Cite as: Fu DL, Chen DJ, Ren L, Hou XL. Relationship between Th1/ Th2 cytokines and severity of acute lung injury secondary to sepsis [J]. Chin J Clin Res, 2025, 38(8):1197-1201.

DOI: 10.13429/j.cnki.cjcr.2025.08.012

Relationship between Th1/Th2 cytokines and severity of acute lung injury secondary to sepsis

FU Daoliang, CHEN Dejian, REN Lei, HOU Xiaolin

Emergency Department, Zigong First People's Hospital, Zigong Academy of Medical Sciences, Zigong, Sichuan 643000, China

Corresponding author: HOU Xiaolin, E-mail: 25460536@qq.com

Abstract: Objective To analyze the effects of helper T cells (Th)1 and Th2 cytokines on the severity of acute lung injury (ALI) secondary to sepsis and to analyze their roles in evaluating the occurrence of ALI secondary to sepsis. **Methods** Clinical data of 206 patients with sepsis from Zigong First People's Hospital from January 2021 to June 2024 were retrospectively collected, and they were divided into ALI group (62 cases) and simple group (144 cases) according to whether ALI was secondary or not. Serum Th1 cytokines [interferon-γ (INF-γ), tumor necrosis factor α (TNF-α)] and Th2 cytokines [interleukin (IL)-4, IL-10] were measured and the Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were performed for all patients at admission. Patients in ALI group were divided into mild-risk group (<10, 25 cases), moderate-risk group (10-20, 20 cases) and high-risk group (>20, 17 cases) according to APACHE II scores. The effects of Th1 and Th2 cytokines on the severity of ALI secondary to sepsis and their roles in predicting to occurrence of ALI were analyzed. **Results** In patients of ALI secondary to sepsis, the levels of IL-4 and IL-10 decreased, while the levels of IFN-γ and APACHE II scores increased, in the order of mild-risk group, moderate-risk group and high-risk group, with statistical significance (P<0.05). The level of TNF-α in mild-risk group was lower than that in moderate-risk group and high-risk group (P<0.05). IL-4 and IL-10 were negatively correlated with APACHE II scores (r=-0.720, -0.537, P<0.01), while IFN-γ and TNF-α were positively correlated with APACHE II scores (r=0.696, 0.551, P<0.01). Logistic regression analysis showed that low oxygenation index (β=-0.202, P<0.01), low IL-4 level (β=-0.230, P<0.01), high IFN-γ level (β=1.106, P<0.01), and high TNF-α level (β =0.012, P<0.05) were independent risk factors for ALI secondary to sepsis. The area under the receiver operating characteristic curve of oxygenation index, IL-4, IFN-γ, TNF-α in the evaluation of ALI secondary to sepsis was 0.929, 0.920, 0.661, 0.679, respectively. **Conclusion** Th1/Th2 cytokines are closely related to the severity of ALI secondary to sepsis. High levels of oxygenation index and IL-4, and low levels of IFN-γ and TNF-α can promote more severe ALI secondary to sepsis, and these four indicators have certain clinical reference value for evaluating the prediction of ALI secondary to sepsis.

Keywords: Sepsis; Acute lung injury; Helper T cells 1; Helper T cells 2; Cytokines; Oxygenation index

Fund program: National Natural Science Foundation of China (81802079)

Sepsis is a systemic inflammatory response syndrome caused by infection, characterized by complex conditions and rapid progression [1]. Sepsis is associated with numerous clinical complications, with acute lung injury (ALI) being one of the most common. ALI refers to the acute inflammatory response and dysfunction of the lungs induced by sepsis. ALI not only significantly increases the mortality rate of patients but also severely affects their prognosis and quality of life [2]. Helper T cells (Th1 and Th2 cells) play a key role in immune responses. Under normal circumstances, there is a dynamic balance between Th1 and Th2 cells to maintain immune homeostasis. However, in pathological conditions like sepsis, this balance is disrupted, leading to immune response imbalance, which further exacerbates tissue damage and organ dysfunction. Studies have shown that the imbalance of Th1/Th2 cytokines in sepsis patients is closely related to the severity of the disease [3]. During sepsis, the body produces a large number of pro-inflammatory cytokines to combat the infection. While these cytokines help eliminate pathogens, their excessive production can lead to an overactivation of the systemic inflammatory response, causing pathological changes such as increased pulmonary microvascular permeability, damage to the alveolar-capillary barrier, and pulmonary edema. Additionally, the overexpression of pro-inflammatory cytokines may suppress the production of anti-inflammatory cytokines [4-5]. This imbalance of Th1/Th2 cytokines further exacerbates lung inflammation and tissue damage. This study aims to explore the relationship between Th1/Th2 cytokine levels in the peripheral blood of sepsis patients and the severity of secondary ALI, and analyze the risk factors for secondary ALI in sepsis, providing a reference for formulating effective treatment strategies.

1. Materials and Methods

1.1 General Data

This study retrospectively collected clinical data from 206 sepsis patients treated at the Zigong First People's Hospital between January 2021 and June 2024. Based on whether ALI developed, patients were divided into the ALI group (62 cases) and the non-ALI group (144 cases).

Inclusion criteria:

(1) Met internationally recognized sepsis diagnostic criteria, such as those outlined in Sepsis-3 definition for sepsis [6]. Patients in the ALI group met the Berlin criteria for acute respiratory distress syndrome (ARDS), which includes the definition of ALI [7].

(2) Aged over 18 years.

(3) Completed the Acute Physiology and Chronic Health Evaluation II (APACHE II) score after admission.

(4) Peripheral blood samples were collected on the day of admission for the measurement of related Th1/Th2 cytokine levels.

(5) Complete examination results.

Exclusion criteria:

(1) ALI caused by other factors (*e.g.*, trauma, aspiration pneumonia, drug reactions).

(2) Presence of severe heart, liver, kidney failure, or other diseases that may affect immune response and cytokine levels.

(3) Long-term use of immunosuppressive drugs or immunodeficiency diseases.

(4) History of severe infections within the past month.

(5) Undergoing treatment that may affect immune response and cytokine levels.

(6) Incomplete data collection or inability to perform analysis for other reasons.

(7) Death within 24 hours after admission or withdrawal from treatment.

This study was approved by the Ethics Committee of Zigong First People's Hospital (Ethics approval number: 20240508).

1.2 ALI Severity Assessment Grouping

Upon admission, the APACHE II score was immediately completed. Based on the APACHE II score, patients in the ALI group were divided into mild-risk group (<10 points, 25 cases), moderate-risk group (10-20 points, 20 cases) and high-risk group (>20 points, 17 cases).

