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Effect of nutritional risk on cognitive function in patients with chronic obstructive pulmonary disease

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Abstract

Objective: We aimed to clarify the cognitive function of patients with chronic obstructive pulmonary disease (COPD) and different nutritional status.

Methods: Among 95 patients with COPD in this retrospective study, we administered the Nutritional Risk Screening 2002 (NRS 2002) and Mini-Mental State Examination (MMSE). We recorded patients' clinical characteristics, comorbidities, and laboratory measurements. According to NRS 2002 scores, patients were divided into two groups: no nutritional risk with NRS 2002 < 3 ($n = 54$) and nutritional risk, with NRS 2002 ≥ 3 ($n = 41$).

Results: We found a negative correlation between NRS 2002 and MMSE scores in participants with COPD ($r = -0.313$). Patients with nutritional risk were more likely to be cognitively impaired than those with no nutritional risk. Multivariate logistic regression analysis indicated that malnutrition was an independent risk factor for cognitive impairment, after adjusting for confounders (odds ratio [OR] = 4.120, 95% confidence interval [CI]: 1.072–15.837). We found a similar association between NRS 2002 and MMSE scores at 90-day follow-up using a Pearson's correlation test ($r = -0.493$) and logistic regression analysis (OR = 7.333, 95% CI: 1.114–48.264).

Conclusions: Patients with COPD at nutritional risk are more likely to have cognitive impairment.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and restricted airflow, usually associated with considerable exposure to harmful particles or gases, resulting in airway and/or alveolar abnormalities. As the disease progresses, ventilatory dysfunction causes the retention of oxygen and carbon dioxide, varying degrees of hypoxemia and hypercapnia, and eventually respiratory failure. It is now widely recognized that COPD comorbidities aggravate the progression of disease and reduce patients' quality of life[1,2] and can lead to the development of cognitive impairment.[3,4] Hypoxemia, serum clusterin levels, depression, and anxiety are associated with cognitive impairment in patients with COPD.[5,6] However, the mechanism of cognitive decline and its related factors have not been rigorously studied.[7]

Recent studies have reported that malnutrition plays an important role in cognitive impairment.[8] Several studies have shown that there is a relationship between nutrition and cognition in some diseases, such as Alzheimer disease and Parkinson disease.[9,10] However, data remain scarce regarding whether malnutrition contributes to the decline in cognition among patients with COPD. In this paper, we examined the association between nutritional risk and cognitive function in patients with COPD.

Methods

Participants

Between February 2018 and February 2019, we performed a retrospective study among patients with COPD from the respiratory ward of the Third Affiliated Hospital of Wenzhou Medical University. The inclusion criteria were patients with a diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria and who consented to voluntarily participate in the study.[11] Exclusion criteria were: 1) neurological and psychotic disorders, such as psychosis or epilepsy,[12] 2) cerebral tumor, trauma, or craniotomy,[13] 3) cerebral hemorrhage, cerebral infarction, or other brain diseases, 4) cancer or pulmonary fibrosis,[12] 5) and Mini-Mental State Examination (MMSE) and Nutritional Risk Screening 2002 (NRS 2002) evaluations could not be completed or were completed with outliers.

This study was approved by the Institutional Ethics Committee review board of the Third Affiliated Hospital of Wenzhou Medical University and was conducted in accordance with the principles of the Declaration of Helsinki. The Ethics Committee approval number was YJ20170015, and the date of approval was November 24, 2017. All patient details were deidentified. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for observational studies.[14]

Data collection

Information on age, sex, body mass index (BMI), education level, smoking and drinking habits, duration of disease, and comorbidities were recorded at hospital admission. Blood samples were collected and used to analyze blood routine parameters, blood biochemistry, and arterial blood gas. Laboratory findings at hospital admission were recorded: force expiratory volume in 1 second (FEV_1), FEV_1 related to the predicted value ($FEV_1\%$), and GOLD stage. After providing their informed consent, patients completed all measures, including the BMI, airflow obstruction, dyspnea and exercise capacity (BODE) index; a COPD assessment test (CAT), the Hospital Anxiety and Depression Scale (HAD), Pittsburgh Sleep Quality Index (PSQI), Morse Fall Scale (MFS), MMSE, and NRS 2002. Patients were evaluated upon hospital admission by the study investigators, who also followed up with participants after 3 months.

