

## Review Article

# Expression and clinical value of IL-6 and PCT in patients with pneumonia

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**Abstract:** This study intended to investigate the changes of IL-6 and PCT in the peripheral blood of patients with pneumonia and their clinical value. Altogether 138 patients with pneumonia from November 2017 to July 2019 were selected as the study group (SG), and 90 healthy people as the control group (CG). Fasting venous blood (4 mL) was obtained. IL-6 and PCT concentrations were tested in serum, and ROC curves were visualized to analyze the early diagnostic value. The changes of IL-6 and PCT were detected before and 7 days after treatment and 30 days after treatment, and the relationship of IL-6, PCT with clinical pathology in the SG was analyzed. Pearson was used to analyze the correlation of IL-6 with PCT, and the factors affecting the prognosis were analyzed. IL-6 and PCT in the SG were higher than in the CG ( $P < 0.001$ ). ROC curve showed that IL-6 and PCT had high sensitivity and specificity. IL-6 and PCT 7 days after treatment in the SG were lower than before treatment ( $P < 0.001$ ), and those 30 days after treatment were lower than 7 days after treatment ( $P < 0.001$ ). Moreover, IL-6 and PCT were closely related to diagnosis, therapy and severity ( $P < 0.001$ ). There was a positive correlation between serum IL-6 and PCT ( $r = 0.7223$ ,  $P < 0.001$ ), and Logistic regression analysis showed that the time of diagnosis and therapy, severity, IL-6, and PCT were independent risk factors affecting prognosis. IL-6 and PCT of patients with pneumonia were increased, which may be involved in the occurrence and development of pneumonia. Detection of IL-6 and PCT levels may be able to diagnose and judge the disease development and prognosis of patients with pneumonia.

**Keywords:** IL-6, PCT, pneumonia, clinical value, adults

## Introduction

Pneumonia is a common respiratory disease, which is usually pulmonary inflammation caused by bacterial or viral infection. With the use of antibiotics and vaccines, the quality of life of patients with pneumonia has been greatly improved [1, 2]. However, with the global aging, the elderly population has poor physical quality and resistance and is more vulnerable to respiratory diseases. According to the report by Bjarnason A et al. [3], the incidence rate of pneumonia was increased with age. With an increased incidence rate, the mortality rate also increases. According to Russell FM et al. [4], pneumonia is the main cause of death for newborns and children under 5 years old, and many deaths are concentrated in low-and middle-income countries due to the limitation of medical care and medical equipment. According

to Miyashita N et al. [5], about 120,000 individuals with pneumonia died in Japan in 2016, 96% of which were elderly patients over 65 years old. Currently, anti-infection and prevention of complications are the main treatments for pneumonia in clinical practice [6, 7]. However, due to the atypical symptoms of pneumonia infections in most patients, it is difficult for patients in the early stages to be detected or it is easy to miss the diagnosis, thus leading to missing the best treatment opportunity [8]. At present, it is difficult to accurately judge the severity of pneumonia in clinical practice. Therefore, finding effective indicators for early diagnosis of pneumonia has gradually become the research focus and direction of scholars in recent years.

Interleukin (IL) is a kind of immune factor that interacts between leukocytes and immune

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cells. Interleukin-6 (IL-6), as an inflammatory factor, it has strong inflammatory activity, can directly act on vascular endothelial cells, increase the permeability, produce a large amount of inflammatory exudate, and participate in the pathogenesis of various chronic inflammatory diseases including tumors [9]. Studies by Sánchez-Zauco N et al. [10] showed that IL-6 can be used for the diagnosis of gastric cancer and can be used to distinguish intestinal gastric cancer from diffuse gastric cancer. Procalcitonin (PCT) is a hormone-free procalcitonin substance produced by thyroid cells, which can be up-regulated in the presence of microbial toxins and some pro-inflammatory mediators such as tumor necrosis factor- $\alpha$  [11]. In the study of Vijayan A L [12], PCT can be used as a promising diagnostic index for sepsis and antibiotic therapy. However, due to the lack of comprehensive reports on the specific role and clinical value of IL-6 and PCT in pneumonia, this study investigated it with the detection of the expression and clinical value of IL-6 and PCT in serum of pneumonia patients, aiming to provide accurate and effective references and indicators for clinical diagnosis and treatment of pneumonia diseases in the future.

