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Sarcopenia and its clinical correlation in elderly chronic obstructive pulmonary disease: a prospective cohort study

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Abstract. – OBJECTIVE: The aim of this study was to examine the effects of sarcopenia on clinical characteristics and short-term outcomes in elderly chronic obstructive pulmonary disease (COPD) patients.

PATIENTS AND METHODS: One hundred twenty elderly COPD patients (age>60) recruited from Beijing Shijingshan Hospital were divided into sarcopenia and non-sarcopenia groups according to the severity of sarcopenia at the first admission. Baseline data, geriatric syndrome, laboratory indicators and body composition analysis were analyzed. One year followed-up by outpatient visits was focused on clinical characteristics and telephone follow-ups for collecting all-cause deaths and acute exacerbations of chronic obstructive pulmonary disease as end-point events. The risk factors for sarcopenia were analyzed by univariate analysis and multivariate logical regression. The proportional hazards model (COX) regression was performed to determine the effect of sarcopenia on COPD patients' prognoses.

RESULTS: One hundred twenty patients (76 men and 44 women) with an average age of 76.7±8.78 years were included, of which 63 patients (52.5%) were diagnosed with sarcopenia. Compared to the non-sarcopenia group, the sarcopenia group exhibited worse lung function and more severe geriatric syndromes with significantly higher incidence ratios of somnipathy and frailty. The sarcopenia group also showed worse muscle indicators and declined body composition. Multivariate analysis showed that the occurrence of sarcopenia in elderly COPD patients was correlated with forced expiratory volume in the first second (FEV1) (OR=0.97, 95% CI: 0.94-1.0, *p*=0.035), body mass index (BMI) (OR=0.80, 95% CI: 0.71-0.89, *p*=0.035) and hemoglobin (OR=0.98, 95% CI: 0.96-1.0, *p*=0.023). Furthermore, the COX regression indicated the association of sarcopenia with acute exacerbations of COPD within the follow-up period (HR=2.4, 95% CI: 1.01-5.72, *p*=0.048).

CONCLUSIONS: Sarcopenia increases the risk of acute exacerbations of chronic obstructive pulmonary disease in the elderly. Sarcopenia incidence in elderly COPD is associated with FEV1, BMI, and hemoglobin and closely monitoring indicators is useful for early diagnosis of sarcopenia.

Key Words:
Chronic obstructive pulmonary disease, Sarcopenia, Comprehensive geriatric assessment, Survival analysis.

Abbreviations

COPD: Chronic obstructive pulmonary disease. AE-COPD: Acute exacerbation of chronic obstructive pulmonary disease. CGA: Comprehensive geriatric assessment. FEV1%: Forced expiratory volume in one second as a percentage of predicted value. FEV1/FVC: Forced expiratory volume in first second/Force vital capacity. CAT: COPD assessment test. mMRC: modified British Medical Research Council. ADL: Activities of daily living. IADL: Instrumental activities of daily living. BMI: Body mass index. SMI: Skeletal muscle index. SMM: Skeletal muscle mass

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most prevalent chronic diseases with high morbidity and mortality, especially in the elderly[1,2]. The incidence of COPD reaches 21.2% in people aged 60-69 and 35.5% in people aged over 70 in China[3]. Among the top 15 diseases with the highest global burden of disease in the elderly,

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COPD ranks third[4]. COPD in the elderly is often accompanied by comorbidities occurring with different degrees of airflow limitation, which has a significant impact on COPD progression, patient consultation, hospitalization and mortality[5-7]. A new model of multidimensional discharge planning can significantly reduce the length of stay and hospitalization costs[7]. The common comorbidities in elderly COPD patients include cardiovascular disease, metabolic syndrome and diabetes, osteoporosis, anxiety and depression, skeletal muscle dysfunction and geriatric syndromes[1].

Improving muscle strength can improve the overall mental and physical quality of life in the senior population[8]. Sarcopenia is defined as the loss of muscle mass and/or reduced muscle function with clinical symptoms including fatigue and decreased physical activity[8,9]. Sarcopenia frequently occurs in patients with COPD and is associated with poor life quality and motility[10]. The prevalence of COPD-related sarcopenia is influenced by a number of risk factors, including the severity of lung disease and other clinical settings, such as systemic inflammatory response, oxidative stress, smoking, hypoxemia, long-term decreased activity, and malnutrition[10]. In addition, sarcopenia is also a common condition in geriatric syndromes, including visual and hearing impairment, polypharmacy, cognitive impairment, anxiety, depression, delirium, malnutrition, frailty and sarcopenia, falls, chronic pain, somnipathy, urinary incontinence[11-15]. The interaction between sarcopenia severity and respiratory dysfunction may be critical for the prognosis or progression of COPD, especially in elderly patients. Some previous studies[16,17] focused on geriatric syndromes among elderly patients with diabetes and coronary heart disease. However, existing studies in the literature have paid little attention to the incidence of sarcopenia and geriatric syndromes in elderly patients with COPD and the impact on the prognosis of elderly COPD patients.

