, OR=4.264), BMI (P<0.001, OR=2.9), Cys-C (P<0.001, OR=0.325), Hb (P< 0.001, OR=3.682), FVC (P=0.001, OR=2.867), FEV1 (P<0.001, OR=5.867), FEV1/FVC (P= 0.002, OR=2.592), and CAT score (P<0.001, OR=0.145) were associated with the occurrence of sarcopenia in COPD patients. Multivariate logistic regression analysis further identified age (P<0.001, OR=0.053), weight (P=0.032, OR=3.321), Cys-C (P=0.018, OR= 0.283), Hb (P=0.001, OR=7.014), FVC (P=0.04, OR=3.605), FEV1 (P=0.001, OR=9.674), and CAT score (P<0.001, OR=0.085) as independent factors predicting the occurrence of sarcopenia (**Table 2**).

Construction and validation of the prediction nomogram model based on independent risk factors

A nomogram prediction model was developed based on the seven independent risk factors:

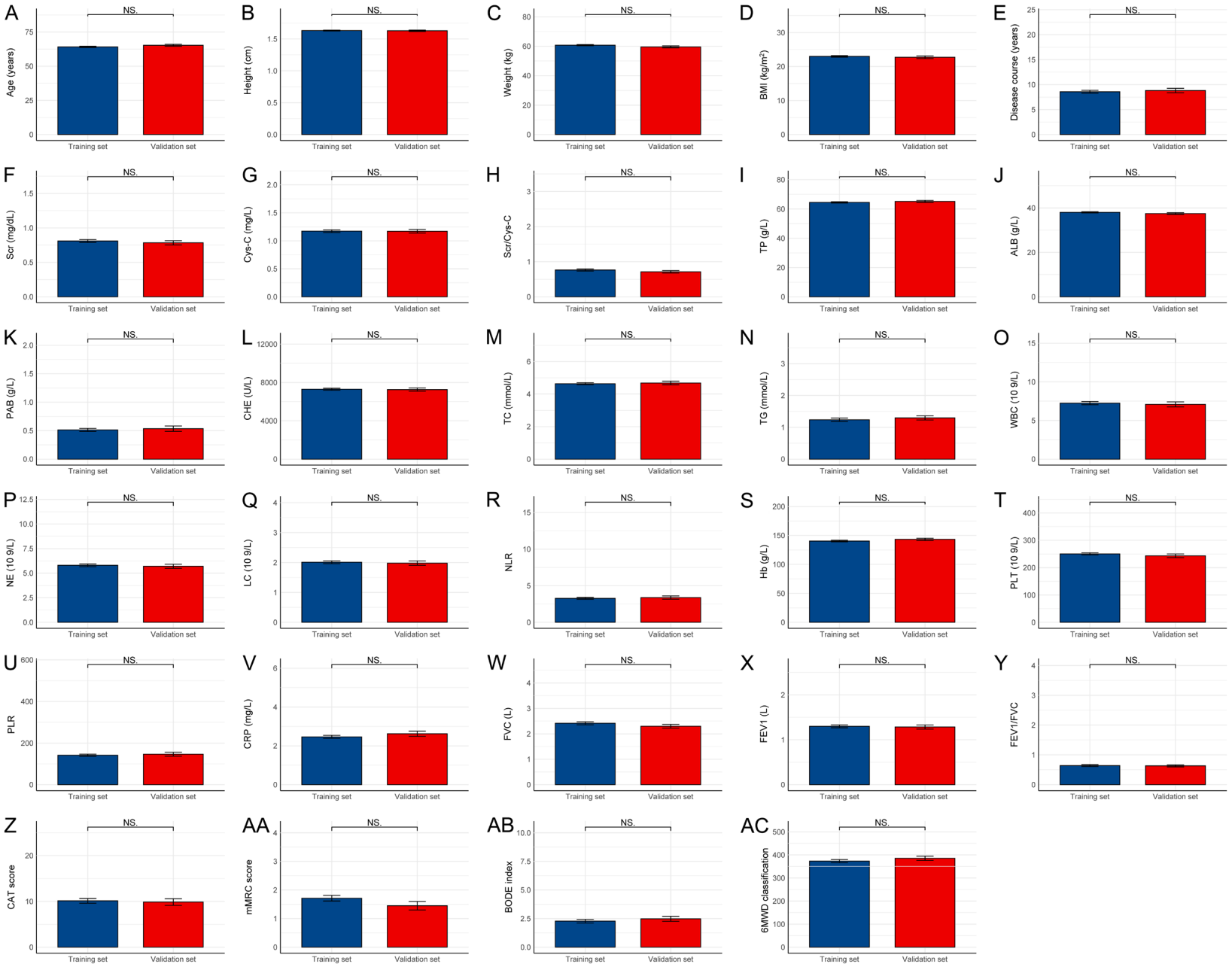
A
Age (years)
B
Height (cm)
C
Weight (kg)
D
BMI (kg/m²)
E
Disease course (years)
F
Scr (mg/dL)
G
Cys-C (mg/L)
H
Scr/Cys-C
I
TP (g/L)
J
ALB (g/L)
K
PAB (g/L)
L
CHE (U/L)
M
TC (mmol/L)
N
TG (mmol/L)
O
WBC (10 9/L)
P
NE (10 9/L)
Q
LC (10 9/L)
R
NLR
S
Hb (g/L)
T
PLT (10 9/L)
U
PLR
V
CRP (mg/L)
W
FVC (L)
X
FEV1 (L)
Y
FEV1/FVC
Z
CAT score
AA
mMRC score
AB
BODE index
AC
6MWD classification
NS.
Training set
Validation set

Figure 3. Comparison of quantitative data between training and validation sets. Note: Body Mass Index (BMI), Serum Creatinine (Scr), Cystatin C (Cys-C), Total Protein (TP), Albumin (ALB), Prealbumin (PAB), Cholinesterase (CHE), Total Cholesterol (TC), Triglycerides (TG), White Blood Cell count (WBC), Neutrophils (NE), Lymphocytes (LC), Neutrophil-to-Lymphocyte Ratio (NLR), Hemoglobin (Hb), Platelet count (PLT), Platelet-to-Lymphocyte Ratio (PLR), C-Reactive Protein (CRP), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, COPD Assessment Test (CAT), Modified Medical Research Council Dyspnea Scale (mMRC), Body Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index (BODE), and 6-Minute Walk Distance Grading (6MWD).

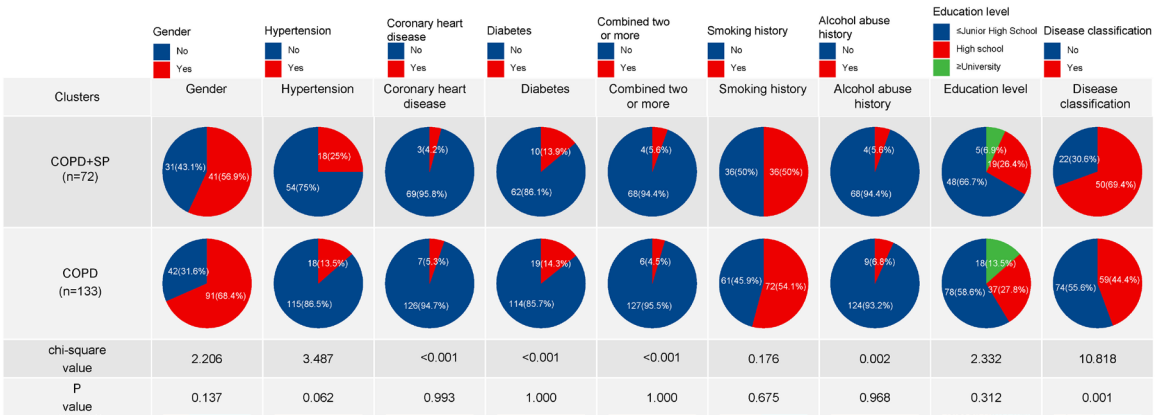

Figure 4. Comparison of counted data between COPD and COPD+SP groups in the training set. Note: Chronic Obstructive Pulmonary Disease (COPD), and Sarcopenia (SP).

