

Original Article

Auxiliary diagnostic value of $\gamma\delta$ T cell, IL-17, and IFN- γ levels in peripheral blood and bronchoalveolar lavage fluid for lung cancer complicated with chronic obstructive pulmonary disease

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Abstract: Objective: To investigate the auxiliary diagnostic value of $\gamma\delta$ T cell, interleukin-17 (IL-17), and interferon- γ (IFN- γ) levels in peripheral blood (PB) and bronchoalveolar lavage fluid (BALF) for lung cancer complicated with chronic obstructive pulmonary disease (COPD). Methods: Seventy-five patients with lung cancer, 81 patients with COPD, 52 lung cancer patients complicated with COPD, and 84 healthy subjects were selected. After PB was drawn from the above 4 groups, the levels of $\gamma\delta$ T cells and total T cells in the mononuclear cells were detected via flow cytometry, and the concentrations of IL-17 and IFN- γ in the PB were measured via enzyme-linked immunosorbent assay. Statistical analysis was performed to study the correlation between research data and clinical data. Results: Compared with normal subjects, lung cancer patients and lung cancer patients complicated with COPD had significantly higher levels of IL-17 and IFN- γ in the PB (all $P < 0.05$), but had significantly smaller $\gamma\delta$ T cell count (both $P < 0.05$), and had no significant difference in total T cell count (both $P > 0.05$). The levels of IL-17 and IFN- γ , $\gamma\delta$ T cell, and total T cell counts in the PB were obviously increased in COPD patients compared with those in normal subjects (all $P < 0.05$). Compared with those in COPD patients and lung cancer patients, lung cancer patients complicated with COPD had obviously higher levels of IL-17 and IFN- γ in the PB and BALF (all $P < 0.05$), but significantly smaller $\gamma\delta$ T cell count (both $P < 0.05$). The total T cell count in lung cancer patients complicated with COPD significantly declined compared with that in COPD patients ($P < 0.05$). Compared with those in lung cancer patients, the levels of IL-17 and IFN- γ in the PB and BALF of lung cancer patients complicated with COPD were remarkably increased (all $P < 0.05$), but the $\gamma\delta$ T cell counts were remarkably decreased (both $P < 0.05$), and the total T cell counts had no significant difference (both $P > 0.05$). Conclusion: The levels of IL-17 and IFN- γ in the PB and BALF of lung cancer patients complicated with COPD were significantly increased compared with those in patients with simple lung cancer (all $P < 0.05$), but the $\gamma\delta$ T cell counts were remarkably decreased (both $P < 0.05$), and there was no significant difference in total T cell counts (both $P > 0.05$).

Keywords: Chronic obstructive pulmonary disease, lung cancer, $\gamma\delta$ T cell, interleukin-17, interferon- γ

Introduction

Lung cancer is one of the malignant tumors with the fastest-growing morbidity and mortality rates in the world. At present, the pathogenesis of lung cancer remains unclear, and a large number of studies have confirmed that lung cancer has an extremely close correlation with smoking [1-3]. Chronic obstructive pulmonary disease (COPD) is also a common pulmonary disease, which is mainly characterized by the

persistent airflow obstruction. With the increase of chronic inflammatory response caused by harmful particles or gases in the human lungs and airways, the prevalence rate of COPD has also been increased [4-6]. Environmental factors and individual susceptibility factors are important factors causing the disease. Both lung cancer and COPD are common diseases in the respiratory medicine, which are closely associated with the body's immune function [7, 8]. $\gamma\delta$ T cells play an important role in the occur-

rence and development of lung cancer and COPD, but they change towards the opposite direction in the two diseases. The level of $\gamma\delta$ T cells in the PB is decreased in lung cancer patients, but increased in COPD patients [9, 10]. However, there are few studies on changes of $\gamma\delta$ T cells in bronchoalveolar lavage fluid (BALF).

