中国临床研究 Chin J Clin Res, November 2024, Vol.37, No.11
Cite as: Tian XY, Yu D, Li XM, Chen XF. Correlation and prognostic value of albumin/fibrinogen ratio with myocardial injury in patients with sepsis[J]. Chin J Clin Res, 2024, 37(11):1709-1713.
DOI: 10.13429/j.cnki.cjcr.2024.11.013

Correlation and prognostic value of albumin/fibrinogen ratio with myocardial injury in patients with sepsis

TIAN Xueyan*, YU Dian, LI Xiaomin, CHEN Xuefeng

**Department of Emergency Medicine, Lianyungang Hospital Affiliated to Xuzhou Medical University, Lianyungang, Jiangsu 222000, China*

Corresponding author: CHEN Xuefeng, E-mail: cxf2010@189.cn

Abstract: **Objective** To investigate the level of albumin/fibrinogen ratio (AFR) and its relationship with prognosis in patients with septic myocardial injury. **Methods** From February 2022 to April 2023, a prospective clinical observational study was conducted to collect 101 patients with sepsis in Lianyungang Hospital Affiliated to Xuzhou Medical University as study subjects. They were divided into myocardial injury group (46 cases) and normal cardiac function group (55 cases) according to whether myocardial injury occurred. The basic clinical data of the two groups were recorded, and peripheral blood was collected within 24 h of admission to test for albumin, fibrinogen, amino-terminal pro–B-type natriuretic peptide (NT-proBNP), high sensitivity troponin I (hsTn I), calcitoninogen (PCT), acute physiology and chronic health evaluation (APACHE II), and sequential organ failure assessment (SOFA). Survival of patients was recorded at 28 days of follow-up. Logistic regression was used to analyze the independent risk factors of septic myocardial injury, ROC curve was used to analyze the clinical diagnostic efficacy of AFR in septic myocardial injury. **Results** Compared with normal cardiac function group, the levels of albumin and AFR were significantly reduced, while the NT-proBNP, hsTn I, APACHE II scores, and fibrinogen were significantly increased in myocardial injury group (P<0.05). Elevated AFR was an independent protective factor for myocardial injury in sepsis (OR = 0.547, 95%CI: 0.384-0.779, P=0.001). When the AFR cutoff value was 7.07, the AUC for the diagnosis of septic myocardial injury was 0.791 (95%CI: 0.693-0.888), but the combination of hs Tn I, NT-proBNP and APACHE II scores had the highest diagnostic value, with an AUC of 0.933 (95%CI: 0.887-0.978). The 28-day survival of sepsis patients with low AFR expression (AFR≤7.07) was significantly lower than that of sepsis patients with high AFR expression (AFR>7.07, P<0.05). **Conclusion** To some extent, AFR can predict the occurrence of myocardial injury and the risk of 28-day death in patients with sepsis.

Keywords: Sepsis; Myocardial injury; Albumin to fibrinogen ratio; Survival
Fund program: Jiangsu Science and Technology Project (BE2020670)

Sepsis is a life-threatening organ dysfunction caused by a systemic inflammatory response triggered by bacterial and other pathogenic microorganism infections [1]. Despite significant progress in treatment, the mortality rate remains high due to the presence of secondary complications. Acute non-ischemic myocardial injury induced by sepsis is commonly diagnosed as sepsis cardiomyopathy (SCM), one of the major complications threatening the lives of sepsis patients. The incidence of SCM has been reported to range from 10% to 70%, and the mortality rate in sepsis patients with SCM is 2 to 3 times higher than that in those without SCM [2]. Therefore, early diagnosis and treatment of SCM should be prioritized. Serum albumin and fibrinogen, both synthesized by the liver, play important roles in the inflammatory response. The albumin to fibrinogen ratio (AFR) has become a research hotspot in recent years and has been widely applied in the diagnosis of various diseases, including cancer, sepsis, and cardiovascular diseases, and is associated with poor prognosis in many conditions. Studies have shown that AFR can be used to predict the occurrence of acute kidney injury caused by sepsis and the prognosis of patients [3]. Recently, research by Li *et al.* further confirmed that AFR is correlated with clinical outcomes and disease severity in sepsis patients [4], but few studies have reported on the role of AFR in sepsis-induced myocardial injury. Currently, known biomarkers of myocardial injury in sepsis include amino-terminal pro–B-type natriuretic peptide (NT-proBNP) and high-sensitivity troponin I (hsTnI). NT-proBNP levels are closely related to the severity of myocardial injury and also play a role in the pathogenesis and progression of sepsis. In patients with myocardial injury, NT-proBNP levels are significantly elevated, and early combined detection can improve diagnostic capability and prognostic assessment [5]. HsTnI is a novel detection method used for diagnosing myocardial injury and cardiovascular diseases. Studies have shown that elevated hsTnI levels in myocardial injury patients have certain value in the early assessment of SCM [6]. Based on existing research on myocardial injury biomarkers, this study explores the correlation between AFR and myocardial injury in sepsis patients, as well as its association with short-term prognosis in sepsis patients.

1 Materials and Methods

1.1 General Information

This prospective observational clinical study included patients with sepsis at the Department of Critical

Care Medicine and Emergency Intensive Care Unit of Lianyungang Hospital, Affiliated to Xuzhou Medical University, between February 2022 and April 2023.

Inclusion criteria: (1) Meeting the diagnostic criteria for adult sepsis and septic shock in the Sepsis 3.0 criteria [7]; (2) Age >18 years; (3) Based on the findings from literature [1], myocardial injury was including left ventricular and/or right ventricular dysfunction and hemodynamic abnormalities.

Exclusion criteria: (1) Patients with chronic heart failure, acute viral myocarditis, severe neurological or mental disorders, or have had a myocardial infarction in the past 6 months; (2) Pregnant or breastfeeding women; (3) Incomplete clinical data; (4) History of heart valve disease or implantation of other cardiac devices; (5) History of hematologic diseases, advanced malignant tumors, or liver diseases.

The study was approved by the Ethics Committee of the First People's Hospital of Lianyungang City, with the ethics approval number KY-20230419001, and informed consent was obtained from all patients.

1.2 Observational Indicators

General information of the patients (including gender, age, length of ICU stays, infection source, etc.), past medical history, and peripheral blood indices (albumin, fibrinogen) within 24 hours of admission were recorded, and the AFR was calculated. The following biomarkers were also recorded: NT-proBNP, hsTnI, procalcitonin (PCT), as well as Acute Physiology and Chronic Health Evaluation (APACHE) II score and Sequential Organ Failure Assessment (SOFA) score at the time of admission. All patients were followed up for 28 days.

