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Analysis of related factors of malnutrition in patients with chronic obstructive pulmonary disease and changes in blood routine parameters with *Ajuga ciliata* Bunge

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Abstract: Chronic obstructive pulmonary disease (COPD), currently one of the most common chronic lung diseases in clinical practice, is the third leading cause of death globally, after ischemic heart disease and stroke. In this study, we analyzed the factors related to malnutrition in chronic obstructive pulmonary disease and found that long-term smoking, body mass index, fasting plasma glucose, and total cholesterol were all independent risk factors. This suggests that in future clinical treatment of chronic obstructive pulmonary disease, attention should be paid to these indicators to prevent malnutrition ($P<0.05$). *Ajuga ciliata* Bunge is one of the drugs commonly used in traditional Chinese medicine for the adjuvant treatment of lung inflammation and sore throat. We found that the addition of *Ajuga ciliata* Bunge to the treatment of COPD can effectively improve the inflammatory response of patients. Meanwhile, the improvement of inflammatory response was more significant in COPD patients who were malnourished among them ($P<0.05$). In addition, the incidence of adverse reactions with *Ajuga ciliata* Bunge was low and improved the patients' treatment satisfaction. These results suggest that *Ajuga ciliata* Bunge has an important application in the treatment of COPD in the future.

Keywords: *Ajuga ciliata* Bunge, analysis of relevant factors, chronic obstructive pulmonary disease, malnutrition

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is still one of the most common chronic lung diseases in clinical practice, especially in the elderly population, with clinical manifestations such as expectoration, dyspnea, and chest tightness [1]. World epidemiological statistics show that the incidence rate of COPD among adults over 20 years of age is about 8.6%, with an increasing prevalence with age, reaching 27.4% at the age of 60 [2]. At present, there are over 100 million cases of COPD in China alone, with approximately 1 million patients ultimately dying from COPD each year [3]. COPD has been defined as the third leading cause of death globally, after ischemic heart disease and stroke [4]. Therefore, the diagnosis and treatment of COPD must be taken seriously by clinical practice.

COPD is a chronic wasting disease that not only affects the lungs, but also causes systemic adverse reactions in patients, which in turn increases energy consumption, hinders digestion and absorption, and leads to malnutrition [5]. Malnutrition may increase the risk of readmission and death and is a main cause of poor prognosis. Therefore, a deep understanding of the related factors of malnutrition in COPD and timely formulation and adoption of targeted intervention measures are of great significance in ensuring the prognosis of COPD patients. However, there are few relevant reports so far.

On the other hand, traditional Chinese medicine (TCM) rehabilitation treatment is becoming increasingly common in clinical practice. For COPD, various types of TCM therapies have begun to receive clinical attention due to their stable effects and excellent safety [6]. Among them, *Ajuga ciliata* Bunge is a perennial herb of Ajuga decumbens Thunb. (*Labiatae*), whose main chemical constituents include flavonoids, triterpenoids and phenolic acids [7]. In China, *Ajuga ciliata* Bunge is very common in clinical practice and has shown excellent application in diabetes mellitus hypertension and helps to improve the progression of lung cancer [8-11]. Studies have shown that *Ajuga ciliata* Bunge is an excellent anti-inflammatory agent used in the treatment of various inflammatory conditions, including COPD [12]. However, its clinical effect in treating COPD remains elusive.

Therefore, this study will provide a reference for future prevention and development of treatment strategies by analyzing the related factors affecting malnutrition in COPD patients. Meanwhile, further observation will be conducted on the therapeutic effect of *Ajuga ciliata* Bunge on COPD to confirm its future application value

MATERIAL AND METHODS

Research participants

This study selected 70 COPD patients admitted to The Affiliated Chuzhou Hospital of Anhui Medical University from January, 2019 to January, 2024, who were divided into a malnourished research group (n=31) and a well-

