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Original Article

Correlation of hs-CRP and T lymphocyte subsets with severity and prognosis in elderly pulmonary infection

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Abstract

Introduction: This study aimed to investigate the correlation between high-sensitivity (hs)-CRP, T lymphocyte subset profiles, disease severity, and treatment outcomes in elderly patients with pulmonary infection.

Methodology: The study included 85 elderly patients with respiratory infections (46 non-severe, 39 severe) and 79 healthy controls. The levels of hs-CRP, T lymphocyte subsets (CD4+/CD8+, CD4+, CD8+), and clinical pulmonary infection score (CPIS) were measured. Correlations with disease severity and CPIS were analyzed. Additionally, pre- and post-treatment levels of hs-CRP and T lymphocyte subsets were compared in patients with different treatment responses.

Results: Patients had lower CD4+ counts and CD4+/CD8+ ratios, but higher hs-CRP, CD8+, and CPIS levels ($p < 0.05$) compared to controls. Severe cases had lower CD4+ and CD4+/CD8+, but higher CD8+, hs-CRP, and CPIS, than non-severe cases ($p < 0.05$). CD4+ and CD4+/CD8+ were negatively correlated with disease severity and CPIS, while hs-CRP and CD8+ were positively correlated ($p < 0.05$). The patients who responded to treatment (responders) had higher increases in hs-CRP, CD4+, and CD4+/CD8+ after 7 days of treatment, compared to non-responders; while CD8+ levels were lower ($p < 0.05$). Receiver operating characteristic (ROC) analysis showed that an hs-CRP difference cutoff of 5.31 had the highest predictive value for treatment outcomes, with 86.67% sensitivity and 68.57% specificity.

Conclusions: hs-CRP and T lymphocyte subsets are closely associated with disease severity and treatment response in elderly patients with pulmonary infection, and their dynamic monitoring may aid in clinical prognosis evaluation.

Key words: infection; hs-CRP; microbiome; lymphocytes; prognosis.

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Introduction

Pulmonary infection refers to lung parenchyma inflammation occurring in the terminal airways, alveolar spaces, and lung interstation [1–2]. Elderly patients often experience fatigue in expectoration and dullness in response, coupled with physical aging and respiratory system function degradation. The decline in systemic and respiratory local defense and immune function leads to persistent pulmonary infection, which can easily progress to severe pneumonia, causing multi-organ functional failure and even death [3]. The pathophysiology of pulmonary infection in the elderly is complex. Current research findings indicate potential associations with regional immunological alterations, particularly in cellular immunity. The quantitative assessment of T-cell subpopulations has been established as a reliable indicator for monitoring host immune status during initial disease stages [4–5]. Additionally, in recent years, clinical attention has gradually shifted to pulmonary infections caused by intestinal flora. Specifically, *Bifidobacteria* can enhance the killing ability of NK cells and proliferate T lymphocytes [6]. As a sensitive inflammatory marker, hs-CRP represents an acute-phase protein that demonstrates rapid elevation following infectious stimuli. Substantial evidence has established its significant role in both the initiation and progression of respiratory tract infections [7], but the prognostic significance of this biomarker in geriatric populations with respiratory tract infections warrants additional

investigation through well-designed clinical studies. Therefore, this study focused on analyzing the relationship between hs-CRP, T lymphocyte subsets, and pulmonary infection; and its efficacy in the elderly, aiming to provide a new insight for clinical efficacy evaluation. It was hypothesized that the severity and prognosis of pulmonary infection in elderly patients are closely associated with systemic inflammation levels (reflected by hs-CRP) and cellular immune status (indicated by T lymphocyte subsets). Specifically, severe cases would show more prominent inflammatory and immune dysregulation, and dynamic changes in these markers could predict treatment response.

Methodology

Study participants

The experimental cohort comprised 85 geriatric cases diagnosed with respiratory tract infections, who were recruited from our medical institution for this investigation from January 2018 to January 2020, including 39 cases of severe infection and 46 cases of non-severe infection. A total of 79 healthy participants who completed routine health screenings contemporaneously served as the reference cohort. Statistical analysis confirmed comparable baseline characteristics across both populations, demonstrating appropriate group matching ($p > 0.05$; Table 1).