age, weight, Cys-C, Hb, FVC, FEV1, and CAT score (**Figure 7A**). The risk formula was as follows: -0.1594 + (age ≤66.5) × -2.8219 + (weight ≤58.75) × 1.6205 + (Cys-C≤1.255) × -1.1191 + (Hb≤130.5) × 1.8841 + (FVC≤2.57) × 1.2313 + (FEV1≤1.265) × 2.2413 + (CAT score ≤9.5) × -2.5508. To evaluate the model's performance, multiple validations were performed within the training group. The ROC curve demonstrated an AUC of 0.886, indicating high discriminative ability (**Figure 7B**). The PR curve exhibited a favorable relationship between precision and recall, reflecting good predictive performance (**Figure 7C**). Additionally, the DCA indicated a positive benefit rate across the 0% to 99% risk threshold range, suggesting the model's practical application value across a wide range of clinical decision thresholds (**Figure 7D**). The calibration curve showed good consistency between the model's predicted probabilities and the actual observed outcomes, as the curve closely aligned with the ideal diagonal line (**Figure 7E**).

Performance evaluation of the nomogram model in the validation set

In the validation set, the nomogram prediction model's performance was assessed through several analyses. The ROC curve revealed an AUC of 0.809, indicating good discriminative ability in the validation group (**Figure 8A**). The PR curve further confirmed the model's predictive performance in this group (**Figure 8B**). The DCA demonstrated a positive benefit rate across the 0% to 76% risk threshold range, highlighting the model's practical utility within various clinical decision-making scenarios (**Figure 8C**). The calibration curve indicated good agreement between predicted probabilities and observed outcomes, since the curve was closely aligned with the ideal diagonal line (**Figure 8D**).

Analysis of nonlinear relationships between seven risk factors and COPD with sarcopenia risk based on restricted cubic splines

Restricted cubic spline model analysis was conducted to reassess the nonlinear relationships between the seven independent risk factors - age, weight, Cys-C, Hb, FVC, FEV1, and CAT score - and the risk of developing COPD with sarcopenia. After adjustment, the analysis revealed that the risk of COPD with sarcopenia increased gradually in the early stages and then significantly as age increased (**Figure 9A**). The relationship between weight and COPD with sarcopenia risk was complex, showing a higher risk at lower weight ranges, a gradual

Table 1. Comparison of quantitative data between COPD and COPD+SP patients in the training group

Variable	Test	COPD+SP (n=72)	COPD (n=133)	Statistic	P
Age (years)	Mann-Whitney U	69.19±7.00	62.00 [58.00, 65.00]	-7.291	<0.001
Height (cm)	t-test	1.63±0.10	1.64±0.09	0.675	0.501
Weight (kg)	t-test	57.76±6.32	62.32±5.75	5.09	<0.001
BMI (kg/m^2)	t-test	22.00±2.97	23.53±3.47	3.325	0.001
Disease course (years)	t-test	8.13±3.88	8.84±4.13	1.228	0.221
Scr (mg/dL)	t-test	0.86±0.30	0.78±0.29	-1.669	0.097
Cys-C (mg/L)	t-test	1.32±0.34	1.09±0.31	-4.851	<0.001
Scr/Cys-C	Mann-Whitney U	0.63 [0.49, 0.81]	0.69 [0.53, 0.93]	1.348	0.178
TP (g/L)	t-test	63.90±6.04	64.88±5.92	1.114	0.267
ALB (g/L)	t-test	37.91±4.29	38.06±3.68	0.253	0.801
PAB (g/L)	Mann-Whitney U	0.43 [0.13, 0.77]	0.47 [0.21, 0.73]	0.626	0.532
CHE (U/L)	Mann-Whitney U	7278.25±1845.50	7375.15 [6615.74, 8209.68]	-0.158	0.876
TC (mmol/L)	t-test	4.70±0.90	4.61±0.86	-0.689	0.492
TG (mmol/L)	Mann-Whitney U	1.17±0.70	1.26 [0.68, 1.75]	0.82	0.413
WBC (10^9/L)	t-test	7.59±2.58	7.05±3.14	-1.31	0.192
NE (10^9/L)	t-test	6.16±1.96	5.61±1.93	-1.916	0.057
LC (10^9/L)	t-test	2.01±0.74	2.01±0.62	0.036	0.971
NLR	Mann-Whitney U	3.28 [2.28, 4.10]	2.71 [1.93, 3.84]	-1.759	0.079
Hb (g/L)	t-test	133.82±17.98	143.84±19.29	3.713	<0.001
PLT (10^9/L)	t-test	251.40±61.75	249.92±57.44	-0.168	0.866
PLR	Mann-Whitney U	126.23 [102.29, 162.48]	120.61 [98.14, 159.81]	-0.638	0.525
CRP (mg/L)	t-test	2.53±1.11	2.43±1.09	-0.647	0.519
FVC (L)	t-test	2.21±0.71	2.53±0.87	2.865	0.005
FEV1 (L)	t-test	1.04±0.45	1.44±0.40	6.452	<0.001
FEV1/FVC	Mann-Whitney U	0.46 [0.35, 0.62]	0.59 [0.41, 0.76]	2.829	0.005
CAT score	Mann-Whitney U	15.00 [5.75, 21.00]	7.00 [3.00, 9.00]	-4.393	<0.001
mMRC score	Mann-Whitney U	1.00 [0.00, 3.00]	2.00 [0.00, 3.00]	0.455	0.642
BODE index	Mann-Whitney U	2.00 [0.75, 4.00]	2.00 [1.00, 4.00]	-0.144	0.884
6MWD classification	Mann-Whitney U	382.50 [323.50, 440.00]	396.00 [349.00, 448.00]	0.962	0.337

Note: Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Body Mass Index (BMI), Serum Creatinine (Scr), Cystatin C (Cys-C), Total Protein (TP), Albumin (ALB), Prealbumin (PAB), Cholinesterase (CHE), Total Cholesterol (TC), Triglycerides (TG), White Blood Cell count (WBC), Neutrophils (NE), Lymphocytes (LC), Neutrophil-to-Lymphocyte Ratio (NLR), Hemoglobin (Hb), Platelet count (PLT), Platelet-to-Lymphocyte Ratio (PLR), C-Reactive Protein (CRP), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, COPD Assessment Test (CAT), Modified Medical Research Council Dyspnea Scale (mMRC), Body Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index (BODE), and 6-Minute Walk Distance Grading (6MWD).

decrease in risk with increasing weight, and an increase in risk at extremely high weights (**Figure 9B**). The level of Cys-C was positively correlated with the risk of COPD with sarcopenia, with significantly higher risk observed at elevated Cys-C levels (**Figure 9C**). Hb levels showed an initial increase in risk followed by a plateau (**Figure 9D**). Increases in FVC and FEV1 were associated with a decrease in the risk of COPD with sarcopenia, suggesting that higher levels of these lung function parameters are linked to lower disease risk (**Figure 9E** and **9F**). Finally, an increase in the CAT score was significantly associated with an increased risk of COPD with sarcopenia, with a sharp rise in risk at higher scores (**Figure 9G**).