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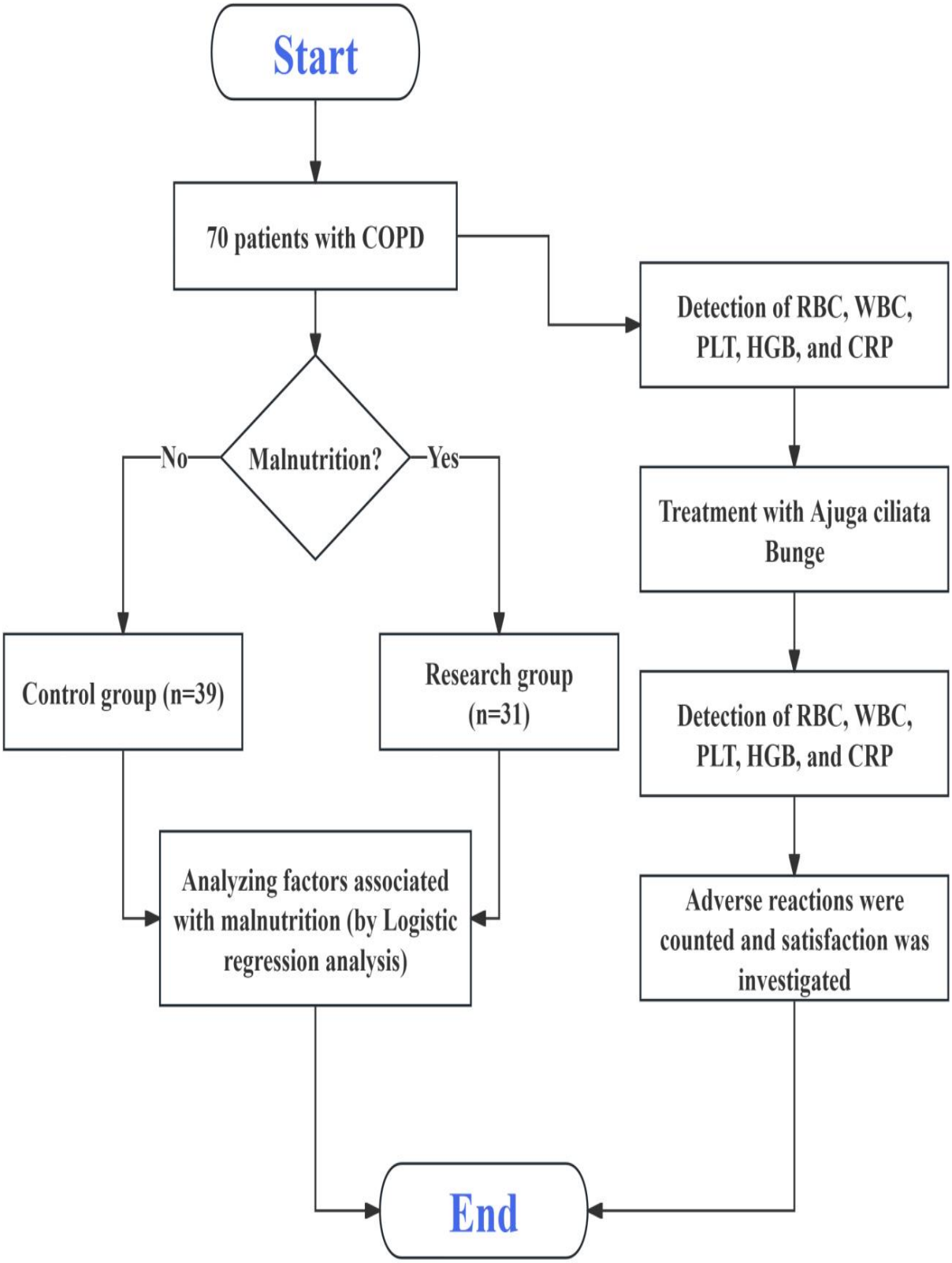

