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Nutritional Status and Inflammation as Mediators of Physical Performance and Delirium in Elderly Community-Acquired Pneumonia Patients: A Retrospective Cohort Study

Jingxian Liao[1], Xiaozhu Shen[1], Zhiqiang Du[2], Xiaojuan Wang[2,*], Lei Miao[2,*]

[1]Department of Geriatrics, The Second People's Hospital of Lianyungang Affiliated to Kangda College of Nanjing Medical University, Lianyungang, Jiangsu, People's Republic of China; [2]Department of Critical Care Medicine, The Second People's Hospital of Lianyungang Affiliated to Kangda College of Nanjing Medical University, Lianyungang, Jiangsu, People's Republic of China

*These authors contributed equally to this work

Correspondence: Lei Miao; Xiaojuan Wang, Department of Critical Care Medicine, The Second People's Hospital of Lianyungang Affiliated to Kangda College of Nanjing Medical University, No. 41, Hailian East Road, Haizhou District, Lianyungang, Jiangsu Province, 222000, People's Republic of China, Email miaolei061@163.com; 56645221@qq.com

Purpose: This study proposes a multiple mediation model to evaluate the association among diminished physical performance, malnutrition, inflammation, and delirium in seniors with community-acquired pneumonia.

Patients and Methods: This retrospective cohort study included elderly patients hospitalized for community-acquired pneumonia at the Geriatrics Department of the Second People's Hospital of Lianyungang from January 1, 2020, to January 1, 2024. Logistic regression analysis was conducted to examine the associations among physical performance, nutritional status, C-reactive protein (CRP) levels, and delirium. Mediation models assessed the effects of nutritional status and CRP on the relationship between physical performance and delirium, with subgroup analyses based on diabetes status.

Results: A total of 379 patients were included, with a mean age of 80.0±7.4 years, and 51.7% were male. The incidence of delirium during hospitalization was 28.5% (n=108). Subgroup analyses revealed significant correlations between physical performance, nutritional status, and CRP (P<0.001), regardless of diabetes status. After adjusting for confounding variables, CRP was positively associated with delirium, while MNA-SF and SPPB scores showed negative correlations with delirium risk (OR=0.852, 95% CI: 0.730–0.995; OR=0.580, 95% CI: 0.464–0.727, P<0.05). Mediation analyses indicated that MNA-SF scores and CRP significantly mediated the association between SPPB and delirium. Specifically, pathways "SPPB→ MNA-SF→ delirium", "SPPB→ CRP→ delirium", and "SPPB→ MNA-SF→ CRP→ delirium" demonstrated significant mediating effects in patients without diabetes, while only the pathway "SPPB→ MNA-SF→ CRP→ delirium" was significant in those with diabetes.

Conclusion: Older patients with community-acquired pneumonia and poor physical performance are more susceptible to delirium, with nutritional status and inflammation as key mediators.

Keywords: delirium, physical performance, nutritional status, inflammation

Introduction

Delirium is a prevalent cognitive impairment among individuals aged 65 and older, closely linked to disease prognosis through timely assessment and intervention.[1] It often manifests as acute confusion, disorientation, and fluctuations in attention during hospitalization or illness in older adults.[2] The underlying mechanisms of delirium remain poorly understood, and there is a lack of standardized clinical identification methods as well as universally effective treatment strategies.[3] Therefore, investigating the risk factors and pathophysiological changes associated with the onset and progression of delirium in elderly patients is crucial.

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The aging process, compounded by chronic diseases, adversely affects bodily functions in older individuals, resulting in a gradual decline in strength, reaction time, coordination, and balance. This decline ultimately impairs physical function.[4] Factors such as multiple health conditions, muscle weakness, and loss of muscle mass contribute to reduced physical function and increased disability among the elderly. Decreased physical function heightens vulnerability to adverse events, including hospitalization, falls, disability, and mortality.[5] Previous studies have demonstrated a connection between diminished physical function and both the occurrence and prognosis of delirium in hospitalized elderly patients.[6–8] Furthermore, comparative analyses within this field emphasize the relevance of our research.[9]

Nutritional status is a key factor in maintaining overall health and well-being, with malnutrition identified as one of the primary factors contributors to delirium.[10,11] Additionally, cognitive impairment has been associated with inflammation, which initiates a cascade of events that disrupt normal brain function, leading to the cognitive impairment and behavioral disturbances typically observed in individuals experiencing delirium.[12] C-reactive protein (CRP) levels are indicative of systemic inflammation, and several studies have established a strong correlation between elevated CRP levels and an increased susceptibility to delirium.[13–15]

Given the robust correlation between nutritional status and physical performance, along with the significant role of inflammation in the development of delirium, this study aims to investigate the impact of both nutritional status and inflammation on the relationship between physical performance and delirium in elderly patients with community-acquired pneumonia (CAP). We will conduct multiple mediation analyses employing statistical models that account for various confounding variables.