1.3 Statistical Methods

Statistical analysis was performed using SPSS 26.0 software. Normally distributed continuous variables are expressed as $\bar{x}\pm s$, and comparisons between two groups were performed using independent samples *t*-test. Skewed data were presented as $M(P_{25}, P_{75})$, with group comparisons conducted using non-parametric tests. Categorical variables were expressed as *n*(%), with comparisons made using the χ^2 test or Fisher's exact test. Logistic regression analysis was used to identify independent risk factors for myocardial injury, and receiver operating characteristic (ROC) curves were drawn to assess the diagnostic value. Kaplan-Meier analysis and the log-rank test were used to analyze the survival prognosis of sepsis patients. GraphPad Prism 9.0 software was used to draw the survival curve. $P<0.05$ was considered statistically significant.

2 Results

2.1 Baseline Data

A total of 101 sepsis patients were included in the study, with 55 patients in the normal cardiac function group (54.46%) and 46 patients in the myocardial injury group (45.54%). There were no statistically significant differences between the two groups in terms of gender, age, body mass index (BMI), underlying diseases, and other baseline characteristics ($P>0.05$). There were statistically significant differences in the APACHE II and SOFA scores within 24 hours between the two groups ($P<0.05$) **[Tab.1]**.

Tab.1 Comparison of general information between two groups [case(%)]

Item	Normal cardiac function group (*n*=55)	Myocardial injury group (*n*=46)	$t/\chi^2/z$ value	*P* value
Age (years) [a]	66.49±11.88	69.33±12.42	1.170	0.245
Gender			1.497	0.221
Male	33(60.0)	22(47.8)		
Female	22(40.0)	24(52.2)		
BMI (kg/m^2) [b]	24.0(22.9, 24.8)	23.9(21.7, 24.7)	1.313	0.189
Length of ICU stay (d) [a]	9.18±2.02	9.85±2.15	1.603	0.112
Heart rate (beats/min) [a]	92.80±11.98	95.26±11.73	1.038	0.302
Main sources of infection			5.525	0.238
Pulmonary	27(49.1)	22(47.8)		
Abdominal	15(27.3)	12(26.1)		
Urinary tract	3(5.5)	8(17.4)		
Soft tissue	5(9.1)	3(6.5)		
Blood	5(9.1)	1(2.2)		
Basic disease [b]				
Hypertension	29(52.7)	20(43.5)	0.858	0.354
Coronary heart disease	10(18.2)	5(10.9)	1.059	0.303
Diabetes	6(10.9)	5(10.9)	0.000	0.995
Cerebral infarction	6(10.9)	7(15.2)	0.415	0.520
Hyperlipidemia	5(9.1)	4(8.7)	0.079	0.779
COPD	4(7.3)	3(6.5)	0.060	0.806
Abnormal renal function	1(1.8)	1(2.2)		1.000[c]
Clinical scoring system				
APACHE II [a]	18.35±2.33	20.89±2.86	4.932	<0.001
SOFA [b]	7(6, 9)	8(6, 10)	2.139	0.032
28 days of death	17(30.9)	22(47.8)	3.024	0.082

Note: [a] meant the data was represent in the form of $\bar{x}\pm s$; [b] meant the data was represent in the form of $M(P_{25}, P_{75})$; c meant it was the result of Fisher's precision probability test.

2.2 Laboratory Indicators

Compared to the normal cardiac function group, the myocardial injury group showed a decreased AFR, and elevated levels of hsTnI and NT-proBNP, with statistically significant differences ($P<0.01$) **[Tab.2]**.

2.3 Risk Factors for Myocardial Injury in Patients with Sepsis

Factors from **Tab.1** and **Tab.2** that showed statistical significance in univariate analysis were included in a multivariate logistic regression analysis. The results indicated that a reduced AFR, elevated hsTnI, APACHE II score, and NT-proBNP were independent risk factors for myocardial injury in sepsis patients ($P<0.05$) **[Tab.3]**.

Tab. 2 Comparison of laboratory indicators between two groups

Group	AFR[a]	hs Tn Ⅰ (pg/mL)[b]	NT-proBNP(pg/mL)[b]	PCT(ng/mL)[b]
Normal cardiac function group(*n*=55)	8.24±1.81	82.21(29.83,155.90)	1196.04(765.09,4562.29)	9.20(5.66,12.80)
Myocardial injury group(*n*=46)	6.29±1.93	231.19(157.33,358.08)	4788.7 (1741,11036)	9.96(7.39,14.20)
***t* /*z* value**	5.244	5.578	2.898	1.483
***P* value**	<0.001	<0.001	0.004	0.138

Note： [a] meant the data was represent in the form of $\bar{x}\pm S$; [b] meant the data was represent in the form of $M(P_{25}, P_{75})$.

Tab. 3 Multivariate logistic regression analysis of influencing factors of myocardial injury in patients with sepsis

Item	*β*	*S.E.*	*Wald*	*P*	*OR*	95%*CI*
AFR	-0.603	0.180	11.179	0.001	0.547	(0.384-0.779)
hsTnI	1.381	0.373	13.728	<0.001	3.980	(1.917-8.264)
NT-proBNP	0.151	0.059	6.542	0.011	1.163	(1.036-1.305)
APACHEII	0.452	0.141	10.222	0.001	1.572	(1.191-2.074)
SOFA	0.277	0.151	3.366	0.067	1.319	(0.981-1.773)

2.4 Diagnostic Efficacy of Various Indicators for Myocardial Injury in Sepsis

ROC analysis showed that when the AFR cutoff value was set at 7.07, the AUC for diagnosing myocardial injury in sepsis was 0.791 (95%*CI*: 0.693–0.888), with a sensitivity of 76.1% and a specificity of 83.6%. However, after combining hsTnI, NT-proBNP, and APACHE II score, the diagnostic efficacy was highest, with an AUC of 0.933 (95%*CI*: 0.887–0.978), sensitivity of 78.3%, and specificity of 96.4% **[Tab.4, Fig.1]**.

2.5 28-day Survival Analysis of Sepsis Patients with Different AFR Levels

The results showed that the 28-day survival rate of patients with AFR≤7.07 was significantly lower than that of patients with AFR>7.07, with a statistically significant difference (P<0.05) **[Fig.2]**.

