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Relationship among depressive symptoms, dyspnea-related fear and sarcopenia in patients with chronic obstructive pulmonary disease: The mediating effect of physical activity

Wenxiu Wang[1], Lili Wang[1], Rongrong Fan[1], Li Xie[1] and Jing Zhu[1]

Abstract

Objectives: Sarcopenia is influenced by multiple factors, including psychological aspects. This study aimed to explore the relationships among depressive symptoms, dyspnea-related fear, and sarcopenia, with a focus on the mediating role of physical activity. **Methods:** A cross-sectional study was conducted among 348 COPD patients at a tertiary hospital in Western China from July 2023 to July 2024. Sarcopenia was assessed according to the 2019 AWGS criteria, including hand bioelectrical impedance analysis (BIA), and grip strength testing. Depressive symptoms, dyspnea-related fear, and physical activity were evaluated through self-reported measures using the depression subscale of the Hospital Anxiety and Depression Scale (HADS), the Breathlessness Beliefs Questionnaire (BBQ), and the International Physical Activity Questionnaire Short Form (IPAQ-SF), respectively. Logistic regressions analyses explored associations among depressive symptoms, dyspnea-related fear, and sarcopenia. Maximum Likelihood (ML) estimation was employed using Mplus software to evaluate the mediating effect of physical activity on the relationships. **Results:** The prevalence of sarcopenia among COPD patients was 60.3%. In the logistic regression analysis with sarcopenia as the dependent variable, physical activity levels (OR = 0.508, $p = 0.019$) and depressive symptoms (OR = 1.079, $p = 0.029$) were statistically significant, while BBQ scores were not (OR = 1.031, $p = 0.070$). Mediating analyses revealed that depressive symptoms directly increased the risk of sarcopenia ($\beta = 0.076$, $p = 0.042$) but did not do so indirectly via physical activity ($\beta = 0.056$, $p = 0.146$). Conversely, dyspnea-related fear had an indirect effect on sarcopenia through physical activity, with a borderline statistical significance ($\beta = 0.053$, $p = 0.049$). **Conclusions:** This study highlights the critical role of psychological factors in sarcopenia development among COPD patients, with physical activity serving as a significant mediator. These findings underscore the need for integrated rehabilitation strategies addressing both psychological and physical activity barriers to improve outcomes for COPD patients.

Keywords

sarcopenia, depressive symptoms, dyspnea-related fear, physical activity, chronic obstructive pulmonary disease

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[1]Department of Pulmonary and Critical Care Medicine, West China Hospital, Sichuan University/West China School of Nursing, Sichuan University, Chengdu, China

Corresponding author:
Jing Zhu, West China Hospital, Sichuan University/West China School of Nursing, Sichuan University, No. 37, Guoxue Alley, Wuhou District, Chengdu 610041, China.
Email: zhu-jing2008@163.com

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disorder characterized by irreversible airflow limitation.[1] Beyond its pulmonary implications, COPD exerts profound systemic effects, including accelerated muscle wasting and dysfunction.[2] Sarcopenia, defined as age-related loss of muscle mass, plus low muscle strength, and/or low physical performance,[3] is frequently observed in COPD patients.[4,5] However, sarcopenia in COPD is not solely an age-related condition, as it is profoundly influenced by disease-specific mechanisms, such as the chronic inflammatory milieu[6] and heightened oxidative stress.[7] These factors synergistically contribute to muscle loss, compounding the physical impairments and adverse outcomes seen in COPD patients.[5]

While physiological factors play a significant role in sarcopenia, psychological factors may also contribute to the development of sarcopenia in COPD patients. Depression, a common comorbidity in COPD, has been identified as a potential risk factor for sarcopenia.[8] A recent systematic review has shown that prevalence of depression in patients with sarcopenia was high relatively.[9] A multicenter cohort study among chronic kidney disease has shown that more depression was associated with a higher likelihood of having sarcopenia.[10] Another critical disease-specific psychological factor in COPD is dyspnea-related fear. As dyspnea is one of the main symptoms in patients with COPD. The subjective perceptions and psychological responses to dyspnea can impact their daily lives and disease management.[11] Patients with COPD often avoid of activities, including exercise and non-exercise activity, due to fear of breathlessness. Several studies have confirmed that fear of breathlessness significantly contributes to reduced physical activity.[12] Additionally, dyspnea-related fear played a significant role in disease progression. While patients with higher dyspnea-related fear have reported higher scores on dyspnea, those who exhibit a stronger decrease in disease-specific fears show more improvement in pulmonary rehabilitation.[11,13] However, the relationship between dyspnea-related fear and sarcopenia remains unclear.