### Data and methods

#### General data

Altogether 138 pneumonia patients admitted to the Affiliated Hospital of Chengde Medical University from November 2017 to July 2019 were selected as the study group, and 90 people who underwent physical examination in the Affiliated Hospital of Chengde Medical University during the same time period were selected as the control group. This experiment has been approved by the Ethics Committee of the Affiliated Hospital of Chengde Medical University. All the patients have signed an informed consent form.

#### Inclusion and exclusion criteria

Inclusion criteria: patients diagnosed with pneumonia through clinical examinations such as chest X-ray, and patients who met the diagnostic criteria for pneumonia; patients who received follow-up treatment in the Affiliated Hospital of Chengde Medical University after diagnosis, and patients who were  $\geq 18$  years old. Exclusion criteria: patients had received

relevant treatment before the experiment; patients with other malignant tumors; patients at the end of the disease; patients with mental disorders who could not cooperate with the treatment; patients with drug allergy; and patients with incomplete clinical and pathological data.

#### Methods

Altogether 138 pneumonia patients were taken as the study group and 90 healthy people were taken as the control group. Fasting venous blood (4 mL) was obtained from all patients. Venous blood was placed in refrigerator at low temperature. After coagulation for 60 min, the blood samples were centrifuged at 4°C (1000 $\times$ g) for 20 min, and the serum was frozen for later use. The concentrations of IL-6 and PCT in serum were detected by enzyme-linked immunosorbent assay (ELISA). The IL-6 ELISA kit was purchased from Shanghai Jingkang Bioengineering Co., Ltd., (JK-(A)-0023). PCT ELISA kit was purchased from Shanghai YuanMu Biological Technology Co. Ltd., (YM-QP11581). The detection process was performed strictly in accordance with the kit instructions.

#### Observation index

The concentrations of IL-6 and PCT in serum of both groups was assessed, and the early diagnostic value of IL-6 and PCT for pneumonia were observed. The study group was tested before treatment, 7 days after treatment and 30 days after treatment to observe the changes of IL-6 and PCT during treatment. The relationship of IL-6 and PCT with clinical pathology in the study group was observed. Pearson was used to analyze the correlation between IL-6 and PCT levels. The factors affecting the prognosis of pneumonia patients were analyzed.

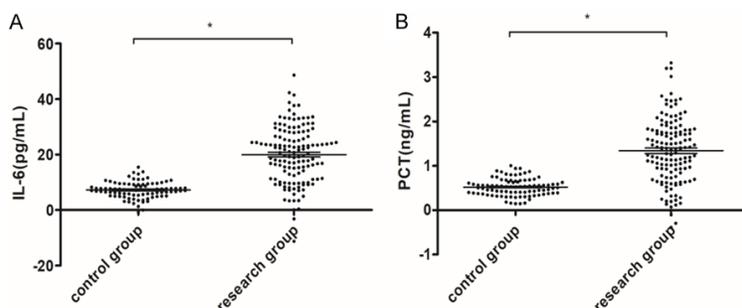
#### Statistical methods

This experiment applied SPSS 24.0 (Shanghai Yuchuang Network Technology Co., Ltd) for analysis and GraphPad 5 to illustrate the required figures. The counting data were expressed in the form of (rate). Chi-square test was used for comparison among multiple groups. The measurement data were expressed in the form of (mean $\pm$ standard deviation), and the comparison between groups was performed with a t test. The comparison at multi-

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**Table 1.** Comparison of clinical data [n (%)]

