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Original Article

Role of lymphoid immune factors in COPD patients complicated with pulmonary infection

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Abstract: Objective: The aim of this study was to explore the role of lymphoid immune factors and their relationship with BODE index in chronic obstructive pulmonary disease (COPD) patients complicated with pulmonary infection. Method: One hundred and ninety-four patients with COPD, who were treated in our hospital, were selected as the study subjects. Among them, 81 cases were complicated with pulmonary infection (group A) and 113 cases were without pulmonary infection (group B). Another 55 healthy subjects were selected as controls (group C). The levels of T lymphocyte subsets ($CD3^+$, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$) in peripheral blood were detected by flow cytometry. The correlation between T lymphocyte subsets and BODE index was analyzed by Spearman's test. Receiver operating characteristic (ROC) curves were used to analyze the diagnostic value of T lymphocyte subsets in patients with COPD complicated with pulmonary infection. Logistic regression analysis was used to analyze the risk factors for COPD complicated with pulmonary infection. Results: The levels of $CD3^+$, CD4, and $CD4^+/CD8^+$ cells in the peripheral blood of group A and group B subjects were significantly lower than in group C subjects ($P < 0.001$). The levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ in the peripheral blood of group A subjects were significantly lower than those in group B subjects ($P < 0.05$). There were no significant difference in the peripheral blood $CD8^+$ cell levels between groups A, B, and C ($P > 0.05$). The levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ cells in the peripheral blood were negatively correlated with the BODE index ($P < 0.001$), while $CD8^+$ cells levels were not associated with BODE index grading ($P > 0.05$). The sensitivity of peripheral blood $CD3^+$ cell levels for the diagnosis of COPD was 72.57% and the specificity was 65.43%, with an optimal cut-off value of 59.05. The sensitivity of peripheral blood $CD4^+$ cell levels for the diagnosis of COPD was 60.40% and the specificity was 77.78%, with an optimal cut-off value of 29.74. The sensitivity of peripheral blood $CD4^+/CD8^+$ cell levels for the diagnosis of COPD was 51.68% and the specificity was 81.73%, with an optimal cut-off value of 1.45. Smoking history, nutritional status, and $CD4^+/CD8^+$ cell levels were independent risk factors for COPD patients complicated with pulmonary infection ($P < 0.05$). Conclusion: T lymphocyte subsets in COPD patients complicated with pulmonary infection are unbalanced, and patients' immune function is low. $CD4^+/CD8^+$ cell imbalance is an independent risk factor for COPD complicated with pulmonary infection. $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ cell levels are associated with the BODE index and T lymphocyte subsets may be predictors of disease assessment and prognosis for COPD patients complicated with pulmonary infection.

Keywords: BODE index, chronic obstructive pulmonary disease, lymphoid immune factors, pulmonary infection, T lymphocyte subsets

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic lung disease, with airflow limitation and progressive development in middle-aged and elderly individuals [1]. In recent years, increasing clinical research on COPD has helped define its characteristics of high incidence and high disability [2]. Pulmonary function progressively degenerates in COPD patients, which leads to a continuous decline in the ability for physical activity and the quality of life. In addition, COPD can cause a series of complications that pose a great threat to the patient's quality of life [3]. Pulmonary infection is one of the most common complications of COPD. It can accelerate the progress of the disease, aggravate the impaired pulmonary function and respiratory tract damage, and make the treatment and recovery of patients more difficult [4]. At present, the pathogenesis of COPD has not been elucidated, but the release

of various inflammatory mediators and immune dysfunction play important roles in its occurrence and development [5, 6]. Studies have shown that long-term chronic inflammation can alter the immune function of COPD patients, which mainly manifests as changes in T lymphocyte subsets ($CD3^+$, $CD4^+$, and $CD8^+$) [7]. The imbalance of cellular immune function is thought to be the cause of concurrent infection in middle-aged and elderly patients. The decline in immune function can reduce the number of T lymphocytes and cause an imbalance of their subpopulations [8]. Half of COPD patients suffer from malnutrition and malignant diseases. Severe malnutrition can affect the function of lymphocytes [9]. Studies have shown that COPD with pulmonary infection is associated with smoking and malnutrition [10]. Other studies have confirmed that factors such as interleukin-6, C-reactive protein, and procalcitonin are associated with pulmonary infection in patients with COPD [11, 12].