In recent years, studies have found that the number of lung cancer patients complicated with COPD has significantly increased, and the prognosis is poor [8]. Therefore, this study aims to better identify and diagnose patients from the changes in levels of interleukin-17 (IL-17), interferon- γ (IFN- γ), and $\gamma\delta$ T cells, so as to intervene as soon as possible and improve the prognosis of patients.

Materials and methods

Materials

A total of 75 lung cancer patients, 81 COPD patients and 52 lung cancer patients complicated with COPD treated in Affiliated Hospital of Taishan Medical University from January 2015 to December 2016 were collected, and another 84 healthy workers in Affiliated Hospital of Taishan Medical University were also enrolled. Among patients with simple lung cancer, there were 46 males and 29 females aged 29-73 years with a median age of 54 years. According to the TNM staging criteria (the 7th Edition) of the International Association for the Study of Lung Cancer, there were 14 patients in stage II, 42 patients in stage III, and 19 cases in stage IV. In terms of pathological type, 30 cases had adenocarcinoma, 27 cases had squamous carcinoma, and 18 cases had small cell carcinoma [11].

Inclusion criteria of COPD patients: Patients not complicated with other cancers; without receiving drug therapy, radiochemotherapy or immunobiological therapy. Exclusion criterion of COPD patients: Patients who used to receive drug therapy, radiochemotherapy or immunobiological therapy. The diagnostic criteria for COPD were based on the revised edition of guideline for diagnosis and treatment of COPD (2013) [12]. Among COPD patients, there were 49 males and 32 females aged 45-76 years old with a median age of 67 years old.

Patients without receiving bioidentical hormone therapy or mechanical ventilation were

included as the lung cancer patients complicated with COPD, while those complicated with tumors and other respiratory diseases were excluded. Among the lung cancer patients complicated with COPD, there were 37 males and 15 females, aged 42-76 years old with a median age of 60 years old. According to the TNM staging criteria, there were 8 patients in stage II, 31 patients in stage III, and 13 cases in stage IV. In terms of pathological type, 11 cases had squamous carcinoma, 29 cases had adenocarcinoma, and 12 cases had small cell carcinoma.

This study was approved by the Ethics Committee of Affiliated Hospital of Taishan Medical University, and informed consent was obtained from all participants.

Specimen collection

At 8 o'clock in the morning at 2 weeks after patients were in stable condition, fasting venous blood was drawn into two tubes. The blood in one tube (3 mL) was anti-coagulated with heparin sodium and used for the detection of $\gamma\delta$ T cells and total T cells. The blood in the other tube (2 mL) was centrifuged, and the plasma was taken and cryopreserved at -80°C for enzyme-linked immunosorbent assay (ELISA). The specimen was also collected from healthy subjects in this way. BALF specimens were collected and treated (excluding healthy subjects) as follows: the focus in patients was positioned via tracheoscopy, and then lavaged with sterile saline (20 mL/each time) at 37°C for 5 times. Then 60% lavage fluid was recycled via vacuum aspiration, filtered through the gauze and centrifuged at 4,000 rpm and 4°C for 15 min. The supernatant was used to detect cytokines (IL-17, IFN- γ) via ELISA, and the cell sediment was used for the detection of $\gamma\delta$ T cells and total T cells [13].

Detection of $\gamma\delta$ T cells and total T cells

The PB collected from lung cancer patients, COPD patients, lung cancer patients complicated with COPD and healthy subjects was divided into a simple lung cancer group, a simple COPD group, a lung cancer with COPD group, and a normal group. Anti-IgG1-FITC9 (ab99772, Abcam, USA) and anti-IgG2-PE (ab-182668, Abcam, USA) were added into normal group, while equal amounts of anti-TCR- $\gamma\delta$ T (FITC; ab25010, Abcam, USA) and anti-CD₃-PE

