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ORIGINAL RESEARCH

Risk Factors of Sarcopenia in COPD Patients: A Meta-Analysis

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Objective: Sarcopenia is a common complication of COPD associated with an age-related reduction in skeletal muscle mass associated with decreased muscle strength and / or reduced mobility. The incidence of sarcopenia in patients with COPD is twice that of non-COPD patients and is associated with poor prognosis, this study aimed to investigate the influencing factors of sarcopenia in COPD patients.

Methods: Selected studies from PubMed, Embase, Web of Science, Cochrane Library, Wanfang, Wanfang, CNKI, CBM, and Wanfang databases as of November 12023. Patients aged 18 were selected; data were then independently extracted by two reviewers using a standard data collection form.

Results: In total, 17 articles reporting on 5408 patients were included. Age (OR = 1.083; 95% CI, 1.024–1.145), ALB (OR = 0.752; 95% CI, 0.724–0.780), BMI(OR = 0.701; 95% CI, 0.586–0.838), smoking (OR = 1.859; 95% CI, 1.037–3.334), diabetes (OR = 1.361; 95% CI, 1.095–1.692), qi deficiency (OR = 9.883; 95% CI, 2.052, 47.593), GOLD C (OR =2.232; 95% CI, 1.866, 2.670) and GOLD D (OR = 2.195; 95% CI, 1.826–2.637) were factors affecting muscle loss in COPD patients.

Conclusion: Sarcopenia is more prevalent in patients with COPD. Age, body mass index, smoking, diabetes mellitus, qi deficiency, ALB, and GOLD grade were the contributing factors for sarcopenia in patients with chronic obstructive pulmonary disease. In the future, medical staff should not only pay attention to the early screening of sarcopenia in high-risk groups, but also provide relevant prevention information.

Keywords: sarcopenia, chronic obstructive pulmonary disease, prevalence, risk factors, meta-analysis

Introduction

Chronic obstructive pulmonary disease (COPD) is a treatable and preventable chronic respiratory disease characterised by persistent respiratory symptoms and incomplete reversible airflow limitation.[1] The European Working Group on Sarcopenia in the Elderly (EWGSOP) defines it as a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with risk of adverse outcomes,[2] characterised by a decline in muscle mass and function, which can increase the risk of falls, fractures, physical disability, and death.[3] The identification of sarcopenia referred to the Asian Working Group for Sarcopenia (AWGS) guideline following the criteria:[4] low muscle mass [bioelectrical impedance (M: <7.0 kg/m^2, F: <5.7 kg/m^2)] and low muscle strength [handgrip strength (M: <28 kg, F: <18 kg)] and/or poor physical performance (five-time chair stand test: ≥12 s). Obesity was defined as body mass index (BMI) ≥ 25.0 kg·m^{-2}. Sarcopenia is a common comorbidity of COPD, specifically a geriatric syndrome of age-related loss of skeletal muscle mass accompanied by decreased muscle strength and/or reduced mobility.[5] Byun et al[6] showed that the prevalence of sarcopenia in COPD patients was 25%, with the elderly, low body mass index, comorbid cardiovascular disease, and high inflammation levels being risk factors for the complication of sarcopenia in COPD patients. Benz et al[7] in a systematic evaluation and Meta-analysis of COPD and sarcopenia noted that patients with COPD are highly susceptible to the complication of sarcopenia, with prevalence rates of 21.6% in clinical studies and up