Interaction analysis reveals independent risk factors for COPD with sarcopenia

Interaction analysis was performed to evaluate the combined impact of multiple variables on the risk of developing COPD with sarcopenia. The results indicated that age (Estimate =-0.203, P<0.001), weight (Estimate =0.143, P=0.001), Cys-C (Estimate =-2.756, P=0.001),

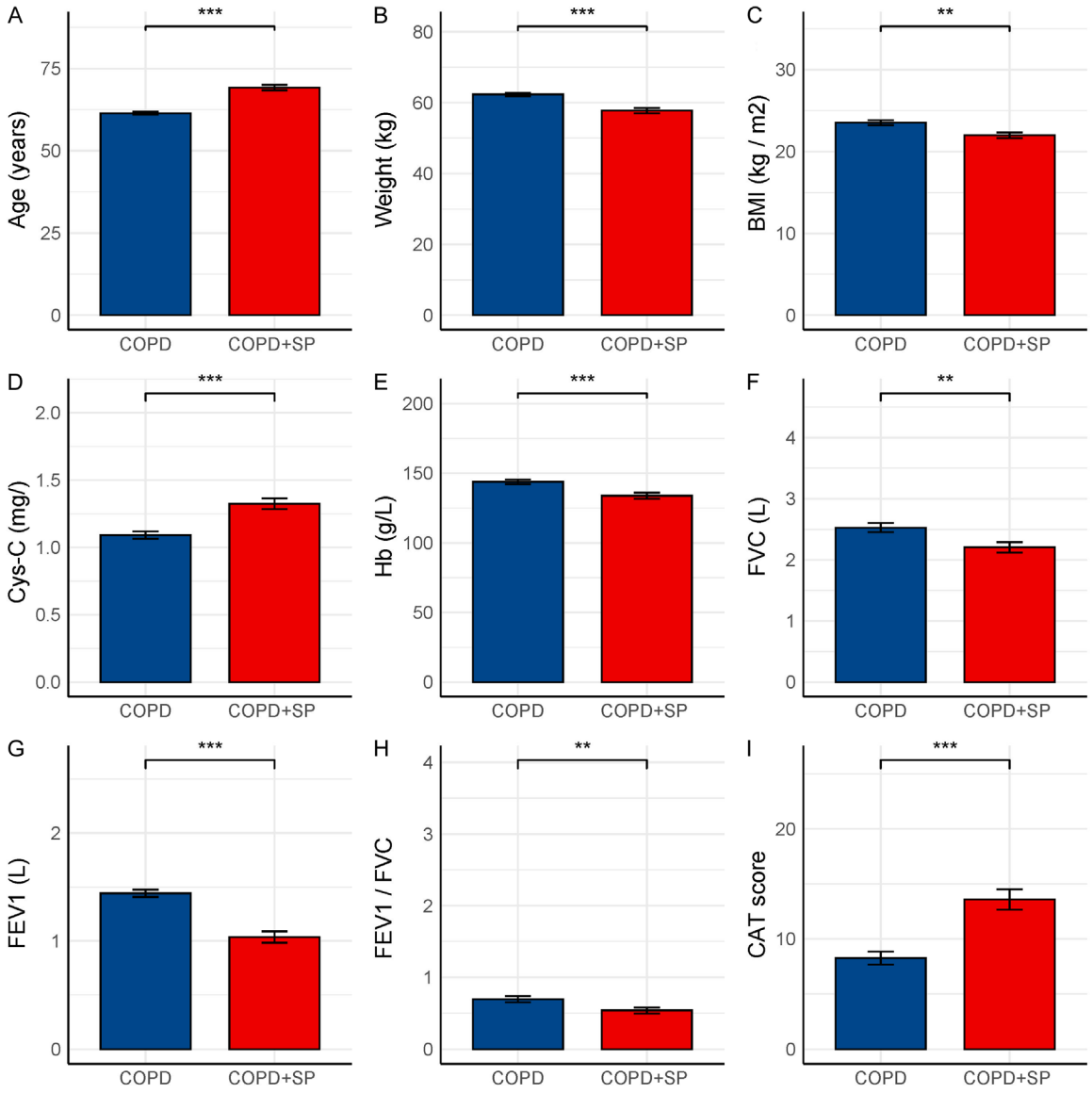

Figure 5. Visualization of significant differences in quantitative data between COPD and COPD+SP groups in the training set. A. Comparison of age between COPD and COPD+SP groups. B. Comparison of weight between COPD and COPD+SP groups. C. Comparison of BMI between COPD and COPD+SP groups. D. Comparison of Cys-C between COPD and COPD+SP groups. E. Comparison of Hb between COPD and COPD+SP groups. F. Comparison of FVC between COPD and COPD+SP groups. G. Comparison of FEV1 between COPD and COPD+SP groups. H. Comparison of FEV1/FVC between COPD and COPD+SP groups. I. Comparison of CAT score between COPD and COPD+SP groups. Note: **P<0.01, ***P<0.001; Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Body Mass Index (BMI), Cystatin C (Cys-C), Hemoglobin (Hb), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, and COPD Assessment Test (CAT).

Hb (Estimate =0.052, P=0.001), FEV1 (Estimate =2.604, P<0.001), and CAT score (Estimate =-0.123, P<0.001) had significant effects, underscoring their crucial roles in patients with COPD and sarcopenia. Although FVC showed a trend towards significance (Estimate =0.421, P=0.148), it did not reach the statistical significance level (**Figure 10**). The interaction plot further illustrated the varying predictive values of these variables between COPD patients with and without sarcopenia.

Expression differences of Cys-C in sarcopenia and COPD patients and possible mechanisms in sarcopenia

Using microarray data from the GEO datasets GSE111006 (sarcopenia) and GSE76925

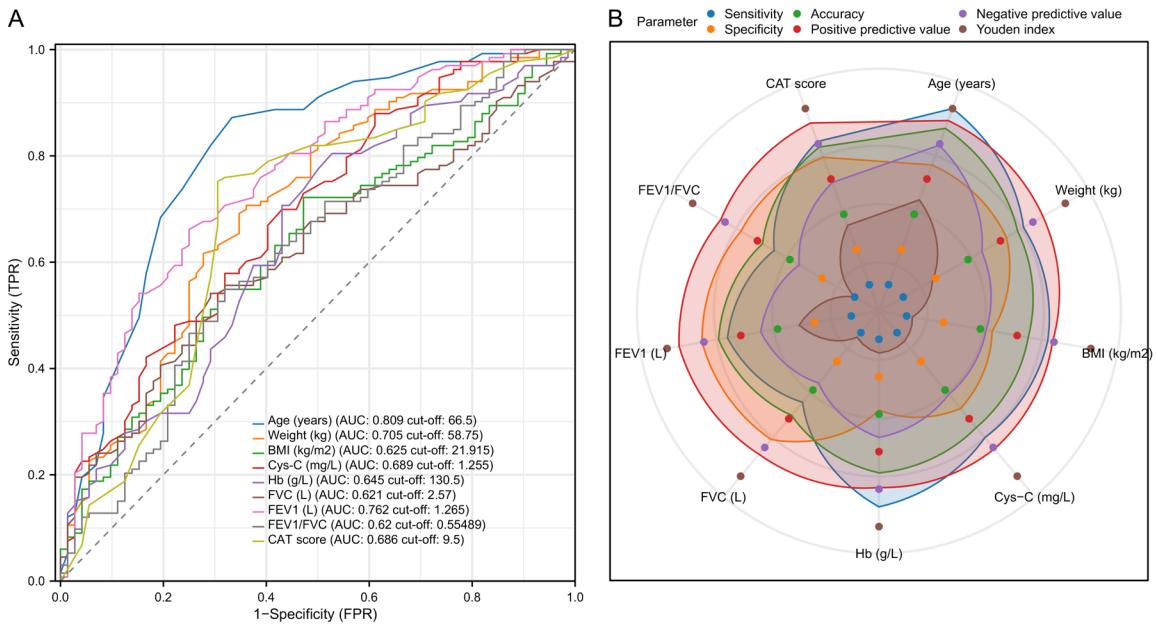

Figure 6. Clinical value of quantitative data in predicting COPD+SP. A. ROC curves for predicting COPD+SP using various clinical data, including age, weight, BMI, Cys-C, Hb, FVC, FEV1, FEV1/FVC ratio, and CAT score. The AUC and cutoff values are provided for each parameter. B. Radar chart illustrating the performance metrics of sensitivity, specificity, accuracy, positive predictive value, negative predictive value, and Youden index for each clinical value used in the ROC analysis. Note: Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Receiver Operating Characteristic (ROC), area under the curve (AUC), Body Mass Index (BMI), Cystatin C (Cys-C), Hemoglobin (Hb), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, and COPD Assessment Test (CAT).