In recent years, there have been many studies on the control of COPD complicated with pulmonary infection [13, 14], but there has been little research on the role of T lymphocyte subsets in the occurrence and development of COPD.

To understand the mechanism of COPD complicated with pulmonary infection, this study examined $CD3^+$, $CD4^+$, and $CD8^+$ T lymphocyte subsets in the peripheral blood of COPD patients. The role of the T lymphocyte subset ratio in the occurrence and development of COPD complicated with pulmonary infection and its relationship with the BODE index were investigated.

Methods

One hundred and ninety-four patients with COPD, who were treated in our hospital, were selected as the study subjects. This included 118 males and 76 females. The subjects were 45-79 years old, with an average age of 61.62± 8.96 years. The length of their medical history was 10-39 years, with an average of 15.43± 5.97 years. There were 81 cases with pulmonary infection (group A) and 113 cases without pulmonary infection (group B). Subjects were included in the study if their diagnosis and treatment occurred in accordance with COPD guidelines [15] and their pulmonary infections were diagnosed by chest X-ray and bacteriological characteristics [16]. This study was approved by the ethics committee of our hospital and all subjects and their families provided signed, fully informed consent. Subjects were excluded if they had used antibiotics, anti-inflammatory drugs, or immunosuppressive drugs within the previous month; had other systemic autoimmune diseases, such as severe liver and kidney dysfunction, connective tissue diseases, or endocrine and metabolic diseases; had hematopoietic dysfunction, cardiac insufficiency, bronchiectasis, tuberculosis, rheumatic diseases, or other chronic inflammation; had other infections; or had psychiatric disorders or a family history of psychiatric disorders. An additional 55 healthy subjects were selected as the control group (group C). This group included 34 males and 21 females ranging in age from 40-61 years, with an average age of 56.62±7.16 years. No abnormalities were found upon physical examination, pulmonary ventilation function was normal, and there was no use of drugs that affect immune function in group C subjects.

Instruments and reagents

The anti-CD3-PE monoclonal antibody, anti-CD4-FITC monoclonal antibody, anti-CD8-APC monoclonal antibody were purchased from Becton Dickinson (Franklin Lakes, NJ, USA). A FACSCalibur automatic flow cytometer (Becton Dickinson) was used for flow cytometry experiments and centrifugation steps were performed using a Beckman Coulter centrifuge (Brea, CA, USA).

Sample collection and experimental procedures

On the morning after admission, 5 mL of peripheral blood was taken and placed into an EDTA anticoagulant tube. The number of T lymphocyte subsets and their ratios were determined using a FACSCalibur automatic flow cytometer. After centrifugation, the upper plasma layer was discarded and 2 mL of the supernatant suspension was added to a 10 mL centrifuge tube. After adding 8 mL of red blood cell lysate, samples were left at room temperature for 10 min and then centrifuged. The supernatant was then discarded and pellets were resuspended in 1 mL of PBS buffer. Red blood cell lysate were transferred to a 1.5 mL centrifuge tube

and after centrifugation, the upper liquid layer was discarded and 500 μL of PBS buffer was added. Aliquots of 100 μL each were then transferred to new 1.5 mL tubes. After staining, $CD3^+$, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ levels were determined by flow cytometry.

Evaluation index

Evaluation and BODE index classification was performed according to the evaluation criteria reported by Celli et al. [17]. The evaluation included measurements of body mass index (BMI), the degree of airflow obstruction, dyspnea, and motor ability. BMI was defined as the ratio of weight/height (kg/m^2) and the degree of airflow obstruction was defined as the forced expiratory volume in 1 second as a percentage of the predicted value. Dyspnea was assessed by the Modified Dyspnea Index (mMRC) and exercise capacity was assessed by a 6-minute walking distance (6MWD) test. BMI was assessed by a two-level scoring method, with either 0 points or 1 point, while the other three parameters were assessed by a four-level scoring method, with 0-3 points. The maximum possible score was 10 points, with a higher score representing a more severe disease state. BODE scoring criteria were then determined as follows: 0-2 points, grade 1; 3-4 points, grade 2; 5-6 points, grade 3; and 7-10 points, grade 4. A higher BODE index grade represented a more severe disease state.