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to 63.0% in nursing homes. The prevalence of muscle loss in Chinese COPD patients is 28.1%, and the risk factors include low body mass index in COPD patients, long duration of disease, advanced age, long-term smoking.[8] According to the data, the prevalence of sarcopenia in patients with COPD is twice as high as in the healthy population, and increases gradually with the severity of COPD, with a higher prevalence in patients with acute exacerbations of COPD.[7,9–11] The study also found that sarcopenia resulted in poorer lung function and exercise capacity, more severe airflow limitation and longer hospital stays in COPD patients.[12] It has been shown that sarcopenia has a sustained negative impact on a range of clinical outcomes associated with COPD, eg sarcopenia is an independent risk factor for respiratory failure in patients with acute exacerbations of COPD, and comorbid sarcopenia in patients with COPD predicts a higher risk of death.[13] However, there is a lack of discussion and summary of risk factors for sarcopenia in COPD patients, and there is a lack of data from Chinese COPD patients with sarcopenia. Early screening for sarcopenia can help to implement interventions to prevent progression of sarcopenia and improve the quality of life of COPD patients. Therefore, the aim of this study was to identify the risk factors for myasthenia gravis in COPD patients, and to provide strategic support for the prevention and treatment of myasthenia gravis in COPD patients.

Materials and Methods

Databases and Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement (PRISMA 2020) 18 principles were followed in this systematic review. A computer-based search of relevant literature publicly available from CNKI, Wanfang Data, SinoMed, VIP, PubMed, Medline, Web of Science, The Cochrane Library, and Embase databases built up to 1 November 2023 was performed. A search strategy was developed with a combination of subject terms and free.We used the following text words: "Chronic Obstructive Lung Disease/Chronic Obstructive Pulmonary Diseases/COAD/COPD/Chronic Obstructive Airway Disease/Chronic Obstructive Pulmonary Disease/Airflow Obstruction, Chronic/Airflow Obstructions", Chronic/Chronic Airflow Obstructions/Chronic Airflow Obstruction, "Sarcopenia/Muscle/Thin tissue/muscle wasting/muscle atrophy/muscle mass/muscle strength/Grip strength", "Incidence/Prevalence/Epidemiology/Frequency", "risk factor/influencing factor/related factor/predictive factor/potential factor/risk/associated factors/dangerous factor". In the Chinese database, the corresponding Chinese terms were used for searching.[14]

Inclusion/Exclusion Criteria

The inclusion criteria were as follows: (1) the study population was COPD patients (GOLD: Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease[15]); (2) assessment of sarcopenia had to be implemented according to the sarcopenia consensus criteria; (3) providing odds ratio (OR) values and 95% confidence interval (CI) or providing raw data that can be converted into the above data; and (4) the study design was a cross-sectional, case-control or cohort study. The exclusion criteria were as follows: (1)full text not available; (2) inclusion of only the most detailed studies in the same sample; (3)inability to extract or transform raw data. (4) studies that were not published in Chinese or English.

Literature Selection and Data Extraction

Results of Searching Various Databases were imported into Endnote software for literature screening and management, and two researchers independently followed the inclusion and exclusion criteria to read the titles and abstracts for initial screening. Two researchers independently followed the inclusion and exclusion criteria to read the titles and abstracts for initial screening, and then read the full text for re-screening to determine the final inclusion. Two researchers independently followed the inclusion and exclusion criteria to read the title and abstract for initial screening, then read the full text for re-screening to determine the final inclusion of literature. In case of disagreement between the two were not in agreement, they were negotiated or third-party advice was sought. The data were extracted using A standardized form template was used to extract the data, including first author, year of publication, country of publication, country of study, study design, type of study, sample size, percentage of males in the sample, diagnosis of sarcopenia, prevalence of sarcopenia, and associated risk factors.

Literature Quality Evaluation

Two investigators independently evaluated the quality of the final included literature, and the cross-sections were rated using the cross-sectional study evaluation criteria recommended by the Agency for Health care Research and Quality (AHRQ),[16] containing 11 entries, with scores of 0 to 3, 4 to 7, and 8 to 11 points were evaluated as low, medium, and high quality, respectively. Case-control, cohort studies were assessed using the Newcastle-Ottawa Scale (NOS),[17] which consists of 8 entries, with a score of ≥6 indicating moderate to high quality literature.

