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Predictive value of combined indexes based on soluble thrombomodulin for sepsis-associated acute kidney injury

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Abstract: Objective To investigate the predictive efficacy of combined indexes based on soluble thrombomodulin (sTM) for acute kidney injury (AKI) in patients with sepsis, and to provide a reference for the early identification of AKI in clinical practice. **Methods** A retrospective study was conducted to collect clinical data of 364 patients with sepsis admitted to the Intensive Care Unit of Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School from January to December 2024. According to the occurrence of AKI during hospitalization [based on the diagnostic criteria proposed by Kidney Disease: Improving Global Outcomes (KDIGO)], the patients were divided into AKI group (171 cases) and non-AKI group (193 cases). The clinical data of the two groups were compared. Multivariate logistic regression analysis was used to screen the risk factors for AKI in sepsis patients. Receiver operating characteristic (ROC) curves were plotted to analyze the predictive value of combined indicators based on sTM for AKI in sepsis patients. **Results** The incidence of sepsis-associated AKI was 46.98%. Compared with the non-AKI group, the AKI group exhibited significantly higher Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, 28-day mortality, and incidence rates of shock, respiratory failure, and liver injury (P<0.05). Levels of sTM, C-reactive protein (CRP), interleukin-6, procalcitonin, prothrombin time, and activated partial thromboplastin time were also significantly higher, whereas platelet count was significantly lower (P<0.05). Multivariate logistic regression analysis identified shock (OR=3.304, 95%CI: 2.001-5.457, P<0.01), liver injury (OR=2.443, 95%CI: 1.399-4.265, P=0.002), high APACHE II score (OR=1.050, 95%CI: 1.016-1.085, P=0.004), high sTM (OR=1.039, 95%CI: 1.018-1.060, P<0.01), and high CRP (OR=1.003, 95% CI: 1.001- 1.006, P=0.034) as independent risk factors for AKI in patients with sepsis. The combined use of sTM, shock, and APACHE II score yielded an area under the curve (AUC) of 0.804 (95%CI: 0.759- 0.850) for predicting AKI, with a sensitivity of 0.754 and a specificity of 0.762. **Conclusion** sTM is an independent risk factor for AKI in sepsis patients, and has certain predictive value for AKI in sepsis patients. The predictive value is more significant when combined with shock and APACHE II score.

Keywords: Soluble thrombomodulin; Acute kidney injury; Sepsis; Shock; Acute Physiology and Chronic Health Evaluation II
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Sepsis refers to life-threatening organ dysfunction caused by a dysregulated host response to infection, and it is one of the leading causes of mortality among patients admitted to the intensive care unit (ICU) [1-2]. Acute kidney injury (AKI) is the most common and severe complication of sepsis with an incidence of 40%–50%, which markedly increases the mortality risk of affected patients [3-4]. At present, the clinical diagnosis of AKI is mainly based on the criteria established by Kidney Disease: Improving Global Outcomes (KDIGO), relying on changes in serum creatinine and urine output. Nevertheless, the elevation of serum creatinine occurs relatively late and is affected by multiple factors including age, muscle mass and fluid balance, making it incapable of achieving early warning of AKI [5]. Therefore, it is of great significance to identify biomarkers that can early, sensitively and specifically predict sepsis-associated AKI. Thrombomodulin is a transmembrane glycoprotein predominantly expressed on the surface of vascular endothelial cells and serves as a pivotal molecule for maintaining vascular endothelial homeostasis. Under septic conditions, uncontrolled inflammatory responses and microcirculatory disorders lead to extensive injury and shedding of vascular endothelial cells, resulting in a significant elevation in plasma soluble thrombomodulin (sTM) levels [6]. The kidney is an organ abundant in capillary networks, and its endothelial cells are particularly vulnerable to damage. The early increase in sTM levels during sepsis may reflect the severity of systemic endothelial injury, especially glomerular endothelial damage, indicating that sTM may act as an early predictive biomarker for sepsis-associated AKI. This study aimed to explore the predictive value of sTM-based combined indicators for AKI occurrence in septic patients.

1 Subjects and Methods

1.1 Study Subjects

A retrospective analysis was conducted on the clinical data of 364 patients with sepsis admitted to the ICU of Drum Tower Hospital Affiliated to Nanjing University Medical School between January and December 2024. **Inclusion criteria**: (1) Age ≥ 18 years old; (2) Meeting the Sepsis-3 diagnostic criteria [1]; (3) Diagnosis of AKI in accordance with relevant KDIGO criteria [7]; (4) Available sTM test results within 24 hours after admission and complete clinical data.

Exclusion criteria: (1) ICU stay duration less than 24 hours; (2) Pre-existing stage 4–5 chronic kidney disease or dependence on renal replacement therapy before admission; (3) Pregnancy status; (4) Acute renal insufficiency induced by other causes such as contrast agents and renal vascular lesions.

All data were extracted from medical records in compliance with medical ethical standards. This study was approved by the Medical Research Ethics Review Committee of Nanjing Drum Tower Hospital (Ethics Approval No.: 2024-646-02).

1.2 Data Collection

General clinical data were collected, including gender, age, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, underlying diseases (hypertension, diabetes mellitus, cardiac insufficiency, cerebral infarction, coronary atherosclerotic heart disease), length of hospital stay, 28-day mortality, and complications (shock, respiratory failure, liver injury). Laboratory parameters detected within 24 hours after admission were also recorded, including white blood cell count (WBC), platelet count (PLT), procalcitonin (PCT), C-reactive protein (CRP), interleukin-6 (IL-6), sTM, prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin-antithrombin complex (TAT), tissue plasminogen activator-inhibitor complex (tPAI-C) and plasmin-antiplasmin complex (PIC).

