

Cite as: Lai Simin, Yu Chan, Wu Mengzhu, Tang Zhanhong. The relationship between serum IL-6, hs-CRP, SAA and acute lung injury in elderly patients with sepsis and their prognostic value [J]. Chin J Clin Res, 2024, 37(11):1700-1704.

DOI: 10.13429/j.cnki.cjcr.2024.11.011

The relationship between serum IL-6, hs-CRP, SAA and acute lung injury in elderly patients with sepsis and their prognostic value

LAI Simin, YU Chan, WU Mengzhu, TANG Zhanhong

Chengdu Eighth People's Hospital, Affiliated Elderly Hospital of Chengdu Medical College, Chengdu, Sichuan 610083, China

Abstract: Objective To analyze the prognostic predictive value of combined serum interleukin-6 (IL-6), high-sensitivity Creactive protein (hs-CRP), and amyloid A (SAA) tests in elderly patients with sepsis combined with acute lung injury (ALI). Methods From May 2021 to May 2023, 50 elderly patients with sepsis (control group), 50 elderly patients with sepsis complicated with ALI (observation group), and 50 elderly healthy subjects (healthy group) admitted in the Affiliated Elderly Hospital of Chengdu Medical College were selected. Patients in observation group were divided into low-risk group (27 cases, 201-300 mmHg), medium-risk group (15 cases, 101-200 mmHg) and high-risk group (8 cases, ≤100 mmHg) according to oxygenation index (OI), and were divided into survival group (42 cases) and death group (8 cases) according to clinical outcomes. Serum levels of IL-6, hs-CRP, SAA and APACHE II scores were compared between each group. Receiver operating curve (ROC) was used to analyze the predictive efficacy of serum IL-6, hs-CRP and SAA on death. Results The levels of serum IL-6, hs-CRP, SAA and APACHE II score in observation group were higher than those in control group and healthy group (P < 0.05). The levels of IL-6, hs-CRP, SAA and APACHE II score in high-risk group were higher than those in medium-risk group and low-risk group (P<0.05). The levels of IL-6, hs-CRP, SAA and APACHE II score in the death group were higher than those in the survival group (P<0.05). The AUC of the combined detection of serum IL-6, hs-CRP and SAA to predict the death of sepsis complicated with ALI was the highest [0.859, 95%C/(0.812-0.952)], the sensitivity was 94.96% and specificity was 90.38%. Conclusion High levels of serum IL-6, hs-CRP, and SAA in elderly sepsis with ALI are closely associated with the severity and prognosis of ALI, and the combined assay can improve the efficacy of predicting the clinical outcome of patients.

Keywords: Interleukin-6; Hypersensitive C-reactive protein; Amyloid A; Sepsis; Acute lung injury

Fund program: National Natural Science Foundation of China (81960342)

Sepsis is an important cause of multiple organ dysfunction and septic shock. It is characterized by high incidence, high mortality, and poor prognosis [1]. Acute lung injury (ALI) is a common complication in patients with sepsis. Conventional oxygen therapy is often insufficient, and if not treated effectively and promptly, it can progress to acute respiratory distress syndrome (ARDS), which poses a significant threat to the patient's life [2-3]. Elderly sepsis patients are at higher risk for developing ALI due to factors such as advanced age, impaired immune function, and multiple comorbidities. The occurrence of ALI exacerbates the primary illness and increases mortality [4]. Therefore, early and accurate diagnosis of the condition and clinical outcomes in elderly sepsis patients with ALI is crucial for guiding targeted clinical treatments. Although inflammatory factors such as interleukin (IL)-6 and high-sensitivity C-reactive protein (hs-CRP) have been clinically proven to be valuable for diagnosing infectious diseases, their diagnostic specificity remains suboptimal [5-6]. Serum amyloid A (SAA) is a cytokine secreted by liver cells, and rapidly increase within 24 hours in response to inflammation or infection, with serum expression levels positively correlated with the degree of infection [7]. Based on this, This article aimed to explore the relationship between serum IL-6, hs-CRP, SAA, and the severity of ALI in elderly sepsis patients, as well as their value in prognostic assessment.

1 Materials and methods

1.1 General information

A total of 50 elderly sepsis patients treated at the Affiliated Elderly Hospital of Chengdu Medical College from May 2021 to May 2023 were selected as the control group. Another 50 elderly sepsis patients with ALI were selected as the observation group, and 50 elderly individuals who underwent health checkups during the same period were selected as the healthy group. There were no significant differences in the general data among the three groups (P > 0.05), as shown in **Table 1**. This study was approved by the hospital's ethics committee (approval number: 20210419).

1.2 Diagnostic criteria

Both the observation and control groups met the diagnostic criteria for sepsis outlined in the "Expert consensus on diagnosis and treatment of sepsis with integrated Chinese and Western medicine" [8]. The observation group also met the diagnostic criteria for ALI as described in the "Expert consensus on diagnosis and treatment of septic lung injury with integrated traditional Chinese and western medicine" [9].

0.062

0.951

 $F/\gamma^2/t$ value

P value

Group	Male/female (case)	Age (year)	BMI (kg/m²)	Sepsis triggers ^a (case)	Duration of ICU stay (d)	Duration of mechanical ventilation (d)
Observation group	28/22	70.82±5.37	23.14±1.29	4/10/11/12/13	16.89±3.01	8.14±1.68
Control group	29/21	71.24±5.12	23.18±1.24	6/9/8/13/14	16.82±3.04	8.16±1.57
Healthy group	26/24	70.24±5.01	23.28±0.97	_	_	_

0.188

0.829

Tab. 1 Comparison of general information among 3 groups $(n=50,\bar{x}\pm s)$

Note: ^aSepsis triggers were hematogenous infection / intracranial infection / urinary tract infection / abdominal infection / pulmonary infection

1.3 Inclusion and exclusion criteria

Inclusion criteria: (1) Age ≥ 60 years, no gender limitation; (2) Mechanical ventilation duration ≥ 48 h; (3) Complete and comprehensive clinical treatment; (4) First occurrence of sepsis and ALI; (5) ICU stay ≥ 2 d.

0.378

0.828

0.472

0.625

Exclusion Criteria: (1) Patients with malignant tumors; (2) Patients with genetic diseases or congenital diseases; (3) Recent use of immunosuppressants or those with immune deficiency diseases within the last 3 months; (4) Participation in other studies or withdrawal due to changes in condition during the study; (5) ALI caused by inhalation of toxic gases, drowning, or lung surgery; (6) Pregnant, breastfeeding, or preparing for pregnancy women; (7) Comorbidity of pulmonary fibrosis, asthma, or other lung diseases; (8) History of lung surgery; (9) Comorbidity of other systemic infectious diseases; (10) Extreme hemodynamic instability; (11) Blood transfusion or organ transplantation within the last 6 months; (12) History of drug dependency, drug abuse, or alcohol addiction.