Statistical methods

SPSS 19.0 (IBM Corp, Armonk, NY, USA) was used for statistical analyses and graphs were prepared using Prism 7 (GraphPad, San Diego, CA, USA). Data are expressed as mean ± standard deviation (SD). An independent samples t-test was used to compare data between groups. Counting data are expressed as both number and percentage [n (%)]. A Chi-square test was used to compare counting data between groups. Single-factor analysis of variance was used to compare means from multiple groups. Two-by-two comparisons were performed using a Dunnett's t-test. Correlations were analyzed by Spearman's test. Diagnostic value was determined using a receiver operating characteristic (ROC) curve. The factors affecting COPD combined with pulmonary infection were analyzed by logistic regression. $P < 0.05$ was considered statistically significant.

Results

General information for the three study groups

There were no significant differences in gender, age, or drinking history among groups A, B, and C ($P > 0.05$). COPD patients' course of disease, history of drinking, history of hypertension, history of heart failure, and history of mechanical ventilation were not associated with pulmonary infection ($P > 0.05$). However, pulmonary infection was associated with smoking history, diabetes history, respiratory failure history, hospitalization time, and nutritional status ($P < 0.05$, **Table 1**).

The levels of peripheral blood T lymphocyte subsets in the three groups

The levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ cells in the peripheral blood of group A subjects were significantly lower than those in group C subjects ($t = 3.681$, $P < 0.001$; $t = 4.584$, $P < 0.001$; $t = 4.969$, $P < 0.001$; respectively). The levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ cells in the peripheral blood of group B subjects were also significantly lower than those in group C subjects ($t = 3.449$, $P < 0.001$; $t = 2.564$, $P = 0.011$; $t = 3.599$, $P < 0.001$; respectively). Furthermore, the levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ cells in the peripheral blood of group A subjects were significantly lower than those of group B subjects ($t = 2.221$, $P = 0.026$; $t = 3.061$, $P = 0.002$; $t = 1.981$, $P = 0.049$; respectively). However, there was no significant difference in peripheral blood $CD8^+$ cell levels among groups A, B, group C ($P > 0.05$, **Table 2** and **Figure 1**).

The relationship between peripheral blood T lymphocyte subsets and BODE index classification

The BODE index for each patient was set to 1, 2, 3, or 4, as described in the "Materials and methods" section. The correlation between peripheral blood T lymphocyte subsets and BODE index grading was analyzed by Spearman's test. The results showed that peripheral blood $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ cell levels were negatively correlated with BODE index ($r = -0.400$, $P < 0.001$; $r = -0.415$, $P < 0.001$; $r = -0.443$, $P < 0.001$; respectively). However, $CD8^+$ cell levels were not associated with BODE index grading ($r = 0.114$, $P = 0.312$; **Figure 2**).

Table 1. General information of study subjects [n (%)]

Category	n	Group A (n = 81)	Group B (n = 113)	Group C (n = 55)	χ^2 value	*P* value
Gender					1.259	0.533
Male	152	53 (65.43)	65 (57.52)	34 (61.82)		
Female	97	28 (34.57)	48 (42.48)	21 (38.18)		
Age)					1.961	0.375
≤ 60	34	8 (9.88)	16 (14.16)	10 (18.18)		
> 60	215	73 (90.12)	97 (85.84)	45 (81.82)		
Course of disease (year)					0.138	0.710
< 15	124	53 (65.43)	71 (62.83)	-		
≥ 15	70	28 (34.57)	42 (37.17)	-		
History of smoking					7.297	0.026
Yes	109	45 (55.56)	43 (38.05)	21 (36.36)		
No	140	36 (44.44)	70 (61.95)	34 (63.64)		
Drinking history					1.569	0.456
Yes	96	35 (43.21)	39 (34.51)	22 (40.00)		
No	153	46 (56.79)	74 (65.49)	33 (60.00)		
History of diabetes					6.845	0.009
Yes	63	30 (37.04)	33 (45.13)	-		
No	131	51 (62.96)	80 (54.87)	-		
History of hypertension					0.260	0.610
Yes	88	35 (43.21)	53 (46.90)	-		
No	106	46 (56.79)	60 (53.10)	-		
History of heart failure						
Yes	45	20 (24.69)	25 (22.12)	-		
No	149	61 (75.31)	88 (77.88)	-		
History of respiratory failure					6.832	0.009
Yes	28	18 (22.22)	10 (8.85)	-		
No	166	63 (77.78)	103 (91.15)	-		
History of mechanical ventilation					2.532	1.591
Yes	134	61 (75.31)	73 (64.60)	-		
No	60	20 (24.69)	40 (35.40)	-		
Hospital stay					4.906	0.027
≥ 12 d	150	69 (85.19)	81 (71.68)	-		
< 12 d	44	12 (14.81)	32 (28.32)	-		
Nutritional status					3.928	0.046
Albumin ≥ 25 g	137	51 (62.96)	86 (76.11)	-		
Albumin < 25 g	57	30 (37.04)	27 (23.89)	-		