Fig. 1: Flow chart of this study

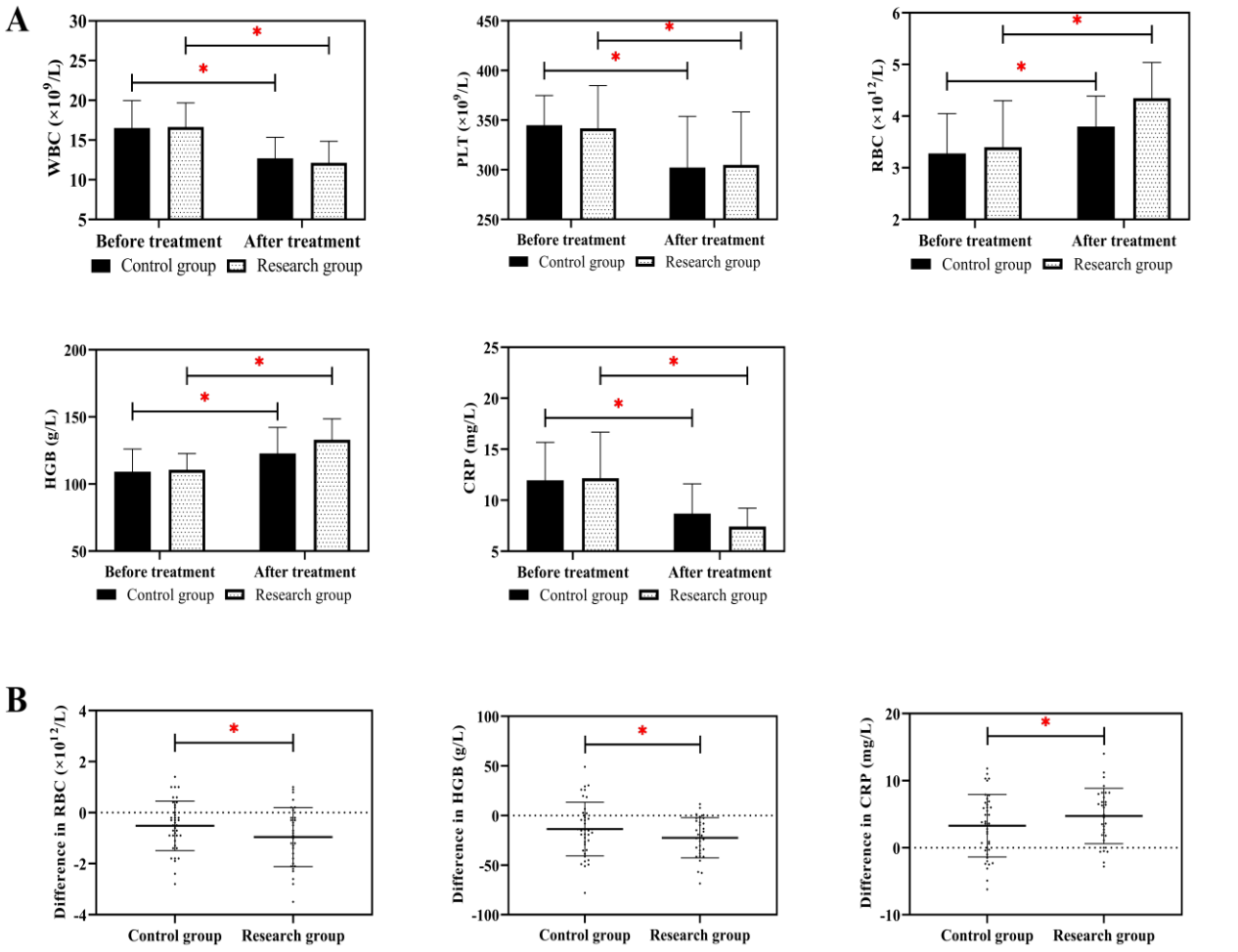

Fig. 2: Changes in blood routine after treatment with Ajuga ciliata Bunge. A) Comparison of RBC, WBC, PLT, HGB, and CRP. B) Comparison of differences in RBC, HGB, and CRP. * means P<0.05. Red blood cell, RBC; White blood cell, WBC; Platelet, PLT; Hemoglobin, HGB; C-reactive protein, CRP.