1.3 Methods

Patient electronic medical records were reviewed to collect relevant clinical indicators:

(1) General data: gender, age, body mass index (BMI), heart rate at admission, systolic and diastolic blood pressure, oxygenation index (OI), underlying conditions such as hypertension, diabetes, coronary artery atherosclerotic heart disease (CHD), chronic obstructive pulmonary disease (COPD), cerebrovascular diseases, and the primary infection type.

(2) APACHE II score at admission: The APACHE II score includes acute physiology score, age score, and chronic health score. The total score is the sum of these three components, with a maximum score of 71 points. The score correlates positively with the severity of the condition.

(3) Laboratory indicators: Serum cytokines secreted by Th1 cells [interferon-γ (INF-γ), tumor necrosis factor (TNF)-α], and cytokines secreted by Th2 cells [interleukin (IL)-4, IL-10]. Specific testing method: 7 mL of blood was collected from the cubital vein at admission, centrifuged at 2 500 rpm for 15 minutes (centrifuge radius 10 cm), and serum was collected. Cytokine levels were detected using enzyme-linked immunosorbent assay (ELISA).

1.4 Statistical Methods

The figures in this study were created using GraphPad Prism software, and data were analyzed using SPSS 22.0 software. Categorical data were expressed as *n*(%), and the chi-square test was performed. For normally distributed continuous variables, data were expressed as $\bar{x} \pm s$. One-way analysis of variance (ANOVA) was used for comparing multiple groups, and pairwise comparisons were made using the LSD-*t* test. Pearson correlation analysis was used to assess correlations. Logistic regression was used to analyze the risk factors for ALI secondary to sepsis, and receiver operating characteristic (ROC) curve analysis was performed to assess the predictive efficacy of various indicators for secondary ALI in sepsis. A P-value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of Data Related to Different Severity Levels of Sepsis-Related ALI

In patients with sepsis-induced ALI, the levels of IL-4 and IL-10 decreased in order from the mild-risk group to the moderate-risk group and high-risk group, while the levels of IFN-γ and APACHE II scores increased, with differences being statistically significant (P<0.05). The TNF-α level in the mild-risk group was lower than in the moderate-risk and high-risk groups (P<0.05). See **Table 1**.

Tab.1 Comparison of related data in patients with different severity of ALI secondary to sepsis

Group	IL-4(ng/L)	IL-10(ng/L)	IFN-γ(ng/L)	TNF-α(pg/L)	APACHE II
Mild-risk group (*n*=25)	76.15±5.59^{ab}	35.14±6.05^{ab}	7.01±1.05^{ab}	306.10±75.64^{a}	7.88±1.36^{ab}
Moderate-risk group (*n*=20)	71.59±5.65^{a}	28.13±5.79^{a}	8.06±1.12^{a}	351.45±80.44	16.15±2.01^{a}
High-risk group (*n*=17)	53.65±10.60	22.45±6.61	9.03±1.02	401.71±81.64	28.06±.97
***F* value**	50.558	22.344	18.506	7.486	463.713
***P* value**	<0.001	<0.001	<0.001	<0.001	<0.001

Note: Compared with high-risk group, ^{a}P<0.05; Compared with moderate-risk group, ^{b}P<0.05.

2.2 Correlation Between Th1/Th2 Cytokines and Severity of Sepsis-Induced ALI

IL-4 and IL-10 were negatively correlated with the APACHE II score (r=-0.720, P<0.01; r=-0.539, P<0.01). IFN-γ and TNF-α were positively correlated with the APACHE II score (r=0.696, P<0.01; r=0.551, P<0.01).

2.3 Univariate Analysis of Factors Affecting Sepsis-Induced ALI

There was no statistically significant difference between the ALI group and the non-ALI group in terms of age, BMI, APACHE II score, admission heart rate, blood pressure, gender, smoking and drinking habits, hypertension, diabetes, coronary heart disease, COPD, CHD, infection site, and IL-10 levels (P>0.05). However, differences in OI, IL-4, IFN-γ, and TNF-α levels were statistically significant (P<0.05). See **Table 2**.

2.4 Multivariate Logistic Regression Analysis of Factors Affecting Sepsis-Induced ALI

Variables with significant differences in the univariate analysis—OI, IL-4, IFN-γ, and TNF-α—were taken as independent variables (continuous variables, original values used). Sepsis-induced ALI was taken as the dependent variable (non-ALI=0, ALI=1), and a binary logistic regression model was applied. The results showed that OI, IL-4, IFN-γ, and TNF-α were independent influencing factors for sepsis-induced ALI (P<0.05). See **Table 3**.

2.5 Predictive Efficacy of OI, IL-4, IFN-γ, and TNF-α for Sepsis-Induced ALI

ROC curve analysis showed that the AUC for the assessment of sepsis-induced ALI using OI, IL-4, IFN-γ, and TNF-α were 0.929, 0.920, 0.661, and 0.679, respectively. The cut-off values were 164.14, 76.750 ng/L, 8.485 ng/L, and 364.395 pg/L, receptively. See **Table 4** and **Figure 1**.

Tab.2 Univariate analysis influencing ALI secondary to sepsis

Indicators	ALI group (n=62)	Non-ALI group (n=144)	t/χ^2 value	P value
Age(years)[a]	47.12±10.12	46.99±10.43	0.083	0.934
BMI(kg/m^2)[a]	22.01±2.43	22.19±2.29	0.508	0.612
APACHE II[a]	16.08±8.48	17.47±7.50	1.173	0.242
Admission HR(beats/min)[a]	102.45±20.10	99.75±20.54	0.871	0.385
Admission SBP(mmHg)[a]	120.44±13.12	121.65±11.07	0.680	0.498
Admission DBP(mmHg)[a]	78.45±8.95	77.15±8.59	0.984	0.326
OI[a]	151.97±12.93	175.46±10.45	12.638	<0.001
Gender[b]				
Male	37(59.68)	85(59.03)	0.008	0.931
Female	25(40.32)	59(40.97)		
Smoking[b]	21(33.87)	45(31.25)	0.137	0.712
Drinking[b]	20(32.26)	40(27.78)	0.421	0.516
Hypertension[b]	19(30.65)	42(29.17)	0.045	0.831
Diabtes[b]	11(17.74)	25(17.36)	0.004	0.947
CHD[b]	10(16.13)	23(15.97)	0.001	0.978
COPD[b]	8(12.90)	19(13.19)	0.003	0.955
Cerebrovascular Disease [B]	8(12.90)	17(11.81)	0.049	0.825
Infection Site [B]				
Respiratory Tract	17(27.42)	36(25.00)		
Abdomen	15(24.19)	37(25.69)		
Urinary System	17(27.42)	39(27.08)	0.191	0.996
Skin Tissue	7(11.29)	18(12.50)		
Other	6(9.68)	14(9.72)		
IL-4(ng/L)[a]	68.51±11.84	84.35±5.21	10.121	<0.001
IL-10(ng/L)[a]	29.40±7.99	30.16±5.77	0.677	0.443
IFN-γ(ng/L)[a]	7.90±1.34	7.11±1.29	3.985	<0.001
TNF-α(pg/L)[a]	346.94±86.84	296.45±65.12	4.108	<0.001

Note: [a], data was represented by $\bar{x}\pm s$; [b], data was represented by n(%).