Criteria

Inclusion criteria

The inclusion criteria were: dry and wet rales were audible on lung auscultation, patchy infiltration shadows were visible in the lungs on computed tomography (CT) or chest X-ray examination, all patients were in the acute exacerbation stage, age > 60 years. The criteria for inclusion in the severe pulmonary infection study group were: the range of lung lesions expanded by 50.0% or more within 2 days of admission, mechanical ventilation was required, serum creatinine was above 177 μmol/L, urine volume was below 400 mL/day, oxygenation index was below 250 mmHg, respiratory rate was above 30 breaths/min, and the lesions involved both lungs. In contrast, the control group showed no patchy infiltration shadows in the lungs on CT or chest X-ray examination and had no clinical symptoms such as cough, fever, or expectoration.

Written informed consent was obtained from each participant prior to study enrollment. The research protocol received formal approval from the Institutional Review Board at our healthcare facility.

Exclusion criteria

The following patients were excluded: patients with organic lesions in vital organs such as kidney and liver; patients with severe myelosuppression; patients with severe craniocerebral injury, congenital heart disease, and other diseases; patients with severe infection, trauma, or active pulmonary tuberculosis in other parts of the body within the past 14 days; patients with alimentary tract hemorrhage, ileus, abdominal infection, or chronic gastrointestinal diseases; patients with abnormal mental behavior.

Sample size calculation

The sample size for this study was determined a priori using G*Power software (version 3.1.9.7). The calculation was based on the primary outcome of comparing the difference in hs-CRP levels between the severe and non-severe patient groups.

An independent samples *t*-test was selected as the appropriate statistical test. A large effect size was anticipated (Cohen's d) of approximately 0.80, based on preliminary data from a pilot study and previous clinical literature, to detect a clinically meaningful difference in hs-CRP levels between groups.

A minimum of 26 participants per group was required to achieve a statistical power (1 - β) of 80% with a two-sided significance level (α) of 0.05. The recruitment target was expanded to account for a potential attrition rate of up to 20% and to ensure robust subgroup analyses. Therefore, a total sample size of 85 patients was deemed sufficient for this study. The final cohort included 39 severe and 46 non-severe cases,

Table 1. General characteristics of the two groups.

	Study group (n = 85)	Control Group（n = 79）	t/χ^2	*p*
Gender (Male/Female)	48/37	44/35	0.010	0.921
Age (year)	61～75 (66.16 ± 2.04)	59～74 (65.84 ± 2.45)	0.911	0.364
BMI (kg/m²)	17.5～23.6 (20.82 ± 1.37)	17.8～23.9 (21.06 ± 1.40)	1.109	0.269
Waist hip ratio	0.7～1.6 (1.28 ± 0.15)	0.9～1.8 (1.30 ± 0.17)	0.800	0.425
Smoking history				
Yes	50 (58.82)	46 (58.23)	0.006	0.938
No	35 (41.18)	33 (41.77)		
Drinking history				
Yes	36 (42.35)	34 (43.04)	0008	0.929
No	49 (57.65)	45 (56.96)		

exceeding the minimum requirement.

Methods

Detection arrangements

hs-CRP was measured before and after 7 days of treatment. A 3 mL sample of venous blood was collected on an empty stomach with vacuum blood collection tubes without anticoagulant (BD, Franklin Lakes, USA). The blood sample was centrifuged (speed: 3500 r/min, time: 8 min, radius: 10 cm) to separate the serum from the blood, and the serum was refrigerated at - 80 ℃ for later use. The electrochemiluminescence kit (Roche, Basel, Switzerland) was used to detect hs-CRP levels.

T-cell subpopulations at baseline and post-treatment intervals were analyzed in venous blood specimens (6 mL) collected in vacuum blood collection tubes containing ethylene diamine tetraacetic acid (K2EDTA) as an anticoagulant (BD, Franklin Lakes, USA), following an 8-hour fasting period using standardized collection procedures. The samples were immediately transferred into anticoagulant-treated vacutainers and maintained at ambient temperature prior to processing. The whole blood samples for flow cytometry analysis were stored at 4 °C and processed within 24 hours to ensure lymphocyte viability and stability. The flow cytometer (BD Biosciences, San Jose, USA) was used to detect CD4+, CD4+/CD8+, and CD8+ levels (Beckman Kurt, Brea, USA).