Statistical Analysis

Stata 16.0 software was used for statistical analysis. In the quantitative analysis of effects, the OR value was chosen as the main statistical index and the corresponding 95% confidence interval (95% CI) was provided. Heterogeneity was assessed by using the χ^2 test (test level α=0.1) in combination with the I^2 test, and the fixed-effects model was used if the $I^2 \leq 50\%$ or P>0.1 suggested that the heterogeneity among the studies was small; the random-effects model was used if the I^2 >50% or $P \leq 0.1$. In addition, sensitivity analysis was performed to test the stability of the results. Funnel plots were drawn and publication bias was tested using the Egger test. A difference of P<0.05 was considered statistically significant.

Ethical Approval Statement

Institutional review board approval was not required because the analysis was based on the secondary processing of data from previously published studies.

Results

Literature Search and Screening Results

A flowchart of the literature selection process is presented in Figure 1. Through database searches of PubMed, Embase, Medline, Web of Science, CNKI and Wanfang, 4952 articles were selected for subsequent filtering. Of these, 2542 duplicate studies were excluded. After checking the title and abstract of each paper and excluding inconsistent literature types, 191 studies were found to be pertinent to the research topic. Among them, 110 articles were excluded due to inaccessible data, 22 articles were excluded after a detailed review of the full text, 28 were review studies, and 14 were case reports. Finally, 17 original studies were included in the meta-analysis.

Summary of Studies

Table 1 shows the characteristics of the 17 included studies[6,9,10,18–28,] with a total of 5408 participants. 2 included studies[10,29] were cohort studies, 10 included studies[6,9,18,19,21,23,25,27,30,31] were cross-sectional studies and 4 included studies[20,22,24,26] were case control study. In the 17 included studies, 3 different definitions of sarcopenia were adopted, including AWGS (8 studies[18–21,25,29–31]) and EWGSOP (8 studies[6,9,10,22–24,26–28]). Literature basic characteristics and quality evaluation results, see Table 1.

Meta-Analysis Results

Influence Factors

The results of the meta-analysis showed that age (11 studies;[6,10,18–20,22–24,26,27,31] odds ratio [OR] = 1.083; 95% CI, 1.024–1.145) was a risk factor for sarcopenia in patients with COPD. BMI (8 studies;[6,18–20,24,26,29,31] OR = 0.701; 95% CI, 0.586–0.838) and ALB(2 studies;[19,24] OR = 0.752; 95% CI, 0.724–0.780), however, was significantly associated with a decreased risk of sarcopenia in patients with COPD. The results of the meta-analysis showed that smoke (6 studies[18,19,22,26–28]; OR = 1.859; 95% CI,1.037–3.334), diabetes (3 studies;[6,19,20] OR = 1.361; 95% CI, 1.095–1.692), Qi deficiency (2 studies;[19,30] OR =9.883; 95% CI, 2.052,47.593),GOLD spirometric classification C (4 studies;[9,21,25,30] OR =2.232; 95% CI, 1.866,2.670), GOLD spirometric classification D (2 studies;[9,21] OR = 2.195; 95% CI, 1.826–2.637) increased the likelihood of sarcopenia in patients with COPD. The results of the risk factors analysis can be found in Table 2