In this study, we examined the sarcopenia occurrence and its clinical correlation with COPD in elderly patients, by performing a prospective pilot study that enrolled 120 elderly COPD patients (age >60) with a year followed-up for the progress of COPD. The clinical indexes were compared between COPD patients with and without sarcopenia; the static correlation of sarcopenia to severity and progression was analyzed. In addition, the risk factors for the incidence of sarcopenia in elderly COPD patients were also analyzed by univariate analysis.

Patients and Methods

The Study Design and the Subjects

This is a prospective cohort study performed between Jan 2019 and Dec 2021 in the Geriatrics Department of Beijing Shijingshan Hospital, Capital Medical University in China. This study protocol was approved by the Ethics Committee of Beijing Shijingshan Hospital (Ethical Review of Scientific Research No. 2018-11). All methods were carried out in accordance with relevant guidelines and regulations, and written informed consent was obtained from all subjects. Patients must have met all of the following inclusion criteria: (1) Patients diagnosed with chronic obstructive pulmonary disease; (2) age ≥60 years; (3) Patients diagnosed with COPD on 2019 GOLD (1); (4) Patients who signed informed consent; (5) The patients could read and write and had no communication disorder. Patients who met one of the exclusion criteria were excluded: (1) refused to test for sarcopenia; (2) unable to communicate or clinical data are not available to determine whether the patient is diagnosed with sarcopenia; (3) end-stage patients with multiple organ failure; (4) severe metabolic diseases, mental disorders, cognitive impairment, progressive nervous system diseases, severe skeletal muscle diseases, tumors.

Data Collection

The participants were interviewed face-to-face to gather information on their gender, height, weight, BMI, and medical history. The venous blood samples were collected the following morning after receiving 12 hours of fasting, and laboratory indicators were examined, including white blood cell (WBC), hemoglobin (HGB), lymphocyte count, serum uric acid (UA), creatinine (CR), cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglycerides (TG), glucose (Glu), glycosylated hemoglobin (HbA1C %), high- sensitivity C-reactive protein (hs-CRP), serum albumin (ALB), serum prealbumin (PA).

Pulmonary function tests were performed on all enrolled patients and the lung function indexes included forced expiratory volume in one second as a percentage of the forced vital capacity (FEV1/FVC %), forced expiratory volume in one second as a percentage of predicted value (FEV1/Pred %), residual volume/total lung capacity (RV/TLC), bronchodilation test indicators (FEV1 improvement rate and absolute increase in FEV1).

All participants completed the Comprehensive Geriatric Assessment (CGA) on the day of the

outpatient visit or within 48 hours after admission. Geriatric syndromes, including urinary incontinence, constipation, visual/hearing impairment, pain, history of falls, somnipathy, oral problems, anxiety and depression, delirium, and frailty were recorded. CGA included geriatric syndromes, cognitive function, psychological assessment, handgrip strength, nutritional status, frailty, and activities of daily living. Cognitive function was assessed using the Mini-Mental State Examination (MMSE). Hamilton Anxiety Rating Scale (HAMA) and Hamilton Depression Rating Scale (HAMD) were used for psychological assessment. Activities of daily living (ADL) scale and Instrumental activities of daily living (IADL) were used to evaluate daily activities. The Mini-Nutritional Assessment (MNA)-SF scale was used for nutritional assessment. Frailty was assessed using the Fried scale. Grip strength was measured using an electronic handgrip dynamometer, and the dominant hand was measured twice to take the maximum value. All assessments were performed by trained personnel in comprehensive geriatric assessment to ensure the consistency of assessment results.

Body composition was analyzed using the in-body S10 body composition analyzer (InBody, Seoul, Korea). Body composition values were measured, including skeletal muscle mass, free mass, protein mass, bone mineral content, skeletal muscle index, basal metabolic rate, and visceral fat area.

Sarcopenia Diagnosis

Sarcopenia was diagnosed according to the 2019 Expert consensus on the diagnosis and treatment of sarcopenia[18] issued by the Asian Working Group (AWGS): (1) Muscle mass measurement (BIA): SMI <5.7 kg/m^2 for females and SMI <7.0 kg/m^2 in males suggested that the skeletal muscle mass was reduced; (2) Muscle strength: grip strength <28 kg in men and <18 kg in women indicated decreased muscle strength; (3) Physical function test: 5 times of sitting up ≥12 seconds or 6-meter walking speed <1 m/s indicated a decline in physical function. Patients with deficiencies in muscle mass and low physical performance or low muscle mass with low muscle strength were diagnosed with sarcopenia. As a result of severe sarcopenia, the patient had decreased skeletal muscle mass, low muscle strength, and low physical performance.