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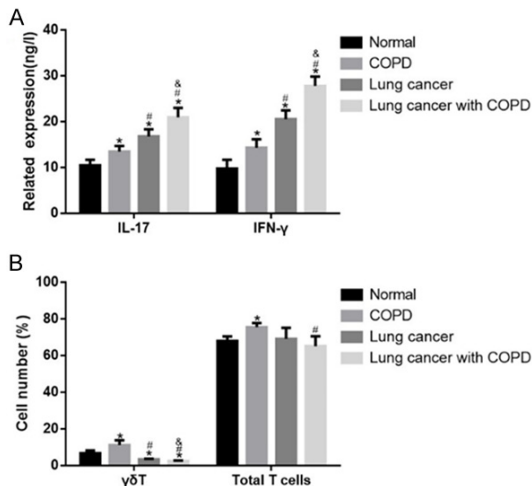


Figure 1. Analytical chart of IL-17, IFN- γ , $\gamma\delta$ T cells, and total T cells in PB of normal subjects, COPD patients, and lung cancer patients and lung cancer with COPD patients. A. ELISA examination; B. Flow cytometry examination. Compared with normal subjects, * $P < 0.05$; compared with COPD, # $P < 0.05$; compared with lung cancer patients, & $P < 0.05$. IL-17, interleukin-17; IFN- γ , interferon- γ ; PB, peripheral blood; COPD, chronic obstructive pulmonary disease; ELISA, enzyme-linked immunosorbent assay.

(ab25531, Abcam, USA) were added into simple lung cancer group, simple COPD group, and lung cancer with COPD group. The mixture was shaken evenly and incubated at room temperature in a dark place for 20 min. After that, 2 mL FACS hemolysin (349202, BD, USA) was added into the test tube and shaken evenly, followed by incubation at room temperature for 10 min. After centrifugation at 10,000 rpm for 5 min, the supernatant was discarded, and the mixture was washed with 2 mL PBS buffer solution twice. Then cells were fixed in 0.5 mL 1% paraformaldehyde, and detected using the flow cytometer within 1 h after fixation. The point diagram was drawn using FSC/SSC, the lymphocyte gate was set up, and then F1/F2 ($\gamma\delta$ TCR/ CD_3) point diagram was drawn. The voltage and threshold value were adjusted using the negative tube. After the experimental tube was adjusted and cells were obtained successfully, the percentage of $\gamma\delta$ TCR/ CD_3 double-positive cells in the PB was analyzed. The experiment was repeated for 3 times.

Detection of serum IL-17 and IFN- γ content

The levels of IL-17 and IFN- γ in serum and BALF were detected using the kits (Article No. 70-EK1172 and 70-EK1802, MultiSciences,

China) according to the instructions of the ELISA kit. The ELISA kit was equilibrated at room temperature for 30 min, and the washing liquid was prepared. The 100 μ L dissolved standard substance was taken and added into the reaction plate, and the standard curve was made. Then 100 μ L specimen (diluted at 1:15) was added into the reaction well, incubated at 37°C for 90 min, washed and added with 100 μ L biotinylated antibody working solution for incubation at 37°C for 1 h. After the plate was washed again, 100 μ L enzyme-conjugated working solution was added for incubation at 37°C for 30 min. After the plate was washed for 3 times, 100 μ L substrate was added for incubation in a dark place at 37°C for 15 min, after which the reaction was terminated using the stop buffer. The optical density value of each tube at 450 nm was measured using a universal microplate reader (BioTek Synergy 2), the standard curve was made based on the optical density value, and the levels of IL-17 and IFN- γ were analyzed. The experiment was repeated 3 times.

Statistical analysis

SPSS 21.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All experiments were repeated for 3 times. Measurement data are presented as mean \pm standard deviation. t test was used for the comparison of measurement data in line with the normal distribution between the two groups, and data were presented as t. Chi-square test was used for the comparison of enumeration data, and data were presented as Chi-square. One-way analysis of variance was used for the comparison among groups, and data were presented as F. Rank sum test was adopted for rank variables, and variables were presented as H. Pearson analysis was adopted for correlation analysis. $P < 0.05$ suggests that the difference is statistically significant.