1.3 Statistical Analysis

SPSS 26.0 statistical software was used for data analysis. Non-normally distributed measurement data were expressed as median (25th percentile, 75th percentile) [M(P_{25}, P_{75})], and the Mann-Whitney *U* test was adopted for intergroup comparison. Enumeration data were presented as case (%), and the chi-square test was used for comparison. Multivariate logistic regression analysis was performed to screen independent risk factors for AKI in septic patients. Receiver operating characteristic (ROC) curve and area under the curve (AUC) were applied to evaluate the predictive efficiency of each indicator for AKI occurrence. A *P* value less than 0.05 was considered statistically significant.

2 Results

2.1 Comparison of General Clinical Data

Among the 364 enrolled septic patients, 171 cases were complicated with AKI (AKI group) and 193 cases were without AKI (non-AKI group), with the incidence rate of sepsis-associated AKI reaching 46.98%. There were no significant differences in age, gender, underlying diseases, length of hospital stay, WBC, TAT and PIC between the two groups (P>0.05). Compared with the non-AKI group, the AKI group had higher APACHE II score, SOFA score, 28-day mortality, higher incidence rates of shock, respiratory failure and liver injury, elevated levels of sTM, CRP, IL-6, PCT, PT, APTT and tPAI-C, as well as decreased PLT level, and all the above differences were statistically significant (P<0.05). **See Table 1.**

2.2 Multivariate Logistic Regression Analysis

Factors with statistical significance in univariate analysis were included in multivariate logistic regression analysis. The results revealed that shock, liver injury, elevated CRP, high APACHE II score and increased sTM level were independent risk factors for AKI in septic patients (P<0.05). See **Table 2.**

2.3 Predictive Efficiency Analysis

ROC curve analysis showed that the AUC values of sTM, shock, APACHE II score and their combination for predicting AKI in septic patients were 0.761, 0.695, 0.674 and 0.804 respectively. See **Figure 1.** The predictive efficacy of sTM, shock, APACHE II score and their combined detection is shown in **Table 3.**

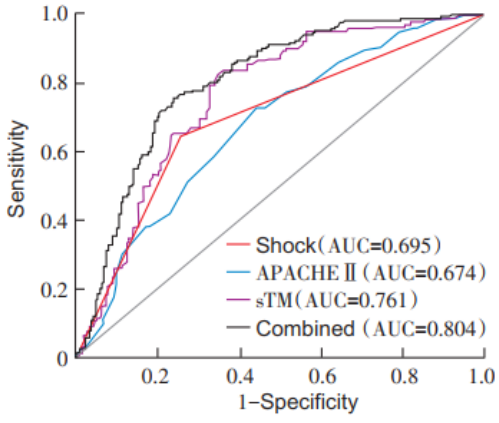

Fig.1 ROC curve for predicting AKI in sepsis based on various influencing factors

Tab.1 Comparison of clinical data between AKI and non-AKI groups

Item	AKI group (n=171)	Non-AKI group (n=193)	Z/χ^2 value	P value
Age (years)*	59.00 (45.00, 72.00)	62.00 (48.00, 73.00)	1.015	0.31
Gender [n (%)]			0.254	0.614
Male	77 (45.03)	92 (47.67)		
Female	94 (54.97)	101 (52.33)		
APACHE II score*	25.00 (20.00, 30.00)	20.00 (13.00, 25.00)	5.752	<0.001
SOFA score*	10.00 (8.00, 12.00)	8.00 (5.00, 10.00)	4.856	<0.001
Underlying diseases [n (%)]				
Hypertension	69 (40.35)	80 (41.45)	0.045	0.831
Diabetes mellitus	36 (21.05)	42 (21.76)	0.027	0.869
Cardiac insufficiency	30 (17.54)	22 (11.40)	2.796	0.095
Cerebral infarction	40 (23.39)	43 (22.28)	0.064	0.801
Coronary heart disease	19 (11.11)	20 (10.36)	0.053	0.818
Complications [n (%)]				
Shock	110 (64.33)	49 (25.39)	55.882	<0.001
Respiratory failure	71 (41.52)	60 (31.09)	4.283	0.038
Liver injury	75 (43.86)	33 (17.10)	31.117	<0.001
Laboratory tests*				
WBC (×10⁹/L)	9.90 (5.80, 15.90)	8.50 (5.80, 13.60)	1.536	0.125
PLT (×10⁹/L)	115.00 (65.50, 183.50)	156.00 (97.00, 229.00)	3.855	<0.001
IL-6 (pg/mL)	137.34 (33.50, 357.38)	59.48 (16.39, 282.19)	2.889	0.004
CRP (mg/L)	81.65 (28.82, 164.08)	50.10 (16.40, 106.30)	3.288	0.001
PCT (ng/mL)	1.11 (0.32, 7.84)	0.33 (0.09, 1.63)	5.182	<0.001
APTT (s)	33.80 (28.42, 41.40)	29.80 (26.30, 34.40)	4.525	<0.001
PT (s)	13.60 (12.20, 16.60)	13.10 (11.80, 14.80)	2.26	0.024
TAT (ng/mL)	13.60 (6.30, 29.43)	11.20 (6.80, 20.60)	1.943	0.052
PIC (μg/mL)	1.39 (0.75, 2.69)	1.33 (0.87, 2.50)	0.197	0.844
sTM (TU/mL)	26.30 (19.40, 36.05)	15.00 (10.60, 22.50)	8.602	<0.001
tPAI-C (ng/mL)	16.90 (10.30, 28.55)	12.30 (7.10, 17.10)	4.785	<0.001
Prognosis				
Length of hospital stay (d)*	23.00 (14.50, 32.50)	21.00 (13.00, 29.00)	1.157	0.247
28-day mortality (%)	39.77	17.62	22.054	<0.001

Note:* Data a are presented as median (P25, P75).