Tab.3 Logistic regression analysis of influencing ALI secondary to sepsis

Variable	*B*	*SE*	*Wald*	*P* value	*OR*(95%*CI*)
OI	-0.202	0.045	19.790	<0.001	0.817(0.748-0.893)
IL-4(ng/L)	-0.230	0.069	11.200	0.001	0.794(0.694-0.909)
IFN-γ(ng/L)	1.106	0.392	7.971	0.005	3.021(1.402-6.508)
TNF-α(pg/L)	0.012	0.005	5.536	0.019	1.012(1.002-1.023)
Constant	39.236	7.088	30.638	<0.001	/

Tab. 4 Analysis of the predictive efficacy of each index for ALI secondary to sepsis

Variable	AUC	*SE*	*P* value	95%*CI*	Cut-Off Value	Yoden index	Sensitivity	Specificity
OI	0.929	.019	<0.001	0.892-0.966	164.14	0.763	0.839	0.924
IL-4(ng/L)	0.920	.020	<0.001	0.881-0.959	76.750	0.716	0.758	0.958
IFN-γ(ng/L)	0.661	.041	<0.001	0.580-0.741	8.485	0.274	0.371	0.903
TNF-α(pg/L)	0.679	.044	<0.001	0.594-0.765	364.395	0.396	0.500	0.896

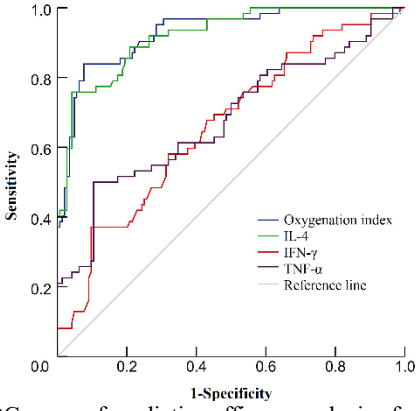

Fig.1 ROC curve of predictive efficacy analysis of each index for ALI secondary to sepsis

3 Discussion

Sepsis is a systemic inflammatory response syndrome triggered by infection, and acute lung injury (ALI) is a common complication of sepsis, posing a significant threat to the patient's life and health [8-9]. The imbalance of Th1/Th2 cytokines plays an important role in the pathogenesis of sepsis and its complications. Multiple studies have shown that the Th1/Th2 ratio is imbalanced in patients with sepsis combined with ALI. This imbalance is closely related to the severity of sepsis-induced ALI, and understanding this relationship can help reveal the immunological mechanisms of disease progression, providing new targets for clinical diagnosis and treatment

[10]. However, existing studies still have limitations in assessing the severity of sepsis-induced ALI and analyzing its influencing factors, especially the specific mechanisms of Th1/Th2 cytokine imbalance and its association with the severity of the disease, which require further exploration. This study aims to analyze the relationship between the severity of sepsis-induced ALI and Th1/Th2 cytokines, as well as the influencing factors of sepsis-induced ALI.

In this study, we compared the levels of Th1/Th2 cytokines in patients with different severity of sepsis combined with ALI. We found that the levels of IL-4 and IL-10 decreased from the mild-risk group to the moderate-risk group and high-risk group, while the levels of IFN-γ and APACHE II score increased. The TNF-α level in the mild-risk group was lower than that in the moderate-risk group and high-risk group. This is consistent with the findings of Fan *et al*. [11], who analyzed the levels of Th1/Th2 cytokines in patients with ARDS from different infection sources. They found that in the moderate- and severe- ARDS group, the pro-inflammatory cytokines IFN-γ and TNF-α levels were higher, and the anti-inflammatory cytokine IL-4 level was lower than in the mild group. Correlation analysis showed that IL-4 and IL-10 were negatively correlated with the APACHE II score, while IFN-γ and TNF-α were positively correlated with the APACHE II score. This suggests that the levels of Th1/Th2 cytokines are closely related to the patient's condition. This may be because, in the mild-risk group with impaired respiratory function, the body can maintain a certain immune homeostasis, and the anti-inflammatory effect of Th2 cytokines is relatively significant, helping to reduce inflammation and organ damage. At the same time, the lower APACHE II score also reflects the patient's relatively mild overall condition and better organ function. In high-risk patients, excessive activation of Th1 cytokines may lead to a severe inflammatory response and significant organ dysfunction, thus significantly increasing the APACHE II score. In contrast, the relative increase in Th2 cytokines may, to some extent, counteract excessive inflammation, slow disease deterioration, and reduce the APACHE II score. This phenomenon is consistent with the findings of Zhao *et al.* [12] in the study of cytokine secretion in ALI in vitro models.

In this study, the sepsis with secondary ALI group had lower OI, lower IL-4 levels, and higher IFN-γ and TNF-α levels compared to the pure sepsis group. Logistic regression showed that OI, IL-4, IFN-γ, and TNF-α are independent factors influencing sepsis with secondary ALI, and the above indicators have certain clinical reference value for predicting sepsis with secondary ALI. This is because a decrease in the OI is a significant marker of sepsis with secondary ALI.

ALI, as a severe complication of sepsis, involves multiple factors in its pathogenesis, including increased permeability of the pulmonary microvasculature, reduced surfactant in the alveoli, atelectasis, and pulmonary edema. These factors collectively lead to severe impairment of the gas exchange function of the alveolar-capillary membrane, preventing oxygen from effectively diffusing into the blood in the alveoli, resulting in a significant decrease in the OI. Although patients in the pure sepsis group also experience some degree of inflammatory response, the lung involvement or lung damage is relatively mild, so the OI remains relatively high [13].

The decrease in IL-4 levels may be related to the immunosuppressive state in patients with sepsis and secondary ALI. IL-4, an important anti-inflammatory cytokine primarily secreted by Th2 cells, plays a role in inhibiting the inflammatory response and promoting tissue repair [14-15]. However, during sepsis with secondary ALI, excessive inflammation and immune cell activation may lead to immune system exhaustion and the onset of an immunosuppressive state. In this case, the production of anti-inflammatory cytokines may be suppressed, leading to a reduction in anti-inflammatory factors, including IL-4 [16-17].