Tab.4 Diagnostic efficacy of individual and combined detection of various indexes for myocardial injury in sepsis

Item	AUC(95%*CI*)	Cut-off value	Sensitivity	Specificity	*P* value
AFR	0.791(0.693-0.888)	7.07	76.1%	83.6%	<0.001
hs TnI	0.823(0.743-0.904)	121.04 pg/mL	84.8%	69.1%	<.0001
NT-proBNP	0.668(0.558-0.778)	3 168.8 pg/mL	67.4%	74.5%	<0.001
APACHE II	0.742(0.645-0.838)	20.5	58.7%	81.8%	<0.001
Combination	0.933(0.887-0.978)	-	78.3%	96.4%	<0.001

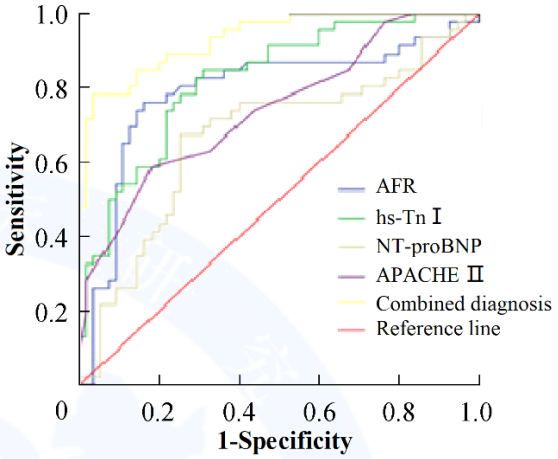

Fig.1 ROC curve of diagnostic efficiency of myocardial injury in sepsis detected by individual or combined detection of each index

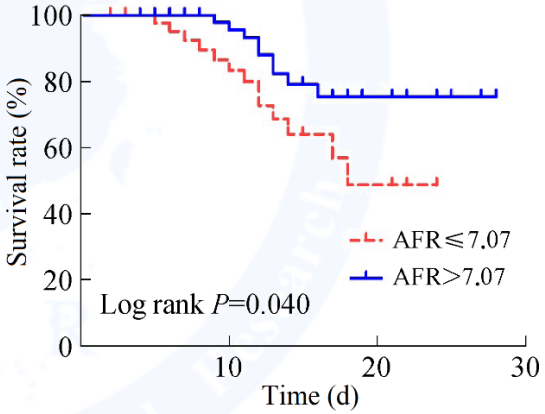

Fig.2 28-day survival curves of sepsis patients with different AFR levels

3 Discussion

Sepsis is a systemic inflammatory response syndrome caused by infection. Patients often present with an acute condition, and if not treated promptly, it can lead to multiple organ dysfunction, being one of the leading causes of non-cardiac death in ICU patients [8-9]. The heart is one of the organs most susceptible to damage in sepsis, and septic myocardial injury and SCM are usually characterized by ventricular dilation, reduced ventricular contractility, and/or dysfunction of both the right and left ventricles, with a decreased volume responsiveness [10].

The occurrence of myocardial injury in sepsis is based on a complex interaction of multiple mechanisms, including immune and coagulation dysfunctions, which are triggered by severe inflammatory responses after infection, leading to cardiac dysfunction [11].

Serum albumin, the most abundant serum protein in the body, reflects the nutritional status and inflammatory state of the body. As a toxin-neutralizing protein, it also influences the pharmacokinetics of antimicrobial agents and plays an important role when the body is infected with toxin-producing microorganisms [12]. During sepsis, excessive inflammatory responses and stress cause a rapid decline in albumin levels [13]. Further studies have shown that low albumin levels are associated with a 30-day mortality in septic patients [14]. Geng *et al.* [15] reported that albumin treatment, especially 20% albumin, could significantly reduce the 90-day mortality in septic shock patients. The results of this study show that the albumin levels were reduced in both patient groups, with a more pronounced decrease in the myocardial injury group.

Fibrinogen, a key component of the body's coagulation system, is involved in normal hemostasis, wound healing, and infection processes. Its diagnostic ability for infection is comparable to other general inflammatory markers, such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) [16-17]. A recent study found that fibrinogen is a reliable diagnostic tool for septic shock, and lower fibrinogen levels are an effective predictor of 30-day all-cause mortality [18]. The results of this study show that fibrinogen levels were higher in the myocardial injury group than in the normal heart function group, which may be related to disease progression, hemodynamic abnormalities, and coagulation system activation in patients with myocardial injury.

As myocardial injury in sepsis is a syndrome involving multiple factors and mechanisms, the author believes that AFR is superior to individual markers like albumin or fibrinogen. AFR not only predicts the level of disease inflammation [19], but also evaluates coagulation function and nutritional status [20-21], and has been confirmed as a predictor of short-term prognosis and disease severity in septic patients. Since septic myocardial injury is secondary to sepsis, it is usually characterized by myocardial cell damage and coagulation dysfunction [22]. These indirect associations may explain why AFR can be used for diagnosing septic myocardial injury and predicting short-term prognosis.

This study explored the role of AFR in septic myocardial injury and found that AFR was significantly lower in the myocardial injury group compared to the normal heart function group. The reason for this decrease in AFR could be that when myocardial injury occurs in sepsis, a large number of inflammatory mediators are released, activating the inflammatory cascade, which leads to a rapid decline in albumin levels as part of the acute-phase response. The drop in albumin levels, in turn, accelerates the inflammatory process through a negative feedback effect on oxidative stress. However, in the early stages of acute inflammation, fibrinogen levels also increase, accelerating platelet activation and leading to coagulation dysfunction [23]. The optimal cutoff point for AFR to predict myocardial injury was found to be 7.07, with an area under the ROC curve of 0.791, a sensitivity of 76.1%, and specificity of 83.6%. This result not only confirms that the inflammatory response was an important mechanism in the occurrence of myocardial injury in sepsis, but also indicated that AFR has predictive value for diagnosing septic myocardial injury, which could help clinicians understand the early progression of sepsis. Specifically, when AFR is higher than 7.07 upon a patient's admission, myocardial injury should be suspected. Compared with other biomarkers such as NT-proBNP and hsTnI for diagnosing myocardial injury in sepsis patients, AFR has certain limitations. However, in this study, combining AFR with NT-proBNP, hsTnI, and APACHE II scores significantly improved diagnostic performance. Furthermore, survival analysis showed that the 28-day survival rate was significantly lower in the AFR≤7.07 group compared to the AFR>7.07 group, suggesting that AFR can stratify the 28-day mortality risk in septic patients, although further studies are needed to validate these findings.

There are limitations to this study, such as being a single-center, prospective observational clinical study with a limited number of cases and laboratory parameters. Since the progression of sepsis can be rapid, most patients may not show signs of myocardial injury until a longer time after admission. Additionally, ICU patients are typically older and have more complex conditions, so further exploration under controlled conditions with various confounding factors is necessary.

AFR may be used as an effective marker to assess the occurrence of myocardial injury in sepsis and may also predict the short-term survival of septic patients to some extent, thereby aiding in the precise diagnosis and treatment of sepsis and improving patient outcomes.