Tab.2 Multivariate logistic regression analysis for AKI in patients with sepsis

Item	*β*	*SE*	*Z*	*P value*	*OR (95%CI)*
Shock	1.195	0.256	4.669	<0.001	3.304 (2.001–5.457)
Liver injury	0.893	0.284	3.14	0.002	2.442 (1.399–4.265)
APACHE II score	0.049	0.017	2.91	0.004	1.050 (1.016–1.085)
CRP	0.003	0.001	2.115	0.034	1.003 (1.001–1.006)
sTM	0.038	0.01	3.697	<0.001	1.039 (1.018–1.060)

Tab.3 The predictive efficacy of various risk factors for AKI in sepsis patients

Item	AUC (95%CI)	*P* value	Cut-off value	Sensitivity	Specificity	Youden index
Shock	0.695 (0.647–0.742)	<0.001	-	0.643	0.746	0.389
APACHE II score	0.674 (0.620–0.729)	<0.001	21.5	0.725	0.56	0.285
sTM	0.761 (0.711–0.811)	<0.001	17.8 TU/mL	0.836	0.642	0.479
Combined prediction	0.804 (0.759–0.850)	<0.001	-	0.754	0.762	0.516

3 Discussion

AKI is a common and serious complication during sepsis progression, which can remarkably increase the mortality of critically ill patients [8-9]. Traditional detection methods based on serum creatinine level and urine output have obvious limitations in the early diagnosis and risk prediction of sepsis-associated AKI. Hence, novel biomarkers with higher sensitivity and specificity are urgently needed in clinical practice to realize early identification of high-risk populations susceptible to severe AKI.

This retrospective study analyzed the clinical data of 364 septic patients, and confirmed that the incidence of sepsis-associated AKI was 46.98%, and the 28-day mortality rate was 39.77% in the AKI group. The high incidence and mortality of sepsis-associated AKI emphasize the necessity of early prediction and timely intervention [3-4,10]. Multivariate logistic regression analysis demonstrated that shock, liver injury, elevated CRP, high APACHE II score and increased sTM were independent risk factors for AKI development in septic patients.

As an independent risk factor, shock contributes to AKI mainly due to insufficient effective circulating blood volume and marked decline in renal perfusion pressure in septic shock. Persistent renal hypoperfusion leads to renal parenchymal ischemia and hypoxia, and ultimately triggers acute tubular necrosis, which is consistent with findings of previous studies [11-14]. As a classic scoring system for evaluating disease severity in critically ill patients, APACHE II score further verified that the occurrence of sepsis-associated AKI is closely correlated with the overall severity of illness. Higher APACHE II score indicates more intense systemic inflammatory response and higher risk of multiple organ dysfunction,

and the kidney, as a high-perfusion organ, is more vulnerable to inflammatory damage [11-12,15-16].

sTM is regarded as a gold standard biomarker for endothelial injury [17]. In the setting of sepsis, inflammatory mediators such as lipopolysaccharide and tumor necrosis factor-α directly damage vascular endothelial cells and destroy endothelial barrier function, resulting in the shedding of thrombomodulin from cell membrane into blood circulation and subsequent elevation of serum sTM levels. The kidney is rich in vascular endothelial cells; systemic inflammation and endothelial injury induced by sepsis can directly impair renal microcirculation, cause intrarenal endothelial damage, thrombosis and insufficient renal tissue perfusion, and eventually induce AKI [14,18].

Accordingly, elevated serum sTM levels not only reflect the degree of systemic vascular endothelial damage, but also indirectly indicate the risk of renal microcirculation impairment, which is the core mechanism underlying its favorable predictive value for sepsis-associated AKI. Since the increase of sTM is derived from endothelial injury, it can indicate AKI occurrence much earlier than renal hypoperfusion and decreased creatinine clearance rate [19-20]. In this study, the sensitivity of sTM in predicting AKI was 0.836, higher than that of shock (0.643) and APACHE II score (0.725), suggesting that sTM can serve as an important reference indicator for clinical screening of sepsis-associated AKI. Multiple clinical studies have also confirmed the high predictive value of elevated sTM expression for sepsis-associated AKI [21-22]. The detection of sTM also provides new clinical evidence for the theory that endothelial dysfunction causes organ damage in sepsis [16].

Although single sTM detection only has a specificity of 0.642 in predicting AKI in septic patients, combined detection with other indicators can significantly improve predictive performance [23-24]. This study found that the combined application of shock, APACHE II score and sTM achieved an AUC of 0.804 and a specificity up to 0.762, which was obviously superior to single-index detection. Therefore, the combination of these three indicators possesses promising clinical application prospects in predicting sepsis-associated AKI.

Several limitations exist in this study. Firstly, inherent defects of single-center retrospective research lead to potential sampling bias. Secondly, only baseline indicators within 24 hours after admission were collected, failing to reflect the dynamic changes of sTM in the early stage of sepsis. Continuous dynamic monitoring of sTM was not performed, so the correlation between sTM fluctuation and AKI progression could not be evaluated.

In conclusion, elevated sTM level is an independent risk factor for AKI in septic patients with favorable predictive efficiency, and combined detection with shock status and APACHE II score can further enhance predictive ability. This combined model facilitates early identification of high-risk patients with sepsis-associated AKI and timely implementation of intervention measures. Large-scale multicenter prospective cohort studies are required to verify the above conclusions and explore the clinical significance of dynamic sTM monitoring in future research.