	Research group (n=138)	Control group (n=90)	t/ $\chi^2$	P
Age	51.26±12.35	48.93±10.27	1.486	0.139
Gender			0.001	0.977
Male	81 (58.70)	53 (58.89)		
Female	57 (41.30)	37 (41.11)		
The time of diagnosis and therapy (d)	4.18±1.24			
Severity				
Mild or moderate	85 (61.59)			
Severe	53(38.41)			
Smoking			0.012	0.914
Yes	42 (30.43)	28 (31.11)		
No	96 (69.57)	62 (68.89)		
Drinking			0.010	0.920
Yes	33 (23.91)	21 (23.33)		
No	105 (76.09)	69 (76.67)		
Residence			2.497	0.114
Urban	89 (64.49)	67 (74.44)		
Rural	49 (35.51)	23 (25.56)		



**Figure 1.** Serum IL-6 and PCT concentrations of the two groups. A. Comparison of IL-6 concentration in serum between the two groups; B. Comparison of PCT concentration in serum of two groups of patients; \* indicates that  $P < 0.001$ .

ple time points was done with variance analysis of repeated measurement. ROC was used to visualize the diagnostic value of IL-6 and PCT in patients with pneumonia. Pearson test was used to analyze the correlation between serum IL-6 and PCT in patients with pneumonia. Logistic regression model was used to analyze the prognostic risk factors of pneumonia patients. At  $P < 0.05$ , the difference was deemed statistically significant.

### Results

#### Comparison of clinical data

There was no significant difference in age, sex, the time of diagnosis and therapy, severity,

smoking, drinking and place of residence between the two groups ( $P > 0.05$ ). See **Table 1**.

#### Concentrations of IL-6 and PCT in serum of the study group and the control group

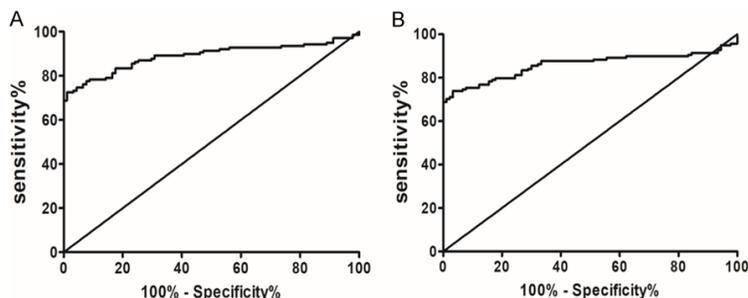
The concentration of IL-6 in the serum of the study group before treatment was  $(20.21 \pm 9.48)$  pg/mL, significantly higher than that of the control group  $(6.84 \pm 2.79)$  pg/mL,  $P < 0.001$ . The PCT concentration in the serum of the study group

was  $(1.42 \pm 0.75)$  ng/mL, significantly higher than that of the control group  $(0.51 \pm 0.18)$  ng/mL,  $P < 0.001$ . See **Figure 1**.

#### Early diagnostic value of IL-6 and PCT for pneumonia

The ROC curve showed that the area under the curve of IL-6 was 0.889, the sensitivity was 72.46%, the specificity was 98.90%, the critical value was 13.940, and the 95% CI was 94.03%-99.97%. The area under the curve of PCT was 0.859, the sensitivity was 73.91%, the specificity was 96.67%, the critical value was 0.899, and the 95% CI was 90.57%-99.31%. Both of them had high sensitivity and specificity to detect pneumonia. See **Figure 2**.

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**Figure 2.** The value of two indicators in early diagnosis of pneumonia. A. The early diagnostic value of IL-6 for pneumonia; B. The early diagnostic value of PCT for pneumonia.

**Table 2.** Changes of serum IL-6 and PCT concentration before and after treatment in study group

	IL-6 (pg/mL)	PCT (ng/mL)
Before treatment	20.21±9.48	1.42±0.75
7 days after treatment	10.63±5.15a	0.91±0.22 <sup>a</sup>
30 days after treatment	7.52±2.87a,b	0.58±0.16 <sup>a,b</sup>
F	145.3	116.5
P	<0.001	<0.001

a: compared with before treatment,  $P < 0.001$ ; b: compared with 7 days after treatment,  $P < 0.001$ .