The authors report no conflict of interest

References

[1] Carbone F, Liberale L, Preda A, et al. Septic cardiomyopathy: from pathophysiology to the clinical setting[J]. Cells, 2022, 11(18): 2833.
[2] Song JQ, Yao Y, Lin SL, et al. Feasibility and discriminatory value of tissue motion annular displacement in sepsis-induced cardiomyopathy: a single-center retrospective observational study[J]. Crit Care, 2022, 26(1): 220.
[3] Mei HF, Zhu ZY, Sun WB, et al. Study on the analysis of the predictive value of AFR on acute kidney injury occurrence and prognosis in the patients with sepsis[J]. Chongqing Med, 2020, 49(15): 2519-2523. **[In Chinese]**
[4] Li ZH, Cheng HX, Wang Y, et al. Predictive value of albumin/fibrinogen ratio for 28-day mortality risk in patients with sepsis[J]. Chin J Emerg Med, 2023, 32(2): 180-185. **[In Chinese]**
[5] Li ZY, Cui SH, Geng LX. Value of combined detection of biomarkers in early diagnosis and prognosis of patients with septic myocardial injury[J]. Chin Crit Care Med, 2021(4): 443-448. **[In Chinese]**
[6] Yang PL, Yuan J, Chen Y, et al. Establishment of a predictive model of septic myocardiopathy based on left ventricular global longitudinal strain[J]. Natl Med J China, 2022, 102(15): 1100-1107. **[In Chinese]**
[7] Evans L, Rhodes A, Alhazzani W, et al. Executive summary: surviving sepsis campaign: international guidelines for the management of sepsis and septic shock 2021[J]. Crit Care Med, 2021, 49(11): 1974-1982.
[8] Fleischmann-Struzek C, Mellhammar L, Rose N, et al. Incidence and mortality of hospital- and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis[J]. Intensive Care Med, 2020, 46(8): 1552-1562.
[9] Wei Y, Li XJ, Lei Y, et al. Effects of blood transfusion on lung epithelial cell activity, lung ultrastructure and SIRT1/PGC-1α in septic rats with

acute lung injury[J]. Chin J Clin Res, 2023, 36(4): 515-520. **[In Chinese]**
[10] Martin L, Derwall M, Al Zoubi S, et al. The septic heart: current understanding of molecular mechanisms and clinical implications[J]. Chest, 2019, 155(2): 427-437.
[11] 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. **[In Chinese]**
[12] Austermeier S, Pekmezović M, Porschitz P, et al. Albumin neutralizes hydrophobic toxins and modulates Candida albicans pathogenicity[J]. mBio, 2021, 12(3): e0053121.
[13] Han T, Deng QM, Wan XY. Research progress of hypoalbuminemia in sepsis patients[J]. Natl Med J China, 2017, 97(3): 228-231. **[In Chinese]**
[14] Turcato G, Zaboli A, Sibilio S, et al. Albumin as a prognostic marker of 30-day mortality in septic patients admitted to the emergency department[J]. Intern Emerg Med, 2023, 18(8): 2407-2417.
[15] Geng L, Tian XX, Gao ZF, et al. Different concentrations of albumin versus crystalloid in patients with sepsis and septic shock: a meta-analysis of randomized clinical trials[J]. J Intensive Care Med, 2023, 38(8): 679-689.
[16] Winearls J, Reade MC, McQuilten Z, et al. Fibrinogen in traumatic haemorrhage[J]. Curr Opin Anaesthesiol, 2021, 34(4): 514-520.
[17] Ciriello V, Ghannadian S, Saracco M, et al. Is fibrinogen a reliable biomarker in the diagnosis of peri-prosthetic joint infection? A systematic review and meta-analysis[J]. Surg Infect, 2022, 23(9): 787-795.
[18] Schupp T, Weidner K, Rusnak J, et al. Fibrinogen reflects severity and predicts outcomes in patients with sepsis and septic shock[J]. Blood Coagul Fibrinolysis, 2023, 34(3): 161-170.
[19] He YJ, Tang JF, Wu BD, et al. Correlation between albumin to fibrinogen ratio, C-reactive protein to albumin ratio and Th17 cells in patients with rheumatoid arthritis[J]. Clin Chim Acta, 2020, 500: 149-154.
[20] Li S, Zhang D, Zeng S, et al. Prognostic value of preoperative albumin-to-fibrinogen ratio in patients with bladder cancer[J]. J Cancer, 2021, 12(19): 5864-5873.
[21] Shang JJ, Jiang SJ, Gong JH, et al. Low albumin-to-fibrinogen ratio predicts adverse clinical outcomes after primary total joint arthroplasty: a retrospective observational investigation[J]. Int Wound J, 2023, 20(9): 3690-3698.
[22] Zhang W, Qi H, Yin WP. Clinical characteristics and influencing factors of elderly septic cardiomyopathy [J]. Chin J Gerontol, 2020, 40(5): 919-922. **[In Chinese]**
[23] Yang WM, Zhang WH, Ying HQ, et al. Two new inflammatory markers associated with disease activity score-28 in patients with rheumatoid arthritis: Albumin to fibrinogen ratio and C-reactive protein to albumin ratio[J]. Int Immunopharmacol, 2018, 62: 293-298.
[24] Yan PX, Wang YY. Value of HMGB1, cTnI, CK-MB and NT-proBNP in myocardial injury caused by sepsis[J]. Chongqing Med, 2023, 52(5): 737-741. **[In Chinese]**

Submission received:2023-11-02 / **Revised:** 2023-12-12

·论　著·

白蛋白/纤维蛋白原比值与脓毒症患者心肌损伤的相关性及预后价值

田雪艳[1]，　俞典[2]，　李小民[1]，　陈雪峰[1]

1. 徐州医科大学附属连云港医院急诊医学科，江苏 连云港 222000；

2. 南京医科大学连云港临床医学院急诊医学科，江苏 连云港 222000

摘要：目的　探讨在脓毒症心肌损伤患者中白蛋白/纤维蛋白原比值（AFR）的水平及其与预后的关系。**方法**　采用前瞻性临床观察研究，收集 2022 年 2 月至 2023 年 4 月徐州医科大学附属连云港医院收治的 101 例脓毒症患者为研究对象。根据是否发生心肌损伤分为心肌损伤组（46 例）和心功能正常组（55 例），记录两组患者的基本临床资料，并于入科 24 h 内采集外周血检测白蛋白、纤维蛋白原、氨基末端 B 型利钠肽前体（NT-proBNP）、高敏肌钙蛋白 I（hsTnI）、降钙素原（PCT）、急性生理学和慢性健康状况评分（APACHE）Ⅱ及序贯器官衰竭评分（SOFA）。随访 28 d，记录患者生存情况。采用 logistic 回归分析脓毒症发生心肌损伤的危险因素；受试者工作特征（ROC）曲线分析 AFR 对脓毒症心肌损伤的诊断效能。**结果**　与心功能正常组相比，心肌损伤组的白蛋白、AFR 水平降低，NT-proBNP、hsTnI、APACHE Ⅱ评分及纤维蛋白原水平升高（$P<0.05$）。AFR 升高为脓毒症发生心肌损伤的独立保护因素（$OR=0.547$，95%CI：0.384～0.779，$P=0.001$）。当 AFR 截断值为 7.07 时，其单独诊断脓毒症心肌损伤的曲线下面积（AUC）为 0.791（95%CI：0.693～0.888），但联合 hsTnI、NT-proBNP 和 APACHE Ⅱ评分后诊断价值最高，AUC 为 0.933（95%CI：0.887～0.978）。AFR 低水平（AFR≤7.07）脓毒症患者的 28 d 生存率明显低于 AFR 高水平（AFR>7.07）脓毒症患者（$P<0.05$）。**结论**　AFR 在一定程度上可以预测脓毒症患者心肌损伤的发生及 28 d 死亡风险。