Table 2. Logistic regression analysis

Variable	Univariate			Multivariate		
	P	OR	95% CI	P	OR	95% CI
Disease classification (Gold 2=1, Gold 3=0)	0.149	1.38	0.9-2.172			
Age (years) (≤66.5=0, >66.5=1)	<0.001	0.073	0.035-0.145	<0.001	0.053	0.015-0.154
Weight (kg) (≤58.75=0, >58.75=1)	<0.001	4.264	2.341-7.932	0.032	3.321	1.132-10.359
BMI (kg/m^2) (≤21.915=0, >21.915=1)	<0.001	2.9	1.601-5.311	0.057	3.013	0.989-9.853
Cys-C (mg/L) (≤1.255=0, >1.255=1)	<0.001	0.325	0.178-0.587	0.018	0.283	0.095-0.783
Hb (g/L) (≤130.5=0, >130.5=1)	<0.001	3.682	1.971-6.983	0.001	7.014	2.399-23.302
FVC (L) (≤2.57=0, >2.57=1)	0.001	2.867	1.572-5.366	0.04	3.605	1.109-13.113
FEV1 (L) (≤1.265=0, >1.265=1)	<0.001	5.867	3.135-11.397	0.001	9.674	2.681-40.545
FEV1/FVC (≤0.55489=0, >0.55489=1)	0.002	2.592	1.433-4.791	0.935	0.942	0.218-3.983
CAT score (≤9.5=0, >9.5=1)	<0.001	0.145	0.075-0.271	<0.001	0.085	0.026-0.241

Note: Body Mass Index (BMI), Cystatin C (Cys-C), Hemoglobin (Hb), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, and COPD Assessment Test (CAT).

(COPD), the expression levels of Cys-C were compared between sarcopenia patients, COPD patients, and normal controls. The analysis revealed that Cys-C expression was significantly higher in sarcopenia patients compared to normal individuals (P<0.05, **Figure 11A**), whereas no significant difference was observed between COPD patients and normal individuals (P>0.05, **Figure 11B**). These findings suggest that Cys-C may play a more critical role in the pathogenesis of sarcopenia, while its expression does not significantly change in COPD patients. Based on this observation, a subgroup analysis of sarcopenia samples in the

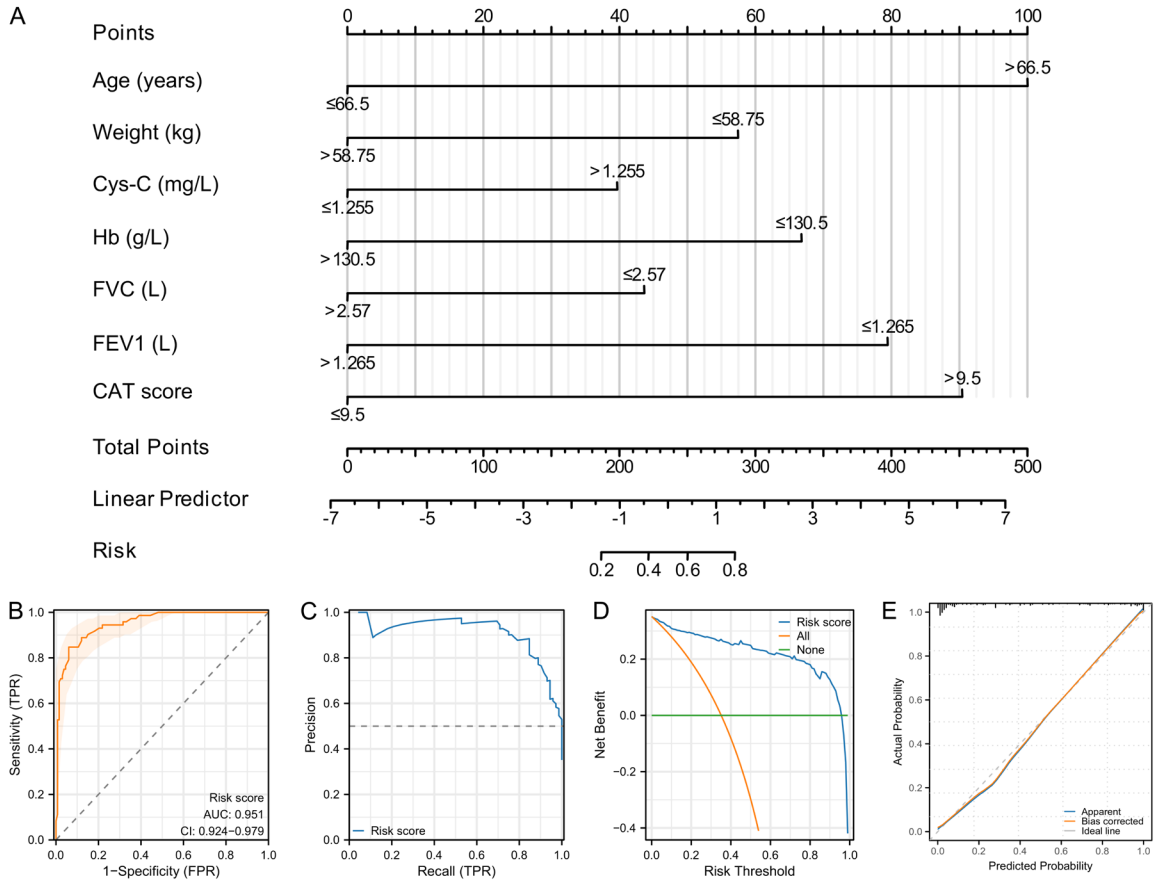

Figure 7. Nomogram model based on 7 independent risk factors for predicting COPD+SP and its validation in the training set. A. Nomogram model based on 7 independent risk factors for predicting COPD+SP. B. ROC curve for the model in the training group. C. PR curve for the model in the training group. D. DCA curve for the model in the training group. E. Calibration curve for the model in the training group. Note: Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Receiver Operating Characteristic (ROC), Precision-Recall (PR), Decision Curve Analysis (DCA), Cystatin C (Cys-C), Hemoglobin (Hb), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, and COPD Assessment Test (CAT).

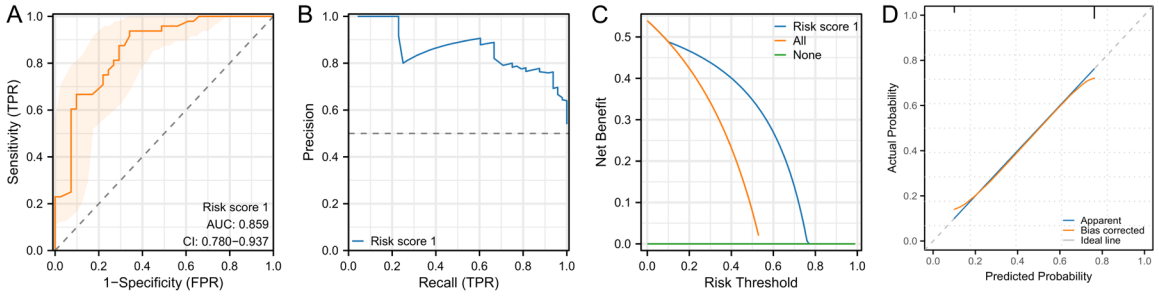

Figure 8. Performance validation of the COPD+SP Prediction nomogram model in the validation group. A. ROC curve for the model in the validation group. B. PR curve for the model in the validation group. C. DCA curve for the model in the validation group. D. Calibration curve for the model in the validation group. Note: Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Receiver Operating Characteristic (ROC), Precision-Recall (PR), Decision Curve Analysis (DCA).