Conflict of Interest: None

Reference

[1] Yang WS, Kang HD, Jung SK, et al. A mortality analysis of septic shock, vasoplegic shock and cryptic shock classified by the third international consensus definitions (Sepsis-3)[J]. Clin Respir J, 2020, 14(9): 857-863.
[2] White KC, Serpa-Neto A, Hurford R, et al. Sepsis-associated acute kidney injury in the intensive care unit: incidence, patient characteristics, timing, trajectory, treatment, and associated outcomes. A multicenter, observational study[J]. Intensive Care Med, 2023, 49(9): 1079-1089.
[3] Fan YW, Jiang SW, Chen JM, et al. A pulmonary source of infection in patients with sepsis-associated acute kidney injury leads to a worse outcome and poor recovery of kidney function[J]. World J Emerg Med, 2020, 11(1): 18.
[4] Pais T, Jorge S, Lopes JA. Acute kidney injury in sepsis[J]. Int J Mol Sci, 2024, 25(11): 5924.
[5] Guo J, Guo FM. Research progress on biomarkers and molecular mechanisms of sepsis-related acute kidney injury[J]. Chin J Emerg Med, 2023, 32(2): 269-274. **[In Chinese]**
[6] Katayama S, Koyama K, Jun SM, et al. Thrombomodulin, plasminogen activator inhibitor-1 and protein C levels, and organ dysfunction in sepsis[J]. Crit Care Explor, 2019, 1(5): e0013.
[7] Khwaja A. KDIGO clinical practice guidelines for acute kidney injury[J]. Nephron Clin Pract, 2012, 120(4): c179-c184.
[8] Yoshimoto K, Komaru Y, Iwagami M, et al. Acute kidney injury in sepsis: evidence from Asia[J]. Semin Nephrol, 2020, 40(5): 489-497.
[9] Xia WH, Yi F, Wang QB. Mortality and differential predictive factors of transient and persistent sepsis-associated acute kidney injury[J]. Clin Nephrol, 2023, 99(3): 119-127.
[10] Suh SH, Kim CS, Choi JS, et al. Acute kidney injury in patients with sepsis and septic shock: risk factors and clinical outcomes[J]. Yonsei Med J, 2013, 54(4): 965.
[11] Hou L, Wu X, Sun ZG. Risk factors and prognosis of acute kidney injury in hospitalised sepsis patients[J]. Arch Esp Urol, 2024, 77(3): 263-269.
[12] Plataki M, Kashani K, Cabello-Garza J, et al. Predictors of acute kidney injury in septic shock patients: an observational cohort study[J]. Clin J Am Soc Nephrol, 2011, 6(7): 1744-1751.
[13] Zuo HZ, Tian LJ, Yang XF, et al. Study on Logistic regression analysis of risk factors for secondary acute kidney injury in patients with sepsis[J]. J Changchun Univ Chin Med, 2023, 39(8): 915-920. **[In Chinese]**
[14] Nguyen VT, Nguyen-Phan HN, Ton TN, et al. Value of serum thrombomodulin as a marker and predictor in patients with sepsis-associated acute kidney injury[J]. Int J Gen Med, 2023, 16: 2933-2941.
[15] Ji XQ, Chen T, Chen C, et al. Value of serum CysC and SAA combined with APACHE Ⅱ score in evaluating prognosis of patients with sepsis complicated with acute kidney injury[J]. Chin J Health Care Med, 2022, 24(2): 125-127. **[In Chinese]**
[16] Quan Z, Han Z, Zeng SY, et al. Stage prediction of acute kidney injury in sepsis patients using explainable machine learning approaches[J]. Front Med, 2025, 12: 1667488.
[17] Takehara K, Murakami T, Kuwahara-Arai K, et al. Evaluation of the effect of recombinant thrombomodulin on a lipopolysaccharide-induced murine sepsis model[J]. Exp Ther Med, 2017, 13(6): 2969-2974.
[18] Deng LX, Chen JH, Tao WY, et al. Cadherin expression in vascular endothelial of sepsis-induced kidney injury rat[J]. J Trop Med, 2021, 21(8): 967-970, 1000. **[In Chinese]**
[19] Ge X. Biomarkers for early diagnosis of sepsis-associated acute kidney injury[J]. Chin J Clin Res, 2024, 37(11): 1649-1654. **[In Chinese]**
[20] Boron M, Hauzer-Martin T, Keil J, et al. Circulating thrombomodulin: release mechanisms, measurements, and levels in diseases and medical procedures[J]. TH Open, 2022, 6(3): e194-e212.
[21] Katayama S, Nunomiya S, Koyama K, et al. Markers of acute kidney injury in patients with sepsis: the role of soluble thrombomodulin[J]. Crit Care, 2017, 21(1): 229.
[22] Wang X, Tao YH, Yang J, et al. Risk factors for sepsis associated-acute kidney injury in intensive care unit patients[J]. J Sichuan Univ Med Sci Ed, 2020, 51(5): 708-713. **[In Chinese]**
[23] Jiang J, Lü JJ, Ye L, et al. Clinical study of soluble thrombomodulin and urinary neutrophil gelatinase-associated lipocalin in early prediction of sepsis-induced acute kidney injury[J]. Chin J Emerg Med, 2020, 29(4): 533-540. **[In Chinese]**
[24] Huang Y, Cui Y, Ao JX, et al. Clinical value of sublingual microcirculation index, APACHEⅡ, NGAL and PCT for predicting sepsis-associated acute kidney injury[J]. J Clin Emerg, 2025, 26(1): 66-72, 78. **[In Chinese]**

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·脓毒症专题·论著·

基于可溶性血栓调节蛋白的联合指标对脓毒症相关急性肾损伤的预测价值

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摘要：目的 探讨基于可溶性血栓调节蛋白(sTM)的联合指标对脓毒症患者发生急性肾损伤(AKI)的预测效能，为临床AKI的早期识别提供参考。**方法** 回顾性分析2024年1月至12月南京大学医学院附属鼓楼医院重症监护病房收治的364例脓毒症患者的临床资料。根据住院期间是否发生AKI[依据改善全球肾脏病预后组织(KDIGO)提出的诊断标准]分为AKI组(n=171)和非AKI组(n=193)，比较两组患者的临床资料。采用多因素logistic回归分析筛选脓毒症发生AKI的危险因素；绘制受试者工作特征(ROC)曲线分析基于sTM的联合指标对脓毒症患者发生AKI的预测价值。**结果** 脓毒症相关AKI的发生率为46.98%，与非AKI组比较，AKI组患者急性生理学与慢性健康状况评分系统Ⅱ(APACHE Ⅱ)评分、序贯器官衰竭评估(SOFA)评分、28 d死亡率以及休克、呼吸衰竭、肝损伤的发生率均更高，sTM、C反应蛋白(CRP)、白细胞介素6、降钙素原、凝血酶原时间、活化部分凝血活酶时间水平更高，血小板水平降低，差异有统计学意义(P<0.05)。多因素logistic回归分析显示，休克(OR=3.304，95%CI：2.001~5.457，P<0.01)、肝损伤(OR=2.442，95%CI：1.399~4.265，P=0.002)、高APACHE Ⅱ评分(OR=1.050，95% CI：1.016~1.085，P=0.004)、高sTM(OR=1.039，95% CI：1.018~1.060，P<0.01)及高CRP(OR=1.003，95%CI：1.001~1.006，P=0.034)是脓毒症患者发生AKI的独立危险因素。sTM、休克以及APACHE Ⅱ评分三者联合预测脓毒症患者发生AKI的ROC曲线下面积为0.804(95%CI：0.759~0.850)，敏感度为0.754，特异度为0.762。**结论** 高sTM是脓毒症患者发生AKI的独立危险因素，对脓毒症患者发生AKI具有一定预测价值，联合休克和APACHE Ⅱ后预测价值更高。