Follow-Up

One year of follow-up was completed by outpatient examination or by telephone. The time and causes of Unscheduled Return Visit (URV) during the follow-up period (acute exacerbation of chronic obstructive pulmonary disease, severe bleeding, peripheral vascular disease, infection, fall/fracture, cardiovascular disease and acute cerebrovascular disease) were recorded. Among the primary end-point events, there were cardiovascular death, acute respiratory failure, acute respiratory distress syndrome (ARDS), and all-cause death.

Statistical Analysis

Normally distributed continuous variables were described as means ± standard deviations (SD), and statistical comparison between two groups was performed using the two-tailed student's *t*-test. The non-normally distributed continuous variables were described as the median and interquartile range (IQR) and the Wilcoxon rank sum test was used for the comparison between the two groups. Categorical variables were depicted as frequency (percentage) and analyzed with the Chi-squared test or Fisher's exact test. The univariate logic regression was performed, followed by multivariate binary logic regression analysis to determine the independent association. Combined with the number of available outcome events, the variables included were selected to ensure the stability of the final model. Kaplan-Meier method was used for statistical description of survival data, and the proportional hazards model (COX) regression was used for statistical tests of exacerbation and survival data. In this study, the test level was 0.05. For statistical analysis and chart drawing, R software version 4.0.3 (R Core Team, 2014, Vienna, Austria) was used.

Results

Sarcopenia was Significantly More Prevalent in Elderly COPD Patients

A total of 123 elderly COPD patients were included consecutively. Body composition analysis was not performed in 3 patients due to pacemaker implantation. Finally, a total of 120 patients (average age: 76.7±8.78 years) were included in further analyses, including 76 males (63.3%) and 44 females (36.7%). Of these patients, 63 patients (52.5%) were diagnosed with sarcopenia, including 36 males (57.1%) and 27 females (42.9%). In terms of age stratification,

60-74 was the early-elderly group, 75-84 was the middle-elderly group and over 85 was the old-age group. Sarcopenia was significantly more prevalent in the old-age group than in the early-elderly and middle-aged groups in terms of age groups (p<0.05) (Table I).

COPD Patients with Sarcopenia Exhibit Worse Lung Function and More Severe Geriatric Syndromes

All patients completed modified British medical research council (mMRC) and COPD assessment Test (CAT) scoring, pulmonary function test, comprehensive geriatric assessment, grip strength and body composition analysis. The baseline characteristics of COPD patients with sarcopenia and without sarcopenia were compared (Table I).

Patients with sarcopenia showed a significantly lower FEV1/pre % (51.7±14.3%) *vs.* the non-sarcopenia group (60.0±13.7%, p=0.001). A higher mMRC (1.89±0.99) and CAT (21.1±7.34) were observed in the sarcopenia group compared to the non-sarcopenia group, but there was no significant difference between them (p=0.116, 0.113, respectively).

A significantly increased number of geriatric syndromes (conditions) were observed in the sarcopenia group (2.19±1.53) *vs.* the non-sarcopenia group (1.63±1.25) (p=0.03). The incidence ratios of somnipathy and frailty, as the consequence of sarcopenia, were significantly higher in the sarcopenia group than those in the non-sarcopenia group [25 (39.7) and 12 (21.1%) (p=0.045 and 0.014, respectively)] (Table II).

Of note, the level of hemoglobin (118±28.7 g/L *vs.* 129±20.4 g/L) and albumin levels (31.75±3.68 g/L *vs.* 36.6±2.77 g/L) were significantly lower than those of non-sarcopenia patients (p=0.012 and p<0.001, respectively). There was no significant difference in other laboratory parameters, including inflammatory indexes (Table III).

Table I. Characteristics of elderly patients with COPD.