Physical activity might play a crucial mediating role in the impact of psychological factors on sarcopenia. Physical inactivity, a recognized risk factor for sarcopenia,[8,14] is highly prevalent in COPD patients due to the disease's inherent characteristics, such as breathlessness and fatigue.[15] The interplay of physical and psychological factors, such as depression and dyspnea-related fear, may further exacerbate physical inactivity. Physical activity often decreases in the early stage of COPD and substantially declined over time. Regular physical activity was recommended to improve health outcomes in COPD by guidelines.[16,17] In aspect of prevention and treatment of sarcopenia, physical exercise has shown beneficial effects.[18–20] Therefore, improving physical activity levels is both necessary and beneficial. However, promoting the physical activity levels in COPD patients remains a significant challenge.[12] Understanding whether psychological factors influence sarcopenia by affecting physical activity levels in COPD patients could provide valuable evidence for developing targeted interventions.

Therefore, the aim of this study is to explore the relationships among depressive symptoms and dyspnea-related fear and sarcopenia in COPD patients, with a particular focus on the mediating role of physical activity levels.

Materials and methods

Participants

We recruited inpatients in the respiratory medicine wards of a tertiary hospital in Western China between July 2023 and July 2024. The inclusion criteria were as follows: (1) a confirmed diagnosis of COPD; (2) normal cognitive function; and (3) provision of informed consent with a voluntary agreement to participate. The following patients were excluded from the study: (1) contraindications for bioelectrical impedance analysis (BIA), such as a pacemaker or implantable cardioverter defibrillator; (2) diagnosis of psychiatric disorders or undergoing professional psychological therapies; (3) other diseases affecting daily activities, such as neurological, muscular, or lower limb joint or vascular diseases; (4) diagnosis of malignant tumor, including lung cancer.

A total of 386 patients were screened for eligibility during the study period. Among them, 2 patients declined to participate, 9 were excluded due to contraindications for BIA, 4 were excluded due to a confirmed diagnosis of psychiatric disorders, 7 were excluded due to other diseases affecting daily activities, and 16 were excluded due to a diagnosis of malignant tumor. Ultimately, 348 COPD patients were included in the final analysis. All assessments were conducted by trained members of the research team to ensure accuracy and consistency. The study was approved by the Human Subjects Ethics Subcommittee of West China Hospital (no. 2023791), and all participants provided informed consent.

Assessment of sarcopenia

Sarcopenia was defined based on the 2019 AWGS criteria,[3] with the presence of low muscle strength and low muscle mass. Muscle strength was evaluated using grip strength measurements obtained with a Xiang Shan CAMRY EH101 dynamometer, participants used their dominant hand for three trials, with at least a 5-min rest between measurements to prevent muscle fatigue. The highest value from

the three trials was used for analysis. Low grip strength was characterized by values below 28 kg for men and below 18 kg for women. Muscle mass was assessed using bioelectrical impedance analysis (BIA) with the InBody S10 device, and the skeletal muscle mass index (SMI) was calculated as the appendicular muscle mass divided by the square of height (kg/m^2). Low muscle mass was defined as SMI values below 7.0 kg/m^2 in men and below 5.7 kg/m^2 in women.

GOLD ABCD assessment tool

The modified Medical Research Council (mMRC) dyspnea scale was used to measure breathlessness. GOLD ABCD assessment tool was used to categorize patients based on their symptoms and risk of exacerbations. Patients were classified into groups A, B, C, or D using a combination of their symptom burden assessed by mMRC scores and exacerbation history. ABCD groups plays a crucial role in the management of COPD by providing a comprehensive assessment and guiding individualized treatment.

Nutritional risk screening 2002 (NRS2002)

Nutritional risk screening was conducted using the NRS2002 scale.[21] The NRS2002 tool evaluates factors such as the severity of illness, changes in appetite and dietary intake, body mass index (BMI), recent weight loss, and age. It consists of three components: a disease score ranging from 0 to 3, a nutrition score ranging from 0 to 3, and an age score, with patients aged 70 years or older receiving an additional point. The total nutritional risk score ranges from 0 to 7. Patients with a total NRS2002 score of 3 or higher were identified as being at high risk for malnutrition, whereas those with a score below 3 were considered to have no nutritional risk or were adequately nourished.