Materials and Methods

Study Design and Participants

This study was designed as a single-center retrospective cohort study that initially included 457 patients aged 65 years and older with a principal diagnosis of community-acquired pneumonia (CAP), who were hospitalized in the Geriatrics Department of the Second People's Hospital of Lianyungang from January 1, 2020 to January 1, 2024. Eligible patients had a minimum hospital stay of 2 days and met the diagnostic criteria for CAP as defined by the 2019 Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) Clinical Practice Guidelines: Diagnosis and Treatment of Adults with Community-Acquired Pneumonia.[16]

Exclusion criteria included patients with acute or chronic neurological diseases, severe hearing or visual impairments that hindered communication, the inability to perform physical activity tests, the requirement for sedatives, and those lacking a nutritional assessment, delirium assessment, or physical performance assessment during hospitalization. After applying these criteria, a total of 379 older patients with CAP were included in this study. This research was approved by the Ethics Committee of the Second People's Hospital of Lianyungang (Ethics number: 2022K040). Due to the retrospective nature of the study, only medical records were analyzed, and informed consent was waived by the Ethics Committee for Clinical Research of the Second People's Hospital of Lianyungang.

Data Collection

Clinical data were collected by trained researchers proficient in electronic medical record systems. Baseline characteristics, including age at admission, sex and chronic diseases, were recorded. Additionally, information regarding the hospital stay, such as length of stay, mortality, nutritional assessments (using the Mini Nutritional Assessment Scale-Short Form), and physical performance assessments (using the Short Physical Performance Battery), were documented. Key clinical parameters including heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP), were recorded. Laboratory test results included white blood cell (WBC) count, platelet (PLT) count, hemoglobin (HB) levels, triglycerides (TG), total cholesterol (TC), serum creatinine (Scr), albumin (Alb), C-reactive protein (CRP), and blood glucose (Glu).

Physical Performance Assessment

Physical performance was evaluated using the Short Physical Performance Battery (SPPB), which comprises three components: (1) a 4-meter walking test; (2) a balance assessment involving three standing positions: feet together, standing with one foot forward, and standing with feet positioned front and back; and (3) a sit-to-stand test in which participants, seated in a chair with their arms crossed over their chest, were instructed to complete five sit-to-stands as quickly as possible, with the time taken for completion recorded. The overall SPPB score ranges from 0 to 12 points, with lower scores indicating poorer physical function.[17]

Nutritional Assessment

Nutritional status was assessed using the Mini Nutritional Assessment Scale-Short Form (MNA-SF), evaluating recent weight loss, body mass index (BMI), physical activity, the presence of acute illness or stressors, mental state, and the ability to self-feed. The total score from the MNA-SF can reach a maximum of 14 points; individuals scoring 7 points or below were classified as malnourished.[18]

Delirium Assessment

The Confusion Assessment Method (CAM) was utilized to diagnose acute delirium in hospitalized patients presenting with disorientation, confusion, and altered levels of consciousness.[19] The CAM identifies delirium by assessing four core features: Feature 1 (acute onset and fluctuating course), Feature 2 (inattention), Feature 3 (disorganized thinking), and Feature 4 (altered level of consciousness). According to the Diagnostic and Statistical Manual of Mental Disorders (5th edition; DSM–5; American Psychiatric Association, 2013), a diagnosis of delirium necessitates the presence of both criteria 1 and 2, along with either criterion 3 or 4.[20]

Statistical Analysis

Statistical analysis were conducted using IBM SPSS Statistics version 21 and PROCESS version 4.1. Normality tests were performed on continuous data; results are expressed as mean ± standard deviation (SD) for normally distributed data and as medians (interquartile range, IQR) for non-normally distributed data. Independent *t*-tests and non-parametric Mann–Whitney *U*-tests were applied for inter-group comparisons. Categorical variables were presented as frequencies and percentages, and Chi-squared tests were utilized for group comparisons. Statistical significance was determined using a two-tailed P-value <0.05. Additionally, binary logistic regression analysis was conducted to explore the associations among the Short Physical Performance Battery (SPPB), nutritional status (MNA-SF), CRP levels, and delirium in elderly patients with CAP. Model goodness of fit was evaluated using omnibus tests and the Hosmer-Lemeshow test. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to contextualize the findings. The bootstrap method was employed to estimate mediation effects, as it does not rely on distributional assumptions and provides a less biased estimation compared to traditional methods. To enhance the accuracy of our results, we included potential confounding variables in our analysis, which comprised age, gender, and underlying health conditions, given their recognized impact on delirium and physical performance as supported by existing literature. The bootstrap approach involved 5000 resampling iterations to analyze the mediating effects of nutritional status and CRP on the relationship between physical performance and delirium. A mediating effect was considered statistically significant if zero was not included in the 95% confidence interval.