Item	Total N=120	Non-sarcopenia N=57	Sarcopenia N=63	*p*-value
Age, years	76.7±8.78	75.9±8.06	77.5±9.39	0.317
>=85, n (%)	25 (20.8)	5 (20)	20 (80)	0.008**
75-84, n (%)	42 (35.0)	22 (52.4)	20 (47.6)	
60-74, n (%)	53 (44.2)	30 (56.6)	23 (43.4)	
Sex				0.197
Male, n (%)	76 (63.3)	40 (70.2)	36 (57.1)	
Female, n (%)	44 (36.7)	17 (29.8)	27 (42.9)	
CAT	20.1 ±7.07	19.1±6.66	21.1±7.34	0.113
mMRC	1.77±0.91	1.63±0.79	1.89±0.99	0.116
FEV1/pre %	55.6±14.6	60.0±13.7	51.7±14.3	0.001**
Gold stage, n (%)				0.176
1	5(4.17)	2 (3.51)	3 (4.76)	
2	72 (60.0)	39 (68.4)	33(52.4)	
3-4	43 (35.8)	16 (28.1)	27 (42.9)	
Smoking, n (%)	107 (89.2)	52 (91.2)	55 (87.3)	0.691
Comorbidity	4.19±2.30	4.09±2.20	4.29±2.40	0.638
BMI kg/m^2	24.1±4.32	25.8±3.79	22.5±4.21	
<0.001**				
ADL	82.0±23.3	85.4±22.1	79.0±24.1	0.133
IADL	4.85±2.87	5.21±2.95	4.52±2.78	0.193
Hand Grip Strength, kg	19.9±8.71	21.7±8.98	18.3±8.19	0.037*
Malnutrition, n (%)	17 (14.2)	7 (12.3)	10 (15.9)	0.571
Polypharmacy, n (%)	85 (70.8)	40 (70.2)	45 (71.4)	1.000
Social Support				0.460
Caregiver, n (%)	2 (1.67)	1 (1.75)	1 (1.59)	
Solitude, n (%)	10 (8.33)	3 (5.26)	7 (11.1)	
Spouse, n(%)	66 (55.0)	36 (63.2)	30 (47.6)	
Nursing home, n (%)	3 (2.50)	1 (1.75)	2 (3.17)	
Offspring, n (%)	39 (32.5)	16 (28.1)	23 (36.5)	

BMI: body mass index; CAT: COPD assessment Test; mMRC: modified British medical research council; FEV1/pre%: forced expiratory volume in one second as a percentage of predicted value; GOLD stage: Global Initiative for Chronic Obstructive Lung Disease stage; ADL: activities of daily living; IADL: instrumental activities of daily living. *p<0.05; **p<0.01.

Table II. The geriatric syndromes of elderly patients with COPD.

Item	Total N=120	Non-sarcopenia N=57	Sarcopenia N=63	*p*-value
Geriatric syndromes	1.93±1.43	1.63±1.25	2.19±1.53	0.030*
Urinary incontinence, n (%)	4 (3.33)	2 (3.51)	2 (3.17)	1.000
Fall, n (%)	24 (20.0)	11 (19.3)	13 (20.6)	1.000
Hearing impairment, n (%)	33 (27.5)	15 (26.3)	18 (28.6)	0.943
Visual impairment, n (%)	38 (31.7)	14 (24.6)	24 (38.1)	0.163
Constipation, n (%)	27 (22.5)	12 (21.1)	15 (23.8)	0.887
Delirium, n (%)	6 (5.00)	1 (1.75)	5 (7.94)	0.210
Cognitive impairment, n (%)	22 (18.3)	8 (14.0)	14 (22.2)	0.357
Chronic pain, n (%)	13 (10.8)	7 (12.3)	6 (9.52)	0.848
Somnipathy, n (%)	37 (30.8)	12 (21.1)	25 (39.7)	0.045*
Oral problems, n (%)	13 (10.8)	4 (7.02)	9 (14.3)	0.325
Anxiety/Depression, n (%)	51 (42.5)	23 (40.4)	28 (44.4)	0.789
Frailty, n (%)	75 (62.5)	29 (50.9)	46 (73.0)	0.014*

*p<0.05; **p<0.01.

Table III. Laboratory indexes of the COPD patients with or without sarcopenia.

Item	Total N=120	Non-sarcopenia N=57	Sarcopenia N=63	*p*-value
WBC, 10^9/L	8.09±4.97	8.19±3.81	8.01±5.86	0.842
NEUT, 10^9/L	6.42±6.88	7.05±8.12	5.85±5.53	0.351
LYM, 10^9/L	1.96±4.02	1.94±3.58	1.97±4.41	0.975
HCT, %	39.1±17.0	39.9±11.6	38.4±20.8	0.620
PLT, 10^9/L	213±71.0	219±66.6	207±75.0	0.387
HGB, g/L	123±25.6	129±20.4	118±28.7	0.012*
TC, mmol/L	3.96±1.91	3.91±1.08	4.00±2.44	0.809
TG, mmol/L	1.88±6.18	2.58±8.89	1.23±0.77	0.265
HDL-C, mmol/L	1.17±0.41	1.14±0.39	1.21±0.43	0.356
LDL-C, mmol/L	2.44±0.77	2.50±0.78	2.38±0.76	0.420
GLU, mmol/L	6.75±3.37	6.91±3.54	6.61±3.24	0.626
HbA1C, %	6.78±1.57	6.83±1.50	6.73±1.65	0.734
Cr, umol/L	86.6±63.4	81.4±31.0	91.3±82.5	0.379
BUN, mmol/L	6.78±3.94	6.49±2.26	7.04±5.00	0.428
UA, umol/L	328±116	314±96.4	340±130	0.215
ALB, g/L	33.98±4.11	36.6±2.76	31.75±3.68	<0.001**
PA, mg/L	188±133	173±57.6	201±174	0.254
hs-CRP, mg/L	29.0±55.6	30.1±52.4	28.0±58.8	0.838