Diagnostic value of peripheral blood T lymphocyte subset levels in patients with COPD complicated with pulmonary infection

ROC curves were constructed for the use of peripheral blood $CD3^+$, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ cell levels in the diagnosis of COPD complicated with pulmonary infection. The area under the curve (AUC) for the diagnosis of COPD by $CD3^+$ cell levels in the peripheral blood was 0.723 (95% CI: 0.650-0.796), with a diagnostic sensitivity of 72.57%, a specificity of 65.43%, and an optimal cut-off value of 59.05. The AUC for the diagnosis of COPD by $CD4^+$ cell levels in the peripheral blood was 0.687 (95% CI: 0.611-0.763), with a diagnostic sensitivity of 60.40%, a specificity of 77.78%, and an optimal cut-off value of 29.74. The AUC for the diagnosis of COPD by $CD8^+$ cell levels in the peripheral blood was 0.638 (95% CI: 0.635-0.719), with a diagnostic sensitivity of 78.56%, a specificity of 53.41%, and an optimal cut-off value of 34.24.

Table 2. Comparison of peripheral blood T lymphocyte subsets among the three groups (mean ± SD)

T lymphocyte subset	Group A (n = 81)	Group B (n = 113)	Group C (n = 55)	F value	*P* value
$CD3^+$ (%)	57.13±24.49*,#	63.14±12.81*	70.19±11.61	9.387	P < 0.001
$CD4^+$ (%)	24.71±12.67*,#	29.97±11.14*	34.91±12.83	12.040	P < 0.001
$CD8^+$ (%)	32.01±12.68	33.46±12.07	34.13±10.34	0.683	0.506
$CD4^+/CD8^+$	1.02±0.78*,#	1.24±0.75*	1.68±0.73	12.620	P < 0.001

Note: *P < 0.05, compared with group C; #P < 0.05, compared with group B.

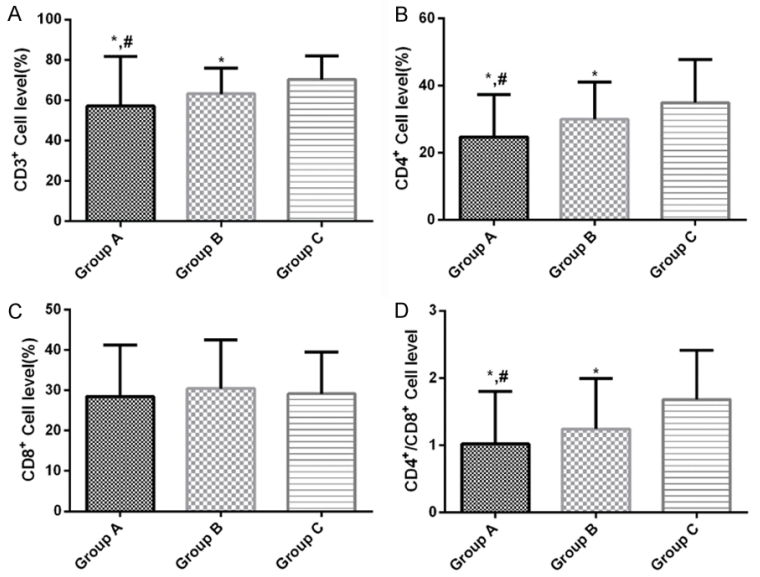

Figure 1. Comparison of peripheral blood T lymphocyte subsets among the three groups. Comparison of $CD3^+$ (A), $CD4^+$ (B), $CD8^+$ (C), and $CD4^+/CD8^+$ (D) cell levels in the peripheral blood of the three study groups. Note: *P < 0.05, compared with group C; #P < 0.05, compared with group B.