Diagnostic criteria

Patients were categorized into severity grades I to IV using spirometry (GOLD I: $FEV_1 \geq 80\%$ predicted; GOLD II: $50\% \leq FEV_1 < 80\%$ predicted; GOLD III: $30\% \leq FEV_1 < 50\%$ predicted; GOLD IV: $FEV_1 < 30\%$ predicted).[15]

We measured the cognitive function of patients with COPD using the MMSE, which is one of the most commonly used standardized tools for assessing cognitive function. The total score of this test is 30 points. Scores of 0 to 26 points indicate cognitive impairment, and scores of 27 to 30 points indicate normal cognitive function.[16,17]

The nutritional status of patients with COPD was evaluated using the NRS 2002. The main purpose of the NRS 2002 is to identify patients who may benefit from nutritional intervention. The NRS 2002 includes three parts: disease status, nutritional status, and age. Scores of 0 to 2 points indicate no nutritional risk whereas scores of 3 to 7 indicate that a nutritional risk exists.[18,19]

Statistical analyses

All statistical analyses were performed using IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Differences between the two groups were analyzed using the chi-square test for categorical variables and the independent samples *t*-test for continuous variables. Subgroup analysis was performed using the chi-square test. The relationship between MMSE and NRS scores was evaluated with the Pearson's correlation test. To identify those variables associated with cognitive impairment, data were initially evaluated using univariate logistic regression analysis. To explain the contribution of nutritional risk to cognitive impairment, multivariable models were constructed for multivariate logistic regression analysis, controlling for confounders including age, sex, duration of disease, education, smoking history, albumin, and MFS scores. Statistical significance was set to $P < 0.05$.

Results

Baseline characteristics of study participants

Among 95 patients with COPD (80 male patients), mean age was 69.94 (SD 8.34) years; 42 (44.21%) were cognitively impaired and 53 (55.79%) were cognitively intact, according to MMSE scores. As for nutritional status assessed using the NRS 2002, 41 participants (43.16%) were at risk of malnutrition and 54 (56.84%) were well nourished.

Based on NRS 2002 scores, the 95 participants were divided into two groups, the group with a risk of malnutrition (NRS 2002 score ≥ 3) and the well-nourished group (NRS 2002 score < 3). Between the two groups, there were no statistical differences in terms of age, sex, education, smoking, drinking, duration of disease, white blood cells, red blood cells (RBC), hemoglobin, platelets, high-density lipoprotein, and results of the CAT, partial pressure of oxygen in arterial blood (PO_2), HAD(A), HAD(D), PSQI, and MFS. However, the values of BMI, albumin, triglycerides, total cholesterol, and low-density lipoprotein, FEV_1, and $FEV_1\%$ of patients with a risk of malnutrition were significantly lower than those of the group with no nutritional risk ($P < 0.001$, $P < 0.001$, $P = 0.001$, $P = 0.025$, $P = 0.010$, $P < 0.001$, and $P < 0.001$, respectively). In contrast, BODE indexes were significantly higher in patients with a nutritional risk ($P < 0.001$). Moreover, there were significantly more patients with GOLD stages I or II and normal cognitive function ($P = 0.015$, $P = 0.042$, respectively) in the well-nourished group (Table 1).

Association between nutritional risk and cognitive function

NRS 2002 scores were found to have a negative correlation with MMSE scores in our participants (Pearson $r = -0.313$, $P = 0.002$; Figure 1a).