Results

Comparisons of T cells and IFN in PB among groups

Results of flow cytometry and ELISA revealed that compared with those in normal subjects, lung cancer patients and lung cancer patients complicated with COPD had significantly higher levels of IL-17 and IFN- γ in the PB (all $P < 0.05$),

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Table 1. Comparison of general data

	Lung cancer patients (n=75)	COPD patients (n=81)	Lung cancer with COPD patients (n=52)	Normal subjects (n=84)	χ^2/H	P
Gender					2.154	0.541
Male	46	49	37	50		
Female	29	32	15	34		
Age (years)					3.158	0.367
≥ 50	39	46	29	37		
< 50	36	35	23	47		
Clinical stage					0.262	0.877
Stage II	14		8			
Stage III	42		31			
Stage IV	19		13			
Pathological type					3.917	0.141
Squamous carcinoma	27		11			
Adenocarcinoma	30		29			
Small cell carcinoma	18		12			

Note: COPD, chronic obstructive pulmonary disease.

but significantly lower $\gamma\delta$ T cell count (both $P < 0.05$), and had no significant difference in the total T cell count (both $P > 0.05$). Compared with normal subjects, the levels of IL-17 and IFN- γ , $\gamma\delta$ T cell and total T cell counts in the PB were obviously increased in COPD patients (all $P < 0.05$). Compared with those in COPD patients, the levels of IL-17 and IFN- γ in the PB of lung cancer patients and lung cancer patients complicated with COPD were obviously increased (all $P < 0.05$), but the $\gamma\delta$ T cell counts were significantly decreased (both $P < 0.05$), and the total T cell count in lung cancer patients complicated with COPD was also significantly decreased ($P < 0.05$). Compared with those in lung cancer patients, the levels of IL-17 and IFN- γ in the PB of lung cancer patients complicated with COPD were remarkably increased ($P < 0.05$), but the $\gamma\delta$ T cell count was remarkably decreased (both $P < 0.05$), and the total T cell count had no significant difference ($P > 0.05$) as shown in **Figure 1**.

The levels of IL-17 and IFN- γ , and $\gamma\delta$ T cell and total T cell counts in the PB of lung cancer patients and lung cancer patients complicated with COPD were not significantly associated with gender, age and pathological type (all $P > 0.05$) as shown in **Table 1**. With the increase of staging, the levels of IL-17 and IFN- γ in lung cancer patients were increased significantly (both $P < 0.05$), and there were no significant differences in $\gamma\delta$ T cell and total T cell counts

(both $P > 0.05$). The clinical stage of lung cancer patients was positively correlated with the levels of IL-17 ($r = 0.7653$, $P < 0.05$) and IFN- γ ($r = 0.7862$, $P < 0.05$), but was not correlated with $\gamma\delta$ T cell and total T cell counts (both $P > 0.05$) as shown in **Table 2**. The clinical stage of lung cancer patients complicated with COPD was also positively correlated with the levels of IL-17 ($r = 0.6371$, $P < 0.05$) and IFN- γ ($r = 0.7315$, $P < 0.05$), but had no correlation with $\gamma\delta$ T cell and total T cell counts (both $P > 0.05$) as shown in **Table 3**.

Sensitivity and specificity of IFN content and T cells in the PB in diagnosing lung cancer complicated with COPD

According to calculation, the sensitivity and specificity of IL-17 in the PB were 85.3% and 63.5%, those of IFN- γ were 89.3% and 69.2%, and those of $\gamma\delta$ T cells were 86.4% and 67.3%. Moreover, the sensitivity and specificity of combined detection of IL-17 and $\gamma\delta$ T cells were 94.3% and 83.5%, and those of combined detection of IFN- γ and $\gamma\delta$ T cells were 95.6% and 85.6% as shown in **Table 4**.