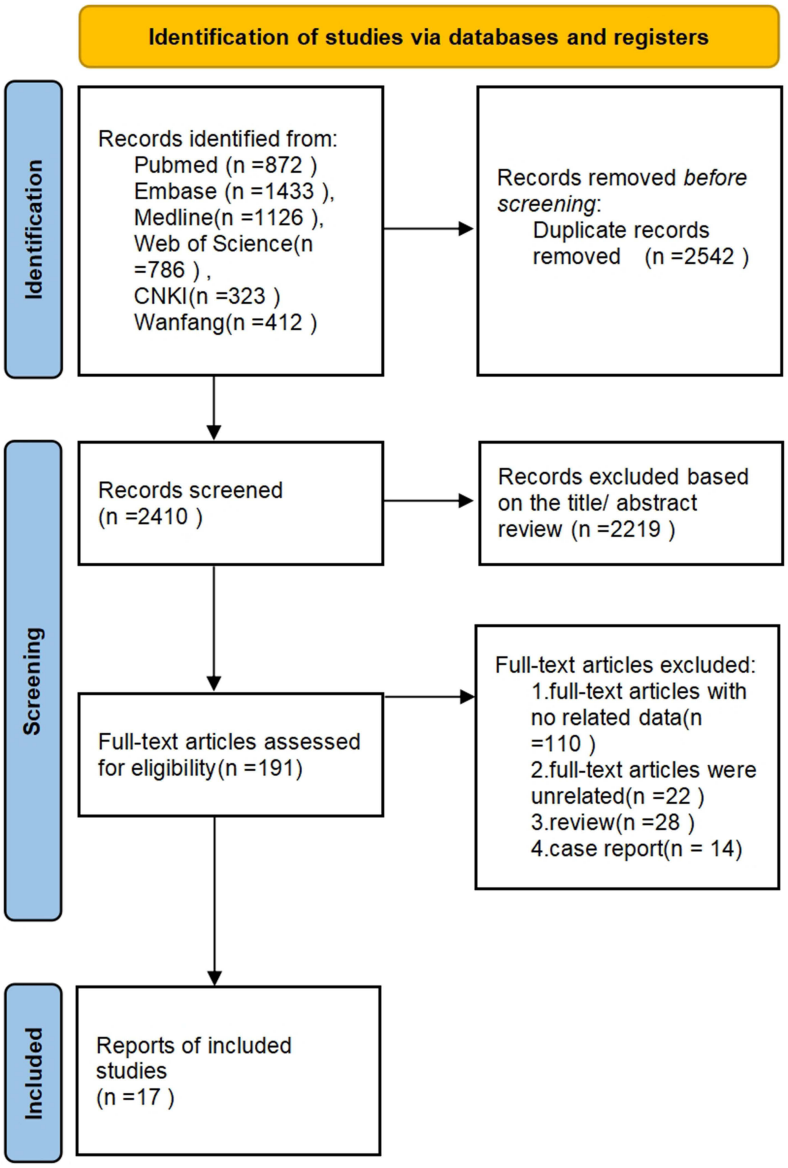

Figure 1 PRISMA flowchart of the meta analysis.

Publication Bias and Sensitivity Analysis

In this study, the funnel plots and Egger test for individual influencing factors with 10 or more included articles were evaluated for publication bias. The results showed that the funnel plot assessed the risk of publication bias showed symmetry, and Egger's test results were t = 2.30 and p=0.787, indicating that there was no publication bias including the studies (Figure 2).

Discussion

Age

The results of this study show that age is a risk factor for the development of sarcopenia in COPD patients. Age itself is associated with muscle loss, fibrosis, reduced mitochondrial efficiency and decreased neuromuscular junction function, and in COPD patients >50 years of age, there is a 1% to 2% muscle loss per year.[32]