Treatment methods

The study group received basic treatments such as oxygen inhalation, electrocardiographic monitoring, and nutritional support. At the same time, physical cooling was provided for patients with a body temperature of 38–38.5 ℃, and symptomatic treatment was given for those with a body temperature > 38.5℃. Type I antibiotic anti-infection treatment was administered based on the pathogenic bacteria results, with continuous treatment for 14 days.

Observatory variables

The levels of hs-CRP, T lymphocyte subsets, and the degree of pulmonary infection were compared between the two groups. The degree of pulmonary infection was evaluated using the clinical pulmonary infection score (CPIS) [8], which assesses five aspects: body temperature, white blood cell count (WBC), respiratory secretions, infiltration on chest X-ray, tracheal aspirate or sputum culture, and oxygenation index. Each dimension was scored from 0 to 2, with the score positively correlated with the degree of pulmonary infection.

The levels of hs-CRP, T lymphocyte subsets, and CPIS scores were compared among patients with different disease severities. The correlation between hs-CRP, T lymphocyte subsets, and disease severity, as well as CPIS scores, were analyzed.

The treatment effect was evaluated in the study group. Effectiveness was defined as the normalization of body temperature, the disappearance of clinical symptoms, and complete absorption or absorption of more than 60.0% of inflammation visible on chest X-ray after 14 days of treatment. Ineffectiveness was defined as not meeting the criteria for effectiveness. The levels of hs-CRP and the difference between before treatment and after 7 days of treatment, T lymphocyte subsets, and their difference between effective and ineffective patients in the study group before and after treatment were compared. The selection of the 7-day post-treatment time point was based on established clinical practice and the pharmacokinetics of inflammatory markers. While guidelines recommend assessing initial clinical response within 48–72 hours, a one-week interval is widely adopted in clinical research for evaluating early biological response. The predictive value of hs-CRP difference and T lymphocyte subset difference on the efficacy of treatment for pulmonary infection in the elderly were analyzed.

Statistical analysis

Statistical analysis was performed using SPSS version 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA). Continuous variables were presented as mean values with standard deviations and were evaluated through Student's t-test. Categorical variables were shown as frequencies with percentages and were examined using Chi-square analysis. Statistical evaluations included Spearman's rank correlation coefficient for assessing variable associations and receiver operating characteristic (ROC) curve analysis

Table 2. Comparison of hs-CRP, T lymphocyte subsets, and clinical pulmonary infection score (CPIS) between the two groups $(\overline{X} \pm s)$.

Group	n	hs-CRP (mg/L)	$CD4^+/CD8^+$	$CD8^+$ (%)	$CD4^+$ (%)	CPIS score (point)
Study group	85	15.10 ± 5.31	1.01 ± 0.55	32.58 ± 4.41	32.90 ± 3.41	6.41 ± 1.05
Control group	79	2.23 ± 0.38	1.55 ± 0.57	28.95 ± 3.50	44.83 ± 3.88	1.02 ± 0.38
t		21.487	6.173	5.819	20.950	43.072
p		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Table 3. Comparison of hs-CRP, T lymphocyte subsets, and clinical pulmonary infection score (CPIS) score among patients with different disease severity in the study group $(\overline{X} \pm s)$.

Group	n	hs-CRP (mg/L)	$CD4^+/CD8^+$	$CD8^+$ (%)	$CD4^+$ (%)	CPIS (point)
Severe	39	16.89 ± 3.55	0.79 ± 0.41	36.63 ± 4.52	28.82 ± 3.38	7.52 ± 2.26
Non-severe	46	13.58 ± 3.27	1.25 ± 0.56	29.15 ± 3.44	36.36 ± 4.13	5.47 ± 1.64
t		4.471	4.252	8.654	9.104	4.833
p		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

for determining predictive capacity. Results achieving significance levels below 0.05 were regarded as statistically meaningful.