The hospital anxiety and depression scale (HADS)

The depression subscale of the Hospital Anxiety and Depression Scale (HADS-D) was used to assess depressive symptoms.[22] The HADS-D is a validated tool specifically designed to detect the presence and severity of depression in clinical settings, avoiding overlap with somatic symptoms that might overlap with physical illnesses. The subscale consists of 7 items, each scored on a 4-point Likert scale (0 to 3), with a total score ranging from 0 to 21. Depression were defined as a score of $\geq$8, and higher scores indicate more severe depressive symptoms.[22]

Breathlessness beliefs questionnaire (BBQ)

The Breathlessness Beliefs Questionnaire (BBQ) was utilized to assess dyspnea-related fear.[23] It comprises 11 items that assess two dimensions: somatic focus and activity avoidance. Respondents rate their agreement with each item on a five-point Likert scale, ranging from 'strongly disagree' (scored 1) to 'strongly agree' (scored 5). The Chinese version of the BBQ has been proven to be a reliable tool for assessing fear related to breathlessness in patients with respiratory diseases.[24]

International physical activity questionnaire short form (IPAQ-SF)

The physical activity levels of COPD patients were assessed using the International Physical Activity Questionnaire Short Form (IPAQ-SF),[25] which is one of the most widely used self-reported questionnaires to assess physical activity. This questionnaire measures the frequency, duration, and intensity of physical activities, including walking, moderate-intensity, and vigorous-intensity activities during a typical week. The total physical activity was calculated in MET-minutes per week by summing the minutes spent in each activity category, weighted by their respective MET values (walking = 3.3 METs, moderate = 4.0 METs, vigorous = 8.0 METs). The IPAQ-SF has been validated and widely used in various populations, including patients with COPD,[26–29] to estimate physical activity levels and categorize participants into low, moderate, or high physical activity groups based on established guidelines.

Statistical analysis

Continuous variables were described as means ± standard deviations (SD) and compared using t-tests or ANOVA if normally distributed, while non-normally distributed variables were described as medians with interquartile ranges and analyzed using non-parametric tests. Categorical variables were presented as frequencies and percentages and compared using chi-square tests to explore differences sarcopenia and non-sarcopenia groups. Binary logistic regressions analyses were conducted using SPSS 27.0 (IBM Corp., Armonk, NY, USA) to determine the association among depressive symptoms, dyspnea-related fear and sarcopenia among patients with COPD. Physical activity was categorized by combining moderate and high activity levels into one category and comparing it against the low PA group. In model 1, sarcopenia was as the dependent variable, independent variables included age, gender, NRS2002, ABCD group classification, depressive symptoms, and dyspnea-related fear (BBQ score). These variables were selected based on their clinical relevance in COPD management and prior evidence linking them to sarcopenia.[8] In model 2, regression analyses were conducted with physical activity as the dependent variable to confirm its associations with depressive symptoms and

dyspnea-related fear. In model 3, sarcopenia was again the dependent variable, with physical activity included as an independent variable. Subsequently, Mplus Version 8.3 was used to verify the mediating effect of physical activity on the association among depressive symptoms, dyspnea-related fear and sarcopenia. Maximum Likelihood (ML) estimation was used, and 5000 bootstrap samples were drawn to obtain bias-corrected confidence intervals (CI) for indirect, direct, and total effects. All p values were two-tailed and p values <0.05 were considered statistically significant.

Results

A total of 348 patients with COPD were included in this study, and 230 (60.3%) were diagnosed with sarcopenia, 130 (37.4%) had depression. Table 1 presents the characteristic of the participants. Univariate analysis showed that COPD patients with sarcopenia were older than those without sarcopenia, while there were no differences in gender, education level, marital status, or smoking status between patients with sarcopenia and those without. Regarding health status, patients with higher NRS2002 scores, more severe symptoms (mMRC scores), and higher ABCD grades in the COPD assessment were more likely to be found among those with sarcopenia.