关键词：脓毒症；心肌损伤；白蛋白/纤维蛋白原比值；生存率

中图分类号：R631　**文献标识码：**A　**文章编号：**1674-8182(2024)11-1709-05

Correlation and prognostic value of albumin/fibrinogen ratio with myocardial injury in patients with sepsis

TIAN Xueyan*, YU Dian, LI Xiaomin, CHEN Xuefeng

** Department of Emergency Medicine, Lianyungang Hospital Affiliated to Xuzhou Medical University, Lianyungang, Jiangsu 222000, China*

Corresponding author: CHEN Xuefeng, E-mail: cxf2010@189.cn

Abstract: Objective　To investigate the level of albumin/fibrinogen ratio (AFR) and its relationship with prognosis in patients with septic myocardial injury. **Methods**　From February 2022 to April 2023, a prospective clinical observational study was conducted to collect 101 patients with sepsis in Lianyungang Hospital Affiliated to Xuzhou Medical University as study subjects. They were divided into myocardial injury group (46 cases) and normal cardiac function group (55 cases) according to whether myocardial injury occurred. The basic clinical data of the two groups were recorded, and peripheral blood was collected within 24 h of admission to test for albumin, fibrinogen, amino-terminal pro-B-type natriuretic peptide (NT-proBNP), high sensitivity troponin I (hsTnI), calcitoninogen (PCT), acute physiology and chronic health evaluation (APACHE Ⅱ), and sequential organ failure assessment (SOFA). Survival of patients was recorded at 28 days of follow-up. Logistic regression was used to analyze the independent risk

DOI: 10.13429/j.cnki.cjcr.2024.11.013

基金项目：江苏省科技项目（BE2020670）

通信作者：陈雪峰，E-mail：cxf2010@189.cn

出版日期：2024-11-20

QR code for English version

factors of septic myocardial injury, ROC curve was used to analyze the clinical diagnostic efficacy of AFR in septic myocardial injury. **Results** Compared with normal cardiac function group, the levels of albumin and AFR were significantly reduced, while the NT-proBNP, hsTnI, APACHE Ⅱ scores, and fibrinogen were significantly increased in myocardial injury group (P<0.05). Elevated AFR was an independent protective factor for myocardial injury in sepsis (OR=0.547, 95%CI: 0.384-0.779, P=0.001). When the AFR cutoff value was 7.07, the AUC for the diagnosis of septic myocardial injury was 0.791 (95%CI: 0.693-0.888), but the combination of hsTnI, NT-proBNP and APACHE Ⅱ scores had the highest diagnostic value, with an AUC of 0.933 (95%CI: 0.887-0.978).The 28-day survival of sepsis patients with low AFR expression (AFR≤7.07) was significantly lower than that of sepsis patients with high AFR expression (AFR>7.07, P<0.05). **Conclusion** To some extent, AFR can predict the occurrence of myocardial injury and the risk of 28-day death in patients with sepsis.

Keywords: Sepsis; Myocardial injury; Albumin to fibrinogen ratio; Survival rate

Fund program: Jiangsu Science and Technology Project (BE2020670)

脓毒症是由细菌及其他病原微生物感染引起的全身炎症反应可导致危及生命的器官功能障碍[1]。尽管目前在治疗上取得了很大的进展,但由于继发性并发症的存在,患者死亡率仍较高。脓毒症诱发的急性非缺血性心肌损伤通常被诊断为脓毒性心肌病(sepsis cardiomyopathy, SCM),SCM 是威胁脓毒症患者生命的主要并发症之一。据报道,SCM 的发病率为 10%~70%,脓毒症合并 SCM 患者的死亡率比无 SCM 患者高 2~3 倍[2]。因此,要重视 SCM 的早期诊断及治疗。血清白蛋白、纤维蛋白原均由肝脏合成,在炎症反应中扮演着重要角色,白蛋白/纤维蛋白原比值(albumin to fibrinogen ratio, AFR)是近年来的研究热点,已广泛应用于肿瘤、脓毒症、心脑血管类疾病的诊断,与多种疾病不良预后相关。研究发现,AFR 可用于预测脓毒症所致急性肾损伤的发生及患者的预后[3]。李志华等[4]的研究再次证实 AFR 与脓毒症患者临床结局和疾病严重程度相关,但鲜有文章报道 AFR 在脓毒症发生心肌损伤中的作用。目前已知的脓毒症的心肌损伤指标有氨基末端 B 型利钠肽前体(amino-terminal pro-B-type natriuretic peptide, NT-proBNP)、高敏肌钙蛋白 I(high sensitivity troponin I, hsTnI)等。NT-proBNP 水平与心肌损伤严重程度密切相关,也参与脓毒症疾病的发生发展。心肌损伤患者 NT-proBNP 水平明显升高,早期联合检测可提高其诊断的能力及预后评估的价值[5]。hsTnI 是一种新型的检测方法,用于诊断心肌损伤和心肌梗死等心血管疾病。研究表明心肌损伤患者中 hsTnI 水平升高,对 SCM 早期评估有一定的价值[6]。本研究在已有心肌损伤标志物研究的基础上,探讨 AFR 与脓毒症患者发生心肌损伤及脓毒症患者短期预后的相关性。

1　资料与方法

1.1　一般资料　纳入 2022 年 2 月至 2023 年 4 月就诊于徐州医科大学附属连云港医院重症医学科和急诊重症监护病房诊断为脓毒症的患者,进行前瞻性观察性临床研究。纳入标准:(1) 符合《sepsis 3.0 中成人脓毒症、脓毒症休克的诊断标准》[7];(2) 年龄>18 周岁;(3) 根据文献[1]研究结果,心肌损伤分为左心室和/或右心室功能障碍及血流动力学异常。排除标准:(1) 慢性心衰、急性病毒性心肌炎及严重精神-神经功能障碍患者、近 6 个月内发生心肌梗死的患者;(2) 妊娠或哺乳期妇女;(3) 临床资料不完整;(4) 既往心脏瓣膜病病史或其他心脏装置植入史;(5) 既往血液系统疾病、恶性肿瘤晚期及肝脏等疾病;(6) 拒绝参加本研究的患者。本研究已获得连云港市第一人民医院伦理委员会批准(伦理批号:KY-20230419001),并已经获得患者知情同意。