Results

Baseline Characteristics

A total of 379 patients were included in the final analysis based on enrollment and exclusion criteria (Figure 1). The mean age of the participants was 80.0±7.4 years, with 51.7% (196) identified as male. The incidence of malnutrition among the participants was 32.4% (123). During hospitalization, 108 patients experienced delirium, resulting in an incidence rate of 28.5%. The final sample analyzed provided a statistical power of 0.85 to detect significant effects at an alpha level of 0.05, indicating a strong likelihood of identifying true effects in our analyses. Table 1 presents the

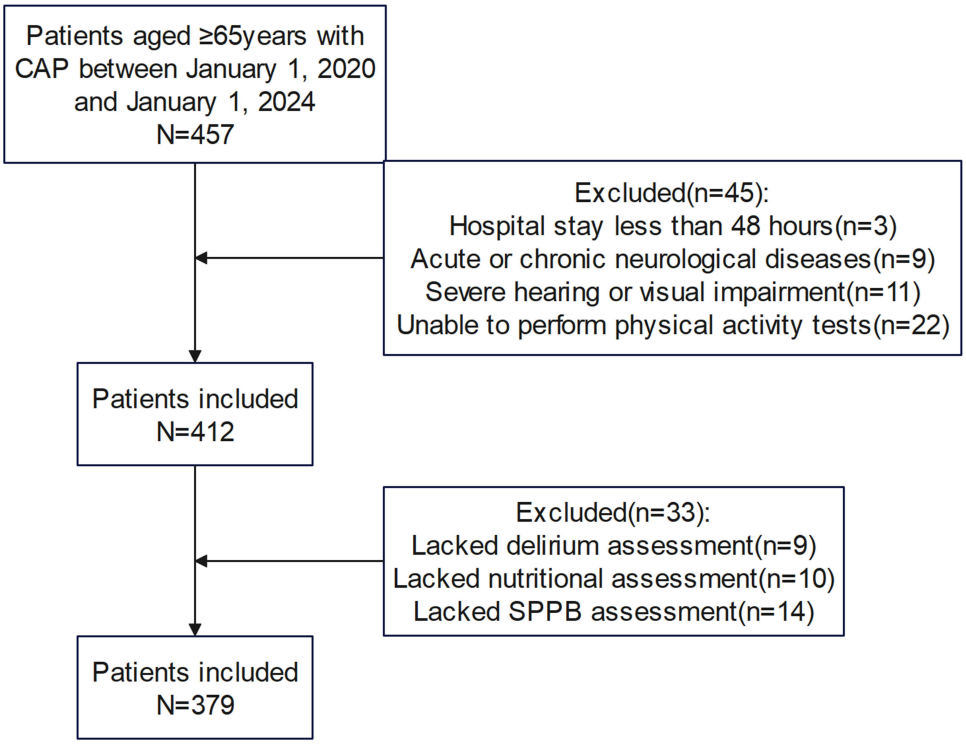

Figure 1 Flow diagram displaying the progress of all participants through the study.

characteristics based on the incidence of delirium. Patients with delirium were more likely to be older (P=0.011) and exhibited a higher incidence of malnutrition and mortality (P<0.001). Delirious patients had lower MNA-SF scores (P<0.001) and SPPB scores (P<0.001). Additionally, delirious patients had lower albumin levels (P=0.043), higher blood glucose levels (P<0.001), and higher CRP levels (P<0.001).

Correlations Among the Variables

The mean total scores of the MNA-SF and SPPB for all patients were 9.3±2.1 (range: 0–14) and 8.9±1.5 (range: 0–12), respectively. Findings from Spearman correlation analysis revealed a significant positive relationship between SPPB and MNA-SF scores (r=0.525, P<0.001), as well as a significant negative correlation between SPPB scores and CRP levels (r=−0.270, P<0.001). Additionally, a negative correlation was observed between MNA-SF scores and CRP (r=−0.374,

Table 1 Baseline Characteristics

Variables	Total (n=379)	Non-delirium Group (n=271)	Delirium Group (n=108)	P-value
Male, n (%)	196(51.7)	142(52.4)	54(50.0)	0.733
Age, mean (SD)	80.0(7.4)	79.4(7.6)	81.5(6.6)	0.011
Mortality, n (%)	42(11.1)	15(5.5)	27(25.0)	<0.001
Combined diseases				
Hypertension, n (%)	175(46.2)	129(47.6)	46(42.6)	0.425
Diabetes, n (%)	153(40.4)	105(38.8)	48(44.4)	0.354
Heart disease, n (%)	124(32.7)	87(32.1)	37(34.3)	0.717
COPD, n (%)	121(31.9)	80(29.5)	41(38.0)	0.115
Antibiotic use				
Use 2 or more antibiotics, n (%)	112(29.6)	77(28.4)	35(32.4)	0.456

(*Continued*)

Table 1 (Continued).