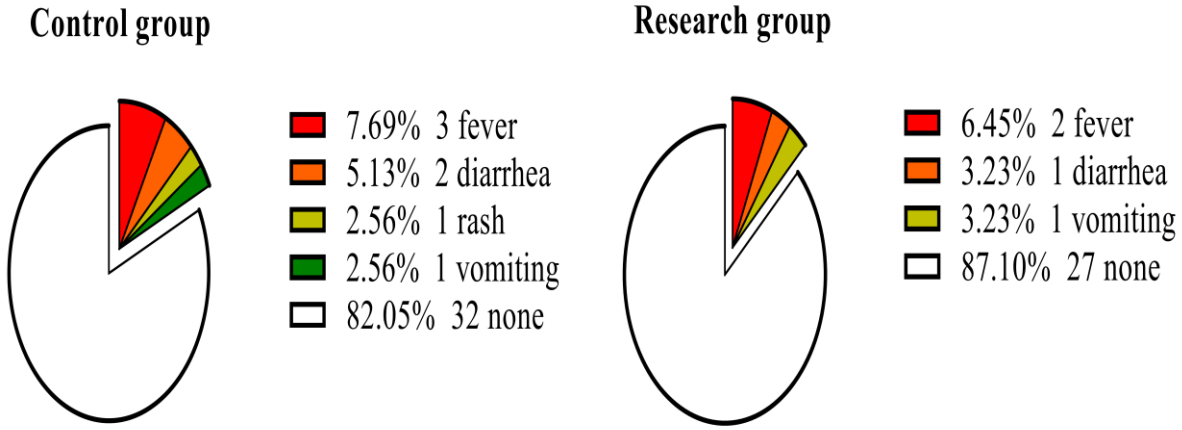

Fig. 3: Therapeutic safety of *Ajuga ciliata* Bunge

investigation results of the Nutrition Risk Screening (NRS 2002) [13]. In addition, both groups were treated with *Ajuga ciliata* Bunge. The Affiliated Chuzhou Hospital of Anhui Medical University's Ethics Committee ratified the study (No. 2019022), and the *Declaration of Helsinki* was strictly followed throughout the research. All the subjects signed an informed consent form.

Eligibility and exclusion criteria

Inclusion criteria: The included patients met the diagnostic guidelines for COPD and volunteered to participate in this study, with complete general information, clinical records, and follow-up data but no having psychiatric disorders or communication barrier. Age > 60 years and duration of COPD > 5 years. Exclusion criteria: Patients with bronchial asthma, malignancies, liver and kidney dysfunction, metabolic abnormalities (such as hyperthyroidism and diabetes mellitus), or surgical procedures in the past 1 month were excluded [14].

Malnutrition determination

At admission, the patients were investigated with a questionnaire designed by our hospital for their age, gender, course of disease, smoking status, etc. Trained professionals gave unified guidance to the patients on how to fill in the questionnaire and explained the matters needing attention. A total of 70 questionnaires were distributed, which were filled out by patients themselves under the supervision of investigators, and then recovered on the spot. All the questionnaires were recovered, with an effective recovery rate of 100%. In addition, patients all completed routine examinations after admission, such as blood sugar, and blood lipid tests. Patients' general information, clinical records, and follow-up data were sorted out, and the height, weight, and body mass index (BMI) were measured. Besides, a nutritional status assessment was carried out by referring to the NRS2002: (1) an age over 70 years was recorded as 1 point. (2) Normal nutritional status was scored 0 points; losing 5% of body weight within 3 months or consuming 50-75% of normal food intake was given 1 point; a 5% decrease in body weight within 2 months or consumption of 25-50% of normal food intake in the previous week was recorded as 2 points; a 5% reduction in body weight within one month, having a BMI<18.5kg/m^2, or consuming 0-25% of normal food intake in the previous week was given 3 points. (3) Hospitalization due to complications without the need for bed rest was scored 1 point; a score of 2 points was given if there was a need for bed rest; 3 points would be given if there is a need for mechanical ventilation support with increased protein requirements that cannot be compensated for by parenteral or enteral nutritional support. An overall score of ≥ 3 was judged to be malnourished and < 3 was considered well-nourished [15].

