

Original Article

Serum procalcitonin levels in predicting the prognosis of severe pneumonia patients and its correlation with white blood cell count and C-reactive protein levels

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Abstract: Objective: To investigate the expression of procalcitonin (PCT) in severe pneumonia patients and its correlation with white blood cell count (WBC) and C-reactive protein (CRP) levels and to further analyze the values of PCT, WBC and CRP levels in predicting the prognosis of severe pneumonia. Methods: First, 74 patients with severe pneumonia were selected as the severe pneumonia group. At the same time, 74 patients with general pneumonia and 74 healthy people were selected as the mild to moderate pneumonia group and control group, respectively. Then, the levels of PCT, WBC and CRP in these three groups was compared, and the correlation between PCT levels and WBC or CRP levels in the severe pneumonia group was analyzed. In addition, the patients in severe pneumonia group were further divided into a survival group (52 cases) and a death group (22 cases) according to the prognosis. PCT, WBC and CRP levels of the survival group and death group were compared, and the clinical value of the individual and combined detection of each index in predicting the prognosis of patients was further analyzed. Results: The level of PCT, WBC and CRP in the severe pneumonia group was significantly higher than that in the mild to moderate pneumonia group and control group ($P < 0.05$). The level of these three indexes in the death group was also significantly higher than that in the survival group ($P < 0.05$). In the severe pneumonia group, PCT level was positively correlated with the level of WBC and CRP (the correlation coefficients are 0.585, 0.774, respectively). ROC curve analysis showed that the area under prognostic curve (AUC) of PCT, CRP and WBC were 0.825, 0.760 and 0.619, respectively; while the prognostic AUC of PCT combined with CRP was 0.834. Conclusion: Significant increases of serum PCT, WBC and CRP levels in severe pneumonia patients were found, and PCT level was positively correlated with both WBC and CRP levels. PCT detection has high clinical value in evaluating the prognosis of severe pneumonia patients.

Keywords: Severe pneumonia, procalcitonin, white blood cell counts, C-reactive protein

Introduction

Severe pneumonia is a critical type of pneumonia, which is mostly induced by bacterial infection [1, 2]. It has the characteristics of critical illness, rapid progress and high mortality, thus early detection has important clinical value for the diagnosis, treatment and prognosis evaluation of severe pneumonia patients [3, 4]. As a new marker of bacterial infection, procalcitonin (PCT) has been widely used in clinical diagnosis. Previous studies have shown that serum PCT can be detected 2 hours post infection,

and the level of PCT is nearly related to the severity of infection. Besides, current studies have also explored the expression of PCT in infectious diseases, and suggest that the level of PCT is an indicator with relatively high sensitivity and specificity [5-7]. White blood cell count (WBC) is widely used in the diagnosis of infectious diseases because it is easy to measure and has wide application, but it is also greatly restricted due to its low specificity and sensitivity. C-reactive protein (CRP) has comprehensive biological activities and has been regarded as one of the most sensitive inflam-

matory markers. However, abnormal expression of serum CRP can be found in cases of viral infection, surgery, cardiovascular diseases and some other factors, so CRP detection lacks specificity for judging infection [8-10]. Our present study further explored the expression of PCT in patients with severe pneumonia and its correlation with WBC/CRP, and analyzed the clinical value of PCT, WBC and CRP in predicting the prognosis of severe pneumonia, aiming to provide a first-line basis for diagnosis and clinical treatment of severe pneumonia.

Materials and methods

Patients source

Patients with severe pneumonia in Tengzhou Central People's Hospital (between January 2015 and January 2019) were selected as the severe pneumonia group. At the same time, 74 patients with general pneumonia and 74 healthy people in our hospital were selected as the general pneumonia group and the control group, respectively. The patients in the severe pneumonia group were followed for 28 days and were further divided into a survival group and a death group according to their survival. All related patients and their family members were informed, and they provided informed consent. The study was approved by the Ethics Committee of Tengzhou Central People's Hospital.