Variables	Total (n=379)	Non-delirium Group (n=271)	Delirium Group (n=108)	P-value
Use antibiotics for 10 days or more, n (%)	138(36.4)	93(34.3)	45(41.7)	0.194
Smoking, n (%)	131(34.6)	90(33.2)	41(38.0)	0.403
Malnutrition, n (%)	123(32.5)	62(22.9)	61(56.5)	<0.001
MNA-SF score, mean (SD)	9.28(2.1)	9.77(2.1)	8.06(1.7)	<0.001
SPPB score, mean (SD)	8.95(1.5)	9.34(1.5)	7.97(1.3)	<0.001
HR, beats/min, mean (SD)	82.62(17.9)	82.08(17.4)	83.96(19.3)	0.358
SBP, mmHg, mean (SD)	131.08(27.5)	129.84(27.9)	134.21(26.5)	0.163
DBP, mmHg, mean (SD)	75.44(15.4)	75.35(15.5)	75.67(15.4)	0.859
CRP, mg/L, median (IQR)	115.6(46.4,156.3)	80.6(37.7,145.7)	143.0(101.8,192.6)	<0.001
WBC, ×109/L, mean (SD)	12.8(3.9)	12.8(4.1)	13.0(3.5)	0.711
PLT, ×109/L, median (IQR)	160.0(130.0,218.0)	161.0(132.0,218.0)	157.0(119.0,210.0)	0.125
HB, g/L, mean (SD)	101.6(22.3)	101.1(22.7)	102.8(21.3)	0.500
TC, mmol/L, median (IQR)	4.7(3.8,5.3)	4.5(3.7,5.3)	4.8(4.0,5.6)	0.159
TG, mmol/L, median (IQR)	1.6(1.2,2.4)	1.6(1.2,2.3)	1.7(1.3,2.8)	0.169
Scr, μmmol/L, median (IQR)	73.0(55.0,117.0)	74.0(58.0,117.0)	69.0(51.8,124.8)	0.601
Alb, g/L, mean (SD)	32.3(4.1)	32.6(3.5)	31.6(5.1)	0.043
Glu, mmol/L, mean (SD)	8.7(2.4)	8.27(2.1)	9.62(2.8)	<0.001

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; MNA-SF, Mini Nutritional Assessment Scale-Short Form; SPPB, Short Physical Performance Battery; HR, Heart Rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; CRP, C-Reactive Protein; TC, Total Cholesterol; TG, Triglyceride; Scr, Serum Creatinine; WBC, White Blood Cell; PLT, Platelet; HB, Hemoglobin; Alb, Albumin; Glu, Glucose; SD, Standard Deviation; IQR, Interquartile Range.

P<0.001). Significant differences in blood glucose levels between the non-delirium and delirium groups are presented in Table 1. Consequently, a correlation analysis was conducted for the diabetes subgroup. Among the patients without diabetes mellitus (n=226), the mean MNA-SF and SPPB scores were 9.4±2.2 and 9.0±1.5, respectively. In contrast, patients with diabetes mellitus (n=153) had mean scores of 9.2±2.0 and 9.0±1.5, respectively. Subgroup analyses based on diabetes status consistently demonstrated significant correlations among physical performance, nutritional status, and CRP (P<0.001), as shown in Table 2.

Table 2 Correlations Among the Variables

Variables	Mean (SD)	SPPB	MNA-SF	CRP
Total (n=379)				
SPPB Score	8.9(1.5)	NA		
MNA-SF Score	9.3(2.1)	0.525**	NA	
CRP	119.3(91.4)	−0.270**	−0.374**	NA
Non-DM group (n=226)				
SPPB Score	9.0(1.5)	NA		
MNA-SF Score	9.4(2.2)	0.506**	NA	
CRP	112.9(88.4)	−0.292**	−0.370**	NA
DM group (n=153)				
SPPB Score	9.0(1.5)	NA		
MNA-SF Score	9.2(2.0)	0.512**	NA	
CRP	128.9(95.1)	−0.363**	−0.446**	NA

Note: **p<0.001.
Abbreviations: SPPB, Short Physical Performance Battery; CRP, C-Reactive Protein; MNA-SF, Mini Nutritional Assessment Scale-Short Form; DM, Diabetes Mellitus.

Binary Logistic Regression Analysis

Logistic regression analysis was performed to assess the impact of SPPB score, CRP and nutritional status on the likelihood of delirium in elderly patients with CAP. Three models were established. Model 1 demonstrated that CRP is a significant risk factor for delirium (OR=1.007, 95% CI: 1.004–1.010, P<0.05). In contrast, both the MNA-SF and SPPB scores showed significant negative associations with delirium (OR=0.827, 95% CI: 0.714–0.958; OR=0.588, 95% CI: 0.475–0.729, P<0.05). Model 2 indicated that CRP remained significantly positively associated with delirium (P<0.05), while both MNA-SF and SPPB scores continued to exhibit negative associations (OR=0.843, 95% CI: 0.725–0.981; OR=0.577, 95% CI: 0.462–0.720, P<0.05). Additionally, age was positively associated with delirium (P < 0.05). Model 3, which included further adjustments, revealed that CRP maintained a positive association with delirium, while the MNA-SF and SPPB scores consistently demonstrated negative correlations with delirium risk after these adjustments (OR = 0.852, 95% CI: 0.730–0.995; OR = 0.580, 95% CI: 0.464–0.727, P < 0.05). Furthermore, age was significantly positively associated with delirium (P < 0.05) (Table 3).