Results

Comparison of hs-CRP, T lymphocyte subsets, and CPIS score in the two groups

Analysis revealed significantly reduced CD4+ T-cell counts and diminished CD4+/CD8+ ratios in the experimental cohort when contrasted with healthy controls. Conversely, elevated concentrations of high-sensitivity C-reactive protein, increased CD8+ lymphocyte levels, and higher clinical pulmonary infection scores were observed in the intervention group ($p < 0.05$; Table 2).

Comparison of hs-CRP, T lymphocyte subsets, and CPIS score among patients with different disease severity in the study group

Comparative immunological profiling demonstrated that critically ill cases exhibited significantly decreased CD4+ T-cell counts and CD4+/CD8+ ratios; while showing elevated CD8+ levels, CPIS, and hs-CRP concentrations relative to their less severe counterparts ($p < 0.05$; Table 3).

Correlation between various indicators, and disease severity and CPIS score

CD4+ and CD4+/CD8+ were negatively correlated with disease severity and CPIS score. The analysis revealed significant positive associations between elevated hs-CRP concentrations, increased CD8+ lymphocyte counts, and both clinical severity indices and pulmonary infection scoring system values ($p < 0.05$; Table 4).

Effective and ineffective patients' hs-CRP and T lymphocyte subsets before and after treatment in the study group

The therapeutic outcomes analysis demonstrated that 70 patients achieved clinical improvement following the 14-day intervention, whereas 15 cases showed treatment resistance. Baseline characteristics revealed comparable pre-treatment values of hs-CRP, CD4+ T-cell counts, CD4+/CD8+ ratios, and CD8+ lymphocyte levels between responsive and non-responsive subgroups ($p > 0.05$). Subsequent evaluation at the 7-day time point indicated statistically significant differences, with treatment-responsive patients exhibiting elevated hs-CRP concentrations, increased CD4+ levels, and enhanced CD4+/CD8+ ratios compared to non-responders, while demonstrating reduced CD8+ lymphocyte counts relative to the treatment-resistant group ($p < 0.05$; Table 5).

Predictive value of therapeutic effect

The ROC curve showed that when the cutoff value for the difference in hs-CRP was 5.31, it yielded the

Table 4. Correlation between the variables and the degree of illness and clinical pulmonary infection score (CPIS).

Observatory variable	Degree of illness		CPIS Score	
	r	*p*	*r*	*p*
hs-CRP	0.688	< 0.001	0.653	< 0.001
$CD4^+/CD8^+$	- 0.633	< 0.001	- 0.651	< 0.001
$CD8^+$	0.549	< 0.001	0.510	< 0.001
$CD4^+$	- 0.561	< 0.001	- 0.564	< 0.001

hs-CRP: high-sensitivity C-reactive protein.

Table 5. Effective and ineffective patients' hs-CRP and T lymphocyte subsets before and after treatment in the study group $(\overline{X} \pm s)$.

Group	n	hs-CRP (mg/L)			$CD4^+/CD8^+$			$CD8^+$ (%)			$CD4^+$ (%)		
		Before treatment	After 7 days of treatment	Difference	Before treatment	After 7 days of treatment	Diference	Before treatment	After 7 days of treatment	Diference	Before treatment	After 7 days of treatment	Diference
Effective	70	15.02 ± 4.28	7.05 ± 2.23	7.97 ± 2.06	1.01 ± 0.48	1.50 ± 0.33	0.49 ± 0.24	32.41 ± 3.65	28.53 ± 3.12	4.46 ± 1.41	32.87 ± 4.05	40.05 ± 3.89	7.18 ± 2.46
Ineffective	15	15.47 ± 4.16	11.01 ± 3.25	4.36 ± 1.33	1.10 ± 0.42	1.25 ± 0.24	0.15 ± 0.03	33.37 ± 4.23	30.32 ± 3.01	3.05 ± 0.34	33.04 ± 3.82	37.78 ± 4.13	4.74 ± 1.42
t		0.371	5.722	6.486	0.672	2.775	5.452	0.899	2.028	3.832	0.149	2.029	3.700
p		0.711	0.000	0.000	0.503	0.007	< 0.001	0.371	0.046	< 0.001	0.882	0.046	< 0.001