1.2　观察指标　记录患者的一般资料(性别、年龄、BMI、ICU 住院天数、感染源等)、既往病史和入科 24 h 内的外周血指标白蛋白、纤维蛋白原,计算 AFR;记录 NT-proBNP、hsTnI、降钙素原(PCT)及入科时的急性生理学和慢性健康状况评分(APACHE)Ⅱ和序贯性器官功能衰竭评估(SOFA)评分。每组患者随访 28 d,记录患者生存情况。

1.3　统计学方法　采用 SPSS 26.0 软件分析数据。符合正态分布的计量资料采用 $\bar{x}\pm s$ 表示,组间比较采用独立样本 t 检验,偏态分布的资料以 $M(P_{25}, P_{75})$ 表示,组间比较采用非参数检验;计数资料以例(%)表示,采用 χ^2 检验或 Fisher 确切概率法;采用 logistic 回归模型分析发生心肌损伤的独立危险因素,绘制受试者工作特征(ROC)曲线分析 AFR 及联合 hsTnI、NT-proBNP 对心肌损伤的诊断价值;Kaplan-Meier 法和 log-rank 检验分析脓毒症患者的生存预后。P<0.05为差异有统计学意义。

2　结　果

2.1　基线资料　共纳入 101 例脓毒症患者,其中心功能正常组 55 例,占 54.46%,心肌损伤组 46 例,占 45.54%。两组间性别、年龄、身体质量指数(BMI)、基础疾病等基线资料差异均无统计学意义($P>0.05$)。两组 24 h 内 APACHE Ⅱ、SOFA 评分差异有统计学意义($P<0.05$)。见表 1。

2.2　实验室指标　与心功能正常组相比,心肌损伤组 AFR 降低,hsTnI、NT-proBNP 升高,差异有统计学意义($P<0.01$)。见表 2。

2.3　脓毒症患者发生心肌损伤的危险因素　将单因素分析中差异有统计学意义的因素纳入多因素 logistic 回归分析,结果显示,AFR 降低,hsTnI、APACHE Ⅱ评分、NT-proBNP 升高为脓毒症患者发生心肌损伤的独立危险因素($P<0.05$)。见表 3。

表 1　两组患者一般资料比较　[例(%)]

Tab. 1　Comparison of general information between two groups　[case(%)]

项目	心功能正常组($n=55$)	心肌损伤组($n=46$)	$t/\chi^2/z$ 值	P 值
年龄(岁)[a]	66.49±11.88	69.33±12.42	1.170	0.245
性别				
男	33(60.0)	22(47.8)	1.497	0.221
女	22(40.0)	24(52.2)		
BMI(kg/m^2)[b]	24.0(22.9, 24.8)	23.9(21.7, 24.7)	1.313	0.189
ICU 住院天数(d)[a]	9.18±2.02	9.85±2.15	1.603	0.112
心率(次/min)[a]	92.80±11.98	95.26±11.73	1.038	0.302
主要感染源				
肺部感染	27(49.1)	22(47.8)		
腹腔感染	15(27.3)	12(26.1)		
泌尿道感染	3(5.5)	8(17.4)	5.525	0.238
软组织感染	5(9.1)	3(6.5)		
血液感染	5(9.1)	1(2.2)		
基础疾病				
高血压	29(52.7)	20(43.5)	0.858	0.354
冠心病	10(18.2)	5(10.9)	1.059	0.303
糖尿病	6(10.9)	5(10.9)	0.000	0.995
脑卒中	6(10.9)	7(15.2)	0.415	0.520
高脂血症	5(9.1)	4(8.7)	0.079	0.779
慢性阻塞性肺疾病	4(7.3)	3(6.5)	0.060	0.806
肾功能异常	1(1.8)	1(2.2)		1.000[c]
临床评分系统				
APACHE Ⅱ评分[a]	18.35±2.33	20.89±2.86	4.932	<0.001
SOFA 评分[b]	7(6, 9)	8(6, 10)	2.139	0.032
28 d 死亡	17(30.9)	22(47.8)	3.024	0.082

注:[a] 表示数据为 $\bar{x}\pm s$;[b] 表示数据为 $M(P_{25},P_{75})$;[c] 表示采用 Fisher 确切概率法。

2.4　各指标单独及联合检测对脓毒症发生心肌损伤的诊断效能　ROC 结果显示,AFR 截断值为 7.07 时,其诊断脓毒症心肌损伤的曲线下面积(AUC)为 0.791(95%*CI*: 0.693~0.888),灵敏度为 76.1%,特异度为 83.6%;但联合 hsTnI、NTproBNP 和 APACHE Ⅱ评分后,诊断效能最高,AUC 为 0.933(95% *CI*: 0.887~0.978),灵敏度为 78.3%,特异度为 96.4%。见表 4、图 1。

2.5　不同 AFR 水平脓毒症患者 28 d 生存分析　用 Graphpad Prism 9.0 软件绘制时间-生存曲线,结果示 AFR ≤7.07 组患者的 28 d 生存率明显低于 AFR>7.07组患者,差异有统计学意义($P<0.05$)。见图 2。

表 2　两组患者实验室指标比较

Tab. 2　Comparison of laboratory indicators between two groups

项目	心功能正常组($n=55$)	心肌损伤组($n=46$)	t/z 值	P 值
AFR[a]	8.24±1.81	6.29±1.93	5.244	<0.001
hsTnI(pg/mL)[b]	82.21(29.83,155.90)	231.19(157.33,358.08)	5.578	<0.001
NT-proBNP(pg/mL)[b]	1 196.04(765.09, 4 562.29)	4 788.70(1 741.00, 11 036.00)	2.898	0.004
PCT(ng/mL)[b]	9.20(5.66,12.80)	9.96(7.39,14.20)	1.483	0.138

注:[a] 表示数据为 $\bar{x}\pm s$;[b] 表示数据为 $M(P_{25},P_{75})$。

表 3　脓毒症患者发生心肌损伤影响因素的多因素 logistic 回归分析

Tab. 3　Multivariate logistic regression analysis of influencing factors of myocardial injury in patients with sepsis

项目	β	*S.E.*	*Wald*	P 值	*OR* 值	95%*CI*
AFR	−0.603	0.180	11.179	0.001	0.547	0.384~0.779
hsTnI	1.381	0.373	13.728	<0.001	3.980	1.917~8.264
NT-proBNP	0.151	0.059	6.542	0.011	1.163	1.036~1.305
APACHE Ⅱ评分	0.452	0.141	10.222	0.001	1.572	1.191~2.074
SOFA 评分	0.277	0.151	3.366	0.067	1.319	0.981~1.773

表 4　各指标单独及联合检测对脓毒症发生心肌损伤的诊断效能

Tab. 4　Diagnostic efficacy of individual and combined detection of various indexes for myocardial injury in sepsis