关键词： 可溶性血栓调节蛋白；急性肾损伤；脓毒症；休克；急性生理学与慢性健康状况评分Ⅱ
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Predictive value of combined indexes based on soluble thrombomodulin for sepsis-associated acute kidney injury

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Abstract: Objective To investigate the predictive efficacy of combined indexes based on soluble thrombomodulin (sTM) for acute kidney injury (AKI) in patients with sepsis, and to provide a reference for the early identification of AKI in clinical practice. **Methods** A retrospective study was conducted to collect clinical data of 364 patients with sepsis admitted to the Intensive Care Unit of Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School from January to December 2024. According to the occurrence of AKI during hospitalization [based on the diagnostic criteria proposed by Kidney Disease: Improving Global Outcomes (KDIGO)], the patients were divided into AKI group (171 cases) and non-AKI group (193 cases). The clinical data of the two groups were

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compared. Multivariate logistic regression analysis was used to screen the risk factors for AKI in sepsis patients. Receiver operating characteristic (ROC) curves were plotted to analyze the predictive value of combined indicators based on sTM for AKI in sepsis patients. **Results** The incidence of sepsis-associated AKI was 46.98%. Compared with the non-AKI group, the AKI group exhibited significantly higher Acute Physiology and Chronic Health Evaluation Ⅱ (APACHE Ⅱ) score, Sequential Organ Failure Assessment (SOFA) score, 28-day mortality, and incidence rates of shock, respiratory failure, and liver injury (P<0.05). Levels of sTM, C-reactive protein (CRP), interleukin-6, procalcitonin, prothrombin time, and activated partial thromboplastin time were also significantly higher, whereas platelet count was significantly lower (P<0.05). Multivariate logistic regression analysis identified shock (OR=3.304, 95%CI: 2.001-5.457, P<0.01), liver injury (OR=2.442, 95%CI: 1.399-4.265, P=0.002), high APACHE Ⅱ score (OR=1.050, 95%CI: 1.016-1.085, P=0.004), high sTM (OR=1.039, 95%CI: 1.018-1.060, P<0.01), and high CRP (OR=1.003, 95%CI: 1.001-1.006, P=0.034) as independent risk factors for AKI in patients with sepsis. The combined use of sTM, shock, and APACHE Ⅱ score yielded an area under the curve (AUC) of 0.804 (95%CI: 0.759-0.850) for predicting AKI, with a sensitivity of 0.754 and a specificity of 0.762. **Conclusion** sTM is an independent risk factor for AKI in sepsis patients, and has certain predictive value for AKI in sepsis patients. The predictive value is more significant when combined with shock and APACHE Ⅱ score.

Keywords: Soluble thrombomodulin; Acute kidney injury; Sepsis; Shock; Acute Physiology and Chronic Health Evaluation Ⅱ

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脓毒症是机体对感染反应失调引起的危及生命的器官功能障碍，是重症监护病房(intensive care unit，ICU)患者死亡的主要原因之一[1-2]。急性肾损伤(acute kidney injury，AKI)是脓毒症最常见且严重的并发症，发生率高，在40%~50%，显著增加患者死亡风险[3-4]。目前，临床上诊断AKI主要参照[改善全球肾脏病预后组织(Kidney Disease：Improving Global Outcome，KDIGO)标准]，依赖血清肌酐和尿量的变化，但血清肌酐升高相对滞后，且受年龄、肌肉量、液体平衡等多种因素影响，无法实现AKI的早期预警[5]。因此，寻找能够早期、灵敏、特异地预测脓毒症相关AKI的生物标志物至关重要。血栓调节蛋白是一种主要表达于血管内皮细胞表面的跨膜糖蛋白，是维持血管内皮稳态的关键分子。在脓毒症状态下，失控的炎症反应和微循环障碍会导致血管内皮细胞广泛损伤和脱落，使血浆中可溶性血栓调节蛋白(soluble thrombomodulin，sTM)水平显著升高[6]。由于肾脏是一个富含毛细血管网的器官，其内皮细胞对损伤尤为敏感。脓毒症早期sTM水平的升高可能反映了全身性内皮损伤，特别是肾小球内皮损伤的严重程度，故可能成为脓毒症相关AKI的早期预测指标。本研究旨在探讨以sTM为基础的联合指标对脓毒症患者发生AKI的预测价值。

1　对象与方法

1.1　研究对象　回顾性纳入2024年1月至12月南京大学医学院附属鼓楼医院ICU收治的脓毒症患者364例。纳入标准：(1) 年龄≥18岁；(2) 符合脓毒症3.0诊断标准[1]；(3) AKI诊断符合KDIGO相关标准[7]；(4) 入院24 h内有sTM检测结果，且临床资料完整。排除标准：(1) 入住ICU时间<24 h；(2) 入院前已存在慢性肾脏病4~5期或依赖肾脏替代治疗；(3) 妊娠期；(4) 其他原因(造影剂、肾血管等)引起的急性肾功能不全。本研究数据均从病历资料中获得，符合医学伦理学标准。研究获得南京鼓楼医院医学科研伦理审查委员会批准(伦理号：2024-646-02)。