1.4 Research methods

5 mL of fasting venous blood was drawn from the subjects. The blood was centrifuged for 10 minutes at 4000 r/mim with a centrifuge radius of 10 cm (model: TD6M; manufacturer: Hunan Hukang Centrifuge Co., Ltd.), and the upper serum was separated and stored at -20 °C. Enzyme-linked immunosorbent assay (ELISA) was used to measure IL-6 and hs-CRP, while turbidimetric method was used to measure SAA. All reagents were provided by Zeye Biotechnology Co., Ltd. All operations were performed following laboratory and reagent standards.

Acute Physiology and Chronic Health Evaluation (APACHE II) score was evaluated. This score includes chronic health status, age, and acute physiology score (APS). The total score is 71, with higher scores indicating more severe illness [10].

Based on their oxygenation index (OI), sepsis patients with ALI were classified into low-risk group (27 cases, OI: 201-300 mmHg), medium-risk group (15 cases, OI: 101-200 mmHg), and high-risk group (8 cases, OI \leq 100 mmHg). Based on clinical outcomes, elderly sepsis patients with ALI were divided into survival group (42

cases) and death group (8 cases). Serum levels of IL-6, hs-CRP, SAA, and APACHE II scores were compared across these groups.

0.116

0.908

1.5 Statistical methods

1.003

0.909

Data were analyzed using SPSS 26.0 software. Normally distributed continuous data were expressed as mean \pm standard deviation ($\bar{x}\pm s$), and comparisons were made using independent-sample t-tests or one-way analysis of variance (ANOVA). Categorical data were presented as case(%) and analyzed using the chi-squared test or Fisher's exact test. Ordered categorical data were analyzed using Ridit analysis. Pearson correlation analysis was used to examine the relationship between serum IL-6, hs-CRP, SAA, and APACHE II scores. Receiver operating characteristic (ROC) curves were plotted to calculate the area under the curve (AUC) and assess the predictive value of serum IL-6, hs-CRP, and SAA for patient mortality. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of serum IL-6, hs-CRP, SAA levels, and APACHE II scores among the three groups

Serum levels of IL-6, hs-CRP, and SAA, as well as APACHE II scores, were higher in the observation group than in the control and healthy groups (P<0.05). The control group showed higher levels of these indicators compared to healthy group (P<0.05), as shown in **Table 2**.

Tab. 2 Comparison of serum IL-6, hs-CRP, SAA levels and APACHE || scores among 3 groups $(n=50,\bar{x}\pm s)$

Group	IL-6 (ng/L)	hs-CRP	SAA (mg/L)	APACHE
		(mg/L)		score
Observation group	13.62±4.88	21.62±6.86	204.62±34.62	51.46±19.52
Control group	8.41±2.72a	14.26±3.17a	$161.88 {\pm} 21.78^a$	$34.88{\pm}12.76^a$
Healthy group	$1.84{\pm}0.34^{ab}$	1.05 ± 0.34^{ab}	$103.52{\pm}16.28^{ab}$	7.16±1.54 ^{ab}
F value	166.843	284.757	199.358	137.572
P value	< 0.001	< 0.001	< 0.001	< 0.001

Note: compared with the observation group, $^{\rm a}P\!\!<\!\!0.05;$ Compared with the control group, $^{\rm b}P\!<\!0.05.$



2.2 Comparison of serum IL-6, hs-CRP, SAA levels, and APACHE II scores among different severity groups

The high-risk group had significantly higher serum levels of IL-6, hs-CRP, SAA, and APACHE II scores than the medium-risk and low-risk groups (P < 0.05), and the medium-risk group had higher levels than the low-risk group (P < 0.05), as shown in **Table 3**.

Tab. 3 Comparison of serum IL-6, hs-CRP, SAA levels, and APACHE II scores among different severity groups $(\bar{x}\pm s)$

Group	IL-6 (ng/L)	hs-CRP (mg/L)	SAA (mg/L)	APACHE score
High-risk	19.15±2.52	30.85±3.44	281.64±51.66	63.55±4.82
Medium-risk	x 13.76±1.82 ^a	$22.81{\pm}2.46^a$	208.05±41.63 ^a	54.55 ± 3.04^{a}
Low -risk	11.90±1.11ab	$18.22{\pm}1.64^{ab}$	179.89±30.04ab	46.16±1.92ab
F value	62.129	100.428	22.700	125.481
P value	< 0.001	< 0.001	< 0.001	< 0.001

Note: compared with the high-risk group, ${}^aP{<}0.05$; Compared with the medium-risk group, ${}^bP{<}0.05$.

2.3 Comparison of serum IL-6, hs-CRP, SAA levels, and APACHE II scores between clinical outcome groups

The death group had significantly higher serum IL-6, hs-CRP, SAA levels, and APACHE II scores compared to the survival group (P < 0.05), as shown in **Table 4**.

Tab. 4 Comparison of serum IL-6, hs-CRP, SAA levels, and APACHE II scores between different clinical outcome groups $(\bar{x}\pm s)$

Group	IL-6 (ng/L)	hs-CRP (mg/L)	SAA (mg/L)	APACHE score
Death group	21.92±4.66	32.75±5.05	310.45±61.88	67.82±3.04
Survival group	12.04±2.82	19.50±4.31	184.46±50.34	48.34±6.82
t value	8.116	7.761	6.259	7.879
P value	< 0.001	< 0.001	< 0.001	< 0.001

Note: compared with the high-risk group, aP <0.05; Compared with the medium-risk group, bP <0.05.

2.4 Correlation between serum IL-6, hs-CRP, SAA, and APACHE II score

Pearson correlation analysis showed that serum IL-6, hs-CRP, and SAA were positively correlated with APACHE II scores (r = 0.392, 0.387, 0.406, P < 0.05).

2.5 Predictive value of serum IL-6, hs-CRP, and SAA for mortality

ROC curve analysis showed that the combination of serum IL-6, hs-CRP, and SAA had the highest AUC for predicting mortality in elderly sepsis patients with ALI, with an AUC of 0.859 (95%CI 0.812–0.952), sensitivity of

94.96%, and specificity of 90.38%, as shown in **Table 5** and **Figure 1**.