As shown in Figure 2a, fewer patients had normal cognition in the group at risk of malnutrition (43.90%) than the well-nourished group (64.81%, $P = 0.042$). We performed subgroup analysis to examine the association between nutritional risk and cognitive function according to sex, duration of disease, and level of education. A higher percentage of cognitively impaired patients in the malnutrition risk group was observed in male participants ($P = 0.028$) or those with longer duration of disease (≥ 5 years, $P = 0.005$) and with higher education levels ($P = 0.019$). However, in female participants or those with shorter duration of disease (< 5 years) and less or no education, there was no significant association between cognitive function and nutritional status (Figure 2b, c, d).

Patients with nutritional risk and cognitive impairment

To gain a deeper understanding of the relationship between a risk of malnutrition and cognitive impairment, we performed univariate and multivariate logistic regression analyses. Based on univariate analysis, risk of malnutrition ($P = 0.044$), age ($P = 0.006$), sex ($P = 0.002$), education ($P < 0.001$), smoking ($P = 0.019$), albumin ($P = 0.032$), and MFS scores ($P = 0.033$) were all found to be significantly correlated with cognitive impairment in patients with COPD (Table 2).

Based on multivariate analysis, we found that malnutrition risk was independently and significantly associated with cognitive impairment. In model 1, relative to well-nourished patients, those who were at risk of malnutrition were significantly more likely to be cognitively impaired (odds ratio [OR] = 2.354, 95% confidence interval [CI]: 1.024–5.409, $P = 0.044$). After adjusting for age, sex, and duration of disease (model 2), the association between nutritional risk and cognitive impairment remained significant, with OR 3.472 (95% CI: 1.283–9.394, $P = 0.014$). Subsequent adjustment for age, sex, duration of disease, education, smoking history, albumin, and MFS scores (model 3) increased the OR to 4.120 (95% CI: 1.072–15.837, $P = 0.039$). These results indicate that malnutrition risk is an independent risk factor of cognitive impairment, and patients with COPD who are at risk of malnutrition are

Table 1. Characteristics of patients with COPD, according to nutritional status.

Variable	Well nourished ($N = 54$)	Risk of malnutrition ($N = 41$)	*P* value
Age (years)	70.83 ± 8.82	68.76 ± 7.59	0.231
Sex (male), *n* (%)	46 (85.19%)	34 (82.93%)	0.765
BMI (kg/m^2)	23.65 ± 2.40	17.86 ± 1.36	<0.001
Education (educated), *n* (%)	39 (72.22%)	27 (65.85%)	0.504
Smoking *n* (%)	42 (77.78%)	33 (82.50%)	0.573
Drinking *n* (%)	26 (49.06%)	17 (43.59%)	0.604
Duration of disease (<5 years), *n* (%)	22 (40.74%)	13 (31.71%)	0.366
WBC ($\times 10^9$/L)	7.75 ± 3.58	6.95 ± 2.70	0.248
RBC ($\times 10^{12}$/L)	4.36 ± 0.45	4.24 ± 0.51	0.255
Hemoglobin (g/L)	132.15 ± 15.40	128.16 ± 15.28	0.225
Platelets ($\times 10^9$/L)	227.78 ± 81.02	217.82 ± 72.34	0.547
Albumin (g/L)	37.14 ± 3.05	34.38 ± 3.87	<0.001
Triglycerides (mmol/L)	1.21 ± 0.59	0.87 ± 0.37	0.001
TC (mmol/L)	4.39 ± 0.83	4.00 ± 0.71	0.025
LDL (mmol/L)	2.76 ± 0.76	2.36 ± 0.64	0.010
HDL (mmol/L)	1.04 ± 0.26	1.14 ± 0.27	0.076
BODE	2.76 ± 1.90	5.18 ± 2.42	<0.001
GOLD I or II, *n* (%)	18 (35.29%)	5 (12.82%)	0.015
CAT	16.69 ± 5.58	18.95 ± 6.34	0.068
PO_2	71.63 ± 10.74	73.38 ± 19.01	0.604
FEV_1	1.09 ± 0.43	0.77 ± 0.33	<0.001
FEV_1%	44.60 ± 13.11	31.52 ± 12.81	<0.001
HAD(A)	1.46 ± 2.43	1.41 ± 2.40	0.923
HAD(D)	3.30 ± 2.73	3.37 ± 3.48	0.913
PSQI	7.40 ± 4.31	7.27 ± 4.02	0.883
MFS	40.38 ± 17.73	45.13 ± 17.34	0.200
Cognitive function (normal), *n* (%)	35 (64.81%)	18 (43.90%)	0.042