1.2　资料收集　收集患者一般临床资料，包括性别、年龄、全身感染相关序贯器官衰竭评估(Sequential Organ Failure Assessment，SOFA)评分、急性生理学与慢性健康状况评分系统Ⅱ(Acute Physiology and Chronic Health Evaluation Ⅱ，APACHE Ⅱ)评分、基础疾病[高血压病、糖尿病、心功能不全、脑梗死、冠状动脉粥样硬化性心脏病(冠心病)]、住院天数、28 d死亡率、并发症(休克、呼吸衰竭、肝损伤)，入院24 h内的实验室指标[白细胞计数(white blood cell count，WBC)、血小板计数(platelet count，PLT)、降钙素原(procalcitonin，PCT)、C反应蛋白(C-reactive protein，CRP)、白细胞介素(interleukin，IL)6、sTM、凝血酶原时间(prothrombin time，PT)、活化部分凝血酶原时间(activated partial thromboplastin time，APTT)、凝血酶-抗凝血酶复合物(thrombin-antithrombin complex，TAT)、组织纤溶酶原激活剂-抑制复合物(tissue plasminogen activator inhibitor complex，tPAI-C)和纤溶酶-抗纤溶酶复合物(plasmin-antiplasmin complex，PIC)]。

1.3 统计学方法 使用SPSS 26.0统计软件进行数据分析。非正态分布的计量资料以$M(P_{25}, P_{75})$表示，两组间比较采用Mann-Whitney U检验。计数资料以例(%)表示，比较采用χ^2检验。采用多因素logistic回归分析脓毒症患者发生AKI的危险因素。采用受试者工作特征(receiver operating characteristic, ROC)曲线及曲线下面积(area under the curve, AUC)评估各指标对脓毒症患者发生AKI的预测效能。P<0.05为差异有统计学意义。

2 结 果

2.1 患者的一般资料比较 364例脓毒症患者中，AKI患者171例(AKI组)，非AKI患者193例(非AKI组)，脓毒症相关AKI的发生率为46.98%。两组的年龄、性别、基础疾病、住院天数、WBC、TAT、PIC比较差异均无统计学意义(P>0.05)。与非AKI组相比，AKI组APACHE Ⅱ、SOFA评分、28 d死亡率以及休克、呼吸衰竭、肝损伤的发生率均更高，sTM、CRP、IL-6、PCT、PT、APTT、tPAI-C水平更高，而PLT更低，差异均有统计学意义(P<0.05)。见表1。

2.2 多因素logistic回归分析 将单因素分析中差异有统计学意义的影响因素纳入多因素logistic回归分析，结果显示：休克、肝损伤、高CRP、高APACHE Ⅱ评分、高sTM是脓毒症患者发生AKI的独立危险因素(P<0.05)。见表2。

2.3 预测效能分析 ROC曲线分析显示，sTM、休克、APACHE Ⅱ评分以及三者联合预测脓毒症患者发生AKI的AUC分别为0.761、0.695、0.674、0.804。见图1。sTM、休克、APACHE Ⅱ评分以及三者联合对脓毒症患者发生AKI的预测效能见表3。

表1 AKI组和非AKI组患者的临床资料比较

Tab.1 Comparison of clinical data between AKI and non-AKI groups

项目	AKI组 (n=171)	非AKI组 (n=193)	Z/χ^2值	P值
年龄(岁)[a]	59.00 (45.00, 72.00)	62.00 (48.00, 73.00)	1.015	0.310
性别[例(%)]				
男	77 (45.03)	92 (47.67)	0.254	0.614
女	94 (54.97)	101 (52.33)		
APACHE Ⅱ评分[a]	25.00 (20.00, 30.00)	20.00 (13.00, 25.00)	5.752	<0.001
SOFA评分[a]	10.00 (8.00, 12.00)	8.00 (5.00, 10.00)	4.856	<0.001
基础疾病[例(%)]				
高血压	69 (40.35)	80 (41.45)	0.045	0.831
糖尿病	36 (21.05)	42 (21.76)	0.027	0.869
心功能不全	30 (17.54)	22 (11.40)	2.796	0.095
脑梗死	40 (23.39)	43 (22.28)	0.064	0.801
冠心病	19 (11.11)	20 (10.36)	0.053	0.818
并发症[例(%)]				
休克	110 (64.33)	49 (25.39)	55.882	<0.001
呼吸衰竭	71 (41.52)	60 (31.09)	4.283	0.038
肝损伤	75 (43.86)	33 (17.10)	31.117	<0.001
实验室检查[a]				
WBC ($\times10^9$/L)	9.90 (5.80, 15.90)	8.50 (5.80, 13.60)	1.536	0.125
PLT ($\times10^9$/L)	115.00 (65.50, 183.50)	156.00 (97.00, 229.00)	3.855	<0.001
IL-6 (pg/mL)	137.34 (33.50, 357.38)	59.48 (16.39, 282.19)	2.889	0.004
CRP (mg/L)	81.65 (28.82, 164.08)	50.10 (16.40, 106.30)	3.288	0.001
PCT (ng/mL)	1.11 (0.32, 7.84)	0.33 (0.09, 1.63)	5.182	<0.001
APTT (s)	33.80 (28.42, 41.40)	29.80 (26.30, 34.40)	4.525	<0.001
PT (s)	13.60 (12.20, 16.60)	13.10 (11.80, 14.80)	2.260	0.024
TAT (ng/mL)	13.60 (6.30, 29.43)	11.20 (6.80, 20.60)	1.943	0.052
PIC (μg/mL)	1.39 (0.75, 2.69)	1.33 (0.87, 2.50)	0.197	0.844
sTM (TU/mL)	26.30 (19.40, 36.05)	15.00 (10.60, 22.50)	8.602	<0.001
tPAI-C (ng/mL)	16.90 (10.30, 28.55)	12.30 (7.10, 17.10)	4.785	<0.001
预后				
住院天数(d)[a]	23.00 (14.50, 32.50)	21.00 (13.00, 29.00)	1.157	0.247
28 d死亡率(%)	39.77	17.62	22.054	<0.001