Tab. 5 Predictive efficacy of serum IL-6, hs-CRP and SAA on

	death								
Indicator	Cut-off	SE	AUC	95%CI	Sensitivit	Specificit			
					y (%)	y (%)			
IL-6	12.38 ng/L	0.155	0.617	0.549~0.732	75.07	71.82			
hs-CRP	19.07 mg/L	0.163	0.591	0.512~0.684	71.74	68.24			
SAA	173.54 mg/L	0.150	0.642	0.578~0.757	78.96	74.82			
Combine	d	0.001	0.859	0.812~0.952	94.96	90.38			

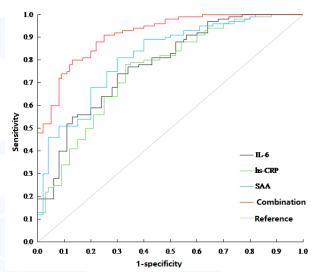


Fig.1 ROC curve of IL-6, hs-CRP and SAA predicting death in elderly patients with sepsis complicated with ALI

3 Discussion

Sepsis can severely damage the function of other tissues and organs, with the lungs being the most commonly affected. This is manifested by excessive release of reactive oxygen species, chemokines, and cytokines, leading to the accumulation of large numbers of neutrophils in the lungs, thereby inducing acute lung injury (ALI), which is one of the leading causes of death in sepsis patients [11-12]. Elderly sepsis patients are at higher risk for developing ALI due to factors such as underlying diseases. Previously, the APACHE II score has been used to assess the severity of sepsis and ALI, but it involves many parameters and is subject to subjective bias from the assessor, resulting in poor sensitivity and specificity. Therefore, finding an indicator that can accurately assess the severity and prognosis of elderly sepsis patients with ALI is of significant clinical importance for guiding treatment strategies.

Clinical studies have indicated that an excessive inflammatory response is the pathological basis for the development of ALI. Persistent inflammatory stimuli can disrupt the alveolar-capillary barrier function, affecting pulmonary ventilation and gas exchange [13]. IL-6 is a cytokine released by monocytes and macrophages, and

during tissue injury or infection, serum IL-6 levels increase rapidly, inducing inflammatory diseases [14]. hs-CRP is synthesized by hepatocytes and is secreted in large amounts in response to inflammation. As the infection subsides and the patient's condition improves, serum hs-CRP levels gradually decrease, returning to normal [15]. SAA is an acute-phase reactant protein. In healthy individuals, SAA levels in the blood are low, but upon stimulation by mycoplasma, viruses, or bacteria, hepatocytes release large amounts of SAA into the bloodstream [16-17]. The present study shows that the levels of serum IL-6, hs-CRP, SAA, and the APACHE II score were all higher in the observation group than in the control and healthy groups. This suggests that elderly sepsis patients with ALI have higher serum levels of IL-6, hs-CRP, and SAA. The likely reason for this is that in patients with ALI, due to lung infection, the body undergoes severe inflammatory and oxidative stress responses, which stimulate the synthesis and release of large amounts of IL-6, hs-CRP, and SAA, thereby exacerbating the primary disease. Furthermore, IL-6, by binding to its receptor, activates the signal transducer and activator of transcription 3 (STAT3) and Janus kinase I (JAK1) signaling pathways, which promote chemotaxis of inflammatory factors and cytokines, and enhance the accumulation and infiltration of macrophages and neutrophils in the lungs. This promotes the acute-phase response, amplifies the inflammatory response, and induces or worsens lung injury. In a study by Wang et al. [18], the serum levels of IL-6 and hs-CRP in children with ALI were significantly higher than those in healthy neonates, which is consistent with our findings and further confirms that abnormally high levels of serum IL-6 and hs-CRP contribute to the occurrence and development of lung injury.

This study indicated that as the severity of ALI increases, serum levels of IL-6, hs-CRP, and SAA rise abnormally. The underlying reason is that increased levels of IL-6, hs-CRP, and SAA exacerbate the body's inflammatory and stress responses, promoting further lung injury. Therefore, clinical interventions that downregulate the expression of IL-6, hs-CRP, and SAA could delay disease progression and reduce lung injury. In this study, by tracking clinical outcomes, we found that abnormal expressions of serum IL-6, hs-CRP, and SAA were associated with patient clinical outcomes. The results showed that the levels of IL-6, hs-CRP, and SAA, as well as the APACHE II score, were higher in the death group than in the survival group. This suggests that elderly sepsis patients with ALI who die have abnormally high serum levels of IL-6, hs-CRP, and SAA. downregulating the expression of these markers can be used as a target to prevent and treat ALI in elderly sepsis patients.

Our study also shows that serum IL-6, hs-CRP, SAA levels are positively correlated with the APACHE II score. This suggests that during the diagnosis and treatment of elderly sepsis with ALI, changes in serum IL-6, hs-CRP, and SAA levels can be used to assess disease severity, thus overcoming the limitations of the APACHE II score, which

is influenced by subjective factors and involves cumbersome evaluation items. Through ROC curve analysis, we found that the combined detection of serum IL-6, hs-CRP, and SAA had an area under the curve of 0.859, with a sensitivity of 94.96% and specificity of 90.38%. This indicates that the combined detection of IL-6, hs-CRP, and SAA has high diagnostic efficiency for predicting the prognosis of elderly sepsis patients with ALI, compensating for the shortcomings of single-marker tests. Moreover, these markers are easy to measure, cost-effective, and highly reproducible, making them suitable for widespread use in the prognosis assessment of elderly sepsis patients with ALI.

In conclusion, the combined detection of serum IL-6, hs-CRP, and SAA has high sensitivity and specificity for predicting patient mortality. Clinically, these markers can be used as biomarkers to predict poor prognosis in elderly sepsis patients with ALI. This study has some limitations, such as the relatively small sample size, retrospective design, and a limited selection period, which may impact the representativeness, generalizability, and universality of the results. Therefore, further clinical studies with larger sample sizes, multi-center, prospective designs, and longer selection periods are needed to provide more evidence for evaluating the diagnostic and prognostic value of serum IL-6, hs-CRP, and SAA in elderly sepsis patients with ALI.