WBC=white blood cell; NEUT=neutrophile granulocyte; LYM=lymphocyte; HCT=hematokrit; PLT=platelet; HGB=hemoglobin; TC=total cholesterol; TG=triglyceride; HDL-C=high density lipoprotein cholesterol; LDL-C=low density lipoprotein cholesterol ;GLU=glucose; HbA1C=glycosylated hemoglobin; Cr=creatinine; BUN=blood urea nitrogen; UA=uric acid; ALB=albumin; PA=prealbumin; hs-CRP= high-sensitivity C-reactive protein. *p<0.05; **p<0.01.

COPD Patients with Sarcopenia Exhibit Worse Muscle Indicators and Body Composition

Sarcopenia patients had significantly lower BMI, grip strength, and skeletal muscle mass than non-sarcopenics. Body composition analysis: skeletal muscle mass (20.0±4.16 *vs.* 25.1±3.93), mineral content (2.84±0.49 *vs.* 3.32±0.45), fat (21.9±9.36 *vs.* 25.8 ±9.69), body cell mass (21.9±9.36 *vs.* 25.8 ±9.69), protein (7.43±1.39 *vs.* 8.96±1.31), fat-free mass (38. 1±8.20 *vs.* 46.7±6.79), visceral fat area (128 ± 59.9 *vs.* 129±55.1) and basal metabolic rate (1204±157 *vs.* 1380 ±1.45) were significantly lower in the sarcopenia group than those in the non-sarcopenia group (Table IV).

Risk Factors for Sarcopenia in Elderly COPD Patients

The univariate logic regression was performed, followed by multivariate logic regression analysis to determine the independent correlation of risk factors to sarcopenia. In these elderly COPD

Table IV. Body composition analysis.

Item	Total N=120	Non-sarcopenia N=57	Sarcopenia N=63	*p*-value
Skeletal Muscle Index, kg/m^2	6.49±1.16	7.28±0.83	5.78±0.94	<0.001**
Skeletal Muscle Mass, kg	22.4±4.76	25.1±3.93	20.0±4.16	<0.001**
Mineral Content, kg	3.06±0.53	3.32±0.45	2.84±0.49	<0.001**
FAT, kg	23.7±9.68	25.8±9.69	21.9±9.36	0.027*
Body Cell Mass, kg	26.6±5.75	29.7±4.32	23.8±5.46	<0.001**
Protein, kg	8.16±1.55	8.96±1.31	7.43±1.39	<0.001**
Fat Free Mass, kg	42.2±8.69	46.7±6.79	38.1±8.20	<0.001**
Visceral Fat Area, cm^2	128±57.4	129±55.1	128±59.9	0.939
Basal Metabolic Rate, kcal	1,287±175	1,380±145	1,204±157	<0.001**

*p<0.05; **p<0.01.

patients, sarcopenia was correlated with FEV1 level (OR=0.97, 95% CI: 0.94-1.0, p=0.035), BMI (OR=0.80, 95% CI: 0.71-0.89, p<0.001) and hemoglobin (OR=0.98, 95% CI: 0.96-1.0, p=0.023). Multivariate binary logic regression mode, with adjustment for the CAT score, mMRC score, ADL score, number of geriatric syndromes and frailty, showed that sarcopenia was significantly correlated with FEV1, BMI, and hemoglobin (Table V).

Sarcopenia is Significantly Correlated with Acute Exacerbation of COPD

In order to evaluate the impact of sarcopenia on the prognosis of elderly COPD patients, a one-year follow-up was performed for the incidence of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and death. A median follow-up time of 16.5 months was observed for all 120 patients, of which 19 patients (15.83%) died during this period, and 43 unscheduled patients (35.63%) visited the hospital unintentionally. Two patients died in the hospital, one with and one without sarcopenia. Seven patients in the non-sarcopenia group and ten patients in the sarcopenia group died during the follow-up period after discharge. 25 cases (20.8%) of AECOPD were found in the unscheduled visit, including 17 cases in the sarcopenia group and 8 in the non-sarcopenia group. Cox regression was further used to analyze the relationship between sarcopenia and poor outcome of COPD. After adjusting by IADL, polypharmacy and LDL-C, the incidence of sarcopenia is a significant independent predictor of acute exacerbations in elderly patients with COPD (HR=2.4, 95% CI: 1.01-5.72, p=0.048), although it was not significantly associated with mortality within the follow-up period (HR=1.15, 95% CI: 1.01-5.72, p=0.75) (Figure 1).