Table 1 Characteristics of the Studies Included in This Review

First Author, Publication Year	Study Region	Study design	Sample (N)	Age	Percentage of Males in the Sample (%)	Definition of Sarcopenia	Prevalence (Total-Male-Female), %	Influencing Factor	Study Quality
Hou 2023[30]	China	Cross-sectional study	275	64.5 (±12.12)	55.27%	AWGS 2019	20%-54.5%-7.9%	Years of onset > 15 years, GOLD Classification, Qi deficiency, spleen, lack of exercise	7
Wu 2023[29]	China	Cohort study	120	76.7±8.78	63.30%	AWGS 2019	52.5%-47.36%-61.36%	FEV1/pre%, BMI, HGB	6
Wang 2023[31]	China	Cross-sectional study	198	-	70.71%	AWGS 2019	36.87%-32.86%-46.55%	Age, BMI, Serum Resistin, Serum TNF-α	7
Tang 2022[18]	China	Cross-sectional study	157	72.90±8.73	75.79%	AWGS 2019	19.7%-23.5%-7.9%	Genders, age, BMI, cigarette smoking	7
Zhang 2021[19]	China	Cross-sectional study	3016	72.86±4.55	83.29%	AWGS 2019	27.49%-27.27%-28.57%	Yang deficiency, qi deficiency, lung function, sputum and dampness, blood stasis, smoking, combined diabetes, duration of disease, CCI, age, duration of exercise, prealbumin, exercise frequency, BMI, and ALB	7
Lei 2021[20]	China	Case control study	150	≥60 y	75.33%	AWGS 2019	27.3%-27.4%-27.0%	Age, genders, BMI, DBP	7
Deng 2020[21]	China	Cross-sectional study	225	60~75	28.0%	AWGS 2019	63.1%-17.8%-21.5%	GOLD Classification	7
Espíndola 2021[10]	Brazil	Cohort Study	208	67.6 ± 10.1	45.2%	EWGSOP	16.3%-20.0%-13.3%	Age, genders, GOLD Classification	6
Chi 2020[22]	China	Case control study	52	61.52±10.23	55.7%	EWGSOP	36.5%-31.0%-43.4%	FVC, PaCO2, cigarette smoking, mMRC, age	6
Demircioğlu 2020[9]	Turkey	Cross-sectional study	219	-	89.5%	EWGSOP	52.1%-52.5%-47.8%	Age groups, GOLD Classification, BMI	7
Lage 2022[23]	Brazil	Cross-sectional study	86	-	72.1%	EWGSOP	51.1%-/-/	Substances reactive to thiobarbituric acid, catalase, MEP	6
Lin 2019[24]	China	Case control study	73	73.21±9.54	80.8%	EWGSOP	38.3%-33.9%-57.1%	Age, BMI, ALB, FEV1/FVC, IL-6, IL-10	6
Limpawattana 2018[25]	Thailand	Cross-sectional study	121	>65	92.6%	AWGS	24.0%-/-/	Age, GOLD Classification, complication, regular medication, history of falling, unexpected admission to hospital, BMI	6
Byun 2017[6]	Korea	Cross-sectional study	80	68.4±8.9	83.8	EWGSOP	25.0%-/-/	Age, genders, BMI, diabetes, angiocardiopathy, GOLD Classification	7
Lian 2017[26]	China	Case control study	96	62.4±7.9	58.3	EWGSOP	28.1%-/-/	Age, genders, cigarette smoking, CAT, bone, BMI	6
Costa 2015[27]	Brazil	Cross-sectional study	121	67.9 ± 8.6	46%	EWGSOP	11.0%-/-/	Age, genders, GOLD Classification, cigarette smoking	7
Tasar 2015[28]	Turkey	Case control study	COPD: 33 all: 211	73.9±7.2	69.7	EWGSOP	66.7%-/-/	Age, genders, GOLD Classification, cigarette smoking, BMI	7

Abbreviations: CCI, Charlson comorbidity index; EWGSOP, European Working Group Older People; AWGS, Asian Working Group on Sarcopenia; CAT, the COPD assessment test; ALB, albumin; MEP, mean effective pressure; DBP, mean diastolic blood pressure.

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Table 2 Analyses of the Risk Factors of Sarcopenia in Patients with COPD