The authors report no conflict of interest

References

- Nam JJ, Wong AI, Cantong D, et al. Sepsis-induced coagulopathy and disseminated intravascular coagulation: what we need to know and how to manage for prolonged casualty care[J]. J Spec Oper Med, 2023, 23(2):118-121.
- [2] Zhang YR, Chen MX, Wang Y, et al. Visualization analysis of global research status and trend of sepsis-induced acute lung injury based on WoSCC database[J]. Chin J Clin Res, 2023, 36(4): 521-526, 531. [In Chinese]
- [3] Cheng DL, Dong YL, Shen ZQ, et al. MicroRNA expression profile in peripheral blood of children with sepsis and acute respiratory distress syndrome[J]. J Chin Pract Diagn Ther, 2022, 36(9): 916-920. [In Chinese]
- [4] Yang HL, Wang DL, Wang J, et al. Application value of neutrophil to lymphocyte rate combined with red blood cell distribution width to platelet count ratio in emergency elderly sepsis patients[J]. Clin Med China, 2022, 38(6): 509-514. [In Chinese]
- [5] Li J, Wang KJ, Liu P. Relationship between serum IL-8, hs-CRP, NLR and the severity of disease as well as prognosis of elderly patients with aspiration pneumonia[J]. Hebei Med J, 2020, 42(8): 1125-1129, 1134. [In Chinese]
- [6] Yan MT, Zheng YT, Sun YM, et al. Analysis of the value of detection of blood CRP, CREA, ALB and IL-6 level in patients with new coronavirus pneumonia to the prognosis of the disease[J]. J Mod Lab Med, 2020, 35(5): 106-109. [In Chinese]
- [7] Chen T, Li XR, Luo FF, et al. Relationship between serum SAA, PCT, CRP levels and prognosis in children with sepsis and analysis of its diagnostic value[J]. Prog Mod Biomed, 2021, 21(10): 1903-1907. [In Chinese]
- [8] Emergency Medicine Professional Committee of Chinese Society of Integrated Traditional and Western Medicine. Expert consensus on diagnosis and treatment of sepsis with integrated Chinese and Western medicine [J]. Chin Crit Care Med, 2013, 25(4): 194-197. [In Chinese]
- [9] Wang XM, Yu JB, Jin SW. Expert consensus on diagnosis and treatment of septic lung injury with integrated traditional Chinese and western medicine[J]. Chin J Surg Integr Tradit West Med, 2020, 26(3): 400-408. [In Chinese]
- [10] Sun W, He YC, Zhang S, et al. The predict value of procalcitonin, common inflammatory indicators combined with critical illness score in diagnosis and prognosis of sepsis in the elderly patients[J]. Geriatr Health Care, 2021, 27(2):

2021, 36(5): 95-99. [In Chinese]

- [11] Julián-Jiménez A, Eduardo Garcí a D, González Del Castillo J, et al. From the 2021 update of the international guidelines of Surviving Sepsis Campaign to new future guidelines proposed by emergency physicians to detect and treat serious infections and prevent progression to sepsis[J]. Emergencias, 2022, 34(6): 471-473.
- [12] 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]
- [13] Ou HY, Duan YJ, Chen L. Diagnostic value of NLRP3 inflammatory corpuscles in peripheral blood mononuclear cells in sepsis patients with acute lung injury[J]. J Pract Med, 2020, 36(3): 380-384. [In Chinese]
- [14] Ling LF, Zou XH, Liu XQ, et al. Clinical application values of procalcitonin, interleukin-6, serum amyloid A and hypersensitive of C-reactive protein detections in the diagnosis of early bloodstream infection[J]. J Mod Lab Med,
- [15] Zhang W, Zhu YL, Du WH, et al. Changes and clinical significance of serum hs-CRP, CTRP-9 and YKL-40 in elderly patients with acute exacerbation of chronic obstructive pulmonary disease[J]. Clin Misdiagnosis Mistherapy, 2021, 34(3): 52-57. [In Chinese]
- [16] Lin GH, Sun RL, Wang Y, et al. Effects of amyloid protein, high-sensitivity C-reactive protein and serum procalcitonin on diagnosis of pulmonary infection in patients with primary lung cancer[J]. Chin J Nosocomiology, 2020, 30(2): 180-183. [In Chinese]
- [17] Liu N, Zou AM, Han S, et al. Correlation analysis of serum SAA, CRP, PCT, IL-6 with disease severity and prognosis in patients with acute pancreatitis[J]. Lab Med Clin, 2023, 9(3): 379-382. [In Chinese]
- [18] Wang J, Sun H. Diagnostic and prognostic predictive value of CD24, IL-6 and hs-CRP in neonatal acute lung injury[J]. Int J Lab Med, 2021, 42(12): 1489-1494. [In Chinese]

Submission received: 2023-10-16/ Revised: 2024-01-31



· 论 著·

血清 IL-6、hs-CRP、SAA 与老年脓毒症患者 急性肺损伤程度的关系及预后评估

赖思敏, 于婵, 吴梦珠, 汤展宏 成都医学院附属老年医院 成都市第八人民医院呼吸科, 四川 成都 610083

摘要:目的 分析血清白细胞介素-6(IL-6)、超敏 C 反应蛋白(hs-CRP)、淀粉样蛋白 A(SAA)联合检测对老年脓毒症合并急性肺损伤(ALI)患者预后的预测价值。方法 选择成都医学院附属老年医院 2021 年 5 月至 2023 年 5 月就诊的 50 例老年脓毒症患者为对照组,50 例老年脓毒症伴 ALI 患者为观察组,以及 50 例老年健康体检者为健康组。根据氧合指数(OI)将脓毒症伴 ALI 患者分为低危组(27 例,OI 为 201~300 mmHg)、中危组(15 例,101~200 mmHg)和高危组(8 例,OI≤100 mmHg),根据患者临床结局将老年脓毒症伴 ALI 患者分为存活组(42 例)和死亡组(8 例),比较各组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分,绘制受试者工作特征(ROC)曲线分析血清 IL-6、hs-CRP、SAA 对患者死亡的预测效能。结果 观察组血清 IL-6、hs-CRP、SAA 水平和 APACHE II 评分均高于对照组和健康组(P<0.05)。高危组血清 IL-6、hs-CRP、SAA 水平和 APACHE II 评分均高于存活组(P<0.05)。血清 IL-6、hs-CRP、SAA 联合检测预测老年脓毒症合并 ALI 死亡的曲线下面积最高,为 0.859(95% CI 0.812~0.952),灵敏度为 94.96%,特异度为 90.38%。结论 老年脓毒症伴 ALI 血清 IL-6、hs-CRP、SAA 水平高,与 ALI 严重程度及预后联系密切,联合检测可提高对患者临床结局的预测效能。

关键词: 白细胞介素-6; 超敏 C 反应蛋白; 淀粉样蛋白 A; 脓毒症; 急性肺损伤中图分类号: R631 文献标识码: A 文章编号: 1674-8182(2024)11-1700-05

The relationship between serum IL-6, hs-CRP, SAA and acute lung injury in elderly patients with sepsis and their prognostic value

LAI Simin, YU Chan, WU Mengzhu, TANG Zhanhong

Department of Respiratory, Affiliated Elderly Hospital of Chengdu Medical College,