Discussion

In this study, we examined the sarcopenia occurrence and its clinical correlation with COPD in elderly patients through a prospective pilot study that enrolled 120 elderly COPD patients (average age: 76.7±8.78 years) with a one-year follow-up for the progress of COPD. 63 patients

Table V. Analysis of risk factors for sarcopenia in elderly COPD.

	Single factor Logic regression analysis		Multifactor binary Logic regression analysis	
Characteristic	OR[CI]	*p*	OR[CI]	*p*
CAT	1.04 [0.99;1.10]	0.113		
mMRC	1.38 [0.92;2.09]	0.116		
FEV1/pre%	0.96 [0.93;0.99]	0.001**	0.97[0.93, 1.00]	0.039*
BMI	0.81 [0.73;0.90]	<0.001**	0.80[0.71, 0.89]	<0.001**
ADL	0.99 [0.97;1.00]	0.133		
Geriatric syndrome	1.35 [1.02;1.79]	0.030*		
Frailty	1.99 [0.87;4.62]	0.014*		
HGB	0.98 [0.96;1.00]	0.012*	0.98 [0.96, 1.00]	0.043*

FEV1/pre%=forced expiratory volume in one second; BMI=body mass index; ADL=activity of daily Living; HGB=hemoglobin.
*p<0.05; **p<0.01.