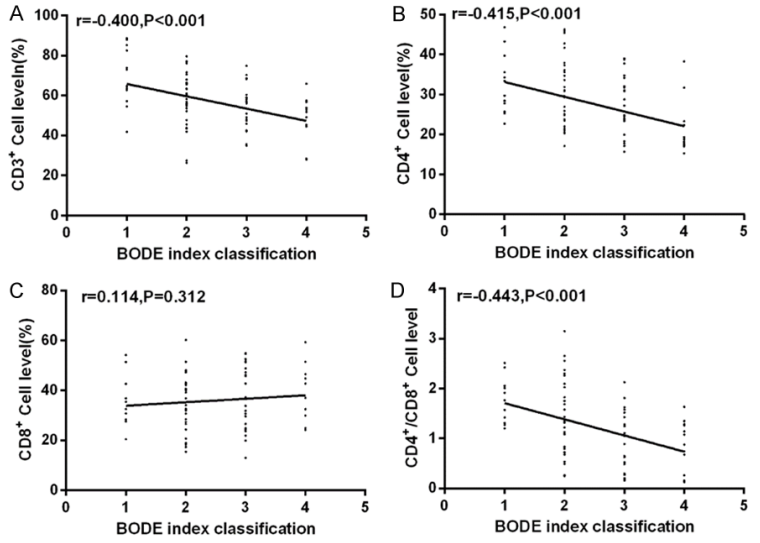

Figure 2. Relationship between peripheral blood T lymphocyte subsets and BODE index grading. The relationship between $CD3^+$ (A), $CD4^+$ (B), $CD8^+$ (C), and $CD4^+/CD8^+$ (D) cell levels in the peripheral blood of COPD patients and BODE index grading.

The AUC for the diagnosis of COPD by $CD4^+/CD8^+$ cell levels in the peripheral blood was 0.671 (95% CI: 0.594-0.749), with a diagnostic sensitivity of 51.68%, a specificity of 81.73%, and an optimal cut-off value of 1.45 (**Table 3** and **Figure 3**).

Risk factors for COPD complicated with pulmonary infection

The optimal cut-off value of peripheral blood T lymphocyte subsets for the diagnosis of COPD complicated with pulmonary infection was used as the critical value. Logistic multivariate analysis showed that smoking history, nutritional status, and $CD4^+/CD8^+$ cell levels were independent risk factors for COPD complicated with pulmonary infection (P < 0.05). However, history of diabetes or respiratory failure; length of hospital stay; and $CD3^+$, $CD4^+$, or $CD8^+$ cell levels had no association with COPD complicated with pulmonary infection (P > 0.05; **Tables 4**, **5**).

Discussion

COPD is a chronic respiratory disease with a high prevalence in humans. The high incidence and mortality in elderly and middle-aged individuals has resulted in a significant social and economic burden [18]. COPD can affect human lungs and cause systemic adverse

Table 3. Diagnostic value of peripheral blood T lymphocyte subsets in patients with COPD complicated with pulmonary infection

Diagnostic indicator	AUC	95% CI	Standard error	Cut-off	Sensitivity (%)	Specificity (%)
$CD3^+$	0.723	0.650-0.796	0.037	59.05	72.57	65.43
$CD4^+$	0.687	0.611-0.763	0.039	29.74	60.40	77.78
$CD8^+$	0.638	0.635-0.719	0.037	34.24	78.56	53.41
$CD4^+/CD8^+$	0.671	0.594-0.749	0.039	1.45	51.68	81.73