GSE111006 dataset was conducted, dividing them into high-expression and low-expression groups based on Cys-C levels. GSEA was then performed on these groups. The results demonstrated significant enrichment of pathways related to oxidative phosphorylation, fatty acid

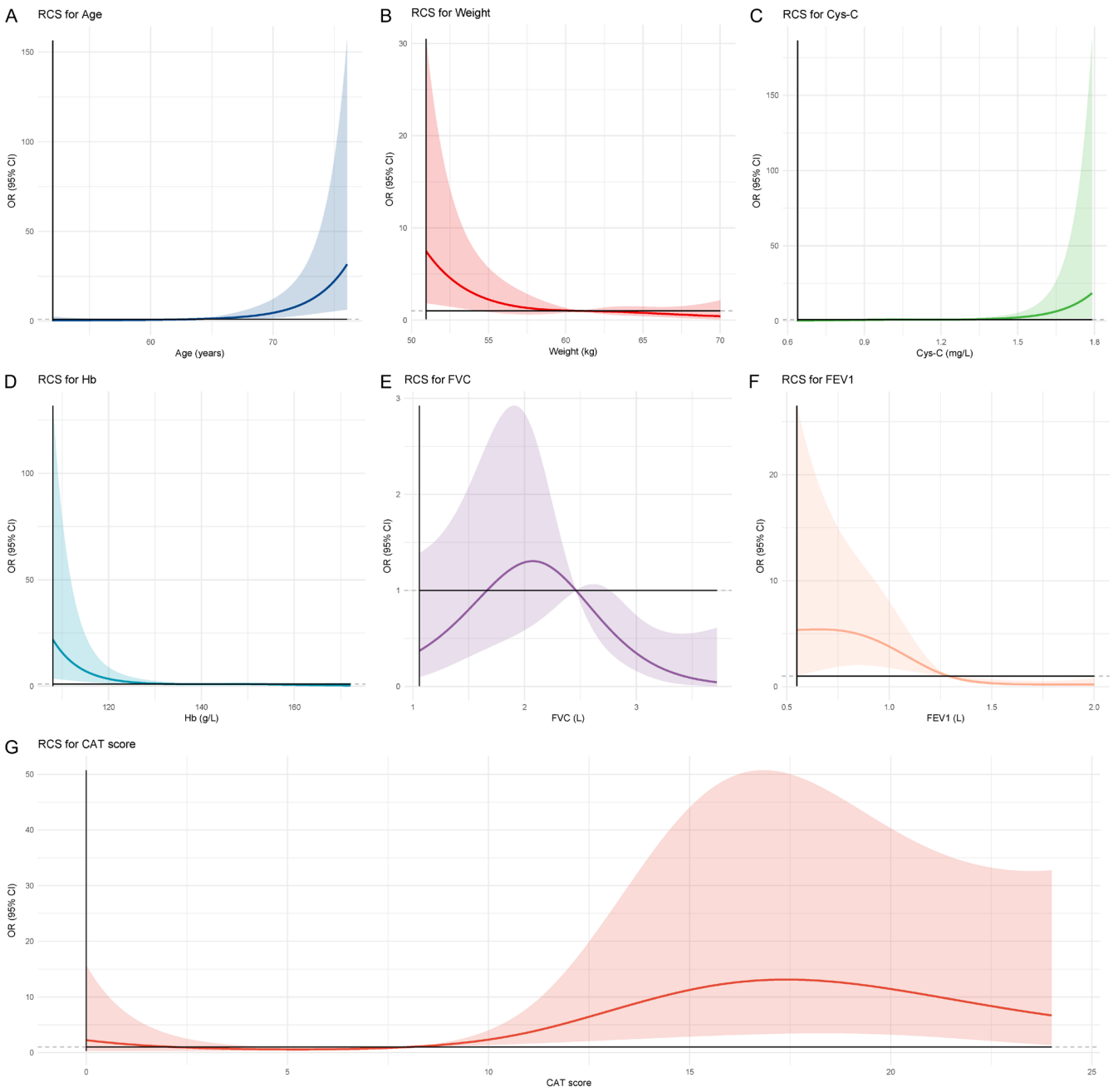
A
RCS for Age
OR (95% CI)
Age (years)
B
RCS for Weight
OR (95% CI)
Weight (kg)
C
RCS for Cys-C
OR (95% CI)
Cys-C (mg/L)
D
RCS for Hb
OR (95% CI)
Hb (g/L)
E
RCS for FVC
OR (95% CI)
FVC (L)
F
RCS for FEV1
OR (95% CI)
FEV1 (L)
G
RCS for CAT score
OR (95% CI)
CAT score

Figure 9. Restricted cubic spline plots of the nonlinear relationships between 7 independent risk factors and COPD+SP Risk. A. Nonlinear relationship between age and COPD+SP risk. B. Nonlinear relationship between weight and COPD+SP risk. C. Nonlinear relationship between Cys-C and COPD+SP risk. D. Nonlinear relationship between Hb and COPD+SP risk. E. Nonlinear relationship between FVC and COPD+SP risk. F. Nonlinear relationship between FEV1 and COPD+SP risk. G. Nonlinear relationship between CAT score and COPD+SP risk. Note: Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Cystatin C (Cys-C), Hemoglobin (Hb), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, and COPD Assessment Test (CAT).