Logistic regression analyses were conducted to explore the relationships between depressive symptoms, dyspnea-related fear, physical activity, and sarcopenia. In model 1, sarcopenia was significantly related to depressive symptoms (OR = 1.090, $p = 0.012$) and BBQ scores (OR = 1.042, $p = 0.010$) after controlling for age, gender, NRS2002 scores, ABCD grades. In model 2, when physical activity level was set as the dependent variable, both depressive symptoms (OR = 0.920, $p = 0.017$) and BBQ scores (OR = 0.924, $p = 0.001$) were significantly correlated to the physical activity. In model 3, when controlled for physical activity level in regression with sarcopenia as the dependent variable, both physical activity levels (OR = 0.508, $p = 0.019$) and depressive symptoms (OR = 1.079, $p = 0.029$) were associated with sarcopenia, while BBQ scores did not remain significant (OR = 1.031, $p = 0.070$) (Table 2).

The mediation effect analysis (Table 3) demonstrated the impact of depressive symptoms, dyspnea-related fear and physical activity level on sarcopenia. The direct effect of depressive symptoms on sarcopenia was statistically significant ($\beta = 0.076$, $p = 0.042$), while the indirect effect through physical activity was not statistically significant ($\beta = 0.056$, $p = 0.146$), with a total effect of $\beta = 0.132$ ($p = 0.017$). For dyspnea-related fear, the indirect effect on sarcopenia via physical activity was observed with a borderline statistical significance ($\beta = 0.053$, $p = 0.049$), resulting in a significant total effect ($\beta = 0.084$, $p = 0.005$).

Discussion

The aim of this study was to explore the relationships between depressive symptoms, dyspnea-related fear, and sarcopenia in COPD patients, with a particular focus on the mediating role of physical activity levels. Our results showed that the direct effect of depressive symptoms on sarcopenia was notable, while the impact of dyspnea-related fear on sarcopenia was mediated by physical activity levels. These findings suggest that psychological factors may play a critical role in the development of sarcopenia in COPD patients, and that physical activity could be a key mediator in this process.

The prevalence of sarcopenia in our study (60.3%) is higher than the overall prevalence of 21.6% reported in the meta-analysis,[4] which included populations from various settings, including community-dwelling individuals, outpatient clinics, and nursing homes. Our findings are more in line with hospital-based studies, where sarcopenia prevalence tends to be higher due to more severe disease profiles. For example, two studies reported sarcopenia rates of 55%[30] and 86.5%[31] among COPD patients in pulmonary rehabilitation settings. Sarcopenia is associated with poorer quality of life, higher disability rates, and increased mortality among affected individuals.[32–34] The high proportion of sarcopenia in hospital-based study are alarming, indicating an urgent need for identification and evidence-based early intervention.

Our study demonstrate that depressive symptoms may significantly increase the risk of sarcopenia in COPD patients. This finding is consistent with previous research showing a high prevalence of depression among individuals with sarcopenia.[9] Additionally, A longitudinal cohort study also indicated that individuals with worsening or persistent depression was more likely to develop sarcopenia.[35,36] The mediation analysis in our study further revealed that depressive symptoms influence sarcopenia, with a significant direct and total effect. Previous studies have linked depression to increased inflammation[37] and metabolic dysregulation,[38] both of which can independently contribute to muscle loss. These mechanisms provide a plausible explanation for the direct effect of depressive symptoms on sarcopenia observed in our study. Although previous studies indicated that depression leads to decreased physical activity,[39,40] and physical activity can slow the progression of sarcopenia,[18] but in our study indirect effect of depressive symptoms through physical activity was not statistically significant among COPD patients, This lack of significance may be attributed to the inclusion of more disease-specific psychological factor (dyspnea-related fear) in our analysis.

Dyspnea-related fear is a psychological construct closely associated with respiratory diseases, similar to the fear of pain observed in patients with pain conditions.[23] Patients with COPD often avoid physical activity due to the fear that

Table 1. Characteristics and univariate analysis of sarcopenia in COPD patients.