Chengdu Eighth People's Hospital, Chengdu, Sichuan 610083, China

Abstract: Objective To analyze the prognostic predictive value of combined serum interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), and amyloid A (SAA) tests in elderly patients with sepsis combined with acute lung injury (ALI). Methods From May 2021 to May 2023, 50 elderly patients with sepsis (control group), 50 elderly patients with sepsis complicated with ALI (observation group), and 50 elderly healthy subjects (healthy group) admitted in the Affiliated Elderly Hospital of Chengdu Medical College were selected. Patients in observation group were divided into low-risk group (27 cases, 201−300 mmHg), medium-risk group (15 cases, 101−200 mmHg) and high-risk group (8 cases, ≤100 mmHg) according to oxygenation index (OI), and were divided into survival group (42 cases) and death group (8 cases) according to clinical outcomes. Serum levels of IL-6, hs-CRP, SAA and APACHEII scores were compared between each group. Receiver operating characteristic (ROC) curve was used to analyze the predictive efficacy of serum IL-6, hs-CRP and SAA on death. Results The levels of serum IL-6, hs-CRP, SAA and APACHEII score in observation group were higher than those in control group and healthy group (P<0.05). The levels of

DOI: 10. 13429/j. enki. ejer. 2024. 11. 011 基金项目: 国家自然科学基金 (81960342)

出版日期: 2024-11-20



IL-6, hs-CRP, SAA and APACHE [I] score in high-risk group were higher than those in medium-risk group and low-risk group (P<0.05). The levels of IL-6, hs-CRP, SAA and APACHE [I] score in the death group were higher than those in the survival group (P<0.05). The area under the curve of the combined detection of serum IL-6, hs-CRP and SAA to predict the death of sepsis complicated with ALI was the highest [0.859, 95%CI (0.812–0.952)], with the sensitivity of 94.96% and specificity of 90.38%. **Conclusion** High levels of serum IL-6, hs-CRP, and SAA in elderly sepsis with ALI are closely associated with the severity and prognosis of ALI, and the combined assay can improve the efficacy of predicting the clinical outcome of patients.

Keywords: Interleukin-6; Hypersensitive C-reactive protein; Amyloid A; Sepsis; Acute lung injury **Fund program:** National Natural Science Foundation of China (81960342)

脓毒症是诱发多器官功能障碍、脓毒症休克的重 要因素,具有高发病率、高死亡率、预后差等特征[1]。 急性肺损伤(ALI)是脓毒症患者较常见的一种并发 症,常规吸氧难以纠正,如不给予及时有效的治疗,容 易发展成为急性呼吸窘迫综合征(ARDS),对患者生 命安全构成一定威胁[2-3]。老年脓毒症患者由于年 龄较大、免疫功能减退、合并较多基础病等因素的影 响,发生 ALI 的风险更高, ALI 的发生会加重患者原 发病,增加死亡率[4]。因此,及早对老年脓毒症合并 ALI 患者病情及临床结局作出准确的诊断,对于指导 临床展开针对性治疗具有重要意义。虽然,目前白细 胞介素(IL)-6、超敏 C 反应蛋白(hs-CRP)等促炎因 子在感染性疾病诊断中的应用价值得到了临床证实 与认可,但单一诊断特异度较差^[5-6]。淀粉样蛋白 A (SAA)是由肝细胞分泌的一种细胞因子,在受到炎 症、感染等刺激后,24 h 内可迅速增高,血清表达量 与机体感染程度呈正相关[7]。基于此,本文探讨血 清 IL-6、hs-CRP、SAA 与老年脓毒症患者 ALI 程度的 关系及对预后的评估价值。报道如下。

1 资料与方法

- 1.1 一般资料 选择成都医学院附属老年医院 2021年5月至2023年5月就诊的50例老年脓毒症患者为对照组,50例老年脓毒症伴ALI患者为观察组,以及同期体检中心50例老年健康体检者为健康组。3组一般资料比较差异无统计学意义(P>0.05)。见表1。本研究经医院伦理委员会审批(批准号;20210419)。
- 1.2 诊断标准 观察组、对照组均符合《脓毒症中西 医结合诊治专家共识》^[8]中对"脓毒症"诊断标准。 观察组符合《脓毒症肺损伤中西医结合诊治专家共 识》^[9]中对"ALI"诊断标准。
- 1.3 纳入与排除标准 纳入标准:(1)年龄≥60周岁,性别不限;(2)机械通气时间≥48h;(3)临床治疗齐全、完整;(4)均为首次发生脓毒症、ALI;(5)ICU住院时间≥2d。排除标准:(1)合并恶性

肿瘤者;(2)有遗传性、先天性疾病;(3)近3个月应用过免疫抑制剂或伴有免疫缺陷性疾病者;(4)同期参与其他研究或中途因病情变化退出者;(5)由于吸入有毒气体、溺水、肺部手术等因素引发的ALI者;(6)哺乳、备孕、妊娠期女性;(7)合并肺纤维化、支气管哮喘等其他肺部疾病者;(8)既往有肺部手术史;(9)合并其他全身感染性疾病者;(10)血流动力学极度不稳定者;(11)近6月存在输血史、器官移植史者;(12)存在药物依赖史、吸毒史、酒精成瘾史者。

表 1 3 组一般资料比较 $(n=50, \bar{x}\pm s)$ **Tab. 1** Comparison of general information among three groups $(n=50, \bar{x}\pm s)$

组别	男/女	年龄(岁)	BMI	脓毒症诱因ª	住 ICU	机械通气
组 加	(例)	平瞬(夕)	(kg/m^2)	(例)	时间(d)	时间(d)
观察组	28/22	70.82±5.37	23.14±1.29	4/10/11/12/13	16.89±3.01	8.14±1.68
对照组	29/21	71.24±5.12	23.18±1.24	6/9/8/13/14	16.82±3.04	8.16±1.57
健康组	26/24	70.24 ± 5.01	23.28±0.97	_	_	_
$F/\chi^2/t$ 值	0.378	0.472	0.188	1.003	0.116	0.062
P 值	0.828	0.625	0.829	0.909	0.908	0.951

注: * 脓毒症诱因分别为血源性感染/颅内感染/泌尿系感染/腹腔感染/肺部感染。

1.4 研究方法 抽取受检者 5 mL 空腹静脉血;采用低速离心机(型号: TD6M;生产企业: 湖南沪康离心机有限公司)离心 10 min,离心速率 4 000 r/min,离心半径 10 cm,将上层清液分离后保存在-20 ℃环境,以酶联免疫吸附法(ELISA)检测 IL-6、hs-CRP,以透射比浊法检测 SAA,试剂盒均由泽叶生物科技有限公司提供,一切操作谨遵实验室、试剂标准完成。急性生理学与慢性健康状况评分(APACHE II):包括慢性健康状况评分、年龄评分、急性生理学评分 3 部分,总分是 71 分,病情越严重,分值越高[10]。