Simple Mediation Analyses

The simple mediation model revealed that the nutritional status mediated the relationship between SPPB and delirium, with an indirect effect of −0.194 (95% CI: −0.301 to −0.098), accounting for 27.02% of the total effect. Similarly, CRP mediated the relationship between SPPB and delirium, with an indirect effect of −0.123 (95% CI: −0.193 to −0.069), accounting for 16.10% of the total effect. We conducted a subgroup analysis based on diabetes status. In patients without diabetes mellitus, nutritional status mediated the relationship between SPPB and delirium, resulting in an indirect effect of −0.200 (95% CI: −0.346 to −0.081), accounting for 24.94% of the total effect. The indirect effect of CRP mediating SPPB on delirium was −0.141(95% CI:-0.244 to −0.069), accounting for 16.85% of the total effect. In patients with diabetes mellitus, nutritional status also mediated the relationship between SPPB and delirium, with an indirect effect of −0.189 (95% CI: −0.384 to −0.027), accounting for 30.05% of the total effect. The indirect effect of CRP mediating SPPB on delirium in this group was −0.100 (95% CI: −0.223 to −0.027), which accounted for 14.68% of the total effect. The 95% confidence interval from the bootstrap analysis did not include zero, indicating a significant mediation effect. Figure 2 illustrates nutritional status or CRP as mediators in the relationship between physical performance and delirium.

Multiple Mediation Analyses

In the multiple mediation analyses, adjustments were made for potential confounding variables. To ensure the accuracy of our results, we included the following confounding variables, including age, gender, and underlying health conditions. Figure 2

Table 3 Regression Analyses Across Different Models

Model	Hosmer-Lemeshow Test p-value	Variables	β	P-value	OR	95% CI Lower	95% CI Upper
Model 1	0.226	CRP	0.007	<0.001	1.007	1.004	1.010
		SPPB Score	−0.531	<0.001	0.588	0.475	0.729
		MNASF Score	−0.190	0.012	0.827	0.713	0.958
Model 2	0.366	CRP	0.008	<0.001	1.008	1.004	1.011
		SPPB Score	−0.550	<0.001	0.577	0.462	0.720
		MNASF Score	−0.171	0.027	0.843	0.725	0.981
		Age	0.051	0.005	1.052	1.016	1.090
Model 3	0.389	CRP	0.007	<0.001	1.007	1.004	1.010
		SPPB Score	−0.544	<0.001	0.580	0.464	0.727
		MNASF Score	−0.160	0.043	0.852	0.730	0.995
		Age	0.047	0.009	1.048	1.012	1.086

Notes: Model 1: without adjusting for confounders; Model 2: adjusted for age and gender; Model 3: further adjusted for variables that demonstrated statistically significant differences in Table 1, including Albumin and Glucose.
Abbreviations: SPPB, Short Physical Performance Battery; CRP, C-Reactive Protein; OR, Odds Ratio; CI, Confidence Interval.