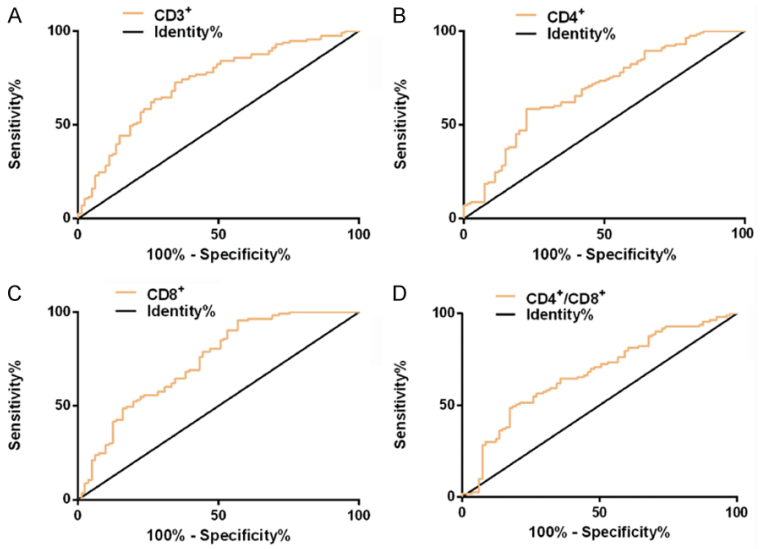

Figure 3. ROC curves of peripheral blood $CD3^+$, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ cell levels for the diagnosis of COPD with pulmonary infection. ROC curves of peripheral blood $CD3^+$ (A), $CD4^+$ (B) $CD8^+$ (C), and $CD4^+/CD8^+$ (D) cell levels for the diagnosis of COPD complicated with pulmonary infection.

Table 4. Variable assignments of logistic regression analysis

Factor	Assignment
History of smoking	Yes = 1, No = 2
History of diabetes	Yes = 1, No = 2
History of respiratory failure	Yes = 1, No = 2
Hospital stay	≥ 12 d = 1, < 12 d = 2
Nutritional status	≥ 25 g = 1, < 25 g = 2
$CD3^+$	≥ 59.05 = 1, < 59.05 = 2
$CD4^+$	≥ 29.74 = 1, < 29.74 = 2
$CD8^+$	≥ 34.24 = 1, < 34.24 = 2
$CD4^+/CD8^+$	≥ 1.45 = 1, < 1.45 = 2

reactions, including malnutrition, weight loss, and skeletal muscle dysfunction. It can also cause pulmonary infection, with inflammation, glandular hypersecretion, and bronchial mucosal edema as the main clinical features. These complications have a serious impact on the patient's quality of life [19-21].

T lymphocyte subsets are the most important cell types of the immune system and each T lymphocyte subgroup interacts with each other to maintain normal immune system function [22]. The body maintains normal humoral and cellular immune functions through T lymphocyte subsets, complement C3 and C4, and immunoglobulin [23]. Previous studies have shown that abnormal levels of T lymphocytes and their subsets and an imbalance of immune function are important factors in the pathogenesis of COPD. Abnormal levels of apoptosis of $CD3^+$, $CD4^+$, and $CD8^+$ cells in the peripheral blood of COPD patients can cause an imbalance of T lymphocyte subsets [24, 25]. Freeman et al. [26] showed that the number of $CD8^+$ cells in the lung is related to the severity of COPD. The proinflammatory cytokines and cytotoxic molecules produced by $CD8^+$ cells in the lung can cause damage to lung tissue. Wu et al. [27] found that immune dysfunction in patients with severe acute COPD is mainly manifested as a decrease in the number of $CD3^+$ and $CD4^+$ cells in the peripheral blood. Our results showed that the levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ cells in the peripheral blood of group A and B subjects were significantly decreased compared with the levels in group C subjects. The decrease in $CD3^+$ cell levels was due to a decrease in the total number of T lymphocytes, which was mainly caused by a decrease in the number of $CD4^+$ cells. Freeman et al. [28] showed that peripheral blood $CD4^+$ and $CD8^+$ cells decreased during acute exacerbation of COPD and T cells could infiltrate into the sites of inflammation or lymphoid tissue. In our study, the decrease in the number of $CD8^+$ cells was

Table 5. Logistic multivariate analysis of risk factors for COPD complicated with pulmonary infection