根据氧合指数(OI)将脓毒症伴 ALI 患者分为低 危组(27 例,OI:201~300 mmHg)、中危组(15 例,OI: 101~200 mmHg)和高危组(8 例,OI: ≤ 100 mmHg),根据患者临床结局将老年脓毒症伴 ALI 患者分为存活组(42 例)和死亡组(8 例)。比较各组血清 IL-6、

hs-CRP、SAA 水平及 APACHE II 评分。

1.5 统计学方法 使用 SPSS 26.0 软件处理数据。符合正态分布的计量资料以 $\bar{x}\pm s$ 表示,比较采用成组 t 检验及单因素方差分析;计数资料以例表示,比较采用 X^2 检验及 Fisher 精确检验,等级资料比较采用 Ridit 分析。Pearson 法分析血清 IL-6、hs-CRP、SAA 水平与 APACHE II 评分的相关性,绘制受试者工作特征(ROC)曲线,计算曲线下面积(AUC),分析血清 IL-6、hs-CRP、SAA 对患者死亡的预测效能。P<0.05 为差异有统计学意义。

2 结 果

- 2.1 3组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分比较 观察组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分高于对照组和健康组(P<0.05),对 照组以上指标高于健康组(P<0.05)。见表 2。
- 2.2 不同疾病严重程度组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分比较 高危组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分均高于中危组和低危组(P<0.05),中危组以上指标均高于低危组(P<0.05)。见表 3。
- 2.3 不同临床结局组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分比较 死亡组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分均高于存活组(P<0.05)。见表 4。
- 2.4 血清 IL-6、hs-CRP、SAA 与 APACHE II 评分的相 关性 Pearson 相关分析显示,血清 IL-6、hs-CRP、SAA 水平与 APACHE II 评分均呈正相关(r=0.392、0.387、0.406、P<0.05)。
- 2.5 血清 IL-6、hs-CRP、SAA 对患者死亡的预测效能 ROC 曲线显示,血清 IL-6、hs-CRP、SAA 联合检测预测老年脓毒症合并 ALI 死亡的 AUC 最高,为 0.859(95% CI: 0.812~0.952),灵敏度为 94.96%,特异度为 90.38%。见表 5、图 1。

表 2 3 组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分比较 $(n=50, \bar{x}\pm s)$

Tab. 2 Comparison of serum IL-6, hs-CRP, SAA levels and APACHE II scores among 3 groups $(n=50, \bar{x}\pm s)$

组别	IL-6(ng/L)	hs-CRP(mg/L)	SAA(mg/L)	APACHEⅡ 评分(分)
观察组	13.62±4.88	21.62±6.86	204.62±34.62	51.46±19.52
对照组	8.41±2.72a	14.26±3.17 ^a	161.88±21.78 ^a	34.88±12.76 ^a
健康组	$1.84\!\pm\!0.34^{ab}$	$1.05\!\pm\!0.34^{\rm ab}$	$103.52\!\pm\!16.28^{\rm ab}$	$7.16\!\pm\!1.54^{ab}$
F 值	166.843	284.757	199.358	137.572
P 值	< 0.001	< 0.001	< 0.001	< 0.001

注:与观察组比较, ^aP<0.05; 与对照组比较, ^bP<0.05。

表 3 不同疾病严重程度组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分比较 ($\bar{x}\pm s$)

Tab. 3 Comparison of serum levels of IL-6, hs-CRP, SAA and APACHE II scores among different disease severity groups $(\bar{x}\pm s)$

组别	例数	IL-6(ng/L)	hs-CRP(mg/L)	SAA(mg/L)	APACHE Ⅱ
高危组	8	19.15±2.52	30.85±3.44	281.64±51.66	呼分(分) 63.55±4.82
中危组	15	13.76±1.82 ^a	22.81±2.46 ^a	208.05±41.63 ^a	54.55±3.04 ^a
低危组	27	11.90±1.11 ^{ab}	18.22 ± 1.64^{ab}	$179.89\!\pm\!30.04^{ab}$	$46.16\!\pm\!1.92^{ab}$
F 值		62.129	100.428	22.700	125.481
P 值		< 0.001	< 0.001	< 0.001	< 0.001

注:与高危组比较, *P<0.05; 与中危组比较, *P<0.05。

表 4 不同临床结局组血清 IL-6、hs-CRP、SAA 水平及 APACHE II 评分比较 (x̄±s)

Tab. 4 Comparison of serum IL-6, hs-CRP, SAA levels and APACHE [] scores among different clinical outcome groups $(\bar{x}\pm s)$

组别	例数	IL-6(ng/L)	hs-CRP(mg/L)	SAA(mg/L)	APACHEⅡ 评分(分)
死亡组	8	21.92±4.66	32.75±5.05	310.45±61.88	67.82±3.04
存活组	42	12.04±2.82	19.50±4.31	184.46±50.34	48.34 ± 6.82
t 值		8.116	7.761	6.259	7.879
P 值		< 0.001	< 0.001	< 0.001	< 0.001

表 5 血清 IL-6、hs-CRP、SAA 对患者死亡的预测效能 Tab. 5 Predictive efficacy of serum IL-6, hs-CRP and SAA on death

因素	截断值	标准误	AUC	95% <i>CI</i>	灵敏度 (%)	特异度 (%)
IL-6	12.38 ng/L	0.155	0.617	0.549~0.732	75.07	71.82
hs-CRP	19.07~mg/L	0.163	0.591	$0.512 \sim 0.684$	71.74	68.24
SAA	173.54 mg/L	0.150	0.642	$0.578 \sim 0.757$	78.96	74.82
联合		0.001	0.859	0.812~0.952	94.96	90.38

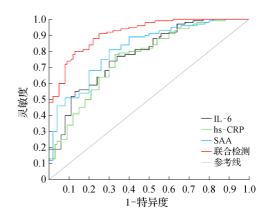


图 1 IL-6、hs-CRP、SAA 预测老年脓毒症 合并 ALI 患者死亡的 ROC 曲线图

Fig. 1 ROC curve of IL-6, hs-CRP and SAA predicting death in elderly patients with sepsis complicated with ALI