	All	No sarcopenia (n = 138, 39.7%)	Sarcopenia (n = 210, 60.3%)	t/χ^2	*p*-value
Age, mean (SD)	64.67 ± 11.69	60.86 ± 12.44	67.17 ± 10.47	0.049	<0.001
BMI, kg/m^2, mean (SD)	22.35 ± 3.70	24.77 ± 3.20	20.75 ± 3.09	0.727	<0.001
Gender, n (%)					
Female	130 (37.4%)	57 (41.3%)	73 (34.8%)	1.523	0.217
Male	218 (62.6%)	81 (58.7%)	137 (65.2%)		
Education level, n (%)					
Junior high school and below	240 (69.0%)	91 (65.9%)	149 (71.0%)	0.977	0.323
Senior high school and above	108 (31.0%)	47 (34.1%)	61 (29.0%)		
Marital status, n (%)					
Married	317 (91.1%)	126 (91.3%)	191 (91.0%)	0.013	0.910
Unmarried, divorced or widowed	31 (8.9%)	12 (8.7%)	19 ((9.0%)		
Smoking, n (%)					
Yes	48 (13.8%)	20 (14.5%)	28 (13.3%)	4.192	0.123
Quit	154 (44.3%)	52 (37.7%)	102 (48.6%)		
never	146 (42.0%)	66 (47.8%)	80 (38.1%)		
NRS2002 scores, n (%)					
<3	192 (55.2%)	100 (72.5%)	92 (43.8%)	27.646	<0.001
≥3	156 (44.8%)	38 (27.5%)	118 (56.2%)		
mMRC scores, n (%)					
0-1	86 (24.7%)	56 (40.6%)	30 (14.3%)	30.045	<0.001
2–4	262 (75.3%)	82 (59.4%)	180 (85.7%)		
ABCD grades n (%)					
A	51 (14.6%)	38 (27.5%)	13 (6.2%)	46.273	<0.001
B	161 (46.3%)	63 (45.7%)	98 (46.7%)		
C	35 (10.1%)	18 (13.0%)	17 (8.1%)		
D	101 (29.0%)	19 (13.8%)	82 (39.0%)		
Physical activity level, n (%)					
Low	216 (62.1%)	57 (41.3%)	159 (75.7%)	41.938	<0.001
Medium	110 (31.6%)	67 (48.6%)	43 (20.5%)		
High	22 (6.3%)	14 (10.1%)	8 (3.8%)		
Depression, mean (SD)	6.35 ± 4.68	4.85 ± 4.33	7.34 ± 4.65	0.546	<0.001
No depression	218 (62.6%)	103 (74.6%)	115 (54.8%)	14.058	<0.001
With depression	130 (37.4%)	35 (25.4%)	95 (45.2%)		
BBQ, mean (SD)	39.18 ± 9.73	36.01 ± 10.39	41.17 ± 8.95	0.037	<0.001

Note: Data are presented as mean ± standard deviation or number (%).
BMI: body mass index; NRS2002: nutritional risk screening 2002; mMRC: the modified medical research council; ABCD grades: classification based on symptom burden and exacerbation risk; BBQ: breathlessness beliefs questionnaire.

it will worsen their breathlessness. Our study highlights the potential significant role of dyspnea-related fear in sarcopenia development. Although the direct effect of dyspnea-related fear on sarcopenia was not statistically significant, its indirect effect through physical activity was significant. This suggests that fear of breathlessness negatively impacts physical activity, which in turn contributes to sarcopenia development. This result further supports the conclusions of previous study, showing dyspnea-related fear was negatively correlated with exercise perception and physical activity.[41] Sarcopenia presents with distinct features across various patient populations, and these disease-specific factors should be carefully considered in intervention strategies.

Physical inactivity is a well-established risk factor for sarcopenia, and in our study, 61% of participants were classified as having low physical activity levels. This finding underscores the widespread prevalence of physical inactivity among COPD patients. Increasing physical activity levels in COPD patients remains a significant challenge, particularly confronted with worsening physical symptoms such as dyspnea. This emphasizes depression and dyspnea-related fear should be integrated into pulmonary rehabilitation interventions. Tailored strategies

Table 2. Logistic regression results for depressive symptoms, dyspnea-related fear, physical activity, and sarcopenia.