项目	AUC(95%*CI*)	截断值	灵敏度(%)	特异度(%)	P 值
AFR	0.791(0.693~0.888)	7.07	76.1	83.6	<0.001
hsTnI	0.823(0.743~0.904)	121.04 pg/mL	84.8	69.1	<0.001
NT-proBNP	0.668(0.558~0.778)	3 168.8 pg/mL	67.4	74.5	<0.001
APACHE Ⅱ评分	0.742(0.645~0.838)	20.5 分	58.7	81.8	<0.001
四者联合	0.933(0.887~0.978)	—	78.3	96.4	<0.001

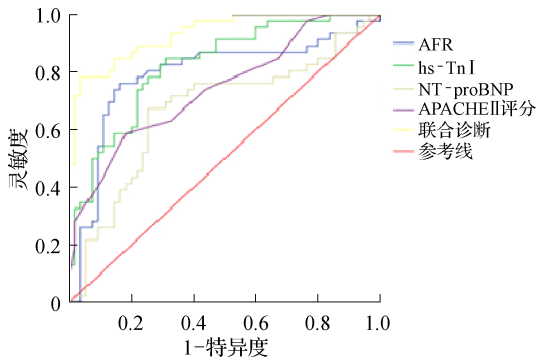

图 1　各指标单独及联合检测对脓毒症发生心肌损伤诊断效能的 ROC 曲线

Fig. 1　ROC curve of diagnostic efficiency of myocardial injury in sepsis detected by individual or combined detection of each index

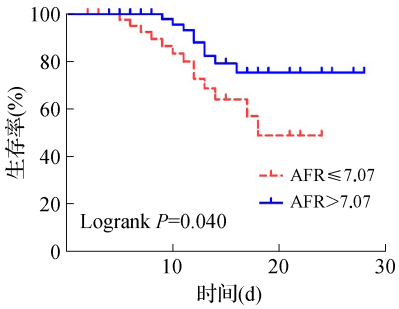

图 2　不同 AFR 水平脓毒症患者 28 d 生存曲线
Fig. 2　28-day survival curves of sepsis patients with different AFR levels

3　讨　论

脓毒症是由感染引起的的全身炎症反应综合征，患者通常病情急骤，如不及时治疗可引发机体多器官功能障碍，是 ICU 患者非心脏疾病死亡的主要原因[8-9]。心脏是脓毒症患者最易受累的器官之一，脓毒症心肌损伤或 SCM 患者通常表现为心室扩张、心室收缩力降低和/或右心室和左心室功能障碍，容量反应性降低[10]。脓毒症发生心肌损伤是基于严重炎症反应后，细胞外或心肌本身因素引起免疫、凝血功能紊乱等多种机制相互作用，导致患者心功能紊乱[11]。

血清白蛋白是人体中最丰富的血清蛋白，可反映机体的营养状况和炎症状态。作为一种毒素中和蛋白，其对抗菌药物的药代动力学有一定影响，在机体感染产毒微生物时发挥重要作用[12]。当患者发生脓毒症时，过度炎症反应、应激状态使其水平迅速下降[13]。进一步研究发现，低白蛋白水平与脓毒症患者 30 d 的死亡相关[14]。Geng 等[15]报道，白蛋白治疗，特别是 20%白蛋白治疗，可显著降低脓毒性休克患者 90 d 的死亡率。本研究结果示，两组患者的白蛋白水平均有所降低，且心肌损伤组降低更为明显。

纤维蛋白原作为机体凝血系统的重要组成成分，参与组织正常止血、创伤及感染的发生等多种过程，且其诊断感染的能力不逊色于一般炎症指标如 C 反应蛋白或红细胞沉降率等[16-17]。国外一项研究表明，纤维蛋白原是脓毒性休克的可靠诊断工具，且较低的纤维蛋白原是 30 d 全因死亡率的有效预测指标[18]。本研究结果示，心肌损伤组的纤维蛋白原较心功能正常组高，这可能与患者疾病的进展、血流动力学异常及心肌损伤激活凝血系统等有关。

由于脓毒症患者发生心肌损伤是一种涉及多因素、多机制的综合征，笔者认为 AFR 优于单一的白蛋白或纤维蛋白原指标检测。AFR 既可以预测疾病的炎症活动程度[19]，也可以用于评估机体凝血功能和营养状况[20-21]，且被证实是脓毒症患者短期预后和病情严重程度的预测因子。由于脓毒症心肌损伤继发于脓毒症，通常以心肌细胞受损、凝血功能障碍为主要特征[22]，或许这些间接性关联能诠释 AFR 可用于脓毒症心肌损伤诊断及患者短期预后预测的原因。

本研究结果发现，心肌损伤组患者的 AFR 显著低于心功能正常组。考虑 AFR 降低的原因：脓毒症患者继发心肌损伤时，大量炎症介质释放，激活炎症级联反应，从而导致作为急性反应期的白蛋白水平骤降；白蛋白降低通过负反馈作用宿主的氧化应激，从而加速炎症反应过程；然而急性炎症状态初期，体内纤维蛋白原也会相应增加，加速血小板的活化，患者进而发生凝血功能障碍[23]。AFR 预测心肌损伤的最佳临界点为7.07，AUC 为 0.791，灵敏度为 76.1%，特异度为 83.6%，这一结果不仅证实了炎症反应是脓毒症发生心肌损伤的重要机制之一，也说明了 AFR 对诊断脓毒症心肌损伤有一定的预测能力，从而有助于临床医师对脓毒症患者疾病进展情况的早期了解，即当脓毒症患者入院时的 AFR>7.07 时，应警惕心肌损伤的发生。临床上对脓毒症心肌损伤的诊断应结合多种因素。与文献中诊断脓毒症患者心肌损伤的指标 NT-proBNP[6,24]、hsTnI 等相比，AFR 诊断心肌损伤有一定的局限性，但本研究中联合 NT-proBNP、hsTnI 及 APACHE Ⅱ 评分后诊断效能明显提高。此外生存分析结果示，AFR≤7.07 组患者的 28 d 生存率明显低于 AFR>7.07 组，即 AFR 在一定程度上可对脓毒症患者 28 d 死亡风险进行分层，但尚需更多研究进一步验证。

本研究尚存在不足之处，如本研究为单中心前瞻性观察性临床研究，病例及采用的实验室指标数量有限；由于脓毒症患者的病情进展迅速，多数患者入院后可能更长时间才出现心肌损伤，且重症病房患者年龄通常较大、病情复杂，因此需在控制多种混杂因素的条件下进行进一步的探索。

综上所述，AFR 可能用于有效评估脓毒症心肌损伤的发生，又可能在一定程度上预测脓毒症患者的短期生存，进而有助于临床精准诊治，改善患者预后。

利益冲突　无

参考文献

[1] Carbone F, Liberale L, Preda A, et al. Septic cardiomyopathy: from pathophysiology to the clinical setting[J]. Cells, 2022, 11

(18): 2833.