注：[a]数据以$M(P_{25}, P_{75})$表示。

表 2　脓毒症患者发生 AKI 的多因素 logistic 回归分析

Tab.2　Multivariate logistic regression analysis for AKI in patients with sepsis

项目	*β*	*SE*	*Z* 值	*P* 值	*OR*(95%*CI*)	VIF	
休克	1.195	0.256	4.669	<0.001	3.304 (2.001 ~ 5.457)	0.770	1.298
肝损伤	0.893	0.284	3.140	0.002	2.442 (1.399 ~ 4.265)	0.838	1.193
APACHE Ⅱ 评分	0.049	0.017	2.910	0.004	1.050 (1.016 ~ 1.085)	0.389	2.569
CRP	0.003	0.001	2.115	0.034	1.003 (1.001 ~ 1.006)	0.921	1.086
sTM	0.038	0.010	3.697	<0.001	1.039 (1.018 ~ 1.060)	0.776	1.289

注：自变量赋值，28 d 死亡、休克、呼吸衰竭、肝损伤（否=0，有=1）；APACHE Ⅱ 评分、SOFA 评分、sTM、CRP（原值录入）；VIF 为方差膨胀因子。

表 3　各危险因素对脓毒症患者发生 AKI 的预测效能

Tab.3　The predictive efficacy of various risk factors for AKI in sepsis patients

项目	AUC(95%*CI*)	*P* 值	截断值	敏感度	特异度	约登指数
休克	0.695(0.647~0.742)	<0.001		0.643	0.746	0.389
APACHE Ⅱ 评分	0.674(0.620~0.729)	<0.001	21.5 分	0.725	0.560	0.285
sTM	0.761(0.711~0.811)	<0.001	17.8 TU/mL	0.836	0.642	0.479
联合预测	0.804(0.759~0.850)	<0.001		0.754	0.762	0.516

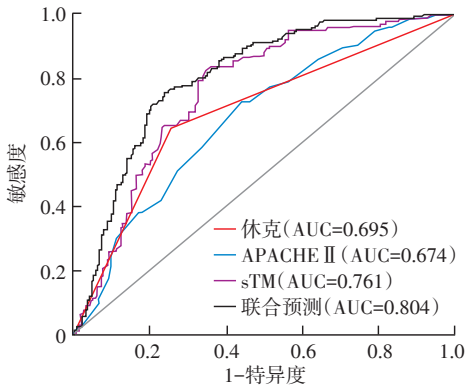

图 1　各项影响因素预测脓毒症发生 AKI 的 ROC 曲线

Fig.1　ROC curve for predicting AKI in sepsis based on various influencing factors

3　讨　论

AKI 是脓毒症进展过程中常见且严重的并发症，可显著增加重症患者的死亡率[8-9]。传统血清肌酐水平或尿量变化的检测，在脓毒症相关 AKI 的早期诊断与风险预测中存在明显局限。因此，临床上亟需探索敏感度与特异度更高的新型生物标志物，从而实现对重度 AKI 高危人群的早期识别。

本研究对 364 例脓毒症患者的临床资料进行回顾性分析，结果显示，脓毒症相关 AKI 的发生率为 46.98%，AKI 组 28 d 死亡率为 39.77%。脓毒症相关 AKI 的高发生率及高死亡率提示了早期预测及干预的必要性[3-4,10]。多因素 logistic 回归分析表明，休克、肝损伤、高 CRP、高 APACHE Ⅱ 评分及高 sTM 是脓毒症患者发生 AKI 的独立危险因素。休克作为脓毒症相关 AKI 的独立危险因素，其机制与脓毒性休克时有效循环血量不足、肾灌注压显著下降有关，持续的肾脏低灌注可导致肾实质缺血、缺氧，进而引发急性肾小管坏死，这与已有研究的结论一致[11-14]。APACHE Ⅱ 评分作为评估重症患者疾病严重程度的经典评分，其结果印证了脓毒症相关 AKI 的发生与疾病整体严重程度密切相关，APACHE Ⅱ 评分越高，全身炎症反应越剧烈，多器官功能损伤风险越高，肾脏作为高灌注器官更易受累[11-12,15-16]。

sTM 被认为是内皮受损的黄金标志物[17]。在脓毒症时，脂多糖、肿瘤坏死因子-α等炎症介质可直接损伤血管内皮细胞，导致内皮屏障功能破坏，细胞膜表面的血栓调节蛋白脱落入血，使 sTM 水平升高；而肾脏富含血管内皮细胞，脓毒症引发的全身炎症反应与内皮损伤可直接累及肾脏微循环，导致肾内血管内皮损伤、血栓形成及肾组织灌注不足，最终诱发 AKI[14,18]。因此，血 sTM 水平升高不仅反映了全身血管内皮损伤的程度，也间接提示肾脏微循环受损的风险，这可能是其能够有效预测脓毒症相关 AKI 的核心机制。sTM 水平升高主要源于内皮细胞损伤，相比于肾脏低灌注及肌酐清除率降低能更早提示 AKI 的发生[19-20]。本研究中，sTM 预测脓毒症患者发生 AKI 的敏感度为 0.836，高于休克和 APACHE Ⅱ 的敏感度（分别为 0.643 和 0.725），可作为临床筛查脓毒症相关 AKI 的重要参考指标。其他临床研究亦显示 sTM 高表达对脓毒症相关 AKI 有较高预测价值[21-22]。因此，sTM 检测为脓毒症内皮细胞功能障碍导致器官损伤的理论提供了新的临床佐证[16]。

虽然单独检测 sTM 预测脓毒症患者发生 AKI 的特异度仅 0.642，但联合其他指标能明显提高预测效

能[23-24]。本研究发现，休克、APACHE Ⅱ评分、sTM 三者联合预测脓毒症患者发生 AKI 的 AUC 为 0.804，其特异度提高至 0.762，明显优于单一检测指标。因此，该三项指标联合预测脓毒症相关 AKI 具有很好的临床应用价值。