Patients selection

Inclusion criteria: (1) Patients with severe pneumonia who met the diagnostic criteria as follows [11]: Main criteria: 1. Rely on invasive mechanical ventilation; 2. Vasoactive drugs are still needed after active fluid resuscitation in septic shock. Minor criteria: 1. Respiratory rate (RR) > 30 times/min; 2. PaO₂/FIO₂ < 250 mmHg; 3. Multilobular infiltration; 4. Patients with consciousness or orientation disorders; 5. The level of urea nitrogen > 7 mmol/L; 6. Hypotension requires active fluid resuscitation. Patients with severe pneumonia can be diagnosed by meeting one main criterion or three or more minor criteria. (2) General pneumonia patients should meet the relevant standards of Guidelines for the diagnosis and treatment of community-acquired pneumonia in adults in China, 2016 Edition [12]: 1. Community onset. 2. Relevant clinical manifestations: a. T >

37.3°C; b. Cough, expectoration or worsening of the original respiratory symptoms with or without chest pain, hemoptysis and dyspnea; c. Wet rale or pulmonary consolidation sign; d. WBC in peripheral blood > 10×10⁹/L or < 4×10⁹/L. 3. X-ray examination shows new signs such as patchy infiltration, consolidation of lobe or segment of lung, ground-glass opacity or interstitial changes, with or without pleural effusion. Patient with general pneumonia can be diagnosed by meeting any standard of 1, 2 and 3 and excludes other pulmonary diseases. (3) Initial treatment after onset of pneumonia. (4) Aged between 18 and 65.

Exclusion criteria: (1) Patients complicated with other infections or serious diseases. (2) Patients with liver, kidney, heart, brain and other organ dysfunction. (3) Patients with low compliance.

Methods

Five mL of venous blood from every selected patient was collected on an empty stomach early in the morning on the day after hospitalization. WBC was tested using the automatic blood routine analyzer (Beckman Kurt AU5800). The levels of PCT and CRP were examined using corresponding enzyme-linked immunosorbent assay kit (Beyotime Biotechnology CO., LTD., Shanghai).

Statistical analysis

Statistical analysis was carried out using SPSS 22.0. The numeration data are presented as the frequency and percentage. The measurement data are shown as mean ± standard deviation.

Differences of measurement data among groups were carried out by one-way analysis. Post hoc LSD-t pairwise comparison was used when the homogeneity of variance was used. The numeration data was compared using the χ^2 test. The correlation between PCT levels and WBC or CRP levels was analyzed using Pearson correlation coefficient method. Clinical values of individual detection of each index in predicting prognosis was analyzed by Receiver Operator Characteristic (ROC) curve. The clinical value of combined detection of various indicators in predicting prognosis was evaluated by constructing a bivariate Logistic regression

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Table 1. Comparison of general data among the three groups

Index	Severe pneumonia group (n=74)	General pneumonia group (n=74)	The control group (n=74)	t/ χ^2	P value
Age (year)	59.9±9.20	58.6±10.00	58.2±8.50	0.725	0.486
Gender					
Male (%)	41 (55.41)	44 (59.46)	45 (60.81)	0.483	0.786
Female (%)	33 (44.59)	30 (40.54)	29 (39.19)		
Protopathy (Cases)					
Pneumonia	32 (43.24)	37 (50.00)		0.916	0.633
Chronic obstructive pulmonary disease (COPD)	25 (33.78)	24 (32.43)			
Bronchopneumonia	17 (22.97)	13 (17.57)			

Table 2. The comparison of PCT, CRP and WBC level among the three groups

Group	PCT (ng/mL)	CRP (mg/L)	WBC ($\times 10^9/L$)
Severe pneumonia group	1.86±0.30* [#]	127.42±15.43* [#]	15.57±3.64* [#]
General pneumonia group	0.82±0.18*	64.87±5.96*	9.87±3.72*
Control group	0.09±0.02	2.37±0.24	5.52±1.34

Note: *P < 0.05 versus the control group; [#]P < 0.05 versus the general pneumonia group.