3 讨论

脓毒症极易损害其他组织、器官功能,以肺脏受 累最为常见,具体表现为活性氧、趋化因子、细胞因子 过度释放,肺部聚集大量的中性粒细胞,从而诱发 ALI,是导致脓毒症患者死亡的重要原因之一^[11-12]。 老年脓毒症患者受基础病等因素的影响,发生 ALI 的 风险更高。既往临床应用 APACHE II 评分评估脓毒症 ALI 患者病情严重程度,测评项目较多,且容易受 到测评者主观因素的影响,灵敏度、特异度较差。因 此,寻求一种可准确评估老年脓毒症合并 ALI 患者病 情严重程度及预后的指标,对于临床制定治疗方案具 有重要的指导意义。

临床有研究表明,过度炎症反应是诱发 ALI 的病 理基础,持续性的炎症刺激会破坏肺泡-毛细血管屏 障功能,影响肺通气、换气功能[13]。IL-6 是由单核巨 噬细胞释放的一种细胞因子,在机体发生组织损伤或 感染时,血清 IL-6 表达量会迅速增高,诱发炎症性疾 病[14]。hs-CRP 由肝细胞合成,在机体受到炎症刺激 时会分泌大量的 hs-CRP, 随着感染程度的减轻及病 情好转,血清 hs-CRP 水平会逐渐降低,直至恢复正 常[15]。SAA 是一种急性时相反应蛋白,健康人群机 体血清 SAA 表达量较低,在受到支原体、病毒、细菌 刺激后,肝细胞会分泌大量的 SAA 到血液循环 中[16-17]。本研究显示,观察组血清 IL-6、hs-CRP、 SAA 水平及 APACHE Ⅱ 评分均高于对照组和健康 组。提示合并 ALI 的脓毒症患者血清 IL-6、hs-CRP、 SAA 表达量相对更高,分析原因可能是发生 ALI 的 患者,由于肺部感染,机体会发生严重的炎症反应、氧 化应激反应,从而刺激机体合成、释放大量的 IL-6、 hs-CRP、SAA,加重原发病。另外,IL-6 通过结合其受 体,激活转录激活子3(STAT3)、J激酶I(JAKI)-信号 转导子通路, 趋化炎性因子、细胞因子生化, 促进巨噬 细胞、中性粒细胞在肺部聚集、浸润,促进急性期反 应,放大炎症反应,诱发 ALI 或加重肺损伤程度。王 军等[18]研究中,ALI 患儿机体血清 IL-6、hs-CRP 显著 高于健康新生儿,本研究报道与文献接近,证实了血 清 IL-6、hs-CRP 异常高表达参与了 ALI 发生、发 展中。

本研究显示,随着 ALI 严重程度的加重,血清 IL-6、hs-CRP、SAA 水平会异常增高,究其原因是血清 IL-6、hs-CRP、SAA 水平增高,会加重机体炎症反应及应激反应,促进肺损伤,故临床可通过下调血清 IL-6、hs-CRP、SAA 水平延缓患者疾病进展,减轻肺损伤程度。本研究对脓毒症合并 ALI 患者通过追踪临床结局,发现血清 IL-6、hs-CRP、SAA 异常表达与患者临床结局存在一定的联系,结果显示临床结局为死亡的老年脓毒症合并 ALI 患者,血清 IL-6、hs-CRP、SAA 呈异常高表达,临床可将下调血清 IL-6、hs-CRP、SAA

表达量作为预防、治疗老年脓毒症患者发生 ALI 的靶点与方向。

本研究显示,血清 IL-6、hs-CRP、SAA 与APACHE II 评分均呈正相关。提示临床在老年脓毒症合并 ALI 疾病诊治过程中,可通过检测血清 IL-6、hs-CRP、SAA 水平变化,评估疾病严重程度,弥补了APACHE II 评分容易受测评者主观因素及测评项目繁琐等因素影响的不足。本研究通过 ROC 曲线分析,发现血清 IL-6、hs-CRP、SAA 联合检测预测老年脓毒症合并 ALI 死亡的 AUC 是 0.859,灵敏度为94.96%,特异度为90.38%,提示血清 IL-6、hs-CRP、SAA 联合检测在预测老年脓毒症合并 ALI 患者预后方面具有较高的诊断效能,弥补了单一检测的不足,且以上指标检测具有操作方便、价格低廉、可重复性强等优点,在老年脓毒症合并 ALI 患者预后评估中具有广阔的应用前景。

综上所述,血清 IL-6、hs-CRP、SAA 联合检测在 预测患者死亡方面灵敏度、特异度较高,临床可将其 作为预测老年脓毒症合并 ALI 患者预后不良的生物 标记物。本研究存在几点不足,例如样本病例数较 小,为回顾性研究,病例选取时限较短,对结果的代表 性、一般性、普遍性等有所影响。因此,仍需要临床扩 大样本病例数,展开多中心、大样本前瞻性研究,延长 病例选取时限开展进一步研究。

利益冲突 无

参考文献

- [1] Nam JJ, Wong AI, Cantong D, et al. Sepsis-induced coagulopathy and disseminated intravascular coagulation; what we need to know and how to manage for prolonged casualty care [J]. J Spec Oper Med, 2023, 23(2);118-121.
- [2] 张怡人,陈梦晓,王毅,等.脓毒症急性肺损伤全球研究现状与趋势的 WoSCC 数据库可视化分析[J].中国临床研究,2023,36 (4):521-526,531.
 - Zhang YR, Chen MX, Wang Y, et al. Visualization analysis of global research status and trend of sepsis-induced acute lung injury based on WoSCC database [J]. Chin J Clin Res, 2023, 36(4): 521-526, 531.
- [3] 程东良,董跃丽,申志强,等.脓毒症及脓毒症并发急性呼吸窘迫综合征患儿外周血单个核细胞 miRNA 表达谱分析[J].中华实用诊断与治疗杂志,2022,36(9):916-920.
 - Cheng DL, Dong YL, Shen ZQ, et al. MicroRNA expression profile in peripheral blood of children with sepsis and acute respiratory distress syndrome $[\ J\]$. J Chin Pract Diagn Ther, 2022, 36 (9): 916–920.
- [4] 杨海龙,王冬利,王晶,等.中性粒细胞与淋巴细胞比值联合红细胞分布宽度与血小板计数比值在急诊老年脓毒症患者中的应