Treatment methods

All patients were treated with *Ajuga ciliata* Bunge capsule (Huangshan Tianmu Pharmaceutical Co., Ltd., Z34020366): packing specification: 0.45g×24 capsules. 3 capsules/times, 3 times/d, continued treatment for 1 week.

Endpoints

The related factors affecting malnutrition in COPD patients were analyzed. In addition, patients' fasting venous blood was collected before and after treatment with *Ajuga ciliata* Bunge. Red blood cell (RBC), white blood cell (WBC), and platelet (PLT) counts, as well as hemoglobin (HGB) and C-reactive protein (CRP) levels, were detected by a blood cell analyzer, and the differences in blood routine indexes before and after treatment were compared (Fig. 1).

STATISTICAL ANALYSIS

SPSS24.0 software was used for statistical analysis. Count data were represented by [n (%)], and Chi-square tests were used for comparisons between groups. Measurement data were expressed as ($\bar{\chi} \pm s$), and the inter-group and intra-group comparisons employed independent sample t-tests and paired t-tests, respectively. Logistic regression analysis was used to analyze related factors. Results were considered statistically significant when P<0.05.

RESULTS

Univariate analysis of malnutrition in COPD patients

By comparison, we found that the two groups were similar in gender, routine blood test (P>0.05). However, the BMI, fasting plasma glucose (FPG), and total cholesterol (TC) were all in the research group compared with the control group (P<0.05), suggesting that the above indicators as potential factors affecting malnutrition in COPD patients (Table 1).

Multivariate analysis of malnutrition in COPD patients

After assigning the above indicators with statistical differences (Table 2) as independent variables and taking the nutritional status of patients as a dependent variable, a Logistic regression analysis was conducted. The results showed that live alone was not an independent risk factor for malnutrition in COPD, but long-term smoking, BMI, FPG and TC were independent factors influencing malnutrition in COPD (P<0.05) (Table 3).

***Changes in blood routine after treatment with Ajuga ciliata* Bunge**

In both groups, WBC, PLT, and CRP decreased after treatment, while RBC and HGB increased (P<0.05). Comparin g the difference before and after treatment in the two groups, it can be seen that the difference in WBC and PLT was not statistically significant between groups (P>0 .05), but the difference in CRP, HGB, and RBC was greater in the research group compared with the control group (P<0.05) (Fig. 2).

***Therapeutic safety of Ajuga ciliata* Bunge**

According to statistics, both groups of patients developed adverse reactions such as fever and diarrhea during the treatment, with an incidence of 17.95% in the research group and 12.90% in the control group, showing no statistical difference (P>0.05) (Fig. 3).

Treatment satisfaction survey

Finally, the survey results of patients' satisfaction showed that the treatment satisfaction of the research group was 93.55%, and the difference was not statistically significant when compared with the treatment satisfaction of 87.18% in the control group (P>0.05) (Table 4).

DISCUSSION

In recent years, research on COPD, a respiratory disease with high morbidity and mortality among the elderly, has focused on the influence of the disease on patients' lung function [16, 17]. With the deepening of research, it has been found that the nutritional risk is prevalent in COPD, especially for elderly people with weak digestive function, with the presence of malnutrition being a direct determinant of their prognosis and recovery status [18]. COPD, as an irreversible chronic progressive disease, not only causes lung damage, but also leads to systemic adverse reactions, which further increase the body's energy consumption, trigger digestive and absorption dysfunction, and ultimately lead to malnutrition [19]. Malnutrition can exert a negative impact on the treatment of patients, hinder disease recovery, increase hospital stay and medical expenses, and even cause serious adverse consequences such as systemic inflammation and death [20]. Therefore, understanding the nutritional status of elderly COPD patients, identifying influencing factors, and proposing relevant prevention and treatment measures are of great significance for improving patient prognosis.