Table 3. The comparison of PCT, CRP and WBC level between the survival and death groups

Group	PCT (ng/mL)	CRP (mg/L)	WBC ($\times 10^9/L$)
The survival group	1.64±0.16	118.08±7.89	14.54±3.79
The death group	1.95±0.27	131.37±16.18	16.00±3.52
T value	4.585	3.663	2.134
P value	< 0.001	< 0.001	0.045

model using the indicator as the index variable. P-value < 0.05 was considered to indicate statistical significance.

Results

General data of the severe pneumonia group, general pneumonia group and the control group

The results below show that there was no statistical difference in the general data among these three groups (P > 0.05, **Table 1**).

The comparison of PCT, CRP and WBC level

The PCT, CRP and WBC levels in the severe pneumonia group were all significantly higher than that of the the general pneumonia group and the control group. At the same time, the level of every index in the general pneumonia

group was clearly higher than that in the control group (P < 0.05, **Table 2**).

The comparison of PCT, CRP and WBC levels between the survival and death groups

The results show that the level of PCT, CRP and WBC in the death group was higher than that in the survival group (P < 0.05, **Table 3**).

The correlation analysis between PCT and WBC or CRP levels in the severe pneumonia group

The results show that PCT was positively correlated with both CRP and WBC levels (r=0.774, 0.585; P < 0.001, **Figure 1**).

Prognostic value of PCT, CRP and WBC levels

The results show that the AUC of PCT, CRP and WBC levels for evaluating the prognosis of severe pneumonia was 0.825, 0.760 and 0.619, respectively. Among which, the sensitivity (80.8%) and specificity (77.3%) are better when the cut-off value of PCT is 1.685 ng/mL. Relevant parameters of each index are shown in **Table 4** and **Figure 2**.

Prognostic value of combined detection of various indicators

The results show that the AUC of PCT combined with CRP in evaluating the prognosis of severe pneumonia was 0.834. Relevant parameters of each index are shown in **Table 5** and **Figure 3**.

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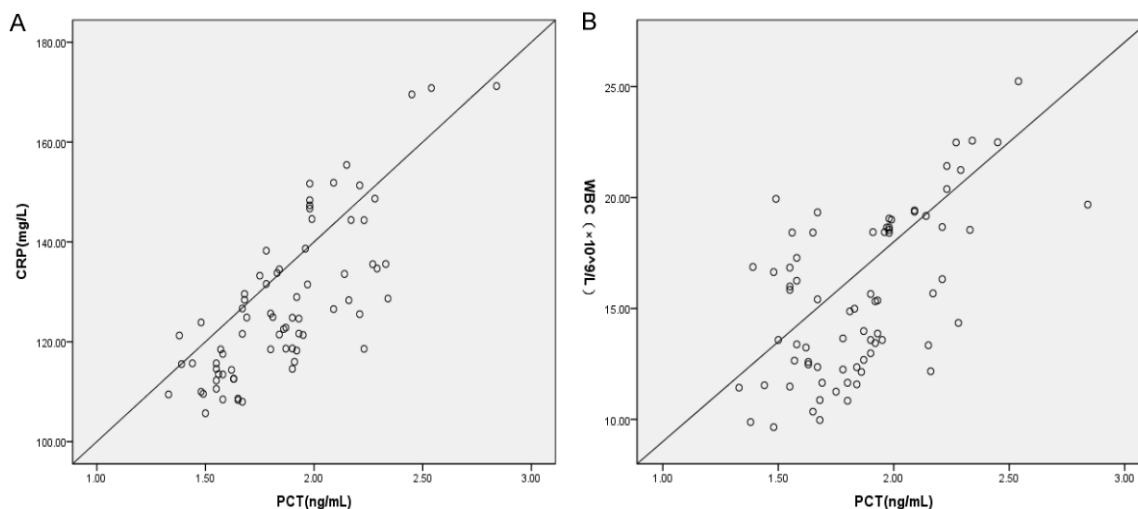


Figure 1. The correlation analysis between PCT and WBC or CRP level. A: PCT and CRP; B: PCT and WBC.