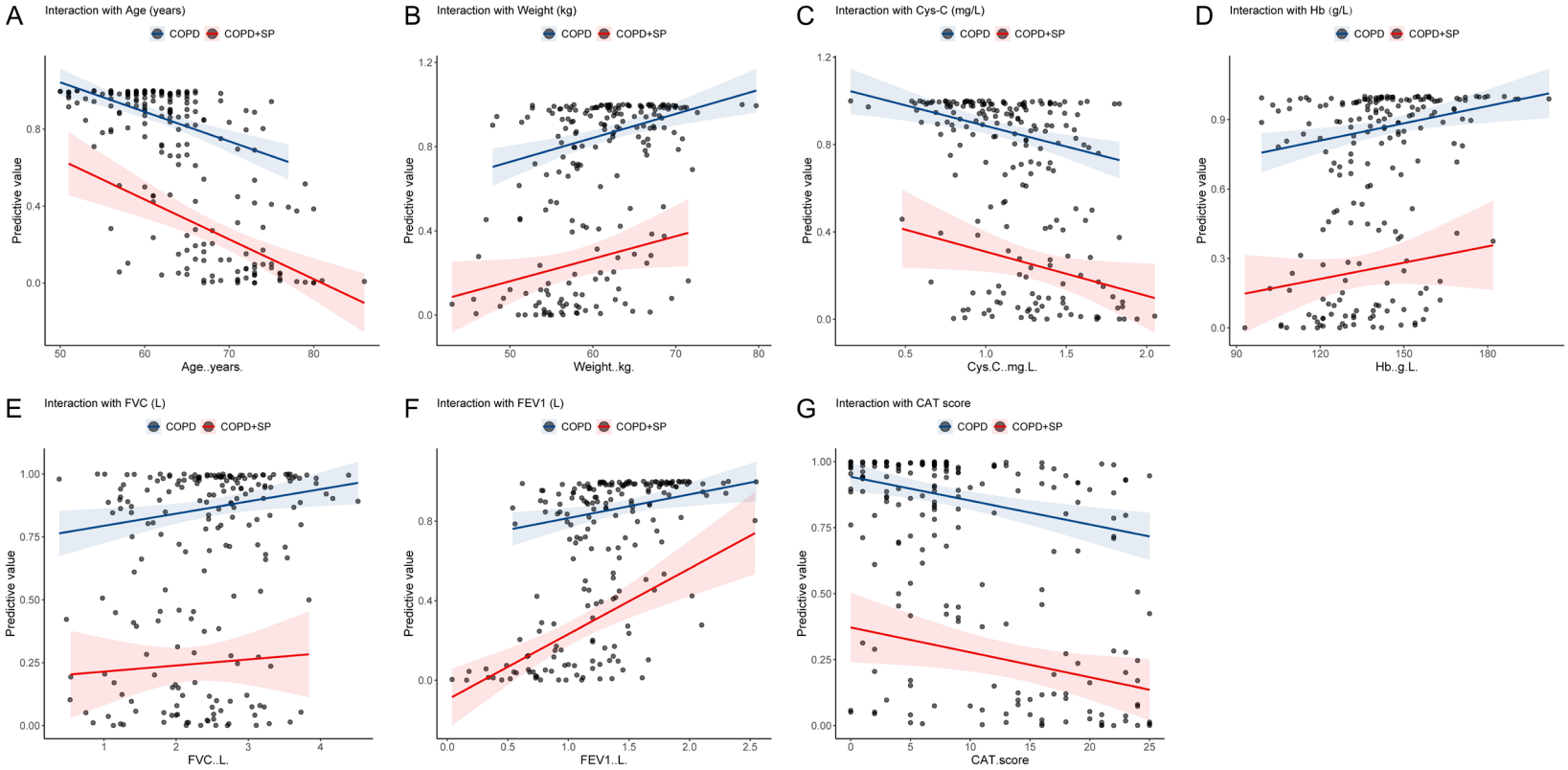

Figure 10. Interaction analysis of independent risk factors for COPD+SP. A. Prediction value of COPD+SP decreases with increasing age. B. Weight gain is associated with an increased risk of COPD+SP. C. Higher Cys-C levels are associated with a higher risk of COPD+SP. D. Higher Hb levels are associated with an increased risk of COPD+SP. E. Although a trend towards increased risk of COPD+SP is shown, significance was not reached. F. Increased FEV1 is significantly associated with an increased risk of COPD+SP. G. Higher CAT scores are associated with a lower risk of COPD+SP. Note: Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Cystatin C (Cys-C), Hemoglobin (Hb), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC ratio, and COPD Assessment Test (CAT).

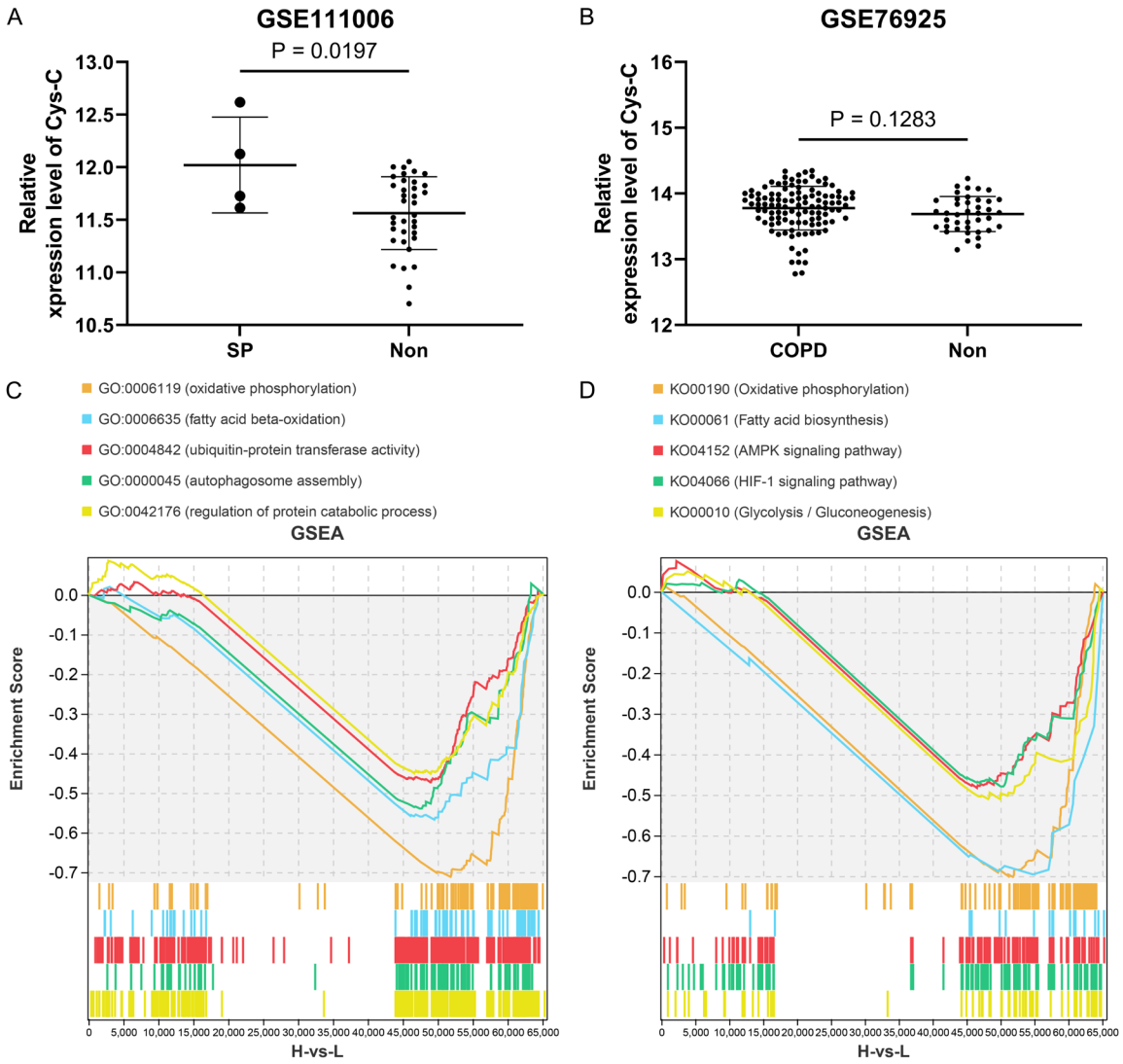

Figure 11. Cys-C expression levels in sarcopenia and COPD patients compared to healthy controls. A. Cys-C expression levels in sarcopenia patients. B. Comparison of Cys-C expression levels between COPD patients and healthy controls. C. GSEA of GO terms in sarcopenia patients with high Cys-C expression. D. GSEA of KEGG pathways in sarcopenia patients with high Cys-C expression. Note: Chronic Obstructive Pulmonary Disease (COPD), Sarcopenia (SP), Gene Set Enrichment Analysis (GSEA), and Cystatin C (Cys-C).

biosynthesis, the AMP-activated protein kinase signaling pathway, the hypoxia-inducible factor one signaling pathway, and glycolysis/gluconeogenesis in the high-expression group. These pathways are implicated in mitochondrial function, energy metabolism, and hypoxic response, which may play important roles in sarcopenia. Furthermore, GO enrichment analysis indicated significant enrichment of processes such as fatty acid β-oxidation, ubiquitin-mediated protein degradation, autophagosome assembly, and regulation of protein catabolism in the high-expression group. These findings imply that elevated Cys-C expression may influence muscle mass and metabolism by enhancing protein degradation and autophagy processes (**Figure 11C** and **11D**). Collectively, these results reveal possible mechanisms by which Cys-C contributes to sarcopenia, particularly through the regulation of energy balance and muscle protein metabolism.

Discussion

There is a close relationship between COPD and sarcopenia, with both conditions sharing

multiple pathophysiologic mechanisms that mutually exacerbate disease progression [24]. Chronic inflammation in COPD leads to the release of pro-inflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6, which accelerate muscle protein breakdown and hinder muscle regeneration, thereby triggering sarcopenia [25]. Additionally, oxidative stress, a key factor in COPD, damages muscle proteins and mitochondria, further impairing muscle function [26]. Hypoxia, commonly seen in COPD patients, restricts oxygen supply to muscles, leading to muscle fatigue and atrophy, while reduced physical activity further increases the risk of sarcopenia [27].

In this study, multivariate logistic regression analysis identified seven independent risk factors significantly associated with the coexistence of COPD and sarcopenia. These risk factors can be classified into three categories based on their nature: age-related factors, metabolic and hematological indicators, and lung function indicators. First, age-related factors include age and weight. Age was a significant independent risk factor for the coexistence of COPD and sarcopenia, with the risk increasing significantly with age, likely due to the natural decline in muscle mass and function in the elderly [28]. Additionally, weight was closely related to the occurrence of the coexistence of COPD and sarcopenia, with lower weight often indicating reduced muscle mass, which may exacerbate the progression of sarcopenia [29]. Interaction analysis further revealed that the interaction between age and weight significantly increased the risk of the coexistence of COPD and sarcopenia, particularly in elderly patients with lower weight. These findings underscore the importance of age and body weight as critical factors in the development of sarcopenia among patients with COPD.