IFN-γ and TNF-α, as typical pro-inflammatory cytokines, show higher levels in patients with sepsis and secondary ALI [18]. IFN-γ is primarily secreted by Th1 cells and natural killer cells and promotes macrophage activation and enhances antigen presentation [19]. TNF-α is a pleiotropic cytokine that induces the production of various inflammatory mediators and mediates the inflammatory response. During the progression of sepsis with secondary ALI, due to increased lung damage and the persistent presence of pathogens, the immune system may attempt to clear the pathogens and repair tissue damage by upregulating the expression of these pro-inflammatory cytokines. However, excessive pro-inflammatory responses may further exacerbate the pathological changes in the lungs, forming a vicious cycle [20]. A large amount of pro-inflammatory cytokines can act as damage-associated molecular patterns, triggering lung inflammation and potentially leading to ALI/ARDS [21].

In summary, Th1/Th2 cytokines are closely related to the severity of sepsis with secondary ALI. OI, IL-4, IFN-γ, and TNF-α are independent factors affecting sepsis with secondary ALI, and the above indicators have certain clinical reference value in predicting sepsis with secondary ALI.

Conflict of Interest None

References

[1] Kellum JA, Formeck CL, Kernan KF, et al. Subtypes and mimics of sepsis[J]. Crit Care Clin, 2022, 38(2): 195-211.
[2] Zhang H, Wu D, Wang Y, et al. METTL3-mediated N6-methyladenosine exacerbates ferroptosis via m6A-IGF2BP2-dependent mitochondrial metabolic reprogramming in sepsis-induced acute lung injury[J]. Clin Transl Med, 2023, 13(9): e1389.
[3] Gao LJ, Li XL, Ning WH, et al. Clinical significance of Th1/Th2 ratio and cytokines in children with sepsis complicated with acute lung injury[J]. Lab Med Clin, 2022, 19(21): 2922-2925. [**In Chinese]**
[4] Liao Y, Qu MJ, Liu J, et al. Effects of ultrashort wave on inflammatory response and intercellular adhesion molecule-1 in rats with acute lung injury[J]. Chin J Gerontol, 2022, 42(15): 3711-3715. [**In Chinese]**
[5] Liu YY, Yao JR, Lin JY, et al. Systemic metabolic changes caused by inflammation progression in patients with acute lung injury[J]. Chin J Clin Med, 2022, 29(4): 565-571. [**In Chinese]**
[6] Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3)[J]. JAMA, 2016, 315(8): 801-810.
[7] ARDS Definition Task Force Ranieri VM, Rubenfeld GD, Thompson BT,

et al. Acute respiratory distress syndrome: the Berlin Definition[J]. JAMA, 2012, 307(23): 2526-2533.
[8] Ling XY, Wei SY, Ling DD, et al. Irf7 regulates the expression of Srg3 and ferroptosis axis aggravated sepsis-induced acute lung injury[J]. Cell Mol Biol Lett, 2023, 28(1): 91.
[9] Wang W, Liu CF. Sepsis heterogeneity[J]. World J Pediatr, 2023, 19(10): 919-927.
[10] Cao YX, Chi XC, Bao CF, et al. Study on the protective mechanism of Ginsenoside Rg1 through TNF-α/TNFR1/RIPKs pathway to regulate acute lung injury induced by acute kidney injury[J]. Chin J Clin Anat, 2023, 41(4): 409-415. [**In Chinese]**
[11] Fan H, Suo T, Su MR, et al. Clinical significance of blood Th1, Th2 cells and their cytokines in evaluating the condition and prognosis of patients with infection-induced acute respiratory distress syndrome[J]. J Clin Pulm Med, 2021, 26(8): 1189-1192, 1197. [**In Chinese]**
[12] Zhao K, Xiao Y, Yang C, et al. Protective effect of interleukin-4 in lipopolysaccharide induced acute lung injury models[J]. J Kunming Med Univ, 2022, 43(8): 41-46. [**In Chinese]**
[13] Huang JY, Liu WM. Mechanism of interleukin-4 negatively regulating NF-κB pathway to inhibit inflammatory response[J]. Tianjin Med J, 2019, 47(10): 1025-1029. [**In Chinese]**
[14] Chen SK, Zhuo Y, Xue T, et al. The clinical value of Th1/Th2 cytokine detection in the identification of sepsis with different pathogens[J]. China J Emerg Resusc Disaster Med, 2021, 16(3): 293-296. [**In Chinese]**
[15] Tang NJ, Liu D, Liu JY, et al. Peripheral blood Th1/Th2 cell balance and the changes of cytokine levels in the patients with severe post-traumatic sepsis[J]. Chin J Crit Care Med, 2023, 43(7): 510-517. [**In Chinese]**
[16] Du JF. Relations between inflammatory factors, Th1/Th2 and sepsis related acute lung injury and the protective mechanism of high concentration hydrogen on lipopolysaccharide induced acute lung injury in mice[D]. Shijiazhuang: Hebei Medical University, 2022. [**In Chinese]**
[17] Chen Q, Jiang WQ, Wang CH, et al. Relationship between IFN-γ/IL-4 and Th1/Th2 levels in peripheral blood and prognosis of patients with acute lung injury caused by sepsis[J]. Med J West China, 2024, 36(11): 1659-1665. [**In Chinese]**
[18] Shi JX, Feng LX, Zhao J. Expression of interferon-γ, CD47 and lymphocyte subsets in patients with sepsis and their relationships with prognosis[J]. J Clin Med Pract, 2024, 28(12): 107-111. [**In Chinese]**
[19] Huang LC, Jiang LY, Zhang BX, et al. Interferon-γ Correlation with the severity of septic shock in patients and its prognostic value[J]. J Pract Med, 2024, 40(12): 1725-1730. [**In Chinese]**
[20] Zhao J, Feng LX, Shi JX, et al. Guiding significance of immune factors and T lymphocyte subsets in immunomodulatory therapy for sepsis[J]. Chin J Immunol, 2024, 40(12): 2614-2622. [**In Chinese]**
[21] Fu XZ, Wang Y. The mechanism and treatment outlook of lung injury in sepsis[J]. Chin J Clin Res, 2023, 36(10): 1445-1448. [**In Chinese]**