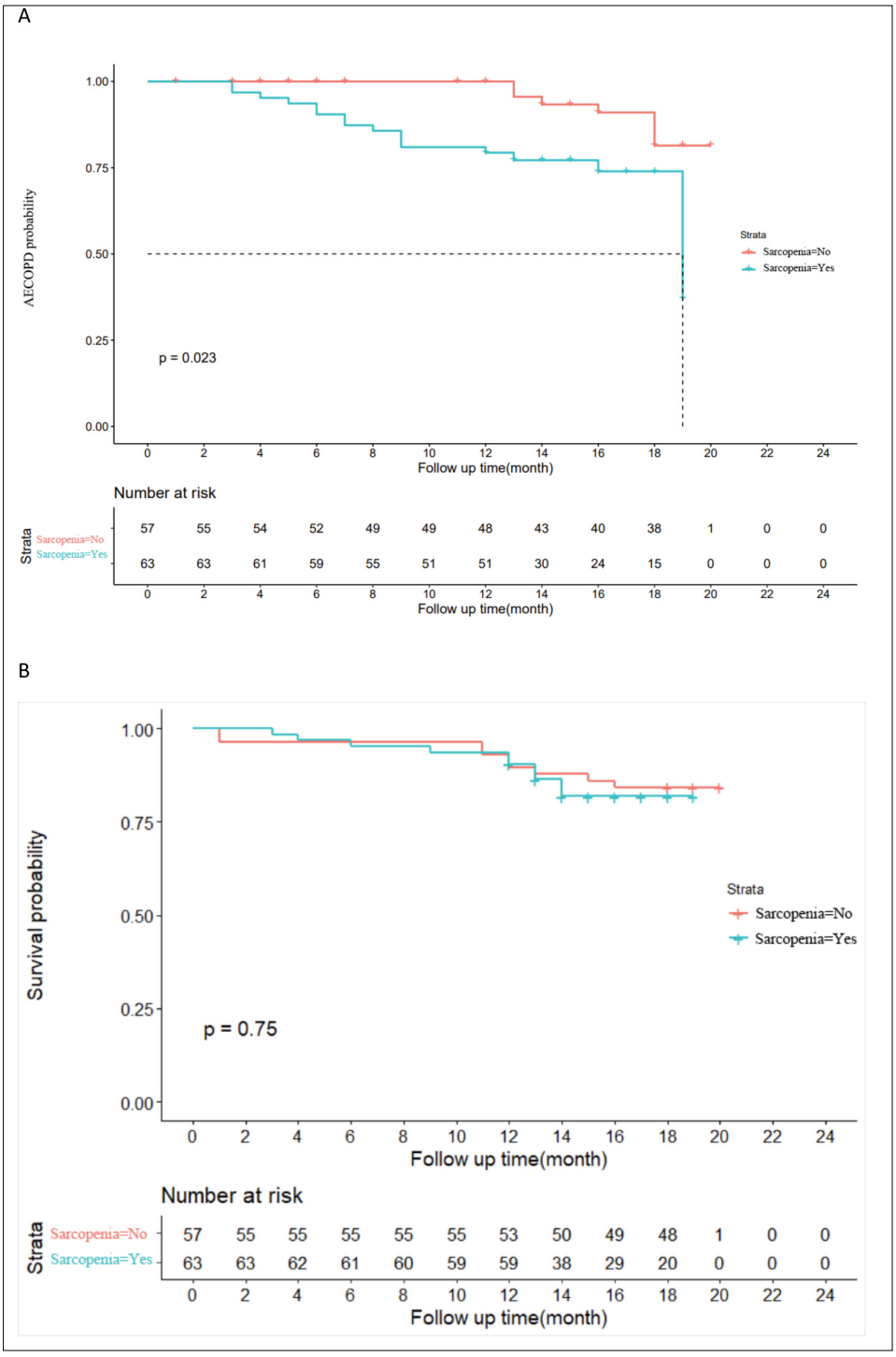

Figure 1. Cox regression was further used to analyze the relationship between sarcopenia and poor outcome of COPD. **A**, K-M curves for whether COPD patients with sarcopenia have acute exacerbations; (**B**) K-M curves for whether COPD patients with sarcopenia have acute exacerbations.

(52.5%) diagnosed with sarcopenia showed significantly more geriatric syndromes. There was a significantly higher occurrence rate of somnipathy and frailty in the sarcopenia group. Multivariate analysis showed that the occurrence of sarcopenia in elderly COPD patients was correlated with FEV1 (OR=0.97, 95% CI: 0.94-1.0, p=0.035), BMI (OR=0.80, 95% CI: 0.71-0.89, p=0.035)

and hemoglobin (OR=0.98, 95% CI: 0.96-1.0, p=0.023). The Cox regression analysis further showed that sarcopenia was associated with acute exacerbations of COPD. Our findings indicated that sarcopenia increased the risk of acute exacerbations of chronic obstructive pulmonary disease in the elderly. Sarcopenia incidence in the elderly with COPD is associated with FEV1, BMI, and hemoglobin and closely monitoring indicators is useful for an early diagnosis.

Sarcopenia is common in patients with COPD, with a prevalence of 7.9 to 66.7%, and is associated with poor prognosis[19]. Recent studies[20,21] have shown that sarcopenia affects 9.2% to 16.2% of healthy elderly (age >60 years), while its prevalence ranges from 7.9% to 66.7% in COPD populations. The variability in the prevalence of sarcopenia can be attributed to differences in the severity of lung disease and clinical settings. Consistently, we found that sarcopenia affected 52.5% of elderly COPD patients (mean age: 76.7±8.78 years), according to the diagnostic criteria of AWGS 2019. This incidence ratio is significantly higher than that in healthy elderly individuals, which is consistent with the observations on aged patients in previous studies[22,23]. Our study further indicates that elderly patients with COPD have a higher risk of impairment in muscle mass and function, due to aging, reduced physical activity resulting from decreased lung function, long-term hypoxemia, oxidative stress, and chronic inflammation[24-26].

In our study, although there was no significant difference in age between sarcopenia and non-sarcopenia groups, a significantly higher prevalence of sarcopenia was observed in the old-age group compared to the early and middle elderly groups, which was consistent with the fact that sarcopenia becomes more prevalent with age[27]. This finding indicates the high prevalence of sarcopenia in elderly COPD patients and underscores the crucial importance of earlier diagnosis and intervention of sarcopenia in these COPD patients. In addition, elderly patients over 80 years old consistently showed lower ADL scores and grip strength compared to the other two groups, suggesting lower physical function, mobility, and more severe muscle damage. In the early and middle-aged patient groups, active daily activities may have benefits against muscle dysfunction. It is worthy of investigating further the risk factors associated with the incidence of sarcopenia, such as quantifying the number of daily activities in each group.

As the population ages, respiratory physicians and geriatricians face an increasing number of patients with complex geriatric medical needs[28,29]. Comprehensive Geriatric Assessment (CGA) is an essential tool to evaluate potential health issues that may affect elderly patients' functional status and customize treatment plans accordingly[30]. Our study found a significant increase in the incidence ratio of geriatric syndromes in elderly COPD patients with sarcopenia (p=0.03), including constipation, visual impairment, hearing impairment, somnipathy, anxiety and depression, especially a significantly increased incidence of frailty and somnipathy. Further analysis of risk factors for sarcopenia in elderly COPD patients consistently indicated that geriatric syndromes and frailty are significantly associated with the incidence of sarcopenia (p=0.014 and 0.03, respectively).