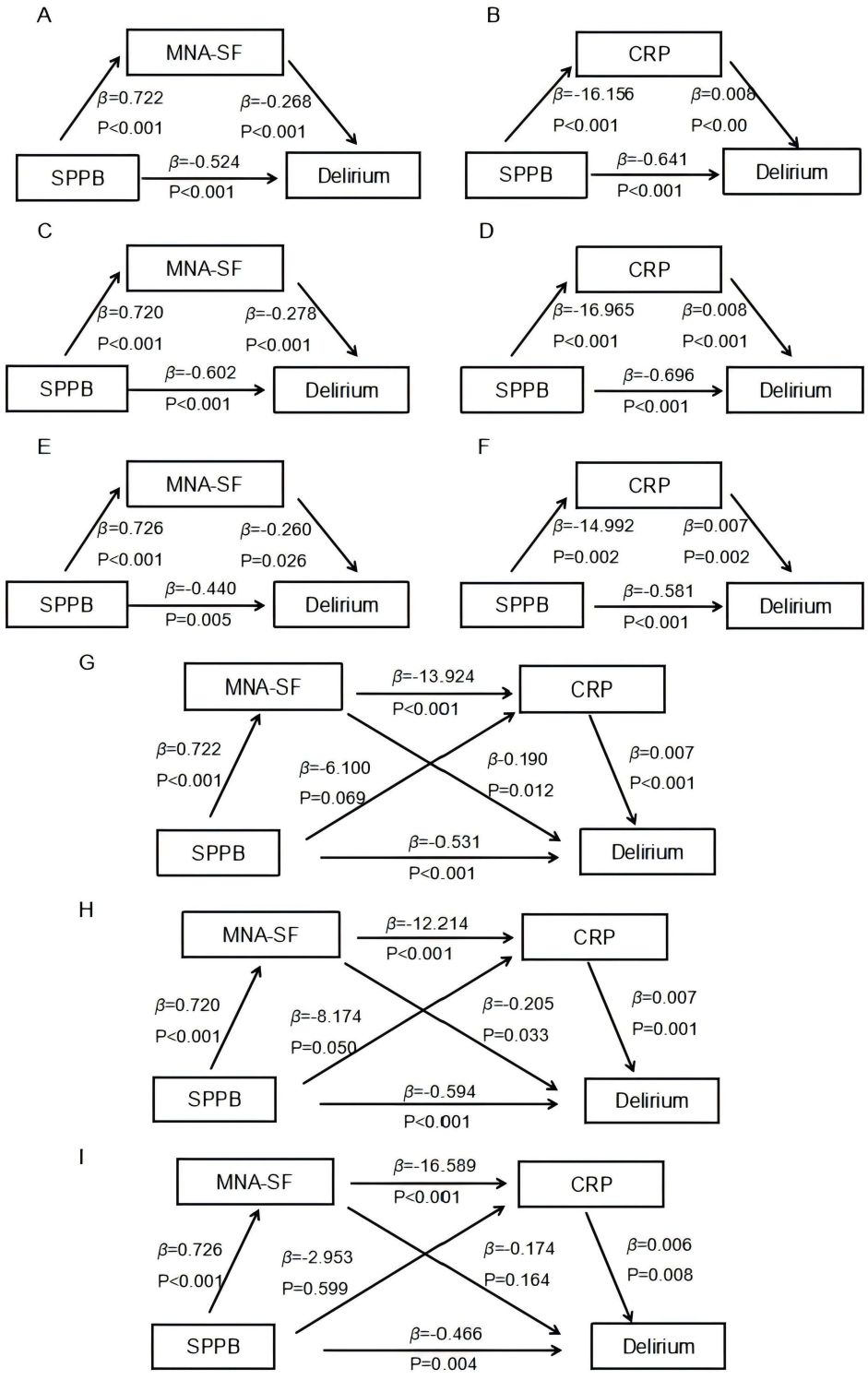

Figure 2 Simple and multiple mediation analyses.
Note: mediation analysis includes all patients (**A** and **B**); patients without diabetes (**C** and **D**); patients with diabetes (**E** and **F**); multiple mediation analysis of all patients (**G**); multiple mediation analysis of patients without diabetes (**H**); multiple mediation analysis of patients with diabetes (**I**).
Abbreviations: SPPB, Short Physical Performance Battery; CRP, C-Reactive Protein; MNA-SF, Mini Nutritional Assessment Scale-Short Form.

presents the results of the effects of nutritional status and CRP on the relationship between physical performance and delirium. Table 4 indicates that the total indirect effect was −0.245 (95% CI: −0.368 to −0.144), suggesting that physical performance serves as a protective factor against delirium, highlighting a partial mediating effect. The mediating effects of the pathways

Table 4 Indirect Effects of Physical Performance on Delirium Through C-Reactive Protein and Nutritional Status

Effect	Coefficients	SE	95% CI
Total indirect effect	−0.245	0.057	−0.368 to −0.144
SPPB→MNA-SF→delirium	−0.137	0.055	−0.251 to −0.035
SPPB→CRP→delirium	−0.041	0.022	−0.087 to −0.004
SPPB→MNA-SF→CRP→delirium	−0.067	0.020	−0.112 to −0.035
Non-DM group			
Total indirect effect	−0.272	0.077	−0.446 to −0.143
SPPB→MNA-SF→delirium	−0.147	0.072	−0.305 to −0.022
SPPB→CRP→delirium	−0.060	0.030	−0.128 to −0.013
SPPB→MNA-SF→CRP→delirium	−0.065	0.027	−0.124 to −0.022
DM group			
Total indirect effect	−0.213	0.097	−0.424 to −0.040
SPPB→MNA-SF→delirium	−0.126	0.095	−0.327 to 0.061
SPPB→CRP→delirium	−0.017	0.038	−0.100 to 0.054
SPPB→MNA-SF→CRP→delirium	−0.070	0.035	−0.153 to −0.020

Abbreviations: SPPB, Short Physical Performance Battery; CRP, C-Reactive Protein; MNA-SF, Mini Nutritional Assessment Scale-Short Form; DM, Diabetes Mellitus.