Comparison of T cells and IFN in BALF among groups

Results of flow cytometry and ELISA also showed that compared with those in COPD patients, the levels of IL-17 and IFN- γ in BALF of

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Table 2. Clinical data analysis of IL-17, IFN- γ content, $\gamma\delta$ T cell, total T cells in PB of normal subjects, COPD patients, lung cancer patients

Pathological data	Case	IL-17 (ng/L)	t/H/F	P	IFN- γ (ng/L)	t/H/F	P	$\gamma\delta$ T cell (%)	t/H/F	P	Total T cell (%)	t/H/F	P
Normal subjects	84	10.52 \pm 1.21			9.82 \pm 1.89			6.85 \pm 1.52			68.12 \pm 2.51		
COPD patients	81	13.52 \pm 1.22			14.35 \pm 1.84			11.32 \pm 2.52			75.63 \pm 2.55		
Lung cancer patients	75												
Clinical stage													
Stage II	14	13.71 \pm 1.02	95.250	<0.0001	17.08 \pm 1.25	84.320	<0.0001	3.95 \pm 0.35	1.159	0.319	69.81 \pm 7.52	0.113	0.893
Stage III	42	15.89 \pm 1.11			18.37 \pm 1.24			3.86 \pm 0.37			69.76 \pm 6.78		
Stage IV	19	19.02 \pm 1.23			22.00 \pm 1.02			4.01 \pm 0.38			68.84 \pm 8.52		
Pathological type													
Squamous carcinoma	27	16.18 \pm 2.10	0.210	0.811	20.12 \pm 2.62	0.245	0.783	3.75 \pm 0.36	2.606	0.080	68.61 \pm 5.52	0.296	0.744
Adenocarcinoma	30	15.92 \pm 1.98			19.65 \pm 2.47			3.62 \pm 0.34			69.62 \pm 7.52		
Small cell carcinoma	18	15.81 \pm 1.94			19.95 \pm 2.64			3.52 \pm 0.30			70.05 \pm 6.45		

Note: IL-17, interleukin-17; IFN- γ , interferon- γ ; PB, peripheral blood; COPD, chronic obstructive pulmonary disease.

Table 3. Clinical data analysis of IL-17, IFN- γ content, $\gamma\delta$ T cell, total T cells in PB of lung cancer with COPD patients (n=52)

Pathological data	Case	IL-17 (ng/L)	t/H/F	P	IFN- γ (ng/L)	t/H/F	P	$\gamma\delta$ T cell (%)	t/H/F	P	Total T cells (%)	t/H/F	P
Clinical stage													
Stage II	8	25.62 \pm 2.86	6.201	0.004	37.65 \pm 3.26	7.280	0.001	2.27 \pm 0.21	1.614	0.209	65.42 \pm 6.21	0.145	0.865
Stage III	31	27.52 \pm 2.91			40.52 \pm 2.97			2.31 \pm 0.23			64.22 \pm 6.03		
Stage IV	13	30.23 \pm 3.53			42.95 \pm 3.37			2.43 \pm 0.24			64.84 \pm 5.86		
Pathological type													
Squamous carcinoma	11	29.86 \pm 3.03	1.222	0.303	40.25 \pm 2.97	0.288	0.750	2.50 \pm 0.30	1.621	0.208	66.61 \pm 6.32	1.454	0.243
Adenocarcinoma	29	30.52 \pm 3.01			41.06 \pm 3.02			2.43 \pm 0.21			67.62 \pm 6.02		
Small cell carcinoma	12	28.92 \pm 2.96			40.65 \pm 3.42			2.33 \pm 0.20			64.05 \pm 6.10		

Note: IL-17, interleukin-17; IFN- γ , interferon- γ ; PB, peripheral blood; COPD, chronic obstructive pulmonary disease.