Submission received: 2024-08-13/ **Revised:** 2024-12-30

·论 著·

Th1/Th2细胞因子与脓毒症继发急性肺损伤严重程度的关系

傅道亮， 陈德建， 任磊， 侯晓林
自贡市第一人民医院 自贡市医学科学院急诊科，四川 自贡 643000

摘要：目的 分析辅助性T细胞（Th）1和Th2细胞因子对脓毒症继发急性肺损伤（ALI）严重程度的影响及其在评估脓毒症继发ALI中的作用。**方法** 回顾性收集自贡市第一人民医院2021年1月至2024年6月收治的206例脓毒症患者临床资料，根据是否继发ALI分为ALI组（62例）和单纯组（144例）。入院时对所有患者进行血清Th1细胞因子[γ干扰素（INF-γ）、肿瘤坏死因子α（TNF-α）]、Th2细胞因子[白细胞介素（IL）-4、IL-10]检测及急性生理学与慢性健康状况（APACHE Ⅱ）评分评估，并根据APACHE Ⅱ评分将ALI组患者分为低危组（＜10分，25例）、中危组（10~20分，20例）和高危组（＞20分，17例）。分析Th1和Th2细胞因子对脓毒症继发ALI严重程度的影响，及其在预测ALI发生中的作用。**结果** 脓毒症继发ALI患者中，IL-4、IL-10水平依低危组、中危组、高危组之序递降，IFN-γ水平及APACHE Ⅱ评分递升，差异均有统计学意义（$P<0.05$）；低危组TNF-α水平低于中危组、高危组（$P<0.05$）。IL-4、IL-10与APACHE Ⅱ评分呈负相关（$r=0.720, -0.539, P<0.01$），IFN-γ、TNF-α与APACHE Ⅱ评分呈正相关（$r=0.696, 0.551, P<0.01$）。Logistic回归分析显示，氧合指数低（$\beta=-0.202, P<0.01$）、IL-4水平低（$\beta=-0.230, P<0.01$）、IFN-γ水平高（$\beta=1.106, P<0.01$）、TNF-α水平高（$\beta=0.012, P<0.05$）为脓毒症继发ALI的独立危险因素。氧合指数、IL-4、IFN-γ、TNF-α评估脓毒症继发ALI的受试者工作特征（ROC）曲线下面积（AUC）分别为0.929、0.920、0.661、0.679。**结论** Th1/Th2细胞因子与脓毒症继发ALI病情严重程度存在密切联系，低水平的氧合指数和IL-4，高水平的IFN-γ、TNF-α可促使脓毒症继发更严重的ALI，且该四项指标对脓毒症继发ALI的预测有一定临床参考价值。

关键词： 脓毒症；急性肺损伤；辅助性T细胞1；辅助性T细胞2；细胞因子；氧合指数
中图分类号： R655.3 R631 **文献标识码：** A **文章编号：** 1674-8182(2025)08-1197-05

Relationship between Th1/ Th2 cytokines and severity of acute lung injury secondary to sepsis

FU Daoliang, CHEN Dejian, REN Lei, HOU Xiaolin
Emergency Department, Zigong First People's Hospital, Zigong Academy of Medical Sciences, Zigong, Sichuan 643000, China
Corresponding author: HOU Xiaolin, E-mail: 25460536@qq.com

Abstract: Objective To analyze the effects of helper T cells (Th) 1 and Th2 cytokines on the severity of acute lung injury (ALI) secondary to sepsis and to analyze their roles in evaluating the occurrence of ALI secondary to sepsis. **Methods** Clinical data of 206 patients with sepsis from Zigong First People's Hospital from January 2021 to June 2024 were retrospectively collected, and they were divided into ALI group (62 cases) and simple group (144 cases) according to whether ALI was secondary or not. Serum Th1 cytokines [interferon-γ (INF-γ), tumor necrosis factor α (TNF-α)] and Th2 cytokines [interleukin(IL)-4, IL-10] were measured and the Acute Physiology and Chronic Health Evaluation Ⅱ (APACHE Ⅱ) scores were evaluated for all patients at admission. Patients in ALI group were divided into low-risk group (＜10, 25 cases), medium-risk group (10-20, 20 cases) and high-risk group (＞20, 17 cases)

DOI: 10.13429/j.cnki.cjcr.2025.08.012
基金项目： 国家自然科学基金（81802079）
通信作者： 侯晓林，E-mail: 25460536@qq.com
出版日期： 2025-08-20

QR code for English version

according to APACHE Ⅱ scores. The effects of Th1 and Th2 cytokines on the severity of ALI secondary to sepsis and their roles in predicting the occurrence of ALI were analyzed. **Results** In patients of ALI secondary to sepsis, the levels of IL-4 and IL-10 decreased, while the levels of IFN-γ and APACHE Ⅱ scores increased, in the order of low-risk group, medium-risk group and high-risk group, with statistical significance (P<0.05). The level of TNF-α in low-risk group was lower than that in medium-risk group and high-risk group (P<0.05). IL-4 and IL-10 were negatively correlated with APACHE Ⅱ scores (r=−0.720, −0.537, P < 0.01), while IFN-γ and TNF-α were positively correlated with APACHE Ⅱ scores (r=0.696, 0.551, P<0.01). Logistic regression analysis showed that low oxygenation index (β=−0.202, P<0.01), low IL-4 level (β=−0.230, P<0.01), high IFN-γ level (β=1.106, P<0.01), and high TNF-α level (β=0.012, P<0.05) were independent risk factors for ALI secondary to sepsis. The area under the receiver operating characteristic curve of oxygenation index, IL-4, IFN-γ, TNF-α in the evaluation of ALI secondary to sepsis was 0.929, 0.920, 0.661, 0.679, respectively. **Conclusion** Th1/ Th2 cytokines are closely related to the severity of ALI secondary to sepsis. High levels of oxygenation index and IL-4, and low levels of IFN-γ and TNF-α can promote more severe ALI secondary to sepsis, and these four indicators have certain clinical reference value for evaluating the prediction of ALI secondary to sepsis.

Keywords: Sepsis; Acute lung injury; Helper T cells 1; Helper T cells 2; Cytokines; Oxygenation index

Fund program: National Natural Science Foundation of China (81802079)

脓毒症是一种由感染引起的全身炎症反应综合征，具有病情复杂、进展迅速的特点[1]。脓毒症临床并发症较多，急性肺损伤(acute lung injury，ALI)是脓毒症常见的并发症，指脓毒症引起的急性肺部炎症反应和功能障碍。ALI不仅可显著增加患者病死率，还严重影响患者的预后和生活质量[2]。辅助性T细胞(helper T cell，Th)1和Th2细胞在免疫应答中起着关键作用。正常情况下，Th1、Th2细胞之间保持动态平衡，以维持机体免疫稳态。然而在脓毒症等病理状态下，这种平衡被打破，机体可出现免疫应答失衡，进而加剧组织损伤和器官功能障碍。有研究表明，脓毒症患者体内Th1/Th2细胞因子失衡与疾病严重程度密切相关[3]。脓毒症时，机体为了对抗感染会产生大量的促炎细胞因子，这些细胞因子虽然有助于清除病原体，但过度产生会导致全身炎症反应过度激活，引起肺微血管通透性增加、肺泡-毛细血管屏障损伤和肺水肿等病理改变，同时，促炎细胞因子的大量表达还可能抑制抗炎细胞因子生成[4-5]。这种Th1/Th2细胞因子失衡进一步加剧了肺部的炎症反应和组织损伤。本研究旨在通过检测脓毒症患者外周血中Th1/Th2细胞因子水平，探讨其与脓毒症继发ALI病情严重程度的关系，并分析脓毒症继发ALI的危险因素，为制定有效的治疗策略提供参考依据。