Second, metabolic and hematologic indicators such as Cys-C and Hb levels showed important associations in patients with both COPD and sarcopenia [30, 31]. Cys-C, as an indicator reflecting renal function and metabolic status, may be associated with muscle breakdown and metabolic dysfunction at high levels, while low Hb levels may reflect malnutrition or the impact of chronic diseases, which was another factor contributing to the increased risk of the coexistence COPD of and sarcopenia [32]. In interaction analysis, the interaction between Cys-C and Hb levels was found to significantly increase the risk of sarcopenia in COPD patients. These metabolic and hematologic factors play a crucial role in the interplay between COPD and sarcopenia, highlighting targets for intervention.

Lastly, lung function indicators such as FVC, FEV1, and CAT scores are also important predictors of the coexistence of COPD and sarcopenia. The decrease in FVC and FEV1 typically reflects worsening lung function, which is closely related to the severity of COPD [33-35]. At the same time, a higher CAT score reflects the severity of symptoms and is positively correlated with the occurrence of the coexistence of COPD and sarcopenia. Interaction analysis showed that when the CAT score was high, further decreases in FVC and FEV1 significantly increased the risk of sarcopenia in COPD patients. These lung function indicators are pivotal in assessing the risk and progression of sarcopenia in patients with COPD.

In the value analysis of the model, the primary role of constructing the nomogram model is to provide an effective tool to assess the risk of the coexistence of COPD and sarcopenia by integrating multiple independent risk factors, thereby assisting clinicians in early diagnosis and intervention. The nomogram model constructed in this study demonstrated high predictive ability, with an AUC of 0.886 in the training group and 0.809 in the validation group, indicating high accuracy in distinguishing COPD patients with sarcopenia from those without. Additionally, the PR curve and DCA further validated the stability and clinical application value of the model. Similar studies have also shown that nomogram models based on multiple factors have significant advantages in identifying high-risk patients. For example, Huang et al. [36] constructed the AB3C model to predict the risk of sarcopenia in community-dwelling elderly, with an AUC of 0.930 in the training group and 0.897 in the validation group, demonstrating excellent predictive performance. Tu et al. [37] showed that the Scr/Cys-C has good diagnostic accuracy for sarcopenia in hospitalized elderly patients, with an AUC of 0.717, and also exhibits important value in predicting adverse clinical outcome. These results affirm the utility of nomogram models in enhancing the predic-

tive accuracy and clinical decision-making process for sarcopenia in COPD patients.

At the end of the study, Cys-C, identified as an independent risk factor, sparked significant interest. Further exploration using the GEO database revealed that Cys-C did not exhibit differential expression in COPD patients but was significantly elevated in patients with sarcopenia, suggesting that Cys-C may play a key role in the pathogenesis of sarcopenia by contributing to muscle metabolic imbalance or muscle function decline. GSEA demonstrated that high expression of Cys-C in sarcopenia patients was associated with abnormal activation of multiple metabolic pathways, such as oxidative phosphorylation, AMP-activated protein kinase signaling, and fatty acid β-oxidation. These pathways are critical for energy metabolism and muscle function regulation, suggesting that Cys-C may promote muscle breakdown or function decline by affecting these pathways. This supports the role of Cys-C as a potential biomarker for sarcopenia, especially in patients with COPD complicated by sarcopenia, where Cys-C may serve as an important indicator for assessing disease severity and progression. Although our findings are primarily based on indirect evidence, they provide a plausible link between Cys-C and sarcopenia in the context of COPD, warranting further investigation.

This study suggests that Cys-C, as an independent risk factor for the coexistence of COPD and sarcopenia, has clinical significance, but there are some limitations. First, this study did not directly use samples from COPD patients with sarcopenia but rather used samples from COPD and normal individuals, and sarcopenia and normal individuals, leading to results that can only indirectly infer the role of Cys-C in COPD complicated by sarcopenia. Second, although the GEO database provides rich gene expression information, sample heterogeneity and differences in experimental conditions may affect the generalizability of the analysis results. Additionally, since the samples mainly come from specific populations and databases, the applicability of the results may not be generalizable to the broad patient population. Lastly, this study primarily used logistic regression analysis and GSEA, which rely on model assumptions and data quality. If the assumptions are not met or the data quality is insufficient, the results may be biased.

Conclusion

This study identified seven independent risk factors influencing the occurrence of COPD complicated by sarcopenia through multivariate logistic regression analysis and successfully constructed a nomogram model that demonstrated high accuracy and clinical application value for predicting the risk of the coexistence of COPD and sarcopenia. Additionally, it was found that Cys-C was not differentially expressed in COPD patients but was significantly elevated in sarcopenia patients, suggesting that Cys-C may play a key role in the pathogenesis of sarcopenia. Although the results reveal a potential role of Cys-C as a biomarker, further clinical studies are needed to validate these findings and explore its specific mechanisms in these patients.

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Disclosure of conflict of interest

None.

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References

[1] Kahnert K, Jörres RA, Behr J and Welte T. The diagnosis and treatment of COPD and its comorbidities. Dtsch Arztebl Int 2023; 120: 434-444.

[2] Zhao X, Liu G, Liu D, Zou L, Huang Q, Chen M, Li D, Wu B, Wu H, Huang D and Wu D. Clinical and economic burden of anxiety/depression among older adult COPD patients: evidence from the COPD-AD China registry study. Front Psychiatry 2024; 14: 1221767.

[3] Chen W, FitzGerald JM, Sin DD and Sadatsafavi M; Canadian Respiratory Research Network. Excess economic burden of comorbidities in COPD: a 15-year population-based study. Eur Respir J 2017; 50: 1700393.

[4] Zhong N, Wang C, Yao W, Chen P, Kang J, Huang S, Chen B, Wang C, Ni D, Zhou Y, Liu S, Wang X, Wang D, Lu J, Zheng J and Ran P. Prevalence of chronic obstructive pulmonary disease in China: a large, population-based