It has been shown[31,32] that up to 65% of COPD patients were identified as frail, though frailty assessment tools and population differences cause variability in estimates. Herein, the frailty scale assessment showed a significantly higher incidence (62.5%) in the elderly sarcopenia COPD patients *vs.* non-sarcopenic patients. This observation was consistent with the fact that sarcopenia is one of the mechanisms contributing to frailty[33,34]. Identifying and intervening earlier in frailty among elderly COPD patients is critical to improve their quality of life and prognosis, as they are at a higher risk of falls, hospitalization, disability and mortality. In addition, somnipathy, another common comorbid condition among COPD patients (30-60% of prevalence), is a risk for acute exacerbations in COPD patients[35,36]. Our study also showed a significantly increased incidence of somnipathy in sarcopenia COPD patients, which was consistent with previous findings[37] that somnipathy was closely related to the sarcopenia process, and the interventions for somnipathy reduced muscle loss. Mechanical studies[38] showed that somnipathy is associated with chronic hypoxia and systemic inflammatory responses, which normally occur in COPD patients. Therefore, in sarcopenia, COPD patients, worse pulmonary function could lead to somnipathy, and poor sleep quality exacerbates muscle decline in these patients. It is essential for clinicians to pay attention to the sleep status of elderly COPD patients with somnipathy, especially those who are sarcopenic.

In our elderly COPD cohort, sarcopenia COPD patients showed decreased FEV1, BMI, and hemoglobin levels *vs.* non-sarcopenia COPD patients. Multivariate linear regression further showed that FEV1, BMI, and hemoglobin were negatively associated with sarcopenia, suggesting that decli-

ned levels of FEV1, BMI, and hemoglobin could be the independent risk factor for sarcopenia in elderly COPD. Mechanically, pulmonary function decline-induced hypoxia, systemic chronic inflammatory response and oxidative stress can cause muscle proteolysis and apoptosis[32]. Moreover, it has been shown[39] that respiratory muscle mass and function decline similarly with aging. In line with these studies[32,39], the observation in our elderly cohort also indicates an important correlation between lung function change and sarcopenia. Therefore, active screening for sarcopenia while monitoring lung function is necessary in elderly COPD patients.

Decreased hemoglobin level, which reflects the body's nutritional status, was an independent risk factor for sarcopenia in our cohort. Malnutrition can lead to the development of sarcopenia, and reduced hemoglobin levels can accelerate the loss of muscle tissue and function, resulting in hypoxia in muscle tissue[40,41]. Furthermore, older people have higher hemoglobin requirements, and even if the Hb level is 1-2 g/L above the WHO threshold (130 g/L for men and 120 g/L for women), elders still face higher risks of mortality, hospitalization, and functional decline[42]. Anemia increases mortality and the risk of falls in elderly patients, leading to decreased physical and muscle function. Therefore, it is necessary to actively increase the level of hemoglobin for elderly patients, especially for those with sarcopenia[40].

Our short-term follow-up showed that comorbidities with sarcopenia were independently predictive of acute exacerbations in elderly patients with COPD, rather than the mortality, within the follow-up period. Previous research[43,44] has found that COPD patients with sarcopenia have an increased risk of mortality, but the small sample size and short follow-up time of our study may have affected the results. Further large-scale studies with longer follow-up periods are needed to investigate sarcopenia's role in mortality risk in COPD patients.

Limitations

There are some limitations in this study: (1) This prospective study included a small sample size from a single-center cohort, which may limit the statistical power. (2) The short follow-up time makes it challenging to observe how sarcopenia affects mortality in elderly COPD patients. (3) Due to the patients' age and poor coordination during the examination, indicators reflecting respiratory muscle strength were not included in the lung function assessment. Future follow-up studies should have a larger sample size, longer follow-up time, and increased intervention measures to improve patient outcomes.

Conclusions

Elderly COPD patients are more likely to suffer from sarcopenia, which is independently predictive of exacerbations of COPD. The incidence ratio of geriatric syndromes, such as somnipathy and frailty, is significantly higher in COPD patients with sarcopenia. The levels of FEV1, BMI, and hemoglobin are negatively correlated with the development of sarcopenia in elderly COPD patients. It is necessary to actively screen for sarcopenia through a comprehensive assessment of aging and pay attention to indicators such as FEV1, BMI, and hemoglobin for elderly COPD patients. This can help physicians in making treatment decisions and judging prognosis for elderly COPD patients.

Authors' Contributions

JW, JJ and YM contributed to the conception and design of the study; JW, JJ, PC, XW, FY, YL carried out the studies and participated in collecting data; JW and JJ performed the statistical analysis and wrote the manuscript. All authors read and approved the final version of the manuscript.

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Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to the ownership of these data but are available from the corresponding author upon reasonable request.

Ethics Approval

The study protocol was approved by the Ethical Review of Scientific Research (No. 2018-11) at Shijingshan Teaching Hospital of Capital Medical University.

Informed Consent

Written informed consent was obtained from all participants.

Conflict of Interest
The authors declare that they have no competing interests.

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