[2] Song JQ, Yao Y, Lin SL, et al. Feasibility and discriminatory value of tissue motion annular displacement in sepsis-induced cardiomyopathy: a single-center retrospective observational study[J]. Crit Care, 2022, 26(1): 220.

[3] 梅海峰,朱志云,孙文斌,等.AFR 在脓毒症患者急性肾损伤发生及预后中的价值研究[J].重庆医学,2020,49(15):2519-2523.
Mei HF, Zhu ZY, Sun WB, et al. Study on the analysis of the predictive value of AFR on acute kidney injury occurrence and prognosis in the patients with sepsis[J]. Chongqing Med, 2020, 49(15): 2519-2523.

[4] 李志华,成慧昕,王毅,等.白蛋白/纤维蛋白原比值对脓毒症患者 28 d 死亡风险的预测价值[J].中华急诊医学杂志,2023,32(2):180-185.
Li ZH, Cheng HX, Wang Y, et al. Predictive value of albumin/fibrinogen ratio for 28-day mortality risk in patients with sepsis[J]. Chin J Emerg Med, 2023, 32(2): 180-185.

[5] 李志宇,崔少华,耿立霞.生物标志物联合检测对脓毒性心肌损伤患者早期诊断及预后评估的价值[J].中华危重病急救医学,2021(4):443-448.
Li ZY, Cui SH, Geng LX. Value of combined detection of biomarkers in early diagnosis and prognosis of patients with septic myocardial injury[J]. Chin Crit Care Med, 2021(4): 443-448.

[6] 杨朋磊,袁静,陈勇,等.基于左心室整体纵轴应变建立脓毒症心肌病预测模型[J].中华医学杂志,2022,102(15):1100-1107.
Yang PL, Yuan J, Chen Y, et al. Establishment of a predictive model of septic myocardiopathy based on left ventricular global longitudinal strain[J]. Natl Med J China, 2022, 102(15): 1100-1107.

[7] Evans L, Rhodes A, Alhazzani W, et al. Executive summary: surviving sepsis campaign: international guidelines for the management of sepsis and septic shock 2021[J]. Crit Care Med, 2021, 49(11): 1974-1982.

[8] Fleischmann-Struzek C, Mellhammar L, Rose N, et al. Incidence and mortality of hospital- and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis[J]. Intensive Care Med, 2020, 46(8): 1552-1562.

[9] 魏燕,李祥军,雷悦,等.输血对脓毒症大鼠急性肺损伤肺上皮细胞活性、肺超微结构及 SIRT1/PGC-1α 的影响[J].中国临床研究,2023,36(4):515-520.
Wei Y, Li XJ, Lei Y, et al. Effects of blood transfusion on lung epithelial cell activity, lung ultrastructure and SIRT1/PGC-1α in septic rats with acute lung injury[J]. Chin J Clin Res, 2023, 36(4): 515-520.

[10] Martin L, Derwall M, Al Zoubi S, et al. The septic heart: current understanding of molecular mechanisms and clinical implications[J]. Chest, 2019, 155(2): 427-437.

[11] 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.

[12] Austermeier S, Pekmezoviz M, Porschitz P, et al. Albumin neutralizes hydrophobic toxins and modulates *Candida albicans* pathogenicity[J]. mBio, 2021, 12(3): e0053121.

[13] 韩涛,邓秋明,万献尧.脓毒症患者低白蛋白血症研究进展[J].中华医学杂志,2017,97(3):228-231.
Han T, Deng QM, Wan XY. Research progress of hypoalbuminemia in sepsis patients[J]. Natl Med J China, 2017, 97(3): 228-231.

[14] Turcato G, Zaboli A, Sibilio S, et al. Albumin as a prognostic marker of 30-day mortality in septic patients admitted to the emergency department[J]. Intern Emerg Med, 2023, 18(8): 2407-2417.

[15] Geng L, Tian XX, Gao ZF, et al. Different concentrations of albumin versus crystalloid in patients with sepsis and septic shock: a meta-analysis of randomized clinical trials[J]. J Intensive Care Med, 2023, 38(8): 679-689.

[16] Winearls J, Reade MC, McQuilten Z, et al. Fibrinogen in traumatic haemorrhage[J]. Curr Opin Anaesthesiol, 2021, 34(4): 514-520.

[17] Ciriello V, Ghannadian S, Saracco M, et al. Is fibrinogen a reliable biomarker in the diagnosis of peri-prosthetic joint infection? A systematic review and meta-analysis[J]. Surg Infect, 2022, 23(9): 787-795.

[18] Schupp T, Weidner K, Rusnak J, et al. Fibrinogen reflects severity and predicts outcomes in patients with sepsis and septic shock[J]. Blood Coagul Fibrinolysis, 2023, 34(3): 161-170.

[19] He YJ, Tang JF, Wu BD, et al. Correlation between albumin to fibrinogen ratio, C-reactive protein to albumin ratio and Th17 cells in patients with rheumatoid arthritis[J]. Clin Chim Acta, 2020, 500: 149-154.

[20] Li S, Zhang D, Zeng S, et al. Prognostic value of preoperative albumin-to-fibrinogen ratio in patients with bladder cancer[J]. J Cancer, 2021, 12(19): 5864-5873.

[21] Shang JJ, Jiang SJ, Gong JH, et al. Low albumin-to-fibrinogen ratio predicts adverse clinical outcomes after primary total joint arthroplasty: a retrospective observational investigation[J]. Int Wound J, 2023, 20(9): 3690-3698.

[22] 张巍, 祁航, 殷文朋. 老年脓毒性心肌病临床特征及发病影响因素[J]. 中国老年学杂志, 2020, 40(5): 919-922.
Zhang W, Qi H, Yin WP. Clinical characteristics and influencing factors of septic cardiomyopathy in the elderly[J].Chin J Gerontol, 2020, 40(5): 919-922.

[23] Yang WM, Zhang WH, Ying HQ, et al. Two new inflammatory markers associated with disease activity score-28 in patients with rheumatoid arthritis: Albumin to fibrinogen ratio and C-reactive protein to albumin ratio[J]. Int Immunopharmacol, 2018, 62: 293-298.

[24] 颜培夏,王媛媛.HMGB1、cTnⅠ、CK-MB 及 NT-proBNP 对脓毒症心肌损伤的诊断价值[J].重庆医学,2023,52(5):737-741.
Yan PX, Wang YY. Value of HMGB1, cTnⅠ, CK-MB and NT-proBNP in myocardial injury caused by sepsis[J]. Chongqing Med, 2023, 52(5): 737-741.

收稿日期:2023-11-02　**修回日期**:2023-12-12　**编辑**:石嘉莹