Table 4. Sensitivity and specificity of IFN content and T cells in the PB in diagnosing lung cancer complicated with COPD (%)

Detection index	Sensitivity	Specificity
IL-17	85.3	63.5
IFN- γ	89.3	69.2
IL-17 + $\gamma\delta$ T cells	94.3	83.5
IFN- γ + $\gamma\delta$ T cells	95.6	85.6

Note: IL-17, interleukin-17; IFN- γ , interferon- γ .

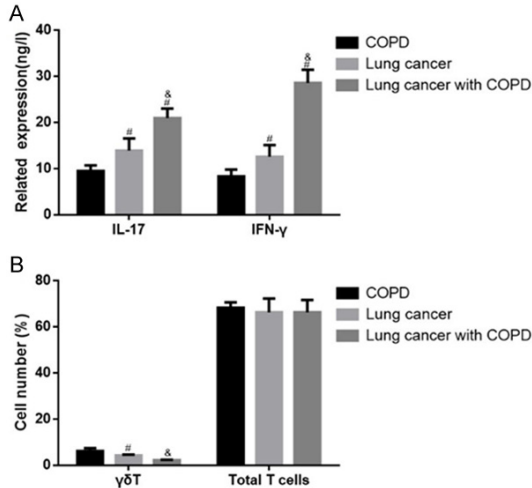


Figure 2. Analytical chart of IL-17, IFN- γ , $\gamma\delta$ T cells, total T cells in BALF of COPD patients, lung cancer patients and lung cancer with COPD patients. A: ELISA examination; B: Flow cytometry examination. Compared with COPD, [#]P<0.05; compared with lung cancer patients, ^{*}P<0.05. IL-17, interleukin-17; IFN- γ , interferon- γ ; BALF, bronchoalveolar lavage fluid; COPD, chronic obstructive pulmonary disease; ELISA, enzyme-linked immunosorbent assay.

lung cancer patients and lung cancer patients complicated with COPD were obviously increased (all P<0.05), but the $\gamma\delta$ T cell counts were significantly decreased (both P<0.05). The total T cell count in lung cancer patients complicated with COPD was significantly reduced compared with that in COPD patients (P<0.05). Compared with those in lung cancer patients, the levels of IL-17 and IFN- γ in BALF of lung cancer patients complicated with COPD were remarkably increased (both P<0.05), but the $\gamma\delta$ T cell count was remarkably decreased (P<0.05), and the total T cell count had no significant difference (P>0.05) as shown in **Figure 2**.

The levels of IL-17 and IFN- γ , $\gamma\delta$ T cells, and total T cell counts in BALF of lung cancer patients

and lung cancer patients complicated with COPD were not obviously associated with pathological type (all P>0.05). With increased staging, the levels of IL-17 and IFN- γ , and $\gamma\delta$ T cell count in BALF of lung cancer patients were increased significantly (all P<0.05), and there was no significant difference in the total T cell count (P>0.05). The levels of IL-17 and IFN- γ in BALF of lung cancer patients complicated with COPD were increased significantly (both P<0.05), and there were no significant differences in $\gamma\delta$ T cell and total T cell counts (P>0.05) as shown in **Tables 5, 6**.

Sensitivity and specificity of IFN content and T cells in BALF in diagnosing lung cancer complicated with COPD

According to calculation, the sensitivity and specificity of IL-17 in BALF were 82.6% and 62.3%, those of IFN- γ were 87.6% and 67.3%, and those of $\gamma\delta$ T cells were 85.7% and 68.4%. Moreover, the sensitivity and specificity of combined detection of IL-17 and $\gamma\delta$ T cells were 92.7% and 84.9%, and those of combined detection of IFN- γ and $\gamma\delta$ T cells were 94.5% and 86.2% as shown in **Table 7**.