1 资料与方法

1.1 一般资料 回顾性收集自贡市第一人民医院2021年1月至2024年6月收治的206例脓毒症患者的临床资料，根据是否继发ALI分为ALI组(62例)、单纯组(144例)。纳入标准：(1) 所有患者均符合国际公认的脓毒症诊断标准，如符合Sepsis-3对脓毒症的定义[6]。ALI组患者符合急性呼吸窘迫综合征(acute respiratory distress syndrome，ARDS)柏林标准中关于ALI定义[7]。(2) 年龄在18周岁以上。(3) 所有患者入院后完成急性生理学及慢性健康状况评分系统(Acute Physiology and Chronic Health Evaluation Ⅱ，APACHE Ⅱ)评分。(4) 患者入院当天获取外周血样本并完成相关Th1/Th2细胞因子水平检测。(5) 检查结果完整。排除标准：(1) 存在其他原因(如创伤、吸入性肺炎、药物反应等)引起的ALI；(2) 合并严重心、肝、肾等器官功能衰竭等可能影响免疫应答和细胞因子水平的疾病；(3) 长期使用免疫抑制剂或患有免疫缺陷疾病；(4) 近期(一个月内)有严重感染史；(5) 正在接受可能影响免疫应答和细胞因子水平的治疗；(6) 各种原因导致数据收集不完整或无法进行分析；(7) 入院后24 h内死亡或放弃治疗。本研究已获自贡市第一人民医院伦理委员会审批(伦理审批号：20240508)。

1.2 ALI严重程度评估分组 患者入院时即刻完成APACHE Ⅱ评分，根据APACHE Ⅱ评分将ALI组患者分为低危组(<10分)25例、中危组(10~20分)20例和高危组(>20分)17例。

1.3 方法 查阅患者电子病历，收集相关临床指标。(1) 一般资料：性别、年龄、身体质量指数(body mass index，BMI)，入院心率、收缩压、舒张压、氧合指数，有无高血压、糖尿病、冠状动脉粥样硬化性心脏病(冠心病)、慢性阻塞性肺疾病(chronic obstructive pulmonary disease，COPD)、脑血管疾病等基础疾病，

原发感染类型。(2) 入院APACHE Ⅱ评分：APACHE Ⅱ评分包括急性生理评分、年龄评分及慢性健康评分。APACHE Ⅱ评分为3部分总分之和，最高分不超过71分，分数与病情严重程度呈正比。(3) 实验室指标：检测血清Th1分泌的细胞因子[γ干扰素(interferon-γ，INF-γ)、肿瘤坏死因子(tumor necrosis factor，TNF)-α]、Th2分泌的细胞因子[白细胞介素(interleukin，IL)-4、IL-10]。具体检测方法：入院时采集患者肘部正中静脉血7 mL，2 500 r/min离心15 min(离心半径10 cm)，取血清，采用酶联免疫吸附试验(ELISA)进行检测。

1.4 统计学方法 本研究图片由GraphPad Prism软件绘制，数据均采用SPSS 22.0软件分析。计数资料用例(%)表示，进行χ^2检验；符合正态分布计量资料用$\bar{x}\pm s$表示，多组比较采用单因素方差分析，事后两两比较用LSD-t检验；采用Pearson法分析相关性。Logistic回归分析脓毒症继发ALI的危险因素，受试者工作特征曲线(receiver operating characteristic，ROC)分析各指标预测脓毒症继发ALI的效能。P<0.05为差异有统计学意义。

表1 脓毒症继发不同严重程度ALI患者相关资料比较 ($\bar{x}\pm s$)

Tab.1 Comparison of related data in patients with different severity of ALI secondary to sepsis ($\bar{x}\pm s$)

组别	例数	IL-4(ng/L)	IL-10(ng/L)	IFN-γ(ng/L)	TNF-α(pg/L)	APACHE Ⅱ评分
低危组	25	76.15±5.59[ab]	35.14±6.05[ab]	7.01±1.05[ab]	306.10±75.64[ab]	7.88±1.36[ab]
中危组	20	71.59±5.65[a]	28.13±5.79[a]	8.06±1.12[a]	351.45±80.44	16.15±2.01[a]
高危组	17	53.65±10.60	22.45±6.61	9.03±1.02	401.71±81.64	28.06±0.97
F值		50.558	22.344	18.506	7.486	463.713
P值		<0.001	<0.001	<0.001	<0.001	<0.001

注：与高危组比较，[a]P<0.05；与中危组比较，[b]P<0.05。

2 结 果

2.1 脓毒症继发不同严重程度ALI患者相关资料比较 脓毒症继发ALI患者中，IL-4、IL-10水平依低危组、中危组、高危组之序递降，IFN-γ水平及APACHE Ⅱ评分递升，差异均有统计学意义(P<0.05)；低危组TNF-α水平低于中危组、高危组(P<0.05)。见表1。

2.2 Th1/Th2细胞因子与脓毒症继发ALI严重程度的相关性 IL-4、IL-10分别与APACHE Ⅱ评分呈负相关(r=−0.720，P<0.01；r=−0.539，P<0.01)。IFN-γ、TNF-α分别与APACHE Ⅱ评分呈正相关(r=0.696，P<0.01；r=0.551，P<0.01)。

2.3 脓毒症继发ALI影响因素的单因素分析 ALI组与单纯组在年龄、BMI、APACHE Ⅱ评分、入院心率、血压、性别、吸烟及饮酒习惯、高血压、糖尿病、冠心病、COPD、脑血管病、感染位置及IL-10水平上差异均无统计学意义(P>0.05)。但在氧合指数、IL-4、IFN-γ、TNF-α水平上差异有统计学意义(P<0.05)。见表2。

2.4 脓毒症继发ALI的多因素logistic回归分析 将单因素体分析中差异有统计学意义的变量氧合指数、IL-4、IFN-γ、TNF-α作为自变量(连续变量，以原值代入)，将继发ALI作为因变量(未合并ALI=0，合并ALI=1)，纳入二元logistic回归模型，结果显示，氧合指数、IL-4、IFN-γ、TNF-α为脓毒症继发ALI的独立影