This study included a total of 70 COPD patients, of which 31 (44.29%) cases were malnourished, which was consistent with the epidemiological investigation results of COPD, indicating that the current nutritional status of COPD patients is not optimistic. However, a survey by Christensen et al. found that the risk of malnutrition in COPD is only 10-20%, which is significantly lower than the results of this study [21, 22]. We believe that this may be related to differences in patients' region. Through Logistic regression analysis, we found that long-term smoking, BMI, FPG, and TC were independent risk factors for malnutrition in COPD patients. The reasons are as follows: (1) In addition to increased energy consumption due to the influence of the disease, elderly COPD patients are often accompanied by tooth loss, decreased taste, and weakened chewing and swallowing abilities, which reduces appetite, affects gastrointestinal digestion and absorption, and causes insufficient nutrition intake,

Table 1: Univariate analysis of malnutrition in COPD patients

Factors	Control group (n=39)	Research group (n=31)	t (χ^2)	P
Age	69.72±3.89	69.87±5.13	0.142	0.888
BMI (kg/m^2)	20.75±1.67	22.61±2.51	3.713	<0.001
Gender			0.148	0.700
male	26 (66.67%)	22 (70.97%)		
female	13 (33.33%)	9 (29.03%)		
Course of disease (years)	6.97±0.84	6.97±1.30	0.026	0.980
Long-term smoking			5.247	0.022
yes	17 (43.59%)	22 (70.97%)		
no	22 (56.41%)	9 (29.03%)		
Alcohol consumption			1.110	0.292
yes	14 (35.90%)	15 (48.39%)		
no	25 (64.10%)	16 (51.61%)		
WBC (×10^9/L)	12.34±2.79	12.49±.57	0.266	0.791
RBC (×10^{12}/L)	3.28±0.77	3.40±0.90	0.575	0.567
PLT (×10^9/L)	344.89±29.80	341.67±43.11	0.369	0.713
HGB (g/L)	109.24±16.76	110.50±12.23	0.351	0.726
CRP (mg/L)	16.56±3.63	17.75±4.18	0.205	0.838
FPG (mmol/L)	5.29±1.59	6.46±1.32	3.300	0.002
TC (mmol/L)	4.46±0.99	5.11±1.28	2.395	0.019
Live alone			5.440	0.020
yes	13 (33.33%)	19 (61.29%)		
no	26 (66.67%)	12 (38.71%)		

resulting in energy imbalance and the inability to meet the body's needs in the long run, and ultimately leading to malnutrition [23]. (2) Long-term smoking can exacerbate chronic airway inflammation, intensify endothelial inflammation, damage endothelial function, accelerate skeletal muscle cell consumption, promote skeletal muscle cell apoptosis, and hinder muscle cell synthesis, thus increasing protein decomposition and muscle atrophy, leading to malnutrition and even cachexia [24]. (3) With the prolongation of the course of COPD and the increasing severity of the disease, the degree of lung damage is aggravated, the difficulty of clinical treatment is increased, and the negative impact of the disease on the nutritional status of patients is increased. Some patients also have comorbidities such as cardiovascular disease and osteoporosis, and the degree of systemic adverse reactions in patients increases with digestive and absorption dysfunction, leading to an increased risk of malnutrition [25]. (4) BMI is an important indicator commonly used internationally to measure human health, with a low BMI indicating excessive weight loss and malnutrition in patients [26]. As the condition of COPD worsens, energy expenditure also increases. Respiratory muscles constantly consume nutrients, including glycogen, stored locally in the muscles, fat, and amino acids supplied by the blood circulation, to change the muscle fiber structure. Patients with better lung function can better meet the oxygen consumption demand of respiratory muscles, so elderly COPD patients with better lung function have better nutritional status [27]. (5) Indicators such as FPG and TC are biomarkers that reflect the overall metabolic status of blood glucose and blood lipids, with their correlation with nutritional status verified many times [28, 29].