COPD, chronic obstructive pulmonary disease; BMI, body mass index; WBC, white blood cells; RBC, red blood cells; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BODE, BMI, airflow obstruction, dyspnea and exercise capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAT, COPD assessment test; FEV_1, forced expiratory volume in 1 second; FEV_1%, FEV_1 related to predicted value; HAD(A) and HAD(D), Hospital Anxiety and Depression scales; PSQI, Pittsburgh Sleep Quality Index; MFS, Morse Fall Scale.

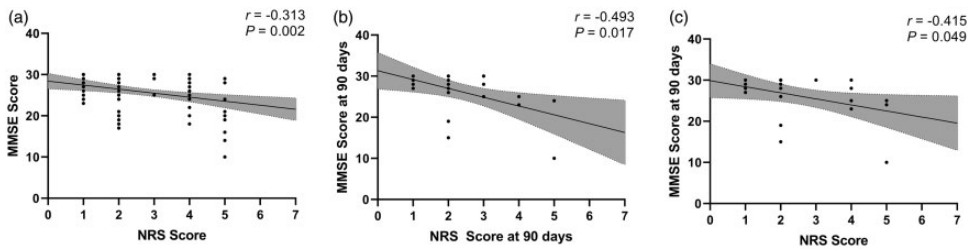

Figure 1. Correlation analyses between NRS 2002 and MMSE scores. (a) Correlation between NRS and MMSE scores at hospital admission, $P = 0.002$; (b) Correlation between NRS and MMSE scores at 90 days of follow-up, $P = 0.017$; (c) Correlation between NRS score at hospital admission and MMSE score at 90 days, $P = 0.049$.
NRS 2002, Nutritional Risk Screening 2002; MMSE, Mini-Mental State Examination.

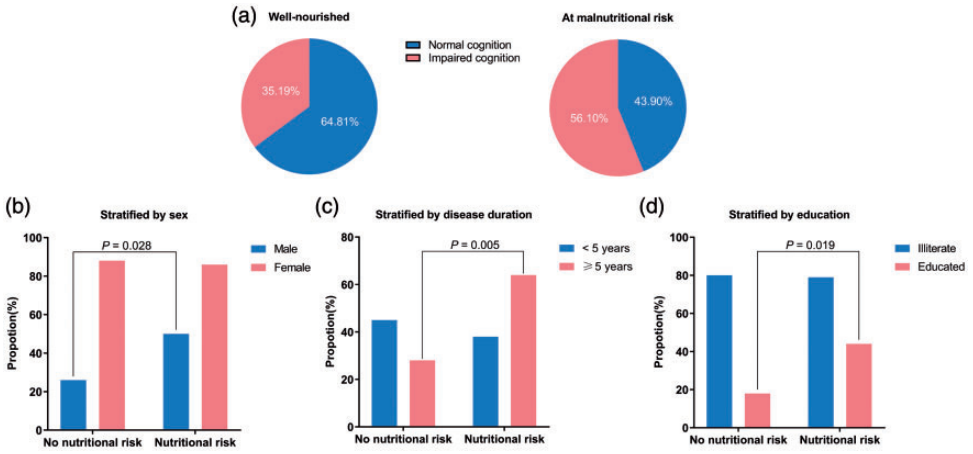

Figure 2. Impaired cognition in patients with COPD with different nutritional status in subgroup analyses. (a) Cognitive function in patients with COPD with different nutritional status. (b) Stratified by sex. (c) Stratified by disease duration. (d) Stratified by education.
COPD, chronic obstructive pulmonary disease.

more likely to have cognitive impairment (Table 3).