Discussion

Previous studies have shown that the level of $\gamma\delta$ T cells in the PB of patients with lung cancer is significantly lower than that in healthy control group, the level of invasive $\gamma\delta$ T cells in lung cancer tissues is significantly higher than that in para-carcinoma tissues, and the level of $\gamma\delta$ T cells in the PB of lung cancer patients after operation is also obviously higher than that before operation [14-16]. The role of $\gamma\delta$ T cells in the pathogenesis of COPD has attracted increasingly more attention, but there is little relevant research. Ekberg-Jansson et al. detected a significant increase in the level of $\gamma\delta$ T cells in the PB and BALF of smokers, suggesting that tobacco irritates the respiratory tract and lung tissues, passing “danger signals” to $\gamma\delta$ T cells [14]. The important function of $\gamma\delta$ T cells is to participate in tissue damage and repair, and they will quickly reach the damage site for tissue repair after receiving the “danger signal”, thus maintaining the tissue homeostasis. Urboniene et al. detected the changes in $\gamma\delta$ T cells in lung tissues of mice at 10, 20, and 30 days after cigarette smoking via flow cytometry, and found that the number of $\gamma\delta$ T cells in

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Table 5. Clinical data analysis of IL-17, IFN- γ content, $\gamma\delta$ T cell, total T cells in BALF of COPD, lung cancer patients

Pathological data	Case	IL-17 (ng/L)	t/H/F	P	IFN- γ (ng/L)	t/H/F	P	$\gamma\delta$ T cell (%)	t/H/F	P	Total T cells (%)	t/H/F	P
COPD patients	81	9.52±1.23			8.35±1.51			6.26±1.22			68.35±2.35		
Lung cancer patients	75												
Clinical stage													
Stage II	14	11.61±1.32	43.560	<0.0001	10.84±1.35	16.740	<0.0001	4.03±0.15	17.610	<0.0001	64.75±5.82	0.609	0.547
Stage III	42	13.63±1.19			12.34±1.62			4.35±0.43			65.76±6.42		
Stage IV	19	15.62±1.24			13.86±1.27			4.73±0.16			63.84±6.82		
Pathological type													
Squamous carcinoma	27	13.14±1.67	0.832	0.439	12.53±1.71	0.753	0.475	4.32±0.41	0.491	0.614	64.63±7.52	0.572	0.567
Adenocarcinoma	30	12.84±1.32			12.62±2.52			4.26±0.29			64.72±7.22		
Small cell carcinoma	18	13.42±1.64			11.85±2.32			4.36±0.35			66.74±6.35		

Note: IL-17, interleukin-17; IFN- γ , interferon- γ ; BALF, bronchoalveolar lavage fluid; COPD, chronic obstructive pulmonary disease.

Table 6. Clinical data analysis of IL-17, IFN- γ content, $\gamma\delta$ T cell, total T cells in BALF of lung cancer with COPD patients (n=52)

Pathological data	Case	IL-17 (ng/L)	t/H/F	P	IFN- γ (ng/L)	t/H/F	P	$\gamma\delta$ T cell (%)	t/H/F	P	Total T cells (%)	t/H/F	P
Clinical stage													
Stage II	8	20.12±2.01	11.050	<0.0001	26.31±2.03	10.310	<0.0001	5.12±0.42	0.770	0.469	70.23±5.72	0.095	0.909
Stage III	31	21.03±2.03			27.34±2.01			5.23±0.13			70.89±6.43		
Stage IV	13	23.84±2.12			29.98±2.13			5.27±0.40			71.46±6.39		
Pathological type													
Squamous carcinoma	11	21.32±2.15	1.796	0.177	27.52±2.03	2.576	0.086	5.43±0.51	1.806	0.175	72.10±7.42	0.140	0.870
Adenocarcinoma	29	20.36±2.01			26.94±2.42			5.23±0.39			71.02±6.98		
Small cell carcinoma	12	19.74±1.89			25.45±2.32			5.09±0.45			70.62±6.72		

Note: IL-17, interleukin-17; IFN- γ , interferon- γ ; BALF, bronchoalveolar lavage fluid; COPD, chronic obstructive pulmonary disease.