Risk Factors	Number of Studies	Heterogeneity		EffectModel	The Results of the Meta-Analysis		
		P	I^2		OR,95% CI	Z	p
Sex	8[6,10,18,20,25–28]	0.002	69.4%	Random	1.429[0.697,2.933)	0.97	0.330
Age, y	11[6,10,18–20,22,24,26,27,31]	<0.001	86.6%	Random	1.083[1.024,1.145]	2.80	0.005
BMI	8[6,18–20,24,26,29]	<0.001	85.5%	Random	0.782[0.677,0.904]	3.33	0.001
Smoke	6[18,19,22,26–28]	0.021	62.4%	Random	1.859[1.037,3.334]	2.08	0.037
Diabetes	3[6,19,20]	0.230	31.9%	Fixed	1.361[1.095,1.692]	2.78	0.005
Qi deficiency	2[19,30]	0.002	89.3%	Random	9.883[2.052,47.593]	2.86	0.004
Exercise	2[19,30]	<0.001	97.5%	Random	4.643[0.250,105.121]	0.96	0.335
ALB	2[19,24]	0.342	0%	Fixed	0.752[0.724,0.780]	15.01	<0.001
GOLD spirometric classification	3[9,21,25]	0.018	75%	Random	3.396[0.555,20.760]	1.32	0.186
B (GOLD spirometric classification Stage A)							
GOLD spirometric classification	4[9,21,25,30]	0.147	44.1%	Fixed	2.232[1.866,2.670]	8.79	<0.001
C (GOLD spirometric classification Stage A)							
GOLD spirometric classification	2[9,21]	0.671	0%	Fixed	2.195[1.826,2.637]	8.38	<0.001
D (GOLD spirometric classification Stage A)							
GOLD spirometric classification	2[6,10]	0.372	0%	Fixed	1.473[−0.077, 3.024]	1.86	0.063
C-D (GOLD spirometric classification Stage A-B)							
Osteoporosis	2[25,26]	0.994	0%	Fixed	0.589[−0.229, 1.406]	1.41	0.158

Abbreviations: BMI, body mass index; OR, odds ratio; GOLD, Global Initiative of Chronic Obstructive Lung Disease.

Bmi

Low BMI was strongly associated with the development of sarcopenia (OR=0.701, 95% CI: 0.586 to 0.838). Low BMI reduces mitochondrial energy conversion in muscle fibres and increases the risk of negative nitrogen balance, leading to accelerated muscle loss.[33] Higher BMI levels may mean that the body has more fat reserves, which help provide energy and nutrients and reduce the likelihood of muscle breakdown, thus maintaining muscle mass.[34] Therefore, while avoiding obesity, adequate nutritional intake and sufficient physical activity should be maintained to maintain muscle mass, strength and function.

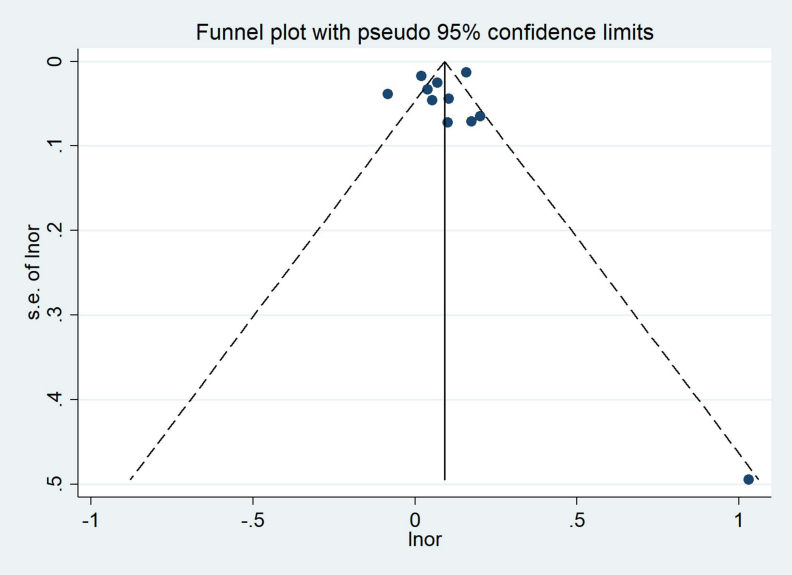

Figure 2 Funnel plot for risk of prevalent sarcopenia in patients with COPD.