Variable	β	SE	Wald	*P* value	OR value	95% CI
History of smoking	1.521	0.620	6.033	0.014	4.583	1.361-14.437
History of diabetes	0.199	0.623	0.131	0.724	1.224	0.362-4.128
History of respiratory failure	0.234	0.738	0.249	0.654	1.337	0.416-4.637
Hospital stay	0.700	0.179	15.313	0.069	2.014	1.418-2.861
Nutritional status	2.483	0.531	18.597	< 0.001	5.583	2.994-21.043
$CD3^+$	0.518	0.586	0.773	0.376	1.686	0.531-5.294
$CD4^+$	1.311	0.543	1.673	0.059	2.695	0.834-4.293
$CD8^+$	0.183	0.634	0.080	0.724	1.194	0.343-4.176
$CD4^+/CD8^+$	0.718	0.363	3.920	0.047	2.114	1.005-4.138

not significantly different among the three groups, which may be related to the redistribution of $CD8^+$ cells. Pulmonary infection may be due to the combined effects of a decrease in the number of $CD4^+$ cells and $CD4^+/CD8^+$ cells. Abnormal levels of $CD3^+$ and $CD4^+/CD8^+$ cells can cause disorders of the immune system and a series of pathological changes, resulting in low overall immune function, impaired cellular immune function in COPD patients and anti-infective immunity in COPD patients.

The BODE index is considered an important index to evaluate the severity and prognosis of COPD patients. A higher score correlates with more severe disease and poorer prognosis [29]. Kumar et al. [30] showed that the BODE index can be used to assess the severity of illness, length of hospital stay, and mortality in patients with COPD. The variables included in the BODE index are simple to measure and can be easily and economically implemented. Therefore, the BODE index is a reliable evaluation method for classifying patients with COPD and making decisions on corresponding treatments to implement. There was been little research on the relationship between the BODE index and COPD immune index. Therefore, we investigated this relationship and found that levels of the peripheral blood T lymphocyte subsets, $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$, were negatively correlated with the BODE index score. This suggests that the condition and prognosis of patients with COPD complicated with pulmonary infection may be related to an imbalance of T lymphocyte subsets. The risk factors for COPD complicated with pulmonary infection are a hot topic in clinical research. Exploring the risk factors of COPD combined with pulmonary infection is of great importance for preventing infection, controlling the disease, relieving clinical symptoms, and improving the lung function of patients [31, 32]. There have been many studies on the risk factors for COPD complicated with pulmonary infection. For example, Mcgown et al. [33] showed that cigarette smoke can affect important pathogens known to cause lung infections in COPD patients. Cigarette smoke extract enhances the pathogenicity of these bacteria, thereby worsening the prognosis of patients with COPD. Yang et al. [34] found that the long-term inhalation of glucocorticoids can increase the risk of upper respiratory tract infection in COPD patients. We performed a logistic regression analysis of the risk factors for pulmonary infection in COPD patients. The results showed that smoking history and nutritional status were independent risk factors for COPD with pulmonary infection, which agrees with results from previous studies. However, there have been no reports on whether T lymphocyte subsets in the peripheral blood can affect the risk of pulmonary infection. Therefore, we constructed ROC curves of COPD with pulmonary infection by peripheral blood T lymphocyte subset and selected the optimal cutoff. The results showed that $CD4^+/CD8^+$ cell level is an independent risk factor for COPD combined with pulmonary infection. Takabatake et al. [35] demonstrated that systemic cell-mediated immune function is impaired in COPD patients and this increases susceptibility to acute respiratory infections. It may be that the imbalance of $CD4^+/CD8^+$ cell levels in COPD patients leads to immune dysfunction and increases the patient's susceptibility to pulmonary infection. Although this study confirmed that T lymphocyte subsets play an important role in COPD with pulmonary infection, there are still some limitations of the study design. First, we did not

analyze disease etiology in these patients. Secondly, we did not conduct in-depth studies of changes in T lymphocyte subsets at the aggravation stage of COPD. These limitations need to be addressed in future research, so that further evidence can be obtained to confirm the results of this study.

In summary, COPD patients with pulmonary infection have an imbalance in T lymphocyte subsets and low immune function. In particular, $CD4^+/CD8^+$ cell imbalance was an independent risk factor for COPD patients with pulmonary infection. $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ cell levels were associated with the BODE index and therefore, T lymphocyte subsets may be a predictor of disease assessment and prognosis for COPD patients with pulmonary infection.

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Disclosure of conflict of interest

None.

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