表2 影响脓毒症继发ALI的单因素分析

Tab.2 Univariate analysis influencing ALI secondary to sepsis

项目	ALI组(n=62)	单纯组(n=144)	t/χ^2值	P值
年龄(岁)[a]	47.12±10.12	46.99±10.43	0.083	0.934
BMI(kg/m^2)[a]	22.01±2.43	22.19±2.29	0.508	0.612
APACHE Ⅱ评分[a]	16.08±8.48	17.47±7.50	1.173	0.242
入院心率(次/min)[a]	102.45±20.10	99.75±20.54	0.871	0.385
入院收缩压(mmHg)[a]	120.44±13.12	121.65±11.07	0.680	0.498
入院舒张压(mmHg)[a]	78.45±8.95	77.15±8.59	0.984	0.326
氧合指数[a]	151.97±12.93	175.46±10.45	12.638	<0.001
性别[b]			0.008	0.931
男	37(59.68)	85(59.03)		
女	25(40.32)	59(40.97)		
吸烟[b]	21(33.87)	45(31.25)	0.137	0.712
饮酒[b]	20(32.26)	40(27.78)	0.421	0.516
高血压[b]	19(30.65)	42(29.17)	0.045	0.831
糖尿病[b]	11(17.74)	25(17.36)	0.004	0.947
冠心病[b]	10(16.13)	23(15.97)	0.001	0.978
COPD[b]	8(12.90)	19(13.19)	0.003	0.955
脑血管病[b]	8(12.90)	17(11.81)	0.049	0.825
感染位置[b]				
呼吸道	17(27.42)	36(25.00)		
腹部	15(24.19)	37(25.69)		
泌尿系统	17(27.42)	39(27.08)	0.191	0.996
皮肤组织	7(11.29)	18(12.50)		
其他	6(9.68)	14(9.72)		
IL-4(ng/L)[a]	68.51±11.84	84.35±5.21	10.121	<0.001
IL-10(ng/L)[a]	29.40±7.99	30.16±5.77	0.677	0.443
IFN-γ(ng/L)[a]	7.90±1.34	7.11±1.29	3.985	<0.001
TNF-α(pg/L)[a]	346.94±86.84	296.45±65.12	4.108	<0.001

注：[a]为数据以$\bar{x}\pm s$表示；[b]为数据以例(%)表示。

响因素（P<0.05）。见表3。

2.5　氧合指数、IL-4、IFN-γ、TNF-α对脓毒症继发ALI预测效能分析　ROC曲线分析发现，氧合指数、IL-4、IFN-γ、TNF-α评估脓毒症继发ALI曲线AUC分别为0.929、0.920、0.661、0.679，最佳截断值分别为164.14、76.750 ng/L、8.485 ng/L、364.395 pg/L。见表4与图1。

表3　影响脓毒症继发ALI的logistic回归分析

Tab.3　Logistic regression analysis influencing ALI secondary to sepsis

变量	β	SE	Waldχ^2	P值	OR(95%CI)
氧合指数	−0.202	0.045	19.790	<0.001	0.817(0.748~0.893)
IL-4	−0.230	0.069	11.200	0.001	0.794(0.694~0.909)
IFN-γ	1.106	0.392	7.971	0.005	3.021(1.402~6.508)
TNF-α	0.012	0.005	5.536	0.019	1.012(1.002~1.023)
常量	39.236	7.088	30.638	<0.001	

表4　各指标对脓毒症继发ALI的预测效能分析

Tab.4　Analysis of the predictive efficacy of each index for ALI secondary to sepsis

变量	AUC	SE	P值	95%CI	截断值	约登指数	敏感度	特异度
氧合指数	0.929	0.019	<0.001	0.892~0.966	164.14	0.763	0.839	0.924
IL-4	0.920	0.020	<0.001	0.881~0.959	76.75 ng/L	0.716	0.758	0.958
IFN-γ	0.661	0.041	<0.001	0.580~0.741	8.48 ng/L	0.274	0.371	0.903
TNF-α	0.679	0.044	<0.001	0.594~0.765	364.40 pg/L	0.396	0.500	0.896

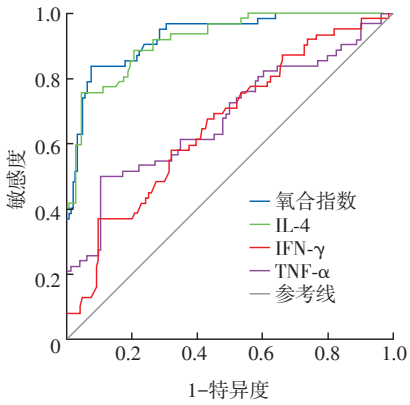

图1　各指标对脓毒症继发ALI预测效能分析的ROC曲线

Fig.1　ROC curve of predictive efficacy analysis of each index for ALI secondary to sepsis

3　讨　论

脓毒症是一种由感染引发的全身炎症反应综合征，ALI是脓毒症常见并发症，对患者生命健康威胁较大[8-9]。Th1/Th2细胞因子的失衡在脓毒症及其并发症的发病机制中扮演重要角色，多项研究表明，脓毒症合并ALI患者体内Th1/Th2比值失衡，这种失衡状态与脓毒症继发ALI的病情严重程度密切相关，深入了解这种联系有助于揭示病情进展的免疫学机制，为临床诊断和治疗提供新的靶点[10]。然而，现有研究在脓毒症继发ALI的病情严重程度评估及影响因素分析方面仍存在不足，特别是在Th1/Th2细胞因子失衡的具体作用机制及其与病情严重程度的关联上尚需深入探讨。本研究旨在分析脓毒症继发ALI严重程度与Th1/Th2细胞因子的关系，及脓毒症继发ALI影响因素。

本研究通过对比不同危重度脓毒症合并ALI患者体内Th1/Th2细胞因子发现，IL-4、IL-10水平依低危组、中危组、高危组之序递降，IFN-γ水平及APACHE Ⅱ评分递升；低危组TNF-α水平低于中危组、高危组，差异均有统计学意义。这与范慧等[11]研究所得结论一致，范慧分析不同病情感染源性ARDS Th1/Th2细胞因子水平发现，中重度组ARDS患者促炎因子IFN-γ、TNF-α水平较轻度组更高，抗炎因子IL-4水平较轻度组更低。相关分析显示，IL-4、IL-10与APACHE Ⅱ评分呈负相关，IFN-γ、TNF-α与APACHE Ⅱ评分呈正相关。说明Th1/Th2细胞因子水平与患者病情存在密切联系。这可能是因为，在呼吸功能受损低危组患者中，机体尚能保持一定的免疫稳态，Th2细胞因子的抗炎作用相对显著，有助于减轻炎症反应和器官损伤。同时，较低的APACHE Ⅱ评分也体现了患者整体病情较轻，器官功能相对较好。在高危组患者中，Th1细胞因子的过度激活可能导致炎症反应剧烈，器官功能严重受损，进而使得APACHE Ⅱ评分显著升高。相反，Th2细胞因子的相对增多可能在一定程度上对抗过度的炎症反应，减缓病情恶化，从而降低APACHE Ⅱ评分。这一现象与赵琨等[12]在ALI体外模型中细胞因子分泌中研究一致。