Table 4. Prognostic value of PCT, CRP and WBC level

Index	Cut-off value	AUC	95% CI	Sensitivity (%)	Specificity (%)
PCT (ng/mL)	1.685	0.825	0.705,0.944	80.8	77.3
CRP (mg/L)	124.835	0.760	0.650,0.869	61.5	81.8
WBC ($\times 10^9/L$)	11.56	0.619	0.467,0.772	96.2	36.4

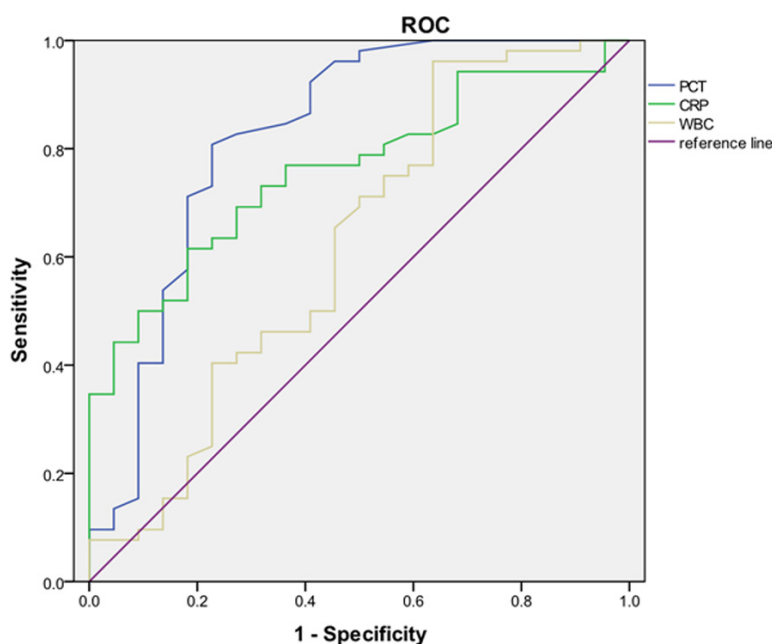


Figure 2. ROC curves of PCT, CRP and WBC levels.

Discussion

Studies have demonstrated that the balance between inflammatory factors and anti-inflam-

matory factors will be disregulated in severe pneumonia patients when the disease is aggravated. Besides, complications and even death can occur with development of the disease [13, 14]. Therefore, the detection of specific indicators has considerable clinical value for the diagnosis, treatment and prognosis evaluation of severe pneumonia patients.

PCT is a kind of pro-calcitonin without hormone activity, which has low serum levels under normal physiological conditions. However, serum PCT level increases rapidly once bacterial infection occurs and reaches its peak 6-8 hours post infection [15, 16]. The change of serum

PCT level is not obvious in non-bacterial infectious diseases due to its high specificity. Previous studies indicated that PCT level was tightly related to the severity of the disease in

Table 5. Prognostic value of combined detection of various indicators

Indicators	AUC	95% CI
PCT+CRP	0.834	0.722, 0.946
PCT+WBC	0.819	0.703, 0.935
CRP+WBC	0.760	0.651, 0.870
PCT+CRP+WBC	0.821	0.709, 0.933

bacterial infections, and it would decrease when the condition was alleviated or controlled [17]. CRP is a kind of stress-antagonistic reactive protein synthesized by the liver and it has been widely used in clinical diagnosis because its content is not affected by interference factors such as antibiotics, immune-suppressants and adrenocortical hormones. In addition, serum CRP level was found to rise rapidly at 4-6 hours post infection and reach a peak at 36-50 hours [18, 19]. Thus, some studies suggest that CRP detection can be used in the diagnosis and treatment of severe pneumonia as CRP level is closely related to the severity of severe pneumonia [20]. However, some others point out that CRP lacks specificity because serum CRP level could increase in the case of some other diseases such as trauma, viral infection, and cancer etc. [21]. As one of the most important cells in human blood, WBC are an important line of defense in immunity. Thus, the rise of WBC is clinically regarded as one of the diagnostic indicators of infection level because it indicates acute/chronic infection in the body or tissues, inflammation or tissue injury. However, the detection of WBC lacks specificity, as the rise of WBC levels can even be induced by physiological fluctuations. Our present study explored the expression of PCT, WBC and CRP in different pneumonia groups and the research results showed that the levels of PCT, WBC and CRP in patients with pneumonia and severe pneumonia were significantly higher than that in healthy people, and the levels were closely related to the severity of the disease. Consistent with previous findings, we suggest that PCT, WBC and CRP are all involved in the inflammatory response of severe pneumonia patients.