- 用价值[J].中国综合临床,2022,38(6):509-514.
- Yang HL, Wang DL, Wang J, et al. Application value of neutrophil to lymphocyte rate combined with red blood cell distribution width to platelet count ratio in emergency elderly sepsis patients [J]. Clin Med China, 2022, 38(6): 509–514.
- [5] 李娟,王开金,刘翩.血清 IL-8、hs-CRP、NLR 与老年吸入性肺炎 患者病情严重程度和预后的关系[J].河北医药,2020,42(8): 1125-1129,1134.
 - Li J, Wang KJ, Liu P. Relationship between serum IL-8, hs-CRP, NLR and the severity of disease as well as prognosis of elderly patients with aspiration pneumonia[J]. Hebei Med J, 2020, 42(8): 1125-1129, 1134.
- [6] 闫美田,郑雨桐,孙艳美,等.新型冠状病毒肺炎患者血液 CRP, CREA, ALB, IL-6 水平检测对疾病预后的应用价值分析[J].现代检验医学杂志,2020,35(5):106-109.
 - Yan MT, Zheng YT, Sun YM, et al. Analysis of the value of detection of blood CRP, CREA, ALB and IL-6 level in patients with new coronavirus pneumonia to the prognosis of the disease [J]. J Mod Lab Med, 2020, 35(5): 106–109.
- [7] 陈婷,李雪茹,罗菲菲,等.脓毒症患儿血清 SAA、PCT、CRP 水平与预后的关系及其诊断价值分析[J].现代生物医学进展,2021,21(10):1903-1907.
 - Chen T, Li XR, Luo FF, et al. Relationship between serum SAA, PCT, CRP levels and prognosis in children with sepsis and analysis of its diagnostic value [J]. Prog Mod Biomed, 2021, 21 (10): 1903-1907.
- [8] 中国中西医结合学会急救医学专业委员会、《中国中西医结合 急救杂志》编辑委员会.脓毒症中西医结合诊治专家共识[J].中 华危重病急救医学,2013,25(4):194-197.
 - Emergency Medicine Professional Committee of Chinese Society of Integrated Traditional and Western Medicine. Expert consensus on diagnosis and treatment of sepsis with integrated Chinese and Western medicine [J]. Chin Crit Care Med, 2013, 25 (4): 194–197.
- [9] 王西墨,余剑波,金胜威.脓毒症肺损伤中西医结合诊治专家共识[J].中国中西医结合外科杂志,2020,26(3):400-408.
 Wang XM, Yu JB, Jin SW. Expert consensus on diagnosis and treatment of septic lung injury with integrated traditional Chinese and western medicine[J]. Chin J Surg Integr Tradit West Med, 2020,
- [10] 孙伟,何燕超,张山,等.血清降钙素原和常用炎症指标与老年脓毒症的相关性及结合重症评分对其预后的评价[J].老年医学与保健,2021,27(2):290-295.

26(3): 400-408.

- Sun W, He YC, Zhang S, et al. The predict value of procalcitonin, common inflammatory indicators combined with critical illness score in diagnosis and prognosis of sepsis in the elderly patients [J]. Geriatr Health Care, 2021, 27(2): 290-295.
- [11] Julián-Jiménez A, Eduardo García D, González Del Castillo J, et al. From the 2021 update of the international guidelines of Surviving

- Sepsis Campaign to new future guidelines proposed by emergency physicians to detect and treat serious infections and prevent progression to sepsis[J]. Emergencias, 2022, 34(6): 471-473.
- [12] 卢强,倪兴国,巩红岩.细菌性血流感染致脓毒症老年患者血清 PCT 和 D-D 及 CRP 及血小板计数变化[J].热带医学杂志, 2022,22(12):1684-1687,1700.
 - Lu Q, Ni XG, Gong HY. Changes of serum PCT, D-D, CRP and platelet count in elderly patients with sepsis caused by bacterial bloodstream infection $[\,J\,]$. J Trop Med, 2022, 22 (12): 1684 1687, 1700.
- [13] 欧海燕,段娅娟,陈兰.外周血单核细胞 NLRP3 炎性小体对脓毒症急性肺损伤患者病情严重程度的诊断价值[J].实用医学杂志,2020,36(3);380-384.
 - Ou HY, Duan YJ, Chen L. Diagnostic value of NLRP3 inflammatory corpuscles in peripheral blood mononuclear cells in sepsis patients with acute lung injury[J]. J Pract Med, 2020, 36(3): 380-384.
- [14] 凌利芬,邹小红,刘小晴,等.血清 PCT,IL-6,SAA,hs-CRP 水平 联合检测对快速筛查早期血流感染的价值[J].现代检验医学杂志,2021,36(5):95-99.
 - Ling LF, Zou XH, Liu XQ, et al. Clinical application values of procalcitonin, interleukin-6, serum amyloid A and hypersensitive of Creactive protein detections in the diagnosis of early bloodstream infection[J]. J Mod Lab Med, 2021, 36(5): 95–99.
- [15] 张巍,朱娅丽,杜维桓,等.老年慢性阻塞性肺疾病急性加重期患者血清 hs-CRP、CTRP-9、YKL-40 水平变化及临床意义[J].临床误诊误治,2021,34(3):52-57.
 - Zhang W, Zhu YL, Du WH, et al. Changes and clinical significance of serum hs-CRP, CTRP-9 and YKL-40 in elderly patients with acute exacerbation of chronic obstructive pulmonary disease [J]. Clin Misdiagnosis Mistherapy, 2021, 34(3): 52–57.
- [16] 牛凯旋,吴淑璐,刘成,等.血清淀粉样蛋白 A 和白细胞介素-6 对脓毒症诊断及病情严重程度评估的临床价值[J].中华全科医学,2022,20(9):1484-1487.
 - Niu KX, Wu SL, Liu C, et al. Clinical value of serum amyloid A and interleukin-6 in the diagnosis and severity evaluation of sepsis [J]. Chin J Gen Pract, 2022, 20(9): 1484-1487.
- [17] 刘娜, 邹爱民, 韩双, 等. 血清 SAA、CRP、PCT、IL-6 水平与急性胰腺炎患者病情严重程度及预后的相关性分析[J]. 检验医学与临床、2023、9(3):379-382.
 - Liu N, Zou AM, Han S, et al. Correlation analysis of serum SAA, CRP, PCT, IL-6 with disease severity and prognosis in patients with acute pancreatitis[J]. Lab Med Clin, 2023, 9(3): 379-382.
- [18] 王军,孙红.CD24、IL-6 和 hs-CRP 对新生儿急性肺损伤的诊断 及预后预测价值[J].国际检验医学杂志,2021,42(12): 1489-1494.
 - Wang J, Sun H. Diagnostic and prognostic predictive value of CD24, IL-6 and hs-CRP in neonatal acute lung injury [J]. Int J Lab Med, 2021, 42(12): 1489–1494.
 - **收稿日期:2023-10-16 修回日期:2024-01-31 编辑:**王宇