Smoke

The results of this study showed that smoking habits is a risk factor for the development of sarcopenia in patients with COPD, and meta-analysis showed[35] that smoking is an independent risk factor for sarcopenia, and that smoking reduces the oxygen transporting capacity of the blood, which leads to a decrease in the supply of oxygen to the mitochondria of myocytes, which ultimately affects the functioning of skeletal muscles.[36] However, Maria Tsekoura et al[37] showed no statistically significant difference of smoking on combined sarcopenia in COPD patients. It is suggested that in the future, the sample size can be expanded and high quality studies can be conducted to further investigate whether smoking is an influential factor on comorbid sarcopenia in patients with COPD.

Diabetes

The results of this study show that diabetes is a risk factor for the development of sarcopenia in COPD patients. Sugimoto et al showed that the prevalence of sarcopenia increased linearly with increasing HbA1c concentration increase in the prevalence of sarcopenia.[38] Yoon et al also found that muscle function declined and the prevalence of sarcopenia increased significantly when glycated haemoglobin exceeded 8.5%.[39] Poor glycaemic control in diabetic patients can exacerbate insulin resistance, and diabetes mellitus.The development of sarcopenia in patients with diabetes mellitus may be associated with a number of causes: increased levels of reactive oxygen clusters can damage the structure and function of skeletal muscle cells.[40] Insulin resistance and insufficient secretion, inflammatory factors, hyperglycaemic state can cause muscle loss, diabetic nephropathy due to the loss of large amounts of proteinuria leads to a decline in muscle mass, there are also studies confirming that a variety of diabetic complications, such as retinopathy, neuropathy, etc., can lead to the decline in tissue and organ function can further lead to the occurrence of hypomyelitis.[41,42]

Qi Deficiency

The results of this study show that qi deficiency is a risk factor for the development of sarcopenia in COPD patients. Modern research has shown that qi deficiency is the most common symptomatic element of lung distension.[43] Qi refers to the vital energy of the body in traditional Chinese medicine(TCM). It maintains blood circulation, warms the body and fights diseases. When qi is deficient, all physiological functions of the body are reduced.[44]

Alb

Low ALB was strongly associated with the development of sarcopenia (OR=0.752, 95% CI: 0.724to 0.780), Same results as Anna Picca's study.[45].The association between higher albumin levels and the absence of sarcopenia in the elderly can be explained by the fact that the major nutrient deficiency in this population is protein.[46] Thus, in the absence of inflammation, albumin is a suitable biomarker of the protein status of the body's viscera, and since albumin is the major protein synthesised by the liver, it may reflect the balance between protein intake and protein consumption. However, the long half-life of albumin of 18–21 days does not reflect acute changes in nutritional status.[47,48]

GOLD Classification

GOLD classification is a risk factor for sarcopenia in COPD patients, and GOLD class C and D are more likely to develop sarcopenia than GOLD class A. Lung function classification is a clinical indicator for assessing the degree of airflow limitation in COPD patients, and it is a clinical indicator for assessing the degree of airflow limitation in COPD patients. The GOLD classification is a clinical indicator for assessing the degree of airflow limitation in COPD patients. COPD patients with longstanding disease are affected by long-term glucocorticoid use and the reduction of protein synthesising hormones in the elderly, both of which affect the synthesis of muscle proteins, accelerating muscle catabolism and depletion.[49,50] With the aggravation of the disease in patients with COPD, the level of oxidative stress is enhanced in the body, which, through the inhibition of PGC-1β, leads to the development of sarcopenia in skeletal muscle satellite cells. This leads to abnormal mitochondrial homeostasis in skeletal muscle satellite cells, impaired myogenic differentiation, inhibition of myofibre repair and direct inhibition of myosin ATPase activity, leading to a decrease in skeletal muscle contractility.[51]

Limitations

The sample size of individual studies included in this study is limited, and the reliability and stability of the conclusions are limited; only Chinese and English literature are included, and the tracking of non-Chinese and English literature is lacking, which may be selection bias; some influencing factors cannot be meta-analyzed due to the insufficient number of literature, and large sample and multi-center studies need to be verified in the future.

Data Sharing Statement

The original contributions presented in this study are included in the article; further inquiries can be directed to the corresponding author.

Author Contributions

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

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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