Previous studies mainly focused on the relationship between PCT, CRP and WBC levels and the severity of the disease. However, there are few reports about the correlation between PCT with CRP or WBC levels. Our present study fur-

ther explored the correlation between PCT and CRP or WBC levels in patients with severe pneumonia. The results showed that PCT was positively correlated with both CRP and WBC levels, indicating that PCT, CRP and WBC are all involved in the appearance and development of severe pneumonia, and there exists a certain relationship among them. However, related mechanism of interaction among these three indicators still needs to be further explored.

Previous reports have shown that PCT has a higher clinical value in the diagnosis and prognosis evaluation of severe pneumonia than CRP and WBC, and serum PCT level is closely related to the severity of severe pneumonia [22, 23]. Another study measured PCT, CRP and WBC levels of 1671 pneumonia patients at admission and the 28-day follow-up results showed that PCT level not only had a significantly higher clinical value compared with CRP and WBC in predicting adverse prognosis (mortality) of pneumonia, but also could identify patients with low mortality risk independently [24]. Moreover, Jain et al. [25] pointed out that the prognosis of patients was better when the serum PCT was lower than 7 ng/mL, and an increased risk of death was shown with high levels of PCT. The results of our present study show that both PCT and CRP have certain clinical significance in evaluating the prognosis of severe pneumonia patients. Clinical value of combined detection of related indicators in evaluating prognosis was also explored and the results showed that the AUC of PCT combined with CRP was 0.834, which is only 0.009 higher than PCT detection alone. Therefore, considering the medical cost and accuracy of prediction, we suggest that PCT detection alone has high clinical value in prognostic evaluation of severe pneumonia.

Taken together, serum PCT, WBC and CRP levels in severe pneumonia patients were found to be increased significantly, and PCT level was positively correlated with both WBC and CRP levels. We conclude that PCT detection has high clinical value in evaluating the prognosis of severe pneumonia patients. However, there are some shortcomings in our study, for instance, lack of dynamic observation of indicator changes and sample source simplification, which need to be further confirmed by subsequent studies.

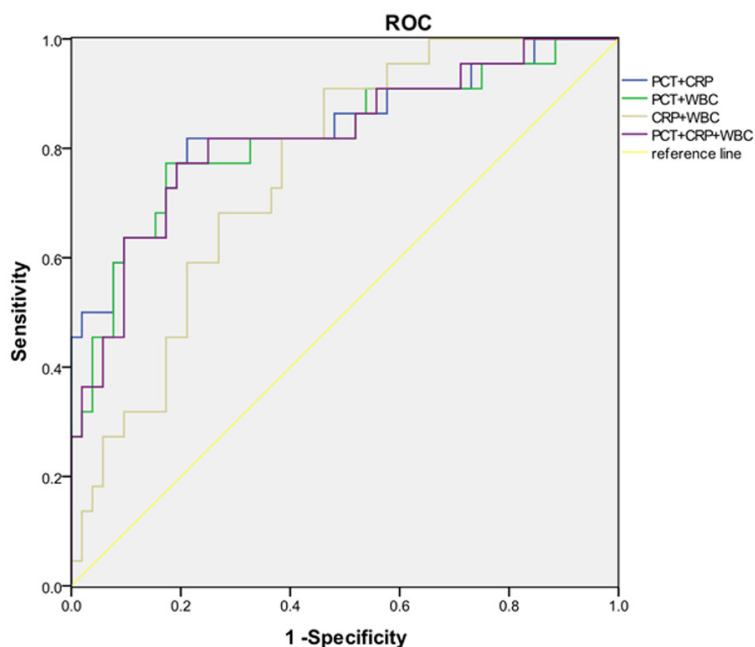


Figure 3. ROC curves of combined detection of various indicators.

Disclosure of conflict of interest

None.

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