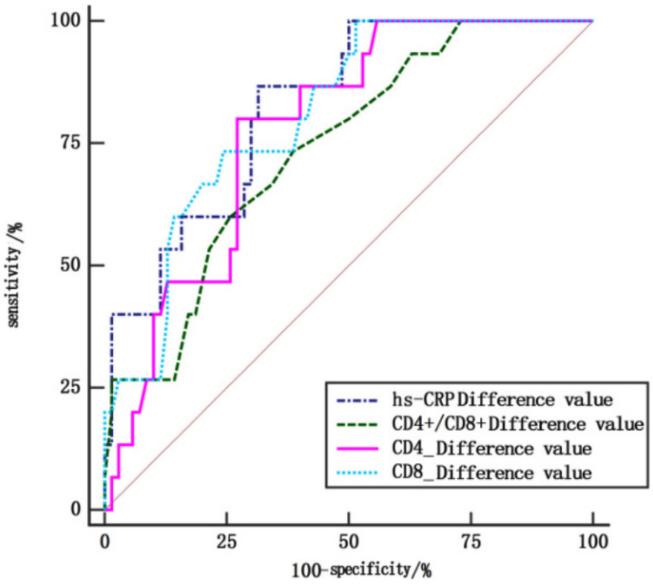
maximum area under curve (AUC) for predicting the efficacy of treatment for pulmonary infection in elderly patients, with a sensitivity and specificity of 86.67% and 68.57%, respectively (Table 6 and Figure 1).

Discussion

Studies indicate that elderly patients with pulmonary infections often have multiple pathogenic infections, which can easily progress to severe pneumonia [9–10], and the fatality rate among elderly patients with severe pneumonia can reach 50% [11]. Antibiotic therapy, as a fundamental treatment for infections, can effectively eliminate pathogenic bacteria. However, some patients may still experience poor treatment outcomes due to increasing drug resistance.

T lymphocyte subsets constitute a crucial cell population for immune system function. Among these, CD4 is a protein molecule present on the cell surface. The identification of CD4+ T-cells is accomplished through the detection of surface CD4 markers, which serve as specific cellular identifiers. These lymphocytes are crucial for orchestrating and modulating the body's immunological defense mechanisms. CD4+ T lymphocytes can recognize antigen peptide-MHC class II molecule complexes presented by antigen-presenting cells, leading to their activation. Activated CD4+ T lymphocytes can further differentiate into various subsets, such as helper T cells (Th), including Th1, Th2, and Th17. These distinct T-cell populations exhibit specialized immunological functions. Th1 lymphocytes predominantly mediate defense mechanisms against intracellular microorganisms through cell-mediated immunity, whereas Th2 cells principally facilitate antibody-dependent immune reactions by supporting B-lymphocyte antibody production. CD4+ T-cells play a crucial role in orchestrating immune system activation, modulation, and homeostasis, contributing substantially to both antimicrobial defense and the pathogenesis of autoimmune disorders. In certain immune-related diseases, such as acquired immune deficiency syndrome, the HIV virus primarily attacks CD4+ T lymphocytes, reducing their numbers and impairing their function. This leads to the collapse of the immune system and triggers various severe infections and tumors [12–13]. On the other hand,

Figure 1. Predictive value of therapeutic effect.