Results in follow-up

To clarify the relationship between malnutrition risk and cognitive impairment over a long period, 23 patients with COPD were followed up for 90 days. We found a similar association between NRS 2002 and MMSE scores at 90 days of follow-up using a correlation test (Pearson $r = -0.493$, $P = 0.017$; Figure 1b) and logistic regression analysis (OR = 7.333, 95% CI: 1.114–48.264, $P = 0.038$; Table 4). We also performed a correlation analysis of NRS 2002 scores at hospital admission and MMSE scores at 90 days (Pearson $r = -0.415$, $P = 0.049$; Figure 1c), which suggested the predictive power of NRS 2002 scores for MMSE scores over a long period.

Discussion

COPD is a progressive disease with a succession of comorbidities. Cognitive impairment as well as nutritional problems are considered frequent comorbidities owing to their high prevalence. López-Torres et al.[12] reported the 48% of patients with COPD had impaired cognitive function according to the Montreal Cognitive Assessment. Parallel results were found by Schure et al.,[20] with a proportion of nearly 30%, and by Yohannes et al.[4] with 32%. Other studies have found a similarly high prevalence of malnutrition, ranging from 17% to 20%.[21,22] Several researchers have focused on this high incidence of cognitive impairment and malnutrition among these patients, and some progress has been made regarding evidence of the relationship between nutritional risk and cognitive function. Metabolic causes may facilitate cognitive dysfunction in patients with diabetes, Alzheimer disease, and epilepsy.[23–25] However, few studies have focused on the association between nutritional risk and cognitive function in patients with COPD.

Our research revealed a robust correlation between nutritional status and cognitive function in patients with COPD, especially in male individuals, patients with higher education levels, and those

Table 2. Univariate logistic regression analyses of factors in cognitive function.

Variables	OR	95% CI	*P* value
Age	1.082	1.023–1.143	0.006
Sex, male	0.087	0.018–0.415	0.002
BMI	0.942	0.838–1.060	0.320
Educated	0.105	0.037–0.300	<0.001
No smoking	3.637	1.242–10.651	0.019
No drinking	2.158	0.923–5.043	0.076
Duration of disease <5 years	0.917	0.395–2.125	0.839
WBC	0.996	0.875–1.133	0.952
RBC	0.516	0.208–1.281	0.154
Hemoglobin	0.977	0.949–1.005	0.101
Platelets	1.005	0.999–1.010	0.116
Albumin	0.868	0.762–0.988	0.032
Triglycerides	0.819	0.369–1.814	0.622
TC	0.810	0.479–1.371	0.432
LDL	0.694	0.386–1.248	0.222
HDL	1.827	0.382–8.741	0.451
BODE	1.080	0.908–1.284	0.387
GOLD I or II	1.071	0.412–2.789	0.888
CAT	1.023	0.956–1.096	0.508
PO_2	0.970	0.940–1.001	0.061
FEV_1	0.423	0.140–1.274	0.126
FEV_1%	1.002	0.973–1.032	0.878
HAD (A)	1.018	0.860–1.205	0.834
HAD (D)	1.137	0.990–1.307	0.070
PSQI	0.968	0.876–1.069	0.516
MFS	1.028	1.002–1.054	0.033
Malnutrition risk	2.354	1.024–5.409	0.044

OR, odds ratio; CI, confidence interval; BMI, body mass index; WBC, white blood cells; RBC, red blood cells; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BODE, BMI, airflow obstruction, dyspnea and exercise capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FEV_1%, FEV_1 related to predicted value; HAD(A) and HAD(D), Hospital Anxiety and Depression scales; PSQI, Pittsburgh Sleep Quality Index; MFS, Morse Fall Scale.

Table 3. Adjusted ORs (95% CIs) for cognitive function.