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Table 7. Sensitivity and specificity of IFN content and T cells in BALF in diagnosing lung cancer complicated with COPD (%)

Detection index	Sensitivity	Specificity
IL-17	82.6	62.3
IFN- γ	87.6	67.3
IL-17 + $\gamma\delta$ T cells	92.7	84.9
IFN- γ + $\gamma\delta$ T cells	94.5	86.2

Note: IL-17, interleukin-17; IFN- γ , interferon- γ .

the early stage of smoking was increased significantly, reached the peak at 20 days, and slightly declined at 30 days, indicating that $\gamma\delta$ T cells are involved in the early formation of COPD [15].

Current studies have demonstrated that the changes in $\gamma\delta$ T cells are in the opposite direction in lung cancer and COPD, two smoking-related diseases [16-20]. Therefore, this study aims to detect the changes in levels of $\gamma\delta$ T cells and its related inflammatory factors (IL-17 and IFN- γ) in the PB and BALF of lung cancer patients complicated with COPD, so as to further investigate the role and function of $\gamma\delta$ T cells in the occurrence and development of lung cancer complicated with COPD. At the same time, it is hoped that a method for early detection and diagnosis of this disease can be found through this study, providing new ideas for the biotherapy of disease in the future.

Results of this study demonstrate that compared with those in normal subjects, the levels of IL-17 and IFN- γ in the PB of lung cancer patients and lung cancer patients complicated with COPD are significantly increased, but $\gamma\delta$ T cell counts are significantly decreased, and there is no significant difference in the total T cell counts. The levels of IL-17 and IFN- γ , $\gamma\delta$ T cell and total T cell counts in the PB were obviously increased in COPD patients. Compared with those in lung cancer patients, the levels of IL-17 and IFN- γ in the PB of lung cancer patients complicated with COPD were remarkably increased, but the $\gamma\delta$ T cell count was remarkably decreased, and the total T cell count had no significant difference. The sensitivity and specificity of combined detection of IL-17 and $\gamma\delta$ T cells in the PB were 94.3% and 83.5%, and those of combined detection of IFN- γ and $\gamma\delta$ T cells were 95.6% and 85.6%.

Compared with those in patients with simple lung cancer, the levels of IL-17 and IFN- γ in

BALF of lung cancer patients complicated with COPD were significantly increased, but the $\gamma\delta$ T cell count was significantly decreased, and there was no significant difference in the total T cell count. The levels of IL-17 and IFN- γ , $\gamma\delta$ T cell and total T cell counts in BALF of lung cancer patients and lung cancer patients complicated with COPD were not obviously associated with pathological type. With the increase of staging, the levels of IL-17 and IFN- γ , and $\gamma\delta$ T cell count in BALF of lung cancer patients were increased significantly, and levels of IL-17 and IFN- γ in BALF of lung cancer patients complicated with COPD were also increased obviously.

The sensitivity and specificity of combined detection of IL-17 and $\gamma\delta$ T cells in BALF were 92.7% and 84.9%, and those of combined detection of IFN- γ and $\gamma\delta$ T cells were 94.5% and 86.2%, respectively.

However, this paper has some limitations. For example, the sample size was not large, and only IL-17 and IFN- γ levels, $\gamma\delta$ T cells, and total T cell counts were measured, but relevant animal experiments were not performed. Animal experiments were not conducted for the pathogenesis of lung cancer complicated with COPD, and changes in relevant factors during the pathogenetic process were not detected continuously. Moreover, the pathogenesis mechanism was not deeply studied. However, this study can provide relevant ideas for the diagnosis of lung cancer complicated with COPD.

In conclusion, with the increased staging, the levels of IL-17 and IFN- γ were significantly increased, and there was no significant difference between $\gamma\delta$ T cells and total T cell counts. The research results can provide a certain basis for early detection and diagnosis of lung cancer complicated with COPD.

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Disclosure of conflict of interest

None.

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Auxiliary diagnostic value of $\gamma\delta$ T cell, IL-17 and IFN- γ levels in PB and BALF

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