本研究中，脓毒症继发ALI组较单纯脓毒症组氧合指数更低，IL-4水平更低，IFN-γ、TNF-α水平更高，logistic回归模型显示，氧合指数、IL-4、IFN-γ、TNF-α为脓毒症继发ALI的独立影响因素，且上述指标对脓毒症继发ALI的预测有一定临床参考价值。这是因为，氧合指数的降低是脓毒症继发ALI的显著标志。ALI作为脓毒症的严重并发症，其发生机制涉及多种因素，包括肺部微血管的通透性增加、肺泡表面活性物质减少、肺不张和肺水肿等。这些因素共同导致

肺泡-毛细血管膜的气体交换功能严重受损，使得进入肺泡的氧气无法有效弥散到血液中，从而表现为氧合指数显著降低。单纯脓毒症组患者虽然也存在一定程度的炎症反应，但尚未累及肺部或肺部损伤较轻，因此氧合指数相对较高[13]。IL-4水平的降低可能与脓毒症继发ALI患者的免疫抑制状态有关。IL-4作为一种重要的抗炎细胞因子，主要由Th2细胞分泌，具有抑制炎症反应和促进组织修复的作用[14-15]。然而，在脓毒症继发ALI的过程中，过度的炎症反应和免疫细胞的活化可能导致免疫系统的耗竭和免疫抑制状态的出现。此时，抗炎细胞因子的产生可能受到抑制，包括IL-4在内的抗炎因子水平因此降低[16-17]。IFN-γ和TNF-α作为典型的促炎细胞因子，在脓毒症继发ALI患者中表现出更高的水平[18]。IFN-γ主要由Th1细胞和自然杀伤细胞分泌，具有促进巨噬细胞活化和增强抗原呈递的作用[19]。TNF-α则是一种多效性的细胞因子，能够诱导多种炎症介质的产生并介导炎症反应。在脓毒症继发ALI的过程中，由于肺部损伤的加剧和病原体的持续存在，免疫系统可能通过上调这些促炎细胞因子的表达来试图清除病原体和修复组织损伤。然而，过度的促炎反应也可能进一步加剧肺部的病理生理变化，形成恶性循环[20]，大量的促炎因子可作为细胞损伤相关的分子模式，引发肺部炎症，可发生ALI/ARDS[21]。

综上所述，Th1/ Th2细胞因子与脓毒症继发ALI病情严重程度存在密切联系，氧合指数、IL-4、IFN-γ、TNF-α为脓毒症继发ALI的独立影响因素，上述指标对脓毒症继发ALI的预测有一定临床参考价值。

利益冲突 无

参考文献

[1] Kellum JA, Formeck CL, Kernan KF, et al. Subtypes and mimics of sepsis[J]. Crit Care Clin, 2022, 38(2): 195-211.

[2] Zhang H, Wu D, Wang Y, et al. METTL3-mediated N6-methyladenosine exacerbates ferroptosis via m6A-IGF2BP2-dependent mitochondrial metabolic reprogramming in sepsis-induced acute lung injury[J]. Clin Transl Med, 2023, 13(9): e1389.

[3] 高刘炯，李小磊，宁文慧，等. 脓毒症合并急性肺损伤患儿Th1/Th2比值及细胞因子临床意义分析[J]. 检验医学与临床，2022，19(21)：2922-2925.

[4] 廖源，屈萌艰，刘静，等. 超短波对大鼠急性肺损伤炎症反应及细胞间黏附分子-1表达的影响[J]. 中国老年学杂志，2022，42(15)：3711-3715.

[5] 刘洋洋，姚杰然，林佳颖，等. 急性肺损伤炎症反应失控所致的系统代谢紊乱及其发生机制[J]. 中国临床医学，2022，29(4)：565-571.

[6] Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)[J]. JAMA, 2016,315(8):801-810.

[7] ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin Definition[J]. JAMA, 2012,307(23):2526-2533.

[8] Ling XY, Wei SY, Ling DD, et al. Irf7 regulates the expression of Srg3 and ferroptosis axis aggravated sepsis-induced acute lung injury[J]. Cell Mol Biol Lett, 2023, 28(1): 91.

[9] Wang W, Liu CF. Sepsis heterogeneity[J]. World J Pediatr, 2023, 19(10): 919-927.

[10] 曹瀛心，迟晓晨，包翠芬，等. 人参皂苷Rg1通过TNF-α/TNFR1/RIPKs通路调控急性肾损伤致急性肺损伤的保护机制研究[J]. 中国临床解剖学杂志，2023，41(4)：409-415.

[11] 范慧，索涛，苏梦茹，等. 感染源性急性呼吸窘迫综合征患者血Th1和Th2细胞及相关细胞因子检测的临床意义[J]. 临床肺科杂志，2021，26(8)：1189-1192，1197.

[12] 赵琨，肖云，杨纯，等. 白细胞介素-4在脂多糖诱导急性肺损伤模型中的保护作用[J]. 昆明医科大学学报，2022，43(8)：41-46.

[13] 黄洁媛，刘文明. 白细胞介素-4负调控NF-κB通路抑制炎症反应的机制研究[J]. 天津医药，2019，47(10)：1025-1029.

[14] 陈尚昆，卓越，薛婷，等. Th1/Th2细胞因子检测在鉴别脓毒症不同病原菌感染中的临床价值[J]. 中国急救复苏与灾害医学杂志，2021，16(3)：293-296.

[15] 唐宁健，刘丹，刘佳雨，等. 严重创伤患者外周血Th1/Th2细胞平衡和细胞因子水平变化及对发生脓毒症的预测价值[J]. 中国急救医学，2023，43(7)：510-517.

[16] 杜俊凤. 炎性因子、Th1/Th2与脓毒症相关急性肺损伤的关系及高浓度氢气对脂多糖诱导小鼠急性肺损伤的保护机制研究[D]. 石家庄：河北医科大学，2022.

[17] 陈谦，蒋文强，王才宏，等. 脓毒症急性肺损伤患者外周血IFN-γ/IL-4、Th1/Th2水平与疾病预后的关系[J]. 西部医学，2024，36(11)：1659-1665.

[18] 史晶心，冯丽霞，赵璟. 干扰素-γ、CD47和淋巴细胞亚群在脓毒症患者中的表达及其与预后的关系[J]. 实用临床医药杂志，2024，28(12)：107-111.

[19] 黄立创，蒋良艳，张碧霞，等. γ干扰素与脓毒性休克患者严重程度的相关性及对预后的评估价值[J]. 实用医学杂志，2024，40(12)：1725-1730.

[20] 赵璟，冯丽霞，史晶心，等. 免疫因子及T淋巴细胞亚群监测在脓毒症免疫调理治疗中的指导意义[J]. 中国免疫学杂志，2024，40(12)：2614-2622.

[21] 付绪哲，王煜. 脓毒症肺损伤的机制及治疗展望[J]. 中国临床研究，2023，36(10)：1445-1448.

收稿日期：2024-08-13 **修回日期**：2024-12-30 **编辑**：石嘉莹