	Model 1				Model 2				Model 3			
	Dependent variable = sarcopenia				Dependent variable = physical activity				Dependent variable = sarcopenia			
	β	OR	95% CI	*p*-value	β	OR	95% CI	*p*-value	β	OR	95% CI	*p*-value
Age	0.033	1.033	1.009–1.058	0.008	−0.025	0.975	0.952–0.998	0.035	0.029	1.030	1.005–1.055	0.018
Gender (ref. = female)	0.491	1.634	0.958–2.788	0.071	−0.503	0.605	0.356–1.028	0.063	0.444	1.560	0.907–2.68	0.108
NRS2002 scores	0.424	1.528	1.261–1.852	<0.001	−0.223	0.800	0.665–0.962	0.018	0.401	1.493	1.229–1.813	<0.001
ABCD grades	0.634	1.886	1.457–2.441	<0.001	−0.380	0.684	0.536–0.872	0.002	0.597	1.816	1.398–2.359	<0.001
Depressive symptoms	0.086	1.090	1.019–1.167	0.012	−0.083	0.920	0.860–0.985	0.017	0.076	1.079	1.008–1.156	0.029
BBQ scores	0.041	1.042	1.010–1.075	0.010	−0.079	0.924	0.895–0.955	<0.001	0.031	1.031	0.997–1.066	0.070
Physical activity (ref. = low activity level)									−0.677	0.508	0.289–0.895	0.019

Notes: BMI: body mass index, NRS2002: nutritional risk screening 2002, ABCD grades: classification based on symptom burden and exacerbation risk, BBQ: breathlessness beliefs questionnaire. OR: odd ratio, CI: confidence interval.

Table 3. Mediating Effect of Physical Activity between Depressive symptom/Dyspnea-related Fear and Sarcopenia.

Path		β	SE	*p*-value	95% CI
Direct effect	Depressive symptoms > sarcopenia	0.076	0.037	0.042*	0.005–0.152
Indirect effect	Depressive symptoms > physical activity > sarcopenia	0.056	0.039	0.146	0.002–0.152
Total effect	Depressive symptoms > sarcopenia	0.132	0.055	0.017*	0.034–0.252
Direct effect	BBQ score > sarcopenia	0.031	0.018	0.082	−0.004–0.066
Indirect effect	BBQ score > physical activity > sarcopenia	0.053	0.027	0.049*	0.006–0.112
Total effect	BBQ score > sarcopenia	0.084	0.03	0.005*	0.028–0.145

Note: BBQ: breathlessness beliefs questionnaire; SE: standard error; CI: confidence interval.

addressing these psychological factors could potentially provide a breakthrough in promoting physical activity thereby preventing and delaying the progression of sarcopenia.

When interpreting the present results, several limitations should be considered. First, the cross-sectional design of the study restricts the ability to infer causality among the variables examined, making it unclear whether psychological factors lead to sarcopenia or vice versa. Second, the study was conducted in a single hospital in Western China, which may limit the generalizability of the findings to other populations or settings. Third, while validated scales were used to assess psychological factors and physical activity levels, the reliance on self-reported measures may introduce response biases, such as social desirability or recall bias. Fourth, this study focused only on depression and dyspnea-related fear as psychological variables, whereas human psychology is inherently complex. Future research should employ longitudinal study designs to better understand causal relationships, include more diverse and representative samples, and use objective measures of physical activity and psychological factors to enhance the robustness of the findings. Additionally, future studies could explore other psychological factors, such as anxiety, to provide a more comprehensive understanding of the relationship between psychological health and sarcopenia.

Conclusion

This study highlights the potential impact of psychological factors, such as depressive symptoms and dyspnea-related fear, on the development of sarcopenia in COPD patients. Our findings suggest that physical activity may play a crucial mediating role in this relationship. However, the cross-sectional design limits causal inference, underscoring the need for longitudinal confirm temporal relationships and underlying mechanisms. A key challenge remains in promoting physical activity and sustaining it over time. This study provides a perspective that future research could explore integrated psychological interventions to address these challenges and slow the progression of sarcopenia.

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ORCID iD

Wenxiu Wang https://orcid.org/0000-0002-4045-3050

Statements and declarations

Ethical approval

The study was approved by the Human Subjects Ethics Subcommittee of West China Hospital (no. 2023791).

Consent to participate

Written informed consent to participate in this study was obtained from all participants.

Author contributions

All the authors contributed to this study. Wenxiu Wang and Jing Zhu conceived and designed the original study protocol. Li Xie and Lili Wang screened the patients and collected data. Rongrong Fan and Wenxiu Wang took responsibility for the integrity of the data and the data analysis. Jing Zhu interpreted the results. Wenxiu Wang drafted and revised the manuscript. Jing Zhu acted as the guarantor for the overall content. All authors critically reviewed and approved the final manuscript.

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Conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data Availability Statement

The data supporting the conclusions of this article are included within the article. All raw data analyzed during the study are available from the first author upon reasonable request.

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