"SPPB→MNA-SF→CRP→delirium", "SPPB→MNA-SF→delirium", and "SPPB→CRP→delirium" were −0.067 (95% CI: −0.112 to −0.035), −0.137 (95% CI: −0.251 to −0.035), and −0.041 (95% CI: −0.087 to −0.004), respectively. Subgroup analyses based on the presence or absence of diabetes mellitus revealed a total indirect effect of −0.272 (95% CI: −0.446 to −0.143) in patients without diabetes mellitus, indicating significant mediating effects in the pathways "SPPB→MNA-SF→delirium", "SPPB→CRP→delirium", and "SPPB→MNA-SF→CRP→delirium". In patients with diabetes mellitus, the total indirect effect was −0.213 (95% CI: −0.424 to −0.040), showing no significant mediating effects in the pathways "SPPB→MNA-SF→delirium" and "SPPB→CRP→delirium". However, the pathway "SPPB→MNA-SF→CRP→delirium", exhibited a significant mediation effect, as indicated by the bootstrap 95% CI not containing zero (Table 4).

Discussion

This study investigated the multiple mediation effects of nutritional status and C-reactive protein on the association between physical performance and delirium in elderly individuals diagnosed with community-acquired pneumonia. The results indicated noteworthy associations among these variables, particularly in patients without diabetes.

Correlation Between Physical Performance and Delirium

One out of every three elderly inpatients aged 70 or older, admitted to general internal medicine wards, exhibits symptoms of delirium.[21] The CAM is a clinically recommended assessment tool that primarily evaluates the following areas: acute onset, fluctuating course, inattention, disorganized thinking, and altered level of consciousness. Its diagnostic accuracy reaches up to 95%, demonstrating high sensitivity and specificity.[22,23]

Frailty is commonly observed in older adults and manifests as reduced physical strength, endurance, and overall physiological function. Recent perspectives suggest that frailty indicates increased vulnerability to stressful occurrences and is linked to unfavorable outcomes among patients.[24] Decreased physical function heightens the likelihood of adverse events, such as hospitalization, falls, disability and death. The Short Physical Performance Battery (SPPB) has been scientifically validated for assessing physical function in elderly individuals residing in communities, demonstrating strong reliability, validity, and response rate.[25] The overall SPPB score ranges from 0 to 12 points, with higher scores indicating superior physical function. A total SPPB score below 10 serves as a predictor of all-cause mortality in the elderly. Additionally, the SPPB can effectively function as a screening tool.[26] The Asian Working Group for Sarcopenia

(AWGS) defines a decline in physical function as an SPPB score of ≤9 points or a time of ≥12 seconds to stand up five times, while the European Working Group on Sarcopenia in Older People (EWGSOP) defines a decline with an SPPB score of ≤8 points.[27,28] Gait speed is a fundamental indicator of health and functionality during aging and disease. Veronese et al found that slow gait speed and low SPPB scores are significant predictors of mortality in the elderly.[29] Patients with poor physical function are more likely to experience delirium during hospitalization. Furthermore, individuals who undergo delirium frequently experience a decline in their physical function, even after their recovery.[30] Numerous studies have verified that reduced SPPB scores are associated with an elevated risk of delirium. Rao et al discovered that elderly patients undergoing aortic valve replacement surgery face an increased risk of delirium as their SPPB scores decrease: scores of 10–12 (28.2%), 7–9 (34.5%), 4–6 (37.5%), and 0–3 (44.1%).[31] Otsuka R et al, on the other hand, observed that preoperative low physical function in cardiovascular surgery patients is not influenced by age but does serve as a risk factor for postoperative delirium onset.[32] Zhang XM et al's study revealed that asthenia increases the likelihood of delirium by 2.96 times, emphasizing the importance of appropriate intervention to control asthenia and potentially reduce adverse clinical outcomes in hospitalized patients.[33] Additionally, Sugi T et al's findings indicate that elderly patients undergoing gastrointestinal surgery with an SPPB score ≤9 are at higher risk for postoperative delirium.[34] Lastly, Lee SY et al's research highlights how frailty significantly raises the chances of experiencing delirium/cognitive impairment among individuals with DKD.[35] Furthermore, recent studies have shown that the prognostic nutritional index (PNI) can effectively predict outcomes in patients with CAP, indicating that nutritional status is a critical factor in managing these patients.[36] Our findings correlate well with the results, demonstrating the relevance of our study's objectives.

In line with these findings, our study further validates the correlation between physical functioning and delirium (OR=4.575, 95% CI: 2.367 to 8.842). There is a growing body of evidence suggesting that reversing the adverse outcomes associated with delirium is challenging, including declines in both physical and cognitive abilities, as well as increased rates of hospital readmission and mortality. Currently, the underlying mechanism of delirium remains unclear, and there appears to be insufficient clinical recognition of this condition. Moreover, there is a lack of standardized and effective treatment approaches available. Therefore, investigating the risk factors and pathophysiological changes involved in the onset and progression of delirium among elderly patients remains a key focus in clinical practice.[3] This hypothesis suggests that poor physical performance may serve as a potentially modifiable risk factor for delirium in elderly individuals diagnosed with CAP.