### *Changes of IL-6 and PCT concentrations in the study group before and after treatment*

The detection of the changes of IL-6 and PCT concentrations in the serum of the patients in the study group after symptomatic treatment such as anti-infection treatment showed that IL-6 and PCT in the patients in the study group 7 days after treatment were significantly lower than those before treatment ( $P < 0.001$ ), and IL-6 and PCT 30 days after treatment were significantly lower than those 7 days after treatment ( $P < 0.001$ ). See **Table 2**.

### *Relationship of IL-6, PCT with clinical pathology of pneumonia*

Analysis of the relationship of the two indexes with the clinical pathology showed that IL-6 and PCT were closely related to the time of diagnosis, therapy and severity of disease ( $P < 0.001$ ). See **Tables 3** and **4**.

### *Correlation analysis between serum IL-6 and PCT in patients with pneumonia*

Through Pearson correlation analysis of the relationship between IL-6 and PCT in serum, it

was found that the expression of IL-6 and PCT was positively correlated ( $r = 0.7223$ ,  $P < 0.001$ ), i.e. the expression of IL-6 increased, and the expression of PCT also increased. See **Figure 3**.

### *Single factor analysis on prognosis of patients with pneumonia*

According to whether the patients in the research group were cured or not after treatment, the patients who were not cured were classified as the group with poor prognosis, and the patients who were cured were classified as the group with good prognosis; including 35 patients in the group with poor prognosis and 103 patients in the group with good prognosis. Single factor analysis of the clinical data collected from the two groups

showed that there was no difference in age, sex and smoking between the two groups ( $P > 0.05$ ), while there was statistical difference in the time of diagnosis and therapy, severity, IL-6 and PCT comparison between the two groups ( $P < 0.05$ ), as shown in **Table 5**.

### *Multivariate analysis on prognosis of patients with pneumonia*

The indicators with differences in single factor analysis were included in the assignment. The multivariate Logistic proportional risk regression model analysis showed that the time of diagnosis and therapy, severity, IL-6 and PCT levels were independent risk factors affecting the prognosis of pneumonia patients ( $P < 0.05$ ), as shown in **Table 6**.

## Discussion

Pneumonia is a common disease of the respiratory system, and is frequently found in the terminal airway, alveoli and pulmonary interstitium. It belongs to the class of pulmonary inflammatory reactive diseases and has serious rate of morbidity and mortality in the world [13]. The incidence of pneumonia among the

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**Table 3.** Relationship of IL-6 with clinicopathology of pneumonia patients

Factor	Cases	IL-6 concentration (pg/mL)	T	P
Age (years)			0.467	0.641
≥51	78	21.09±9.21		
<51	60	20.37±8.65		
Gender			0.579	0.564
Male	81	20.64±8.92		
Female	57	21.55±9.34		
The time of diagnosis and therapy (d)			3.831	<0.001
≥4.2	62	24.36±9.78		
<4.2	76	18.52±8.13		
Severity			3.762	<0.001
Mild or moderate	85	20.04±9.15		
Severe	53	26.25±9.87		
Smoking			0.807	0.421
Yes	42	22.43±8.72		
No	96	21.16±8.41		

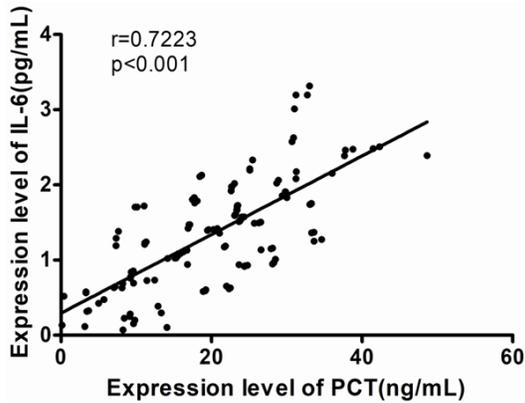
**Table 4.** Relationship between PCT and clinicopathology of pneumonia patients