survey. Am J Respir Crit Care Med 2007; 176: 753-760.
[5] Wang C, Xu J, Yang L, Xu Y, Zhang X, Bai C, Kang J, Ran P, Shen H, Wen F, Huang K, Yao W, Sun T, Shan G, Yang T, Lin Y, Wu S, Zhu J, Wang R, Shi Z, Zhao J, Ye X, Song Y, Wang Q, Zhou Y, Ding L, Yang T, Chen Y, Guo Y, Xiao F, Lu Y, Peng X, Zhang B, Xiao D, Chen CS, Wang Z, Zhang H, Bu X, Zhang X, An L, Zhang S, Cao Z, Zhan Q, Yang Y, Cao B, Dai H, Liang L and He J; China Pulmonary Health Study Group. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. Lancet 2018; 391: 1706-1717.
[6] Choi YJ, Kim T, Park HJ, Cho JH and Byun MK. Long-term clinical outcomes of patients with chronic obstructive pulmonary disease with sarcopenia. Life (Basel) 2023; 13: 1628.
[7] Cho MR, Lee S and Song SK. A review of sarcopenia pathophysiology, diagnosis, treatment and future direction. J Korean Med Sci 2022; 37: e146.
[8] Sayer AA and Cruz-Jentoft A. Sarcopenia definition, diagnosis and treatment: consensus is growing. Age Ageing 2022; 51: afac220.
[9] Cesari M, Penninx BW, Pahor M, Lauretani F, Corsi AM, Rhys Williams G, Guralnik JM and Ferrucci L. Inflammatory markers and physical performance in older persons: the InCHIANTI study. J Gerontol A Biol Sci Med Sci 2004; 59: 242-248.
[10] Byun MK, Cho EN, Chang J, Ahn CM and Kim HJ. Sarcopenia correlates with systemic inflammation in COPD. Int J Chron Obstruct Pulmon Dis 2017; 12: 669-675.
[11] Muraki I. Muscle mass assessment in sarcopenia: a narrative review. JMA J 2023; 6: 381-386.
[12] Storie H. Dysphagia management and sarcopenia. Gastroenterol Nurs 2022; 45: 279-280.
[13] Landi F, Russo A, Liperoti R, Pahor M, Tosato M, Capoluongo E, Bernabei R and Onder G. Midarm muscle circumference, physical performance and mortality: results from the aging and longevity study in the Sirente geographic area (ilSIRENTE study). Clin Nutr 2010; 29: 441-447.
[14] Chan SMH, Selemidis S and Vlahos R. The double-edged sword of ROS in muscle wasting and COPD: insights from aging-related sarcopenia. Antioxidants (Basel) 2024; 13: 882.
[15] M Y, Dave AK, Patel SS, Parbat R, Shah V and Gandhi R. Association between sarcopenia and chronic renal failure (overt and concealed) in chronic obstructive pulmonary disease (COPD) patients: a cross-sectional study. Cureus 2023; 15: e46870.
[16] Ma K, Huang F, Qiao R and Miao L. Pathogenesis of sarcopenia in chronic obstructive pulmonary disease. Front Physiol 2022; 13: 850964.
[17] Singh D, Agusti A, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Criner GJ, Frith P, Halpin DMG, Han M, López Varela MV, Martinez F, Montes de Oca M, Papi A, Pavord ID, Roche N, Sin DD, Stockley R, Vestbo J, Wedzicha JA and Vogelmeier C. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. Eur Respir J 2019; 53: 1900164.
[18] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M and Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019; 48: 16-31.
[19] Bansode PM, Kumar C and M S. Usefulness of cat score in patients with stable COPD and acute exacerbation of COPD and it's co-relation with PFT. J Assoc Physicians India 2022; 70: 11-12.
[20] Rhee CK, Kim JW, Hwang YI, Lee JH, Jung KS, Lee MG, Yoo KH, Lee SH, Shin KC and Yoon HK. Discrepancies between modified medical research council dyspnea score and COPD assessment test score in patients with COPD. Int J Chron Obstruct Pulmon Dis 2015; 10: 1623-1631.
[21] Holland A. The BODE index. J Physiother 2010; 56: 62.
[22] Fermont JM, Masconi KL, Jensen MT, Ferrari R, Di Lorenzo VAP, Marott JM, Schuetz P, Watz H, Waschki B, Müllerova H, Polkey MI, Wilkinson IB and Wood AM. Biomarkers and clinical outcomes in COPD: a systematic review and meta-analysis. Thorax 2019; 74: 439-446.
[23] Boudewijn IM, Faiz A, Steiling K, van der Wiel E, Telenga ED, Hoonhorst SJM, Ten Hacken NHT, Brandsma CA, Kerstjens HAM, Timens W, Heijink IH, Jonker MR, de Bruin HG, Sebastiaan Vroegop J, Pasma HR, Boersma WG, Wielders P, van den Elshout F, Mansour K, Spira A, Lenburg ME, Guryev V, Postma DS and van den Berge M. Nasal gene expression differentiates COPD from controls and overlaps bronchial gene expression. Respir Res 2017; 18: 213.
[24] Benz E, Wijnant SRA, Trajanoska K, Arinze JT, de Roos EW, de Ridder M, Williams R, van Rooij F, Verhamme KMC, Ikram MA, Stricker BH, Rivadeneira F, Lahousse L and Brusselle

GG. Sarcopenia, systemic immune-inflammation index and all-cause mortality in middle-aged and older people with COPD and asthma: a population-based study. ERJ Open Res 2022; 8: 00628-2021.
[25] Gao J, Deng M, Li Y, Yin Y, Zhou X, Zhang Q and Hou G. Resistin as a systemic inflammation-related biomarker for sarcopenia in patients with chronic obstructive pulmonary disease. Front Nutr 2022; 9: 921399.
[26] Lage VKDS, de Paula FA, Dos Santos JM, Costa HS, da Silva GP, Lima LP, Santos JNV, de Almeida HC, Figueiredo PHS, Bernardo-Filho M, Taiar R, Teixeira AL, Lacerda ACR and Mendonça VA. Are oxidative stress biomarkers and respiratory muscles strength associated with COPD-related sarcopenia in older adults? Exp Gerontol 2022; 157: 111630.
[27] Mano Y, Tsukamoto M, Wang KY, Nabeshima T, Kosugi K, Tajima T, Yamanaka Y, Suzuki H, Kawasaki M, Nakamura E, Zhou Q, Azuma K, Nakashima T, Tamura Y, Kozaki K, Nakazato K, Li YS, Kawai K, Yatera K and Sakai A. Oxidative stress causes muscle structural alterations via p38 MAPK signaling in COPD mouse model. J Bone Miner Metab 2022; 40: 927-939.
[28] Kuchi Bhotla H, Meyyazhagan A, Pushparaj K, Pappuswamy M, Chaudhary A, Arumugam VA, Balasubramanian B, Ragu Varman D, Orlacchio A and Rengasamy KRR. Prevalence of cardiovascular diseases in south asians: scrutinizing traditional risk factors and newly recognized risk factors sarcopenia and osteopenia/osteoporosis. Curr Probl Cardiol 2024; 49: 102071.
[29] Sugiura K, Hirasaka K, Maeda T, Uchida T, Kishimoto K, Oarada M, Labeit S, Ulla A, Sakakibara I, Nakao R, Sairyo K and Nikawa T. MuRF1 deficiency prevents age-related fat weight gain, possibly through accumulation of PDK4 in skeletal muscle mitochondria in older mice. J Orthop Res 2022; 40: 1026-1038.
[30] He J, Li H, Yao J and Wang Y. Prevalence of sarcopenia in patients with COPD through different musculature measurements: an updated meta-analysis and meta-regression. Front Nutr 2023; 10: 1137371.
[31] Zhou J, Liu Y, Yang F, Jing M, Zhong X, Wang Y, Liu Y, Ming W, Li H, Zhao T and He L. Risk factors of sarcopenia in COPD patients: a meta-analysis. Int J Chron Obstruct Pulmon Dis 2024; 19: 1613-1622.
[32] Yajima T and Yajima K. Serum creatinine-to-cystatin C ratio as an indicator of sarcopenia in hemodialysis patients. Clin Nutr ESPEN 2023; 56: 200-206.
[33] Wu JF, Jia J, Chen P, Wang XF, Yang FX, Liu Y, Ma YM and Jin JW. Sarcopenia and its clinical correlation in elderly chronic obstructive pulmonary disease: a prospective cohort study. Eur Rev Med Pharmacol Sci 2023; 27: 9762-9772.
[34] Liao L, Deng M, Gao Q, Zhang Q, Bian Y, Wang Z, Li J, Xu W, Li C, Wang K, Zheng Z, Zhou X and Hou G. Predictive and therapeutic value of lipoprotein-associated phospholipaseA2 in sarcopenia in chronic obstructive pulmonary disease. Int J Biol Macromol 2024; 275: 133741.
[35] Costa TM, Costa FM, Moreira CA, Rabelo LM, Boguszewski CL and Borba VZ. Sarcopenia in COPD: relationship with COPD severity and prognosis. J Bras Pneumol 2015; 41: 415-421.
[36] Huang SW, Long H, Mao ZM, Xiao X, Chen A, Liao X, Wang M, Zhang Q, Hong Y and Zhou HL. A nomogram for optimizing sarcopenia screening in community-dwelling older adults: AB3C model. J Am Med Dir Assoc 2023; 24: 497-503.
[37] Tu X, Lin T, Huang L, Tang T, Xie D, Gao L, Jiang T and Yue J. The diagnostic performance of Cr/CysC for sarcopenia and its predictive value on clinical outcomes in hospitalized older patients: a prospective cohort study. Eur Geriatr Med 2024; 15: 579-588.