	OR	95% CI	*P* value
Model 1	2.354	1.024–5.409	0.044
Model 2	3.472	1.283–9.394	0.014
Model 3	4.120	1.072–15.837	0.039

Model 1 is univariate analysis. Model 2 is adjusted for age, sex, and duration of disease. Model 3 is adjusted for age, sex, duration of disease, education, smoking history, albumin, and MFS scores.
OR, odds ratio; CI, confidence interval.

with a longer duration of disease. In multivariate logistic regression analysis, after taking into account covariates such as age, sex, duration of disease, education, smoking history, albumin, and MFS scores, we observed that NRS 2002 scores were independently associated with MMSE scores and patients with COPD with a nutritional risk were more likely to have cognitive impairment. Analogous results were found in an older Taiwanese population with hip fracture.[26]

Table 4. Univariate logistic regression analysis of nutritional status for cognitive function of follow-up.

	Univariate logistic regression		
Variable	OR	95% CI	*P* value
Malnutrition risk	7.333	1.114–48.264	0.038

OR, odds ratio; CI, confidence interval.

Previous findings regarding the potential mechanism underlying how malnutrition influences cognitive function provided a basis for our findings, including the following. 1) Protein insufficiency. Albumin is a useful biochemical indicator of malnutrition.[27] Thus, malnutrition signifies a lower level of serum albumin. Xu et al.[28] deemed that a protein-rich dietary pattern was significantly associated with higher cognitive global scores and verbal memory scores. We obtained similar findings in our study; patients with COPD at risk of malnutrition had a lower level of albumin, and albumin was positively correlated with cognitive function (Table 2). 2) Micronutrient deficiency. According to a scoping review, selected micronutrients in adequate doses, including omega-3 fatty acids, potassium, and vitamins B6, B12, C, D, and E might play an ancillary role in improving cognitive function in older people.[29] 3) Inflammation. Bourassa and Sbarra[30] argued that systemic inflammation is one biologically plausible mechanism through which body mass might influence cognitive function in aging adults. 4) Glucose supply. The vast majority of energy used by brain cells comes from blood glucose, which is involved in the transfer of energy from foods to neurons fundamental to the control of brain function.[31,32]

In our study, during follow-up, we still observed a link between nutritional risk and cognitive function, which implied that malnutrition contributes to cognitive impairment over a long period.

As far as we know, the present study is the first to identify an association between nutritional risk as evaluated by the NRS 2002, and cognitive function as evaluated by the MMSE, in patients with COPD. Although the detailed mechanisms behind this relationship remain to be elucidated, several potential mechanisms of pathogenesis have been suggested. Our research findings may help to guide clinical practice in the future. Nutritional intervention should be performed in randomized controlled trials, to verify its effect in improving cognitive impairment among patients with COPD.

There are some limitations in this study. Most of our study findings are based on the results of questionnaires, which may include information bias. Some patients may have problems with recall owing to poor memory, which would introduce bias in the results of scales based on self-assessment. Only 23 patients were followed up, which is a relatively small cohort and may lead to overrating or underestimation of the association between nutritional risk and cognitive function over time.

Conclusion

Patients with COPD at nutritional risk are more likely to have cognitive impairment. Nutritional status may predict cognitive function in patients with COPD to some extent; however, further studies are needed for confirmation. Specific and detailed evaluation of nutritional status are an

important stage in the assessment of older patients with COPD, to prevent the onset of cognitive impairment.

Quick Look

Current knowledge

A host of studies have proved the important role of nutritional status in cognitive function in many diseases, such as Alzheimer disease and Parkinson disease. However, the relationship between nutritional status and cognitive function in patients with COPD has not been clarified.

What this paper contributes to our knowledge

NRS 2002 scores had a negative correlation with MMSE scores in patients with COPD. Participants with COPD at nutritional risk were more likely to have cognitive impairment, especially male patients, those with longer duration of disease ($\geq$5 years), and those with higher education levels. Malnutrition risk was an independent risk factor for cognitive impairment in patients with COPD, after adjusting for several confounders. A similar association between NRS 2002 and MMSE scores was also found at 90 days of follow-up.

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Authors' contributions

YH and XZ formulated the research question and designed the study. XC, CL, HM, and RZ collected the data. XM, FF, JW, and KD organized the data. JM analyzed the data. JM, BJ, and NY wrote and reviewed the manuscript. All authors read and approved the final manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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