本研究尚有一定的局限性。首先，受单中心回顾性研究设计的固有属性限制，本研究存在一定的抽样误差问题；其次，该研究仅收集入院 24 h 内基线指标，未能反映脓毒症起病初期 sTM 的动态变化；未对 sTM 进行连续动态监测，无法评估其水平变化与 AKI 进展的关联。

综上所述，高 sTM 是脓毒症患者发生 AKI 的独立危险因素，并具有良好的预测价值，联合休克和 APACHE Ⅱ评分预测价值更高，有助于早期识别脓毒症相关 AKI 高危患者并及时开展干预。未来，需要开展大规模、多中心的前瞻性队列研究来验证本研究结果，并探索动态监测 sTM 的临床意义。

利益冲突　无

参考文献

[1] Yang WS, Kang HD, Jung SK, et al. A mortality analysis of septic shock, vasoplegic shock and cryptic shock classified by the third international consensus definitions (Sepsis-3)[J]. Clin Respir J, 2020, 14(9): 857-863.

[2] White KC, Serpa-Neto A, Hurford R, et al. Sepsis-associated acute kidney injury in the intensive care unit: incidence, patient characteristics, timing, trajectory, treatment, and associated outcomes. A multicenter, observational study [J]. Intensive Care Med, 2023, 49(9): 1079-1089.

[3] Fan YW, Jiang SW, Chen JM, et al. A pulmonary source of infection in patients with sepsis-associated acute kidney injury leads to a worse outcome and poor recovery of kidney function[J]. World J Emerg Med, 2020, 11(1): 18.

[4] Pais T, Jorge S, Lopes JA. Acute kidney injury in sepsis[J]. Int J Mol Sci, 2024, 25(11): 5924.

[5] 郭俊，郭凤梅. 脓毒症相关急性肾损伤生物标志物及分子机制的研究进展[J]. 中华急诊医学杂志，2023，32(2)：269-274.

[6] Katayama S, Koyama K, Jun SM, et al. Thrombomodulin, plasminogen activator inhibitor-1 and protein C levels, and organ dysfunction in sepsis[J]. Crit Care Explor, 2019, 1(5): e0013.

[7] Khwaja A. KDIGO clinical practice guidelines for acute kidney injury[J]. Nephron Clin Pract, 2012, 120(4): c179-c184.

[8] Yoshimoto K, Komaru Y, Iwagami M, et al. Acute kidney injury in sepsis: evidence from Asia[J]. Semin Nephrol, 2020, 40(5): 489-497.

[9] Xia WH, Yi F, Wang QB. Mortality and differential predictive factors of transient and persistent sepsis-associated acute kidney injury [J]. Clin Nephrol, 2023, 99(3): 119-127.

[10] Suh SH, Kim CS, Choi JS, et al. Acute kidney injury in patients with sepsis and septic shock: risk factors and clinical outcomes [J]. Yonsei Med J, 2013, 54(4): 965.

[11] Hou L, Wu X, Sun ZG. Risk factors and prognosis of acute kidney injury in hospitalised sepsis patients[J]. Arch Españoles De Urol, 2024, 77(3): 263.

[12] Plataki M, Kashani K, Cabello-Garza J, et al. Predictors of acute kidney injury in septic shock patients: an observational cohort study[J]. Clin J Am Soc Nephrol, 2011, 6(7): 1744-1751.

[13] 左海忠，田六九，杨晓帆，等. 脓毒症患者继发急性肾损伤危险因素 Logistic 回归方程研究[J]. 长春中医药大学学报，2023，39(8)：915-920.

[14] Nguyen VT, Nguyen-Phan HN, Ton TN, et al. Value of serum thrombomodulin as a marker and predictor in patients with sepsis-associated acute kidney injury [J]. Int J Gen Med, 2023, 16: 2933-2941.

[15] 纪小奇，陈婷，陈城，等. 血清 CysC、SAA 联合 APACHEⅡ评分对脓毒症合并急性肾损伤患者预后的评估价值[J]. 中华保健医学杂志，2022，24(2)：125-127.

[16] Quan Z, Han Z, Zeng SY, et al. Stage prediction of acute kidney injury in sepsis patients using explainable machine learning approaches[J]. Front Med, 2025, 12: 1667488.

[17] Takehara K, Murakami T, Kuwahara-Arai K, et al. Evaluation of the effect of recombinant thrombomodulin on a lipopolysaccharide-induced murine sepsis model[J]. Exp Ther Med, 2017, 13(6): 2969-2974.

[18] 邓柳霞，陈继红，陶伍元，等. 脓毒症性肾损伤大鼠血管内皮钙粘蛋白的表达[J]. 热带医学杂志，2021，21(8)：6.

[19] 葛新. 脓毒症相关急性肾损伤早期诊断标志物的研究现状[J]. 中国临床研究，2024，37(11)：1649-1654.

[20] Boron M, Hauzer-Martin T, Keil J, et al. Circulating thrombomodulin: release mechanisms, measurements, and levels in diseases and medical procedures[J]. TH Open, 2022, 6(3): e194-e212.

[21] Katayama S, Nunomiya S, Koyama K, et al. Markers of acute kidney injury in patients with sepsis: the role of soluble thrombomodulin[J]. Crit Care, 2017, 21(1): 229.

[22] 王馨，陶于洪，杨佳，等. 重症监护病房中脓毒症患者并发急性肾损伤的危险因素分析[J]. 四川大学学报（医学版），2020，51(5)：708-713.

[23] 姜洁，吕菁君，叶璐，等. 可溶性血栓调节蛋白及中性粒细胞明胶酶相关脂质运载蛋白早期预测脓毒症相关急性肾损伤的临床研究[J]. 中华急诊医学杂志，2020，29(4)：533-540.

[24] 黄媛，崔艳，敖锦曦，等. 舌下微循环、APACHI Ⅱ评分、NGAL 和 PCT 预测脓毒症相关性急性肾损伤的临床价值[J]. 临床急诊杂志，2025，26(1)：66-72，78.

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