Factor	Cases	PCT concentration (ng/mL)	T	P
Age (years)			0.412	0.681
≥51	78	1.39±0.68		
<51	60	1.44±0.74		
Gender			0.158	0.875
Male	81	1.41±0.72		
Female	57	1.43±0.75		
The time of diagnosis and therapy (d)			3.781	<0.001
≥4.2	62	1.79±0.82		
<4.2	76	1.32±0.64		
Severity			3.623	<0.001
Mild or moderate	85	1.36±0.71		
Severe	53	1.85±0.86		
Smoking			0.247	0.805
Yes	42	1.45±0.69		
No	96	1.42±0.64		

elderly is still relatively high in the world due to poor self-resistance and immune function and the existence of many other concurrent basic diseases. Once the disease occurs and if it is not treated promptly and effectively, it often poses a serious threat to the life and health of patients. According to the research of Arnold FW et al. [14], the incidence rate of community acquired pneumonia among the elderly in the United States is about 2% (2,000 per 100,000 people), and about 360,000 people die each year from it. In Portugal and other countries, pneumonia is the first cause of respiratory

death other than lung cancer [15]. According to Marshall DC et al. [16], about 230,000 people die of pneumonia every year in Europe. Although the mortality rate of pneumonia is reducing in most EU countries, there are still great differences in different countries and different genders. The diagnosis of pneumonia often requires imaging confirmation. Chest X-ray and CT are the main imaging methods for the diagnosis of pneumonia. However, due to the high cost and large radiation amount of these methods, the treatment has always been a major problem perplexing people, and for

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**Figure 3.** Correlation between serum IL-6 level and PCT level in patients with pneumonia.

unstable and severe patients, the above methods are not easy to implement [17, 18]. Therefore, it is particularly important to find early effective indicators for diagnosis of pneumonia, which has become a research hotspot of scholars. At present, the specific pathogenesis of pneumonia is not completely clear. Some studies have shown that age, smoking and environment are all related to the occurrence of pneumonia [19-21]. With the deepening of research, more and more scholars have pointed out that various factors may be involved in the occurrence and development of pneumonia [22, 23], but the roles of IL-6 and PCT in pneumonia are not clear. According to some studies, IL-6 may be related to pneumonia in children [24]. Yang Y [25] et al. said PCT had certain predictive value for infectious diseases, but there is still little research on the specific clinical application value of IL-6 and PCT for pneumonia diseases. Therefore, this experiment aimed to verify the role of IL-6 and PCT in pneumonia by studying the expression of IL-6 and PCT in the serum of patients with pneumonia and analyzing their relationship with the condition, treatment, clinical pathology of pneumonia.

The results of this experiment showed that the concentrations of IL-6 and PCT in peripheral blood of patients with pneumonia were much higher than those of normal people, suggesting that IL-6 and PCT may participate in the occurrence and development of pneumonia. Meanwhile, ROC curve analysis was performed, and it was found that when the cut-off values were 13.940 and 0.899, respectively, IL-6 and PCT had higher sensitivity and specificity for the early diagnosis of pneumonia. However, the lev-

els of IL-6 and PCT after relevant treatment were found to be lower than before treatment, suggesting that the future treatment of pneumonia in patients can be judged by detecting the concentrations of IL-6 and PCT in the peripheral blood of patients. Further analysis of the patient's clinical pathology showed that the concentrations of IL-6 and PCT were closely related to the time of diagnosis and therapy and severity, suggesting that the severity of pneumonia can be judged by detecting the concentrations of IL-6 and PCT in the peripheral blood in the future. IL-6 is a major pro-inflammatory cytokine in the IL family.