Nutritional Status and CRP as Mediators

The C-reactive protein (CRP) serves as a highly responsive indicator of infection and inflammation, with clinical research confirming its significant prognostic value in the diagnosis and stratification of sepsis, bacteremia, and infection.[37] Previous investigations have suggested that the inflammatory response plays a central role in the occurrence and progression of delirium. The release of cytokines through the blood-brain barrier can activate microglia to release pro-inflammatory cytokines, leading to brain inflammation, neuronal damage, and disruption of neurotransmitter synthesis. The inflammatory response caused by cytokine release is believed to be a key factor in cognitive impairment associated with delirium.[12,38] The Global Leadership on Malnutrition Initiative (GLIM) Working Group has outlined five criteria to diagnose malnutrition: unintentional weight loss, low body mass index, decreased muscle mass, reduced food intake or absorption capacity, and disease burden/inflammation.[39] The Mini Nutritional Assessment Scale-Short Form (MNA-SF) is a concise tool comprising of only six items that exhibit strong correlations: ① Recent weight loss, ② BMI, ③ acute illness or stress, ④ activity level, ⑤ mental state, and ⑥ independent eating. This scale can be easily administered to elderly patients.[40] Moreover, a recent study utilizing machine learning identified three immune phenotypes that can aid in risk stratification and prognosis in patients with CAP, further emphasizing the importance of understanding the immune response in this context.[41] The nutritional status and inflammatory response of individuals play crucial roles in the progression of the disease.[42] Imbalance in inflammation and malnutrition are factors that increase the likelihood of delirium in elderly patients diagnosed with CAP. These findings further support our conclusions that both nutritional status and inflammation play significant roles in the onset of delirium.

Recently, mediation analysis has gained popularity as a statistical method for determining the causal relationship between diseases and investigating how exposure factors impact outcomes.[43] It enables us to uncover the specific pathways or mechanisms through which exposure factors influence outcomes.[44,45] Through a series of mediation models, we have identified that nutritional status and CRP levels can serve as mediators in explaining the association between physical performance and delirium among elderly patients with CAP. This study indicates that inadequate physical performance, elevated levels of CRP, and malnutrition all significantly contribute to a higher risk of delirium in older CAP patients. Regardless of diabetes status, there is a significant positive correlation between physical performance and nutritional status, as well as a negative correlation with CRP. Additionally, there is a significant negative correlation between nutritional status and CRP. These findings are in line with the fundamental requirement to analyze the role of nutritional status and CRP in the association between poor physical performance and delirium using multiple mediation analyses. Our results suggest that the indirect effects of the "SPPB→MNA-SF→delirium" pathway account for a higher proportion in patients without diabetes. These findings suggest that nutritional status plays a greater role than CRP in mediating the association between physical performance and delirium. However, in diabetics, the mediating effects of these pathways are not significant. This suggests that physical performance may play a more pronounced role in mediating the onset of delirium through nutritional status and inflammation in elderly CAP patients, particularly those without diabetes. This provides a new approach to the pathogenesis of delirium in elderly pneumonia patients.

The inclusion of these recent studies not only reinforces our findings but also situates our research within the broader context of geriatric medicine. This highlights the significance of our work in addressing the complex interplay between physical performance, nutritional status, and cognitive health in elderly patients with CAP. By understanding these relationships, healthcare providers can better identify at-risk patients and implement targeted interventions to mitigate the risk of delirium, ultimately improving patient outcomes.

In conclusion, our study contributes to the ongoing discourse in the field by emphasizing the importance of assessing nutritional status and inflammation in elderly patients with CAP. Future research should focus on longitudinal studies to further explore these relationships and evaluate the effectiveness of nutritional and inflammatory interventions in preventing delirium.

Limitations

There are several limitations in this study. First, this study is a single-center retrospective study with a limited sample size, which cannot establish the causal relationship between physical performance and delirium. Second, only confounding factors that had a significant impact on the research results were included in this study, while other potential confounding factors were not considered. Additionally, the patients included in this study were selected from the same department, which may introduce selection bias. Future work will need to increase the sample size, perform follow-up in this population to further verify the causal relationship, and validate these findings in other populations.

Conclusion

Our study reinforces the association between physical performance and delirium in elderly patients with community-acquired pneumonia (CAP). We found that nutritional status and inflammation, particularly in patients without diabetes, mediate this relationship. These findings may enhance early screening and management strategies for delirium in this population. If validated by larger cohort studies that include additional relevant confounding factors, these novel findings could offer valuable insights for developing effective screening strategies for patients with delirium.

Ethics Approval and Consent to Participate

This study followed the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Second People's Hospital of Lianyungang (approval number 2022K040), which waived the requirement for informed consent due to the retrospective, non-interventional, and non-intrusive nature of the study.

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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 report no conflicts of interest in this work.

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