CD8+ T lymphocytes represent an important cell population responsible for specific cellular immunity in the immune system. These immune cells are essential for preserving immunological defense mechanisms and maintaining immune system equilibrium (14). Upon activation, cytotoxic T lymphocytes secrete effector molecules including perforin and granzymes, mediating direct cytolysis of target cells. Additionally, they express Fas ligand, which interacts with Fas receptors on target cell membranes, triggering programmed cell death. CD8+ T-cells serve a vital function within the immune system's surveillance network, in identifying and eliminating pathological cells, particularly those compromised by viral infection or malignant transformation. Additionally, CD8+ T lymphocytes participate in the formation of immune memory, enabling a more potent and effective immune response when encountering the same pathogen again. In this study, flow cytometry revealed abnormal expressions of CD4+, CD4+/CD8+, and CD8+ levels in elderly patients with pulmonary infection, which is generally consistent with Xu Ying's viewpoint [15]. This may be attributed to the fact that pulmonary infection stimulates the body's stress state, intensifies oxidative stress damage, and increases the excitability of the hypothalamus-hypophysis-adrenal axis [16–18]. The main manifestations are CD4+ apoptosis, CD8+

Table 6. Predictive value of therapeutic effect.

Observatory variable	AUC	95% CI	Critical value	Sensitivity	Specificity
Difference of hs-CRP	0.825	0.727～0.899	≤ 5.31	86.67%	68.57%
Difference of $CD4^+/CD8^+$	0.737	0.630～0.827	≤ 0.21	73.33%	61.43%
Difference of $CD4^+$	0.808	0.708～0.885	≤ 3.11 %	73.33%	75.71%
Difference of $CD8^+$	0.779	0.675～0.861	≤ 5.5 %	80.00%	72.86%

proliferation, and CD4+/CD8+ imbalance [19–21]. According to Spearman's correlation analysis in this study, there is a certain correlation between CD4+, CD8+, CD4+/CD8+, and the severity of the disease and CPIS score in elderly patients with pulmonary infection, which is similar to the research results of Yan [22]. The mechanism may be that abnormal expressions of CD4+, CD8+, and CD4+/CD8+ levels can massively eliminate activated T lymphocytes, stimulate immune responses in elderly patients with pulmonary infection, and aggravate immune damage, thereby promoting the occurrence and development of the disease. This indirectly indicates that T lymphocyte subsets can serve as a reference indicator for diagnosing severe pulmonary infection in the elderly. It is suggested that clinical practice should adopt the CPIS score combined with T lymphocyte subsets as an auxiliary means to evaluate the severity of respiratory tract infections in geriatric patients.

The previous study indicated that early hs-CRP levels can affect the prognosis of patients with severe pneumonia to some extent [23]. The investigation's findings demonstrate a strong association between hs-CRP concentrations and both clinical status and pulmonary infection severity scores. Significant variations were observed across prognostic groups, aligning with previous research by Ji and colleagues [24]. The data indicate that this inflammatory biomarker serves as a reliable parameter for assessing systemic inflammation and predicting clinical outcomes, potentially emerging as a valuable prognostic tool in clinical practice. Furthermore, in this study, the effective patients in the treatment group after 7 days of therapy had higher hs-CRP difference values, CD4+, CD4+/CD8+ levels, and their respective difference values compared to the ineffective patients; while CD8+ levels and their difference values were lower in the effective patients ($p < 0.05$). This suggests that hs-CRP difference values, CD4+, CD4+/CD8+ levels, and their respective difference values are associated with treatment efficacy. The levels before treatment mainly reflect the disease state, and factors such as treatment interference and individual sensitivity can reduce the predictive value for prognosis. However, the difference values before and after 7 days of treatment reflect the changes in various indicators with treatment. Therefore, this study used difference values to make predictions and found that an hs-CRP difference cut-off value of 5.31 is the most accurate at predicting how well treatment will work in older patients with pulmonary infection. This suggests that better detection can help doctors figure out how well treatment is working for these patients.

Conclusions

Elderly patients with pulmonary infection are closely associated with hs-CRP and cellular immunity. Dynamic monitoring of hs-CRP and cellular immunity can provide a new approach for clinically predicting the efficacy of treatment in elderly patients with pulmonary infection.

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Ethics approval

This research was conducted in compliance with internationally recognized ethical guidelines, adhering to both the principles outlined in the Helsinki Declaration (1964) with subsequent revisions and the regulatory standards established by the national institutional review board for human subject protection. The study was approved by the Ethics Committee of Huzhou Central Hospital.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Data availability statement

All data are provided in this study, and raw data can be requested from the corresponding authors.

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Conflict of interest

No conflict of interest is declared.

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