We also explored the correlation between serum IL-6 and PCT levels in patients with pneumonia by Pearson correlation analysis, and found that IL-6 was positively correlated with PCT expression, which suggested that there might be a close relationship between IL-6 and PCT, but we did not carry out an in-depth exploration. At the end of the study, we analyzed the factors that affect the prognosis of patients with pneumonia. The results showed that the time of diagnosis therapy, severity, and IL-6 and PCT levels were independent risk factors that affect the prognosis of patients with pneumonia. This showed that IL-6 and PCT could be used as clinical indicators to evaluate the prognosis of patients with pneumonia.

IL-6 signals are transmitted through glycoprotein 130 and membrane-bound or soluble IL-6 receptors, which are respectively called classical signals and trans signals [26]. Interestingly, the concentration of IL-6 in this study increased significantly before pneumonia treatment, which is consistent with the research results of Naik SP et al. [27] in asthma. The two results can be mutually verified. It was speculated that the mechanism of IL-6 participating in pneumonia may be that IL-6 regulates antibody production, activates T cells, differentiates B cells, increases the acute phase protein and vascular permeability, and finally leads to inflammatory exudation [28]. PCT is a blood marker of metabolic infection, the level of which is helpful to estimate the possibility of bacterial infection [29]. In the study of Lippi G [30], the concentration of PCT in infectious complications of inflammatory bowel disease increased, which was similar to the results of this experiment and could support our results. PCT is a precursor of calcitonin hormone, which is released into the

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**Table 5.** Univariate analysis on prognosis of patients with pneumonia

Factor	Good prognosis group (n=103)	Poor prognosis group (n=35)	t or $\chi^2$	P
Age (years)	50.96±10.54	51.88±11.28	0.438	0.662
Gender			0.033	0.856
Male	60 (58.25)	21 (60.00)		
Female	43 (41.75)	14 (40.00)		
Time of diagnosis and therapy (d)	3.82±0.89	4.21±1.07	2.125	0.035
Severity			39.170	<0.001
Mild or moderate	79 (76.70)	6 (17.14)		
Severe	24 (23.30)	29 (82.86)		
Smoking			2.026	0.155
Yes	28 (27.18)	14 (40.00)		
No	75 (72.82)	21 (60.00)		
IL-6 (pg/mL)	18.25±8.34	22.13±9.73	2.277	0.024
PCT (ng/mL)	1.27±0.39	1.53±0.47	3.230	0.002

**Table 6.** Multivariate analysis on prognosis of patients with pneumonia

Variable	$\beta$	S.E.	Wald $\chi^2$	OR value (95%CI)	P
Time of diagnosis and therapy	1.021	0.280	8.759	2.545 (1.521-7.344)	<0.05
Severity	0.682	0.283	5.807	1.915 (1.232-3.458)	<0.05
IL-6	1.306	0.575	8.614	8.442 (1.498-3.016)	<0.05
PCT	1.177	0.493	6.326	4.075 (1.425-6.881)	<0.05

systemic circulation within 4 hours after inoculating bacteria or bacterial endotoxin. It was presumed that cytokines were related to bacterial infection, such as IL-6 and TNF- $\alpha$ , and increased the release of PCT [31].

The purpose of this experiment was to explore the concentration and changes of IL-6 and PCT in peripheral blood of patients with pneumonia, and to explore the relationship of IL-6 and PCT with pneumonia. However, due to the limitations of conditions, there are still some deficiencies in this experiment, such as the lack of in-depth study on the specific mechanism of action of IL-6 and PCT with pneumonia. Moreover, due to the small sample base of the research subjects and the relatively single population of research subjects, it is not excluded that the results of this experiment may differ from others with different age groups. Therefore, we will continue to improve this experiment in future research to obtain the most accurate research results.

### Conclusion

The concentrations of IL-6 and PCT in the serum of patients with pneumonia were significantly

increased, which may be involved in the occurrence and development of pneumonia diseases. This may be able to assist with the diagnosis and judge the disease development and prognosis of patients with pneumonia by detecting IL-6 and PCT in the future.

### Disclosure of conflict of interest

None.

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