On the other hand, *Ajuga ciliata* Bunge is an excellent TCM for regulating lung function, with functions such as detoxifying, cooling blood, and reducing swelling [30]. As indicated by TCM pharmacology research, *Ajuga ciliata* Bunge contains flavonoids, triterpenoid saponins, and polysaccharides that possess certain anti-inflammatory effects, which can be used clinically to alleviate joint pain, swelling, and other symptoms, relieve muscle soreness, and inhibit the synthesis and release of prostaglandins, thus achieving the purpose of pain relief [31]. In this study, we observed that after treatment with *Ajuga ciliata* Bunge, both groups showed reduced WBC, PLT, and CRP as well as elevated RBC and HGB, which shows that *Ajuga ciliata* Bunge also has excellent anti-inflammatory, effects in COPD. Besides, the difference in CRP, HGB, and RBC before and after treatment was more significant in the

Table 2: Table of Assignments

Factors	Assignments
Nutritional states	Good = 1, poor = 2
Course of disease (years)	Unassigned
Long-term smoking	No = 1, yes = 2
FPG (mmol/L)	Unassigned
TC (mmol/L)	Unassigned
Live alone	No = 1, yes = 2

Table 3: Multivariate analysis of malnutrition in COPD patients

Factors	Regression coefficient	Standard error	Wald χ^2	P	Odds ratio	95% confidence interval
BMI	1.064	0.342	9.934	0.002	2.765	1.415-5.268
Long-term smoking	0.846	0.216	17.665	0.000	2.226	1.641-3.716
FPG	1.264	0.441	8.971	0.003	2.762	1.634-5.264
TC	1.134	0.542	4.632	0.035	3.106	1.070-8.996
Live alone	0.764	0.451	2.642	0.094	2.144	1.642-3.716

Table 4: Treatment satisfaction survey

Groups	Very satisfied	Satisfied	Dissatisfied	Total satisfaction
Control group (n=39)	12 (30.77%)	22 (56.41%)	5 (12.82%)	87.18%
Research group (n=31)	18 (58.06%)	11 (35.48%)	2 (6.45%)	93.55%
χ^2				0.778
P				0.378

research group compared to the control group, suggesting the more potent anti-inflammatory effect of *Ajuga ciliata* Bunge on malnourished patients. This is because *Ajuga ciliata* Bunge is rich in crude fiber, crude protein, vitamins, dietary fiber, carotene, iron, calcium, and other nutrients, which play a good role in maintaining human health [32-34].Therefore, the use of it can promote the recovery of nutritional status in patients with malnutrition, thereby exerting a more significant effect on symptom improvement. There was no notable inter-group difference in the incidence of adverse reactions, which emphasized the excellent safety profile of *Ajuga ciliata* Bunge. Moreover, the high treatment satisfaction of the two groups of patients once again confirms the future clinical use of *Ajuga ciliata* Bunge.

However, due to the small number of cases, the results of this study may be accidental, which requires the inclusion of more cases for validation. In addition, it is necessary to further confirm the therapeutic effect of *Ajuga ciliata* Bunge on COPD by setting up a control group using conventional treatment schemes to compare differences in inflammatory factors, nutritional proteins, and other indicators.

CONCLUSION

To sum up, long-term smoking, BMI, and FPG are independent factors affecting malnutrition in COPD patients. In the future clinical treatment of COPD patients, we should focus on the the above indicators and implement targeted interventions to prevent malnutrition. Moreover, *Ajuga ciliata* Bunge may be an excellent treatment scheme for COPD, as it has more significant anti-inflammatory and rehabilitation-promoting effects on COPD patients